Yawning in PUBMED 25 octobre 2009

Walusinski, O. (2009). "Yawning in diseases." Eur Neurol 62(3): 180-7.
Yawning is a physiological behavior, an emotional stereotypy that indicates the homeostatic process of the mechanisms regulating rhythms, such as sleeping/waking, hunger/satiety or mating/relaxation, generated by the diencephalon. As with all physiological behaviors, its deregulation reveals disorders. In daily practice, yawning as a symptom is generally neglected. That is why we propose a wide overview of yawning in diseases, its consequences and significance.

Uher, R., A. Farmer, et al. (2009). "Adverse reactions to antidepressants." Br J Psychiatry 195(3): 202-10.
BACKGROUND: Adverse drug reactions are important determinants of non-adherence to antidepressant treatment, but their assessment is complicated by overlap with depressive symptoms and lack of reliable self-report measures. AIMS: To evaluate a simple self-report measure and describe adverse reactions to antidepressants in a large sample. METHOD: The newly developed self-report Antidepressant Side-Effect Checklist and the psychiatrist-rated UKU Side Effect Rating Scale were repeatedly administered to 811 adult participants with depression in a part-randomised multicentre open-label study comparing escitalopram and nortriptyline. RESULTS: There was good agreement between self-report and psychiatrists' ratings. Most complaints listed as adverse reactions in people with depression were more common when they were medication-free rather than during their treatment with antidepressants. Dry mouth (74%), constipation (33%) and weight gain (15%) were associated with nortriptyline treatment. Diarrhoea (9%), insomnia (36%) and yawning (16%) were more common during treatment with escitalopram. Problems with urination and drowsiness predicted discontinuation of nortriptyline. Diarrhoea and decreased appetite predicted discontinuation of escitalopram. CONCLUSIONS: Adverse reactions to antidepressants can be reliably assessed by self-report. Attention to specific adverse reactions may improve adherence to antidepressant treatment.

Shoja, M. M., R. S. Tubbs, et al. (2009). "Vasovagal syncope in the Canon of Avicenna: The first mention of carotid artery hypersensitivity." Int J Cardiol.
Ibn Sina, known as Avicenna in the West, was a celebrated Persian thinker, philosopher, and physician who is remembered for his masterpiece, The Canon of Medicine. The Canon that served as an essential medical encyclopedia for scholars in the Islamic territories and Europe for almost a millennium consisted of 5 books. In the third book, Avicenna described patients with symptoms of carotid hypersensitivity syndrome. These patients, who had excessive yawning, fatigue, and flushing, dropped following pressure on their carotids. Based on such history, it seems that Avicenna was the first to note the carotid sinus hypersensitivity, which presents with vasovagal syncope following compression of the carotid artery. In this paper, we presented a brief account of Avicenna's life and works and discuss his description of the so-called carotid hypersensitivity syncope. Notwithstanding his loyalty to the Greek theory of humoralism, Avicenna set forth his own version of "theory of spirits" to explain the mechanism of this disease. An account of the theory of spirits is also given.

Senju, A., Y. Kikuchi, et al. (2009). "Brief report: does eye contact induce contagious yawning in children with autism spectrum disorder?" J Autism Dev Disord 39(11): 1598-602.
Individuals with autism spectrum disorder (ASD) reportedly fail to show contagious yawning, but the mechanism underlying the lack of contagious yawning is still unclear. The current study examined whether instructed fixation on the eyes modulates contagious yawning in ASD. Thirty-one children with ASD, as well as 31 age-matched typically developing (TD) children, observed video clips of either yawning or control mouth movements. Participants were instructed to fixate to the eyes of the face stimuli. Following instructed fixation on the eyes, both TD children and children with ASD yawned equally frequently in response to yawning stimuli. Current results suggest that contagious yawning could occur in ASD under an experimental condition in which they are instructed to fixate on the yawning eyes.

Pal, S. and P. R. Padala (2009). "A case of excessive yawning with citalopram." Prim Care Companion J Clin Psychiatry 11(3): 125-6.

Nowak, P., D. Nitka, et al. (2009). "Neonatal co-lesion by DSP-4 and 5,7-DHT produces adulthood behavioral sensitization to dopamine D(2) receptor agonists." Pharmacol Rep 61(2): 311-8.
To assess the possible modulatory effects of noradrenergic and serotoninergic neurons on dopaminergic neuronal activity, the noradrenergic and serotoninergic neurotoxins DSP-4 N-(2-chlorethyl)-N-ethyl-2-bromobenzylamine (50.0 mg/kg, sc) and 5,7-dihydroxytryptamine (5,7-DHT) (37.5 microg icv, half in each lateral ventricle), respectively, were administered toWistar rats on the first and third days of postnatal ontogeny, and dopamine (DA) agonist-induced behaviors were assessed in adulthood. At eight weeks, using an HPLC/ED technique, DSP-4 treatment was associated with a reduction in NE content of the corpus striatum (> 60%), hippocampus (95%), and frontal cortex (> 85%), while 5,7-DHT was associated with an 80-90% serotonin reduction in the same brain regions. DA content was unaltered in the striatum and the cortex. In the group lesioned with both DSP-4 and 5,7-DHT, quinpirole-induced (DA D(2) agonist) yawning, 7-hydroxy-DPAT-induced (DA D(3) agonist) yawning, and apomorphine-induced (non-selective DA agonist) stereotypies were enhanced. However, SKF 38393-induced (DA D(1) agonist) oral activity was reduced in the DSP-4 + 5,7-DHT group. These findings demonstrate that DA D(2)- and D(3)-agonist-induced behaviors are enhanced while DA D(1)-agonist-induced behaviors are suppressed in adult rats in which brain noradrenergic and serotoninergic innervation of the brain has largely been destroyed. This study indicates that noradrenergic and serotoninergic neurons have a great impact on the development of DA receptor reactivity (sensitivity).

Major, C. A., B. J. Kelly, et al. (2009). "The anxiogenic drug FG7142 increases self-injurious behavior in male rhesus monkeys (Macaca mulatta)." Life Sci.
AIMS: Self-injurious behavior (SIB), which is deliberate infliction of self-injury without suicidal intent, is a significant human health problem. SIB is not unique to humans but is also manifested in a small percentage of captive macaques, typically as self-directed biting. Although the onset and maintenance of SIB have been linked to increased anxiety in both humans and nonhuman primates, no previous studies have directly tested the anxiety-SIB hypothesis. Here, we determined whether rhesus monkeys increase their self-directed biting following a challenge with the anxiogenic compound N-methyl-beta-carboline-3-carboxamide (FG7142). MAIN METHODS: Ten rhesus monkeys (Macaca mulatta) with a veterinary record of self-wounding (SIB) as well as six age- and weight-matched non-wounding control monkeys were given intramuscular injections of 0.1, 0.3, or 1.0mg/kg FG7142. Behavior was observed following drug administration with special attention to displacement behaviors (scratching, self-grooming, and yawning), locomotor stereotypy, and self-directed biting. Plasma cortisol and ACTH were also measured as physiological indices of stress. KEY FINDINGS: Self-directed biting rates dose-dependently increased in a subset of SIB monkeys, but did not change in control animals. Furthermore, administration of FG7142 led to an increase in scratching, yawning, and locomotor stereotypy in all monkeys, but did not affect the frequency self-grooming. Additionally, there was a dose-dependent increase in plasma cortisol concentrations, but not ACTH, in all animals. SIGNIFICANCE: The present findings indicate that self-biting is anxiety-related in some but not all SIB monkeys, suggesting that this behavioral pathology is heterogeneous as has previously been suggested for SIB in humans.

Hasler, C. T., C. D. Suski, et al. (2009). "The influence of dissolved oxygen on winter habitat selection by largemouth bass: an integration of field biotelemetry studies and laboratory experiments." Physiol Biochem Zool 82(2): 143-52.
In this study, field biotelemetry and laboratory physiology approaches were coupled to allow understanding of the behavioral and physiological responses of fish to winter hypoxia. The biotelemetry study compared dissolved oxygen levels measured throughout the winter period with continually tracked locations of nine adult largemouth bass obtained from a whole-lake submerged telemetry array. Fish habitat usage was compared with habitat availability to assess whether fish were selecting for specific dissolved oxygen concentrations. The laboratory study examined behavioral and physiological responses to progressive hypoxia in juvenile largemouth bass acclimated to winter temperatures. Results from the dissolved oxygen measurements made during the biotelemetry study showed high variance in under-ice dissolved oxygen levels. Avoidance of water with dissolved oxygen <2.0 mg/L by telemetered fish was demonstrated, but significant use of water with intermediate dissolved oxygen levels was also found. Results from the lab experiments showed marked changes in behavior (i.e., yawning and vertical movement) at <2.0 mg/L of dissolved oxygen but no change in tissue lactate, an indicator of anaerobic metabolism. Combined results of the biotelemetry and laboratory studies demonstrate that a dissolved oxygen content of 2.0 mg/L may be a critical threshold that induces behavioral responses by largemouth bass during the winter. In addition, the use by fish of areas with intermediate levels of dissolved oxygen suggests that there are multiple environmental factors influencing winter behavior.

Harr, A. L., V. R. Gilbert, et al. (2009). "Do dogs (Canis familiaris) show contagious yawning?" Anim Cogn 12(6): 833-7.
We report an experimental investigation into whether domesticated dogs display contagious yawning. Fifteen dogs were shown video clips of (1) humans and (2) dogs displaying yawns and open-mouth expressions (not yawns) to investigate whether dogs showed contagious yawning to either of these social stimuli. Only one dog performed significantly more yawns during or shortly after viewing yawning videos than to the open-mouth videos, and most of these yawns occurred to the human videos. No dogs showed significantly more yawning to the open-mouth videos (human or dog). The percentage of dogs showing contagious yawning was less than chimpanzees and humans showing this behavior, and considerably less than a recently published report investigating this behavior in dogs (Joly-Mascheroni et al. in Biol Lett 4:446-448, 2008).

Haker, H. and W. Rossler (2009). "Empathy in schizophrenia: impaired resonance." Eur Arch Psychiatry Clin Neurosci.
Resonance is the phenomenon of one person unconsciously mirroring the motor actions as basis of emotional expressions of another person. This shared representation serves as a basis for sharing physiological and emotional states of others and is an important component of empathy. Contagious laughing and contagious yawning are examples of resonance. In the interpersonal contact with individuals with schizophrenia we can often experience impaired empathic resonance. The aim of this study is to determine differences in empathic resonance-in terms of contagion by yawning and laughing-in individuals with schizophrenia and healthy controls in the context of psychopathology and social functioning. We presented video sequences of yawning, laughing or neutral faces to 43 schizophrenia outpatients and 45 sex- and age-matched healthy controls. Participants were video-taped during the stimulation and rated regarding contagion by yawning and laughing. In addition, we assessed self-rated empathic abilities (Interpersonal Reactivity Index), psychopathology (Positive and Negative Syndrome Scale

in the schizophrenia group resp. Schizotypal Personality Questionnaire in the control group), social dysfunction (Social Dysfunction Index) and executive functions (Stroop, Fluency). Individuals with schizophrenia showed lower contagion rates for yawning and laughing. Self-rated empathic concern showed no group difference and did not correlate with contagion. Low rate of contagion by laughing correlated with the schizophrenia negative syndrome and with social dysfunction. We conclude that impaired resonance is a handicap for individuals with schizophrenia in social life. Blunted observable resonance does not necessarily reflect reduced subjective empathic concern.

Gallup, A. C. and G. G. Gallup, Jr. (2009). "Medical implications of excessive yawning in relation to thermoregulatory dysfunction." Eur J Neurol 16(6): e120.

Gallup, G. G., Jr. and A. C. Gallup (2009). "Excessive yawning and thermoregulation: two case histories of chronic, debilitating bouts of yawning." Sleep Breath.

BACKGROUND: This report details the case histories of two women who suffer from chronic and debilitating episodes of excessive yawning in the absence of sleep problems. METHODS: Each woman independently provided information and answered questions about their excessive yawning symptoms and medical histories. RESULTS: Both women show signs of thermoregulatory dysfunction, and each reports symptom relief and/or the postponement of yawning attacks through means of behavioral cooling. One woman recorded her body temperature before and after bouts of yawning, revealing a significant drop in temperature following each episode ($p < 0.05$). CONCLUSIONS: The trigger for yawning in these patients appears to be related to increases in body/brain temperature. These cases are consistent with growing evidence showing that recurrent episodes of excessive yawning are not necessarily associated with a sleep disorder, but rather may be indicative of thermoregulatory dysfunction.

Gallup, A. C. and G. G. Gallup, Jr. (2009). "Venlafaxine-induced excessive yawning: A thermoregulatory connection." Prog Neuropsychopharmacol Biol Psychiatry.

Di Martino, E. F., V. Nath, et al. (2009). "Evaluation of Eustachian tube function with perfect sequences: technical realization and first clinical results." Eur Arch Otorhinolaryngol.

The aim of this study was the introduction of a specific class of signals, the so-called perfect sequences (PSEQ), in a novel approach for sonotubometry of the Eustachian tube (ET). Sonotubometry using PSEQ stimuli was performed on 20 healthy subjects in order to gauge its potential for clinical applications. In a series of 320 measurements ET opening was probed, which was induced by dry and water swallowing, Toynbee maneuver, and yawning. All sonotubograms were analyzed with respect to their shape, increase of sound intensity, and opening duration. In 298/320 measurements (>93%) the subjects reported subjective ET openings. The evaluation of the recorded sonotubograms showed good detection of ET opening for the inducing maneuvers of swallowing (dry and water swallowing) and the Toynbee maneuver, with 90, 86, and 80% valid sonotubograms, respectively. Yawning led to only 40% valid sonotubograms. In total, 237/320 (~74%) sonotubograms were classified as valid. The evaluation of the sound level increase during ET openings showed that it was significantly higher in measurements with dry and water swallowing, as well as Toynbee maneuvers (mean 17.1, 19.0 and 17.2 dB, respectively), than with yawning (mean 10.17 dB; $P < 0.0001$). Nasal decongestion was found to have little influence on the results ($P > 0.05$). Sonotubometry using PSEQ stimuli is a novel sonotubometry methodology that provides valuable information regarding the auditory tube patency. By further technical refinements of the method, a diagnostic tool with high sensitivity and specificity could be developed.

Depoortere, R., L. Bardin, et al. (2009). "Penile erection and yawning induced by dopamine D2-like receptor agonists in rats: influence of strain and contribution of dopamine D2, but not D3 and D4 receptors." Behav Pharmacol 20(4): 303-11.

Dopamine (DA) is implicated in penile erection (PE) and yawning (YA) in rats through activation of D2-like receptors. However, the exact role of each subtype (D2, D3 and D4) of this receptor family in PE/YA is still not clearly elucidated. We recorded concomitantly PE and YA after treatment with agonists with various levels of selectivity for the different subtypes of D2-like receptors. In addition, we investigated the efficacy of antagonists with selective or preferential affinity for each of the three receptor subtypes to prevent apomorphine-induced PE and YA. Wistar rats were more sensitive than Long-Evans rats to the erectogenic activity of the nonselective DA agonist apomorphine (0.01-0.08 mg/kg), whereas Sprague-Dawley rats were insensitive. However, all the three strains were equally sensitive to apomorphine-induced YA. In Wistar rats, apomorphine (0.01-0.63 mg/kg), the D2/D3 agonists quinelorane and (+)7-OH-DPAT (0.000625-10 mg/kg) or PD 128,907 (0.01-10 mg/kg), but not the D4 agonists PD-168,077, RO-10-5824 and ABT-724 (0.04-0.63 mg/kg), produced PE and YA with bell-shaped dose-response curves. Similarly, ABT-724 and CP226-269 (another D4 agonist) failed to elicit PE and YA in Sprague-Dawley rats. Furthermore, in Wistar rats, PE and YA elicited by apomorphine (0.08 mg/kg) were not modified by selective D3 (S33084 and SB-277011, 0.63-10 mg/kg) or D4 (L-745,870 and RBI-257, 0.63-2.5 mg/kg) antagonists, but were prevented by the preferential D2 blocker L-741,626 (near-full antagonism at 2.5 mg/kg). The present data do not support a major implication of either DA D3 or D4 receptors in the control of PE and YA in rats, but indicate a preponderant role of DA D2 receptors.

Collins, G. T., A. Truccone, et al. (2009). "Pro-erectile Effects of Dopamine D2-like Agonists are Mediated by the D3 Receptor in Rats and Mice." J Pharmacol Exp Ther.

Dopamine D2-like agonists induce penile erection (PE) and yawning in a variety of species, effects that have recently been suggested to be specifically mediated by the D4 and D3 receptors, respectively. The current studies were aimed at characterizing a series of D2, D3, and D4 agonists with respect to their capacity to induce PE and yawning in the rat, as well as the pro-erectile effects of apomorphine in wild-type and D4 receptor (R) knock-out (KO) mice. All D3 agonists induced dose-dependent increases in PE and yawning over a similar range of doses, whereas significant increases in PE or yawning were not observed with any of the D4 agonists. Likewise, D2, D3, and D4 antagonists were assessed for their capacity to alter apomorphine- and pramipexole-induced PE and yawning. The D3 antagonist, PG01037, inhibited the induction of PE and yawning, whereas the D2 antagonist, L-741,626, reversed the inhibition of PE and yawning observed at higher doses. The D4 antagonist, L-745,870, did not alter apomorphine- or pramipexole-induced PE or yawning. A role for the D3 receptor was further supported as apomorphine was equipotent at inducing PE in wild-type and D4R KO mice, effects that were inhibited by the D3 antagonist, PG01037, in both wild-type and D4R KO mice. Together, these studies provide strong support that D2-like agonist-induced PE and yawning are differentially mediated by the D3 (induction) and D2 receptors (inhibition). These studies fail to support a role for the D4 receptor in the regulation of PE or yawning by D2-like agonists.

Chen, C. H. and M. L. Lu (2009). "Venlafaxine-induced excessive yawning." Prog Neuropsychopharmacol Biol Psychiatry 33(1): 156-7.

Chang, C. C. and S. T. Chang (2009). "Excessive yawning induced by stimulation of myofascial trigger point--case report." Eur J Neurol 16 (6): e118-9.

Campbell, M. W., J. D. Carter, et al. (2009). "Computer animations stimulate contagious yawning in chimpanzees." Proc Biol Sci.

People empathize with fictional displays of behaviour, including those of cartoons and computer animations, even though the stimuli are obviously artificial. However, the extent to which other animals also may respond empathetically to animations has yet to be determined. Animations provide a potentially useful tool for exploring non-human behaviour, cognition and empathy because computer-generated stimuli offer complete control over variables and the ability to program stimuli that could not be captured on video. Establishing computer animations as a viable tool requires that non-human subjects identify with and respond to animations in a way similar to the way they do to images of actual conspecifics. Contagious yawning has been linked to empathy and poses a good test of involuntary identification and motor mimicry. We presented 24 chimpanzees with three-dimensional computer-animated chimpanzees yawning or displaying control mouth movements. The apes yawned significantly more in response to the yawn animations than to the controls, implying identification with the animations. These results support the phenomenon of contagious yawning in chimpanzees and suggest an empathic response to animations. Understanding how chimpanzees connect with animations, to both empathize and imitate, may help us to understand how humans do the same.

Baladi, M. G., A. H. Newman, et al. (2009). "Dopamine D3 receptors mediate the discriminative stimulus effects of quinpirole in free-feeding rats." J Pharmacol Exp Ther.

Discriminative stimulus effects of dopamine (DA) D3/D2 receptor agonists are thought to be mediated by D2 receptors. To maintain responding, access to food is often restricted, which can alter neurochemical and behavioral effects of drugs acting on DA systems. This study established stimulus control with quinpirole in free-feeding rats and tested the ability of agonists to mimic and antagonists to attenuate the effects of quinpirole. The same antagonists were studied for their ability to attenuate quinpirole-induced yawning and hypothermia. DA receptor agonists apomorphine and lisuride, but not amphetamine and morphine, occasioned responding on the quinpirole lever. Discriminative stimulus effects of quinpirole were attenuated by the D3 receptor-selective antagonist PG01037 and the nonselective D3/D2 receptor antagonist raclopride, but not by the D2 receptor-selective antagonist L-741,626; the potencies of PG01037 and raclopride to antagonize this effect of quinpirole paralleled their potencies to antagonize the ascending limb of the quinpirole yawning dose-response curve (thought to be mediated by D3 receptors). L-741,626 selectively antagonized the descending limb of the quinpirole yawning dose-response curve and both L-741,626 and raclopride, but not PG01037, antagonized the hypothermic effects of quinpirole (thought to be mediated by D2 receptors). Food restriction (10 g/day/7 days) significantly decreased quinpirole-induced yawning without affecting the quinpirole discrimination. Many discrimination studies on DA receptor agonists use food-restricted rats; together with those studies, the current experiment using free-feeding rats suggests that feeding conditions impacting the behavioral effects of direct-acting DA receptor agonists might also impact the effects of indirect-acting agonists such as cocaine and amphetamine.

Baladi, M. G. and C. P. France (2009). "High fat diet and food restriction differentially modify the behavioral effects of quinpirole and raclopride in rats." Eur J Pharmacol 610(1-3): 55-60.

Nutritional status can impact dopamine systems in a manner that might be important to understanding possible common neurobiological mechanisms that mediate abnormal compulsive food (e.g., obesity) and drug taking. Limiting food intake, for example, can increase sensitivity to the behavioral effects of indirect-acting dopamine receptor agonists. Much less is known regarding possible diet-induced changes in sensitivity to direct-acting dopamine receptor drugs. The present study investigated the effects of a high fat diet and of food

restriction on sensitivity of rats to the behavioral effects of a direct-acting dopamine receptor agonist and a dopamine receptor antagonist. Free access to high fat chow increased sensitivity to quinpirole-induced yawning without changing sensitivity to raclopride-induced catalepsy or quinpirole-induced hypothermia. Food restriction (10 g/day) decreased sensitivity to quinpirole-induced yawning and raclopride-induced catalepsy without affecting sensitivity to quinpirole-induced hypothermia. Free access to a standard chow restored sensitivity to the behavioral effects of both drugs in rats that were previously food-restricted but not in rats that previously ate a high fat diet. These data confirm that food restriction can decrease sensitivity to behavioral effects of direct-acting dopamine receptor drugs, they provide evidence (i.e., no change in hypothermic effects) indicating that these changes are not due to pharmacokinetic mechanisms, and they provide initial evidence showing enhanced sensitivity to behavioral effects of dopamine receptor drugs in rats eating a high fat diet. These changes in sensitivity of dopamine systems could be relevant to understanding the impact of nutrition on therapeutic and recreational drug use.

Arnott, S. R., A. Singhal, et al. (2009). "An investigation of auditory contagious yawning." Cogn Affect Behav Neurosci 9(3): 335-42.
Despite a widespread familiarity with the often compelling urge to yawn after perceiving someone else yawn, an understanding of the neural mechanism underlying contagious yawning remains incomplete. In the present auditory fMRI study, listeners used a 4-point scale to indicate how much they felt like yawning following the presentation of a yawn, breath, or scrambled yawn sound. Not only were yawn sounds given significantly higher ratings, a trait positively correlated with each individual's empathy measure, but relative to control stimuli, random effects analyses revealed enhanced hemodynamic activity in the right posterior inferior frontal gyrus (pIFG) in response to hearing yawns. Moreover, pIFG activity was greatest for yawn stimuli associated with high as opposed to low yawn ratings and for control sounds associated with equally high yawn ratings. These results support a relationship between contagious yawning and empathy and provide evidence for pIFG involvement in contagious yawning. A supplemental figure for this study may be downloaded from http://cabn.psychonomic-journals.org/content/supplemental.

Zilli, I., F. Giganti, et al. (2008). "Yawning and subjective sleepiness in the elderly." J Sleep Res 17(3): 303-8.
Yawning is related to sleep/wake transitions and time of day, probably reflecting the time course of sleepiness. As aging modifies sleep-wake and sleepiness rhythms, we suppose that yawning frequency and its time course vary as a function of age. Thirteen aged healthy subjects (77.15 +/- 4.09 years) and 12 young adults (24.41 +/- 3.31 years) were instructed to keep their habitual sleep schedules for three consecutive work-days, during which they were required to signal every yawning occurrence and to evaluate hourly their sleepiness level. Results showed that aged subjects yawn less frequently than young adults, particularly during morning and mid-afternoon hours. The time course of yawning was different between the two age groups: aged subjects showed earlier morning peak and evening rise compared with young adults; in addition, aged subjects showed two minor peaks in-between. Differences as a function of age in the time course of yawning were associated with differences in the time course of sleepiness. The only exception pertained to the early morning yawning peak, which was close to the awakening but it was not associated with high sleepiness in aged subjects. Our study discloses that aging modifies yawning frequency and its time course. Furthermore, as in the elderly yawning after the awakening is not associated with high sleepiness level as in young adult, we put forward that sleepiness level and the proximity of sleep/wake transitions could separately affect yawning.

Weiss, N., D. Galanaud, et al. (2008). "A combined clinical and MRI approach for outcome assessment of traumatic head injured comatose patients." J Neurol 255(2): 217-23.
Traumatic brain injury (TBI) is associated with substantial consumption of health care resources. No clinical or paraclinical examination can reliably predict neurological evolution. In this study, we evaluated the ability of a combined clinical and MRI approach to predict outcome. METHODS : This prospective study took place between June 2001 and March 2005 in a Neurosurgical Intensive Care Unit in Paris, France. Inclusion criteria were TBI patients still mechanically ventilated and without clinical signs of awareness after 2 weeks. Four clinical signs were assessed after cessation of sedation: grasping, yawning, chewing and paroxysmal sympathetic storm. FLAIR and T2* acquisitions on MRI were used in order to localize brain lesions. Statistically linked regions (clusters) were defined. Outcome was assessed at one year by Glasgow Outcome Scale (GOS). FINDINGS : 73 patients were included: 41 had poor outcome (GOS 1-3) and 32 had good outcome (GOS 4-5). Lesions in the clusters "right upper pons and right lower midbrain"," hypothalamus and basal forebrain","left parietal, left temporal, left occipital lobes and left insula" and the presence of grasping or chewing were associated with poor outcome in multivariate analysis. This combined clinical and MRI approach gives a much better prediction than MRI approach only (P < 0.009), with an area under the ROC curve of 0.94 (95 % CI, 0.89-1.00). INTERPRETATION : These data suggest that MRI associated with clinical assessment improves outcome prediction in severe TBI patients.

Victor, O. U. (2008). "Ageing and urban-rural drift in Nigeria: Coping or dispensing with city accommodation in retirement." Ageing Res Rev.
The massive press attentions attracted by the plight of pensioners in Nigeria appear to provide the extrinsic nudge and popular support for the 2004 pension reform. In some sense, these sets of exposes offered a new peephole into the yawning care and support gap for the elderly in the country. Against the background of counteracting processes of population ageing and receding formal and informal social protection and support mechanisms, the country appears ill-prepared to tackle the unfolding old age bulge and its myriad challenges. The paper addresses one of the most basic needs and choices confronting older people after retirement: the resolve to cope or dispense with city (or urban) accommodation. Such decisions have become increasingly critical not only because they are principal determinants of urban-rural drift but also because of the changing circumstances (of weakening support systems and increased vulnerability) under which they are made. The paper explores these important ageing issue and their implications for policy in Nigeria.

Tsou, C. H., T. Kao, et al. (2008). "Clinical assessment of propofol-induced yawning with heart rate variability: a pilot study." J Clin Anesth 20(1): 25-9.
STUDY OBJECTIVES: To investigate the proportion of propofol-induced yawning and sympathovagal balance during propofol-induced yawning. DESIGN: Prospective, observational, clinical study. SETTING: University hospital and 2400-bed tertiary medical center. PATIENTS: 546 ASA physical status I and II patients undergoing elective surgery with general anesthesia. INTERVENTIONS: Standard induction of anesthesia was performed with intravenous (IV) propofol two to four mg/kg (group P), or pretreatment with atropine 0.1 mg/kg (group AP) or with fentanyl 1 to 3 microg/kg (group FP) before propofol. Continuous standard electrocardiogram for heart rate variability (HRV) was performed in another 20 patients to investigate sympathovagal balance during propofol-induced yawning. MEASUREMENTS AND MAIN RESULTS: The proportions of yawning were 53.5% (207/386), 61.1% (55/90), and 0% (0/50) in the P, AP, and FP groups, respectively. Propofol-induced yawning could be dramatically decreased by pretreatment with IV fentanyl (P < 0.001, chi2 test). Significant increased ratio of low-frequency/high-frequency power was detected during HRV monitoring in 9 patients with yawning in comparison with 11 patients without yawning (P < 0.05, Wilcoxon signed-rank test). CONCLUSIONS: Pretreatment with fentanyl may inhibit propofol-induced yawning. Fluctuations in autonomic function have been noted during propofol-induced yawning.

Tjakkes, G. H., D. J. Rijnvis, et al. (2008). "[A patient with glossopharyngeal neuralgia: a (un)known trap]." Ned Tijdschr Tandheelkd 115 (5): 263-5.
A man visited the dentist regularly during the past 6 years with a complaint about severe pain. Treatment met with uneven success. The patient now complained about severe, radiating pain which resulted from contact between the tongue and the bridge. The teeth that seemed to be involved were inspected and, after diagnostic testing, restoratively and endodontically treated. When the pain persisted, an oral and maxillofacial surgeon was consulted; the surgeon diagnosed the problem as a glossopharyngeal neuralgia. The neuralgia was treated with carbazamzepine, after which the pain diminished. Pain that seems to be pulpitis pain may be caused by a neuralgia, in this case a glossopharyngeal neuralgia. Triggers for the pain can be swallowing, chewing, talking, coughing or yawning. Although the incidence is low, when pain persists after initial treatment, a (glossopharyngeus) neuralgia should be seriously considered.

Taskapilioglu, O., C. Akkaya, et al. (2008). "Pathological yawning in a patient with anxiety and chronic disease anaemia." J Psychopharmacol.
Abstract Yawning, frequent in daily life, is accepted as a complex arousal reflex. Excessive yawning may be due to neurological, psychiatric, infectious, gastrointestinal or metabolic diseases. This reflex has also been associated with different selective serotonin reuptake inhibitors. We report a female patient, with excessive yawning, who was on selective serotonin reuptake inhibitor treatment with the diagnosis of generalised anxiety disorder. She was then found to have endometrial carcinoma. Her complaints of palpitation, shortness of breath and loss of energy might be explained by a psychiatric disease and/or anaemia. Previous anaemic periods and partial response of her psychiatric symptoms during last 3 years alerted us to think about an organic cause. Investigations for chronic disease anaemia resulted in diagnosis of endometrial carcinoma. This case is a good example showing misdiagnosis caused by medical stigmatisation.

Tamaddonfard, E., H. Soraya, et al. (2008). "Central interaction between physostigmine and histamine during yawning in rats." Pharmacol Rep 60(6): 896-903.
In this study, the effects of intraperitoneal (ip) injection of physostigmine, subcutaneous (sc) injection of atropine, and intracerebroventricular (icv) injections of histamine, chlorpheniramine (H(1)-receptor antagonist), and ranitidine (H(2)-receptor antagonist) in separate and combined treatments were investigated during yawning in rats. Physostigmine at a dose of 0.25 mg/kg produced the highest number of yawns. Atropine, used alone, was without effect, but physostigmine (0.25 mg/kg, ip)-induced yawning was blocked by pretreatment with atropine (1 mg/kg, sc). Histamine at the doses of 10, 20 and 40 microg produced yawning. Chlorpheniramine and ranitidine, used alone, had no effect, whereas pretreatments with chlorpheniramine and ranitidine at the same dose of 80 microg prevented histamine (40 microg, icv)-induced yawning. The suppressive effect of chlorpheniramine was more than that of ranitidine. Histamine (10 and 40 microg, icv) enhanced, whereas chlorpheniramine and ranitidine at the same dose of 80 microg suppressed, physostigmine (0.25 mg/kg, ip)-induced yawning. Atropine (1 mg/kg, sc) not only suppressed histamine-induced yawning, but also enhanced the inhibitory effect of chlorpheniramine, but not of ranitidine on yawning induced by histamine. These results indicate that muscarinic receptors mediate yawning induced by physostigmine. Histamine central H(1), and to a lesser extent H(2) receptors, may be involved in histamine-induced yawning. Cholinergic muscarinic receptors, as well as histaminergic H(1) and to a lesser extent H(2) receptors, may lso be involved in the interaction between brain acetylcholine and histamine.

Svensson, P., E. Castrillon, et al. (2008). "Nerve growth factor-evoked masseter muscle sensitization and perturbation of jaw motor function in healthy women." J Orofac Pain 22(4): 340-8.

AIM: To replicate and extend previous findings of nerve growth factor (NGF)-induced mechanical sensitization in healthy young men to women and test for associations between mechanical sensitization and oral motor function. Combined these data would indicate if injection of NGF into the masseter muscle is a valid model of muscle pain related to temporomandibular disorders (TMD). METHODS: A double-blind, placebo-controlled study was conducted on 14 healthy women. Each subject received an injection of NGF (5 microg in 0.2 mL) into 1 masseter muscle and buffered isotonic saline (control, 0.2 mL) into the other. Pressure pain thresholds (PPT) and pressure pain tolerance (PPTOL) as well as self-assessed pain intensity (numeric rating scale of 1 to 10) with the jaw at rest and in relation to various motor activities (chewing, yawning, talking, swallowing, drinking, and smiling) were recorded prior to and 3 hours, 1 day, 7 days, 14 days, and 21 days postinjection. ANOVAs were used to test data. RESULTS: It was found that NGF significantly reduced PPT and PPTOL 3 hours, 1 and 7 days postinjection ($P < .001$). Numerical rating scale (NRS) scores during chewing and yawning were significantly increased 3 hours and 1 day following NGF injection ($P < .001$). After 3 hours, there were significant correlations between relative changes in PPTs and NRS scores during chewing ($r = -0.556$; $P = .037$), between relative changes in PPTOL and NRS scores during yawning ($r = -0.607$; $P = .020$), and between relative changes in PPTOL and maximum unassisted jaw-opening capacity ($r = 0.868$; $P < .001$). CONCLUSION: This study shows that injection of NGF into the masseter muscle of women causes local signs of mechanical allodynia and hyperalgesia that persist for at least 7 days as well as pain during strenuous jaw movement. Taking the authors' previous results on NGF effects in men into consideration, these findings lend additional support to the suggestion that this model may serve as a proxy of some of the clinical features of TMD-related muscle pain.

Sevak, R. J., W. Koek, et al. (2008). "Feeding conditions differentially affect the neurochemical and behavioral effects of dopaminergic drugs in male rats." Eur J Pharmacol 592(1-3): 109-15.

The high co-morbidity of eating disorders and substance abuse suggests that nutritional status can impact vulnerability to drug abuse. These studies used rats to examine the effects of food restriction on dopamine clearance in striatum and on the behavioral effects of amphetamine (locomotion, conditioned place preference), the dopamine receptor agonist quinpirole (yawning), and the dopamine receptor antagonist raclopride (catalepsy). Amphetamine increased locomotion and produced conditioned place preference. Food restriction reduced dopamine clearance, which was restored by repeated treatment with amphetamine or by free feeding. Food restriction also decreased sensitivity to quinpirole-induced yawning and raclopride-induced catalepsy; normal sensitivity to both drugs was restored by free feeding. The same amphetamine treatment that normalized dopamine clearance, failed to restore normal sensitivity to quinpirole or raclopride, suggesting that in food-restricted rats the activity of dopamine transporters and dopamine receptors is differentially affected by pathways that are stimulated by amphetamine. These studies show that modest changes in nutritional status markedly alter dopamine neurotransmission and the behavioral effects of direct-acting dopamine receptor drugs (agonist and antagonist). These results underscore the potential importance of nutritional status (e.g., glucose and insulin) in modulating dopamine neurotransmission and in so doing they begin to establish a neurochemical link between the high co-morbidity of eating disorders and drug abuse.

Prasad, H. (2008). "Amelioration of pathological yawning after tracheostomy in a patient with locked-in syndrome: a thermoregulatory approach." Eur J Neurol 15(12): e114; author reply e115.

Prasad, H. (2008). "Yawning...and why yawns are contagious: A theory on evolution and atavism." Med Hypotheses.

Prasad, H. (2008). "Drug-induced yawning: A vital protective reflex." Med Hypotheses.

Perna, M. K., Z. A. Cope, et al. (2008). "Nicotine sensitization in adult male and female rats quinpirole-primed as neonates." Psychopharmacology (Berl).

RATIONALE: Increases in dopamine D(2)-like receptor function are common in several psychological disorders that demonstrate a four to five fold increase in nicotine abuse compared to the general population. OBJECTIVE: The objective of this study was to analyze the interaction of sex differences and sensitization to nicotine in rats D(2) receptor primed as neonates. MATERIALS AND METHODS: A total of 32 male and 32 female Sprague-Dawley rats derived from eight litters were ontogenetically treated with quinpirole (1 mg/kg) or saline from postnatal days (P) 1-21 and raised to adulthood. At P60, all animals were given an acute injection of quinpirole HCl (100 mug/kg) and yawns were counted for 1 h. Yawning has been shown to be a behavioral event mediated by D(2)-like receptors. Beginning on P61-65, animals were habituated to a locomotor arena and subsequently administered either nicotine (0.5 mg/kg free base) or saline (intraperitoneal) every second day for 3 weeks. Approximately 15 min after each injection, animals were placed into the arena and horizontal activity and vertical rears were recorded. RESULTS: A robust increase of yawning was observed at P60 in D(2) primed as compared to saline controls. Priming of D(2)-like receptors increased the locomotor response to nicotine in horizontal activity in both males and females, but females demonstrated a more robust hypoactive locomotor response to initial nicotine treatment when compared to saline-treated females. Nicotine also produced a significant decrease of vertical rearing in both males and females. CONCLUSIONS: It appears that D(2) receptor priming enhances sensitization to nicotine in adult rats, and females may be more behaviorally sensitive to nicotine than males.

Nahab, F. B., N. Hattori, et al. (2008). "Contagious yawning and the frontal lobe: An fMRI study." Hum Brain Mapp.

We conducted a slow event-related fMRI experiment with naive subjects' passively viewing yawn and various other control videos along with correlative behavioral testing. Specifically associated with the viewing of the contagious yawn was an area of activation in the ventromedial prefrontal cortex. These findings suggest a role for the prefrontal cortex in the processing of contagious yawning, while demonstrating a unique automaticity in the processing of contagious motor programs which take place independently of mirror neuron networks. Hum Brain Mapp 2008. (c) 2008 Wiley-Liss, Inc.

Moyaho, A., M. Barajas, et al. (2008). "Genetic and littermate influences on yawning in two selectively bred strains of rats." Dev Psychobiol.

This study was made to separate genetic from postnatal maternal influences on yawning in two strains of Sprague-Dawley rats selected for high- (HY) and low-yawning frequency (LY). Foster mothers of the two strains reared litters of pups in the four possible combinations and yawning was recorded in a novel environment when the adult offspring were 75-day-old. Yawning frequency of males and females was affected by pup strain but not by the strain of the foster mothers, when litter size was made constant; HY adult offspring yawned more than LY adult offspring. Yawning frequency was higher in HY male offspring than in HY female offspring. An interaction term between pup sex and the strain of the foster mothers revealed that while males reared by LY mothers yawned more than males reared by HY mothers, females reared by HY mothers yawned more than females reared by LY mothers. Mean frequency of yawning increased with the sex ratio of HY litters. These findings indicate that genetic and genotype-correlated littermate effects influence yawning frequency of adult offspring in response to a novel environment. (c) 2008 Wiley Periodicals, Inc.

Millan, P. A., M. I. Montes, et al. (2008). "[Biopercular syndrome: report of two cases and literature review]." Biomedica 28(2): 183-90.

The anterior opercular or biopercular syndrome is a cortical pseudobulbar palsy due to bilateral lesions of the anterior brain operculum. It is characterized by preservation of reflex function and automatic activity, without mental impairment. Two cases are reported herein and the relevant literature reviewed. The first case was a 73-year-old female with a history of a stroke occurring seven years previously, without sequelae in the interim. She presented with sudden loss of consciousness. The neurological examination showed a right facial central palsy and anarthria, with reflex acts such as smiling, blinking and yawning, not elicited by commands; she also had a right hemiparesis and walking impairment. A brain CT scan showed an old ischemic infarction in the region of the right medial cerebral artery. Because the right motor involvement did not correlate with the findings of the initial CT scan, another CT scan two days later showed an acute brain infarction in the vicinity of the left medial cerebral artery. The second case was an 8-year-old girl with mental retardation and impairment of verbal development, caused by of biopercular pachygyria. Facio-pharyngo-glosso-masticatory diplegia and volitional selective palsy of the oro-facial muscles was seen in both patients. The neuropsychological assessment showed cognitive, emotional and social interaction impairment in both cases -as part of the frontal convexity syndrome in the first case and of mental retardation in the second. The two patients had difficulty in mastication and swallowing. The prognosis for recovery of verbal capacity is poor, although generally most patients recover the ability to swallow.

Matikainen, J. and H. Elo (2008). "Does yawning increase arousal through mechanical stimulation of the carotid body?" Med Hypotheses 70(3): 488-92.

Yawning is a stereotyped event that occurs in humans and animals from fish to mammals, but neither its mechanisms nor its functions are entirely known. Its widespread nature suggests that it has important physiological functions. It is associated with stretching of muscles in a large area, but the function of this stretching is understood far from completely. It has been proposed that yawning increases arousal and that it is an arousal defense reflex, whose aim is to reverse brain hypoxia. Whilst yawning has been speculated to have an important role in reversing hypoxia, there is a structure in the neck that is known to be intimately involved in the regulation of oxygen homeostasis, namely the carotid body. It senses acute changes in oxygen levels. In spite of this, a connection has never been proposed either between the carotid body and arousal, or between yawning and the carotid body. We propose that yawning stimulates mechanically the carotid body (and possibly other structures in the neck). We further propose that this stimulation gives rise to increased arousal, alertness and wakefulness and that one important physiological function of yawning is increase of arousal through this stimulation. We also propose that mechanical effects on the shunt system of the carotid body may be involved in this stimulation. Our hypothesis is supported by several facts. For example, yawning causes movements and compressions that may affect the carotid body that is situated strategically at the bifurcation of the common carotid artery. Thus, yawning may stimulate the carotid body. The carotid body is highly vascular and compressions may affect its shunt system and blood flow and for example give rise to release of hormones or other substances. Also several facts related to situations where people yawn or do not yawn support our hypothesis and are discussed. Further support comes from facts related to somnogenic substances, hormones and transmitters, and from facts related to the interconnection of homeostatic mechanisms, sleep, arousal and ventilation.

Marcos, B., T. T. Chuang, et al. (2008). "Effects of 5-HT6 receptor antagonism and cholinesterase inhibition in models of cognitive impairment in the rat." Br J Pharmacol 155(3): 434-40.

BACKGROUND AND PURPOSE: The beneficial effect of 5-HT6 receptor antagonism in cognition remains controversial. This study has been undertaken to reassess the cognition enhancing properties of acute vs subchronic treatment with the selective 5-HT6 receptor antagonist SB-271046 in unimpaired rats, as well as against scopolamine (cholinergic-) or MK-801 (glutamatergic-mediated) deficits. EXPERIMENTAL APPROACH: The Morris water maze was used, measuring behaviour acquisition and retention, and swim speed. Other behavioural measures included yawning and motor activity. SB-271046 was given acutely before each trial or subchronically for 7 days before the trials. The AChE inhibitor galanthamine was also used alone or in combination with SB-271046. KEY RESULTS: Subchronic treatment with SB-271046 improved acquisition in the Morris water maze, while the acute treatment only improved retention. Neither acute nor subchronic SB-271046 treatment reversed scopolamine-induced learning deficits. MK-801 induced learning impairment associated with a behavioural syndrome, reversed by acute, but not subchronic, SB-271046 treatment. Interestingly, combined treatment with galanthamine and SB-271046 reversed the scopolamine- or MK-801-induced learning impairments. Subchronic treatment with SB-271046 did not modify motor activity or the increased number of yawns, a cholinergic-mediated behaviour, induced by single administration of SB-271046. CONCLUSIONS AND IMPLICATIONS: These data suggest a potential therapeutic role of 5-HT6 receptor antagonists such as SB-271046, alone or in combination with galanthamine, in the treatment of cognitive dysfunction, such as those seen in Alzheimer's disease and schizophrenia.

Lewitt, P. A., W. G. Ondo, et al. (2008). "Open-Label Study Assessment of Safety and Adverse Effects of Subcutaneous Apomorphine Injections in Treating "Off" Episodes in Advanced Parkinson Disease." Clin Neuropharmacol.

OBJECTIVE:: To assess the safety and adverse effect profile of continued use of intermittent subcutaneous apomorphine to treat "off" episodes in subjects with advanced Parkinson disease. SUBJECTS AND METHODS:: The study enrolled subjects with Hoehn and Yahr stage II-V Parkinson disease who were experiencing "off&" events despite an optimized oral medication regimen. After baseline assessment and subcutaneous apomorphine dose titration (2-10mg/dose), subjects received >/=12 months of open-label treatment, as needed, for "off" episodes. RESULTS:: Of the 546 subjects in the study population, the majority used apomorphine on a daily basis; the average dose was 4.0 mg. A total of 187 subjects discontinued treatment because of adverse events (AEs). Most AEs were mild to moderate and expected with apomorphine. The AEs most commonly classified as definitely, probably, or possibly treatment related were nausea and vomiting, dyskinesia, dizziness, somnolence, hallucination, yawning, and injection site bruising. Serious AEs occurred in 199 subjects, but only 27 were considered to be probably or possibly treatment related. None of the 45 deaths recorded in the study were attributed to apomorphine. CONCLUSIONS:: Long-term use of intermittent apomorphine dosing for treatment of "off" episodes was generally associated with mild-to-moderate AEs.

Lal, S., J. X. Thavundayil, et al. (2008). "Induction of tolerance of dopaminergic responses in man." J Neural Transm.

Schizophrenia may reflect a sensitization of dopaminergic (DA) function. Apomorphine (Apo), a DA receptor agonist, induces both sensitization and tolerance of DA function in rodents depending on dose intervals. We investigated sensitization and tolerance to Apo in healthy male volunteers. After a period of acclimatization to the experimental setting (Day 1) subjects were assigned randomly to two groups: Group A subjects received seven injections of placebo (physiological saline) (PLA) and Group B subjects received seven injections of Apo HCl (7 mug/kg sc) under double-blind conditions at 2 h intervals commencing at 0930 hours (Day 2) after an overnight fast. Twelve hours after the seventh injection, i.e. on Day 3, after an overnight fast all subjects received an injection of Apo. Serial samples of blood commencing at 0900 hours were drawn after the first and last injection in both groups for assay of growth hormone (GH), prolactin (PRL) and cortisol by radioimmunoassay; sleepiness was measured using the Analog Sleepiness Rating Scale and yawning recorded by video recorder. The GH response in Group B (N = 8) was (a) decreased after the eighth injection of Apo compared with the first injection of Apo (P = 0.03) and (b) decreased after the eighth injection of Apo compared with the first injection of Apo in Group A (N = 10) (P = 0.001). The number of yawns in Group B was significantly decreased after the eighth injection of Apo compared with the first injection of Apo (P = 0.042). PRL, cortisol and sleepiness were not significantly different between the first and eighth injection of Apo. Sensitization was not observed in any of the measures studied. These results are compatible with induction of acute tolerance of DA-mediated GH and yawning responses. The method used provides a safe pharmacological paradigm to examine plasticity of DA mechanisms in man. Results are discussed in the context of possible therapeutic implications for schizophrenia.

Kita, I., N. Kubota, et al. (2008). "Intracerebroventricular administration of corticotropin-releasing factor antagonist attenuates arousal response accompanied by yawning behavior in rats." Neurosci Lett 433(3): 205-8.

We have reported that an arousal response accompanied by yawning behavior can be evoked by electrical and chemical stimulation of the hypothalamic paraventricular nucleus (PVN) in rats, although the mechanism responsible for the arousal response accompanied by yawning evoked by PVN stimulation is still unknown. In the present study, we examined the involvement of corticotropin-releasing factor (CRF) in the arousal response during yawning induced by electrical stimulation of the PVN in anesthetized, spontaneous breathing rats using intracerebroventricular (icv) injection of alpha-helical CRF, a CRF antagonist (4.2 microg, lateral ventricle). The electrocorticogram (ECoG) was recorded to evaluate arousal responses during yawning. Fast Fourier transform was used to obtain the power spectrum in delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-20 Hz) bands. We also recorded the intercostal electromyogram as an index of inspiratory activity and blood pressure (BP) as an index of autonomic function to evaluate yawning response. PVN stimulation induced significant increases in relative powers of theta, alpha, and beta bands, but not delta band, concurrent with yawning events regardless of icv injection, though the relative powers after icv injection of alpha-helical CRF were significantly lower than those after saline injection. These findings suggest that CRF neurons in the PVN are primarily responsible for the arousal response accompanied by yawning behavior.

Joly-Mascheroni, R. M., A. Senju, et al. (2008). "Dogs catch human yawns." Biol Lett 4(5): 446-8.

This study is the first to demonstrate that human yawns are possibly contagious to domestic dogs (Canis familiaris). Twenty-nine dogs observed a human yawning or making control mouth movements. Twenty-one dogs yawned when they observed a human yawning, but control mouth movements did not elicit yawning from any of them. The presence of contagious yawning in dogs suggests that this phenomenon is not specific to primate species and may indicate that dogs possess the capacity for a rudimentary form of empathy. Since yawning is known to modulate the levels of arousal, yawn contagion may help coordinate dog-human interaction and communication. Understanding the mechanism as well as the function of contagious yawning between humans and dogs requires more detailed investigation.

Han, C., C. U. Pae, et al. (2008). "Venlafaxine versus mirtazapine in the treatment of undifferentiated somatoform disorder: a 12-week prospective, open-label, randomized, parallel-group trial." Clin Drug Investig 28(4): 251-61.

OBJECTIVE: We set out to compare the efficacy and tolerability of mirtazapine versus venlafaxine in patients with undifferentiated somatoform disorder (USD) using the Patient Health Questionnaire-15 (PHQ-15). METHODS: This was a 12-week prospective, open-label, randomized, parallel-group trial. The trial consisted of six visits that included baseline and weeks 1, 2, 4, 8 and 12. The primary effectiveness measure was the mean change in PHQ-15 total score from baseline to the end of treatment. Secondary effectiveness measures included the mean changes in total scores on the Beck Depression Inventory (BDI) and the 12-item General Health Questionnaire (GHQ) from baseline to the end of treatment. Ninety-five subjects were randomized to either mirtazapine (n = 50) or venlafaxine (n = 45); 71 subjects completed the study (mirtazapine: n = 39/50 [78%]; venlafaxine: n = 32/45 [71%]). RESULTS: The mean total score on the PHQ-15 decreased by 34.7% (-8.4, p < 0.0001) from baseline to endpoint in the mirtazapine group and by 26.6% (-6.1, p < 0.0001) in the venlafaxine group. A marginally significant between-group difference was observed for the mean change in total score on the PHQ-15 from baseline to endpoint (F = 4.126, p = 0.046). The mean total scores on the GHQ-12 and BDI from baseline to endpoint decreased by -4.9 (29.4%, p < 0.0001) and -13.5 (55.9%, p < 0.0001), respectively, in the mirtazapine group, and by -4.3 (26.2%, p = 0.001) and -9.02 (46.0%, p < 0.0001), respectively, in the venlafaxine group. No between-group difference was observed for the mean changes in total scores on the secondary effectiveness measures from baseline to endpoint. Both treatments were well tolerated. CONCLUSION: Our findings suggest that both mirtazapine and venlafaxine may be effective and well tolerated in the treatment of patients with USD. Double-blind, placebo-controlled and/or head-to-head comparison studies are required to allow definite conclusions to be drawn.

Gronqvist, J., B. Haggman-Henrikson, et al. (2008). "Impaired jaw function and eating difficulties in whiplash-associated disorders." Swed Dent J 32(4): 171-7.

Eating requires mouth opening, biting, chewing and swallowing and should be performed without dysfunction or pain. Previous studies have shown that jaw opening-closing movements are the result of coordinated activation of both jaw and neck muscles, with simultaneous movements in the temporomandibular, atlanto-occipital and cervical spine joints. Consequently, it can be assumed that pain or dysfunction in any of the three joint systems involved could impair jaw activities. In fact, recent findings support this hypothesis by showing an association between neck injury and reduced amplitudes, speed and coordination of integrated jaw-neck movements. This study investigated the possible association between neck injury and disturbed eating behaviour. Fifty Whiplash-associated disorders (WAD) patients with pain and dysfunction in thejaw-face region and 50 healthy age- and sex-matched controls without any history of neck injury participated in the study. All participants were assessed by a questionnaire, which contained 26 items about eating behaviour, jaw pain and dysfunction. For the WAD group there were significant differences in jaw pain and dysfunction and eating behaviour before and after the accident, but no significant differences between WAD before and healthy. The healthy and the WAD group before the accident reported no or few symptoms. The WAD patients after the accident reported pain and dysfunction during mouth opening, biting, chewing, swallowing and yawning and felt fatigue, stiffness and numbness in the jaw-face region. In addition, a majority also reported avoiding tough food and big pieces of food, and taking breaks during meals. Altogether, these observations suggest an association between neck injury and disturbed jaw function and therefore impaired eating behaviour. A clinical implication is that examination of jaw function should be recommended as part of the assessment and rehabilitation of WAD patients.

Goektas, O., F. Fleiner, et al. (2008). "The scent-diffusing ventilator for rehabilitation of olfactory function after laryngectomy." Am J Rhinol 22(5): 487-90.

BACKGROUND: The larynx bypass (LB) is the only device capable of providing laryngectomy patients with the ability to smell. Our findings regarding one-time and long-term use did reveal an improved olfactory function in these patients. Because the LB is difficult to use, however, it is not appropriate for everyday use. Therefore, we devised a new instrument: the scent-diffusing ventilator (SV). METHODS: Between January 2006 and February 2007, we researched the olfactory function of 16 patients who had undergone a laryngectomy (13 men/3 women; median age, 63 years) by using the LB and the SV. Their olfactory function was measured with the Sniffin' Sticks test battery. Further practicability of both methods was determined through a visual analog scale (1-10). RESULTS: The patients' olfactory function significantly improved (SV median 8 versus LB median 7; $p < 0.002$). In addition, the SV was much easier to use than the LB (median, 6 versus 5; $p < 0.001$). CONCLUSION: Further technical improvements are necessary to make the SV an established part of the rehabilitation of the olfactory function after laryngectomy.

Gibbins, S., B. Stevens, et al. (2008). "Pain behaviours in Extremely Low Gestational Age infants." Early Hum Dev 84(7): 451-8.

BACKGROUND: To date, there are over 40 infant pain measures. Despite this plethora of measures, only 8 have included preterm infants and only 2 have included Extremely Low Gestational Age (ELGA; infants <28 weeks GA) in their development. Without reliable, valid and clinically useful indicators for procedural pain in ELGA infants, clinicians have no means to interpret the responses from an immature infant who may respond differently from infants of older GA. OBJECTIVE: To examine the physiological, behavioural and biochemical responses to painful and non-painful procedures in ELGA infants and the influence of GA and sex. DESIGN/METHODS: A prospective crossover design with 50 ELGA infants from one Canadian tertiary level NICU was conducted. Infants were assessed in random order during standardized painful (heel lance) and non-painful (diaper change) procedures. Physiological (heart rate, oxygen saturation) and behavioural (facial and body movement) indicators were continuously collected during 4 phases of the procedures. Biochemical (salivary cortisol) indicators were collected immediately before and 20 min following the procedures. RESULTS: Four facial actions (brow bulge, eye squeeze, nasolabial furrow, vertical mouth stretch) increased immediately following the heel lance. There were no specific changes in physiological, body movement or cortisol indicators following the heel lance. ELGA infants demonstrated greater body movements during the diaper change, which may reflect immature motor coordination. No differences in pain responses were found for infants born between 23-25 6/7 weeks GA and those between 26-28 weeks GA. Similarly, no gender differences were found. CONCLUSIONS: Changes in 4 facial actions were the most sensitive indicators of pain in ELGA infants. This finding is consistent with existing measures where facial actions are the most prominent pain indicators. Specific body movements such as those included in NIDCAP, may provide more information about pain in ELGA infants. Movements such as hand-on-face, finger splaying, fisting, arching or yawning need to be examined in future research.

Ghika, J. (2008). "Paleoneurology: neurodegenerative diseases are age-related diseases of specific brain regions recently developed by Homo sapiens." Med Hypotheses 71(5): 788-801.

Bipedal locomotion and fine motility of hand and larynx of humans introduced musculoskeletal adaptations, new pyramidal, corticostriatal, corticobulbar, nigrostriatal, and cerebellar pathways and expansions of prefrontal, cingular, parieto-temporal and occipital cortices with derived new brain capabilities. All selectively degenerate in aged homo sapiens following 16 syndromic presentations: (1) Parkinsonism: nigrostriatal control for fast automatic movements of hand, larynx, bipedal posture and gait ("simian gait and hand"). (2) Frontal (highest level) gait disorders (lower body parkinsonism, gait apraxia, retropulsion): prefrontostriatal executive control of bipedal locomotion. (3) ataxia: new synergistic coordination of bipedal gait and fine motility. (4) Dyskinesias (chorea, dystonia, tremor...): intrusions of simian basal ganglia motor subroutines. (5) motoneuron diseases: new proximo-distal and bulbar motoneurones, preserving older ones (oculomotor, abdominal...). (6) Archaic reflexes: prefrontal disinhibition of old mother/tree-climbing-oriented reflexes (sucking, grasping, Babinski/triple retraction, gegenhalten), group alarms (laughter, crying, yawning, grunting...) or grooming (tremor=scratching). (7) Dysautonomia: contextual regulation (orthostatism...). (8) REM sleep disorders of new cortical functions. (9) Corticobasal syndrome: melokinetic control of hand prehension-manipulation and language (retrocession to simian patterns). (10) Frontal/temporal lobe degeneration: medial-orbitofrontal behavioural variant: self monitoring of internal needs and social context: apathy, loss of personal hygiene, stereotypia, disinhibition, loss of concern for consequences of acts, social rules, danger and empathy; dorsolateral executive variant: inadequacy to the context of action (goal, environmental changes...); progressive non-fluent aphasia: executive and praxic processing of speech; temporal variant: abstract concepts for speech, gestures and vision (semantic dementia, progressive nonfluent aphasia) (11) Temporomesial-limbic-paralimbic-associative cortical dementias (Alzheimer's disease, Lewy body, progressive amnesia): processing of explicit cognition: amnesic syndrome, processing of hand, larynx and eye: disorientation, ideomotor apraxia, agnosia, visuospatial processing, transcortical aphasia. (12) Focal posterior atrophy (Benson, progressive apraxia): visuomotor processing of what and where. (13) Macular degeneration: retinal "spot" for explicit symbols. (14) "Psychiatric syndromes": metacognition, self monitoring and regulation of hierarchical processing of metacognition: hallucinations, delusions, magic and mystic logic, delusions, confabulations; drive: impulsivity, obsessive-compulsive disorders, mental automatisms; social interactions: theory of mind, autism, Asperger. (15) Mood disorders: control on emotions: anxio-depressive and bipolar disorders, moria, emotional lability. (16) Musculoskeletal: inclusion body myositis: muscles for bipedal gait and fine motility. Paget's disease: bones for bipedal gait and cranium. Understanding of the genetic mechanisms underlying the evolution of these recent human brain regions and paleoneurology my be the key to the focal, asymmetrical or systemic character of neurodegeneration, the pathologic heterogeneity/overlap of syndromic presentations associating gait, hand, language, cognition, mood and behaviour disorders.

Gallup, A. C. and G. G. Gallup, Jr. (2008). "Yawning and thermoregulation." Physiol Behav.

We review a growing body of medical and physiological evidence indicating that yawning may be a thermoregulatory mechanism, providing compensatory cooling when other provisions fail to operate favorably. Conditions such as multiple sclerosis, migraine headaches, epilepsy, stress and anxiety, and schizophrenia have all be linked to thermoregulatory dysfunction and are often associated with instances of atypical yawning. Excessive yawning appears to be symptomatic of conditions that increase brain and/or core temperature, such as central nervous system damage, sleep deprivation and specific serotonin reuptake inhibitors. Yawning is also associated with drowsiness, and subjective ratings of sleepiness are correlated with increases in body temperature. This view of yawning has widespread application for the basic physiological understanding of thermoregulation as well as for the improved diagnosis and treatment of diseases associated with abnormal thermoregulation.

Di Martino, E. F. (2008). "[Sonotubometry - an alternative to tympanometry?]." Laryngorhinootologie 87(10): 694-6.

Di Martino, E., V. Nath, et al. (2008). "[Examination of the eustachian tube activity with perfect sequences.]." Laryngorhinootologie 87(6): 406-11.

INTRODUCTION: Sonotubometry allows an assessment of the Eustachian tube (ET) function under physiological conditions. The application of conventional sinus signals is not reliable enough for routine clinical use. The aim of this study was to investigate ET activity with so-called perfect sequences (PSEQ). PATIENTS AND METHODS: PSEQs generated by a custom-made device were applied in 25 healthy subjects. ET opening was induced by Toynbee manoeuvre, yawning, dry and water swallowing. All sonotubograms were qualitatively analysed according to their shape, and quantitatively according to increase of sound intensity, frequency of opening and opening duration. The sonotubometry results were combined with the patients' perception of tone variation. RESULTS: A number of 400 measurements were performed. In 92.75 % measurements the patients reported ET openings. These were confirmed by 81.5 % valid sonotubograms. The swallowing manoeuvres dry/water swallowing and Toynbee yielded with 94 %/90 % and 93 % valid measurements favourable results. Yawning was associated with 49 % valid measurements. Sound level increase was also significantly different in these manoeuvres when compared to yawning ($p < 0.0001$). Nasal decongestion had no influence on the results ($p > 0.05$). CONCLUSIONS: PSEQs allow an evaluation of ET function. The chosen manoeuvres trigger in healthy subjects objective ET openings with a high reliability. The application of PSEQs can detect ET activity with a high sensitivity and good specificity. By further technical refinements specificity may also be enhanced in future studies.

d'Andrea, C., J. L. Meliet, et al. (2008). "[Peripheral facial palsy secondary to middle-ear overpressure]." Presse Med 37(4 Pt 2): 643-7.

Facial baroparesis is an ischemic neurapraxia of the facial nerve. It occurs after airplane trips or prolonged diving. This paralysis is due to the tympanic promontory. Several promoting factors have been identified, including tubal dysfunction, hypotension, and neurotropic virus. Simple maneuvers can make it disappear: yawning, swallowing, or a Toynbee maneuver. Treatment is based on normobaric or even hyperbaric oxygen therapy. During airplane flights, the paralysis often disappears at landing.

Cooper, N. R., I. Puzzo, et al. (2008). "Contagious yawning: the mirror neuron system may be a candidate physiological mechanism." Med Hypotheses 71(6): 975-6.

Cologno, D., G. Cicarelli, et al. (2008). "High prevalence of Dopaminergic Premonitory Symptoms in migraine patients with Restless Legs Syndrome: a pathogenetic link?" Neurol Sci 29 Suppl 1: S166-8.

In order to assess the prevalence of Dopaminergic Premonitory Symptoms (DPS) in migraine patients with Restless Legs Syndrome (RLS), we chose migraine patients from a large Italian clinical headache population previously investigated for an association between primary headaches and RLS. We evaluated a total sample of 164 patients with migraine, in particular 114 with migraine without aura (MO), 10 with migraine with aura (MA) and 40 with MO and MA in various combinations between them or with episodic tension-type headache (ETTH), defined as a "mixed group". About 20% of all migraine patients referred at least one of the following DPS: yawning, nausea, somnolence or food craving, confirming data already indicated in the literature. Among migraine patients with RLS (25.6%), DPS were referred from about half of the patients (47.6%) compared to those without RLS (47.6% vs. 13.1%; $p<0.001$). Based on migraine subtype, patients with MO referred DPS (26.3%) more frequently compared to the MA group and "mixed group" (12.0%, $p<0.05$), particularly in the presence of RLS (63.0% vs. 20.0%, $p<0.01$). No statistical differences were found between clinical and demographic data of the subgroups or related to medical conditions investigated (anxiety, depression, sleep disorders, body mass index). It is interesting that the chances of having RLS in migraine patients were more than 5 times higher in the presence of DPS. These results could support a hypothetical dopaminergic imbalance in RLS and migraine, as the dopamine is involved in the pathogenesis of both disorders and it is responsible for the migraine DPS reported above.

Collins, G. T. and J. H. Woods (2008). "Narrowing in on compulsions: Dopamine receptor functions." Exp Clin Psychopharmacol 16(6): 498-502.

A series of experiments in rats explored the possibility that D3/D2 dopamine receptors are involved in behaviors that might be related to compulsion. A series of D3/D2 agonists and antagonists were shown to elicit yawning (D3-receptor mediated) and its inhibition (D2-receptor mediated). In rats with histories of cocaine exposure, D3-agonist-elicited yawning was enhanced, and quinpirole led to persistent operant responding only if conditioned stimuli associated with cocaine were presented for responding. Finally, a more selective D3 partial agonist was reported that had a novel profile of activity that could have relevance to the suppression of dopamine-related compulsions. (PsycINFO Database Record (c) 2008 APA, all rights reserved).

Collins, G. T., D. M. Calinski, et al. (2008). "Food restriction alters N'-propyl-4,5,6,7-tetrahydrobenzothiazole-2,6-diamine dihydrochloride (pramipexole)-induced yawning, hypothermia, and locomotor activity in rats: evidence for sensitization of dopamine D2 receptor-mediated effects." J Pharmacol Exp Ther 325(2): 691-7.

Food restriction enhances sensitivity to the reinforcing effects of a variety of drugs of abuse including opiates, nicotine, and psychostimulants. Food restriction has also been shown to alter a variety of behavioral and pharmacological responses to dopaminergic agonists, including an increased sensitivity to the locomotor stimulatory effects of direct- and indirect-dopamine agonists, elevated extracellular dopamine levels in responses to psychostimulants, as well as suppression of agonist-induced yawning. Behavioral and molecular studies suggest that augmented dopaminergic responses observed in food-restricted animals result from a sensitization of the dopamine D2 receptor; however, little is known about how food restriction affects dopamine D3 receptor function. The current studies were aimed at better defining the effects of food restriction on D2 and D3 receptor function by assessing the capacity of N'-propyl-4,5,6,7-tetrahydrobenzothiazole-2,6-diamine dihydrochloride (pramipexole) to induce yawning, penile erection (PE), hypothermia, and locomotor activity in free-fed and food-restricted rats. Food restriction resulted in a suppression of pramipexole-induced yawning, a sensitized hypothermic response, and an enhanced locomotor response to pramipexole, effects that are suggestive of an enhanced D2 receptor activity; no effect on pramipexole-induced PE was observed. Antagonist studies further supported a food restriction-induced enhancement of the D2 receptor activity because the D2 antagonist 3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]methyl-1H-indole (L741,626) recovered pramipexole-induced yawning to free-fed levels, whereas yawning and PE were suppressed following pretreatment with the D3 antagonist N-{4-[4-(2,3-dichlorophenyl)-piperazin-1-yl]-trans-but-2-enyl}-4-pyridine- 2-yl-benzamide hydrochloride (PG01037). The results of the current studies suggest that food restriction sensitized rats to the D2-mediated effects of pramipexole while having no effect on the D3-mediated effects of pramipexole.

Chen, J., G. T. Collins, et al. (2008). "Design, synthesis, and evaluation of potent and selective ligands for the dopamine 3 (D3) receptor with a novel in vivo behavioral profile." J Med Chem 51(19): 5905-8.

A series of compounds structurally related to pramipexole were designed, synthesized, and evaluated as ligands for the dopamine 3 (D3) receptor. Compound 12 has a K(i) value of 0.41 nM to D3 and a selectivity of >30000- and 800-fold over the D1-like and D2 receptors, respectively. Our in vivo functional assays showed that this compound is a partial agonist at the D3 receptor with no detectable activity at the D2 receptor.

Chang, C. C., S. T. Chang, et al. (2008). "Amelioration of pathological yawning after tracheostomy in a patient with locked-in syndrome." Eur J Neurol.

Chan, T. C., R. A. Harrigan, et al. (2008). "Mandibular reduction." J Emerg Med 34(4): 435-40.

Patients who dislocate their mandible often present to the Emergency Department for care. Dislocation can occur after a variety of activities that hyperextend the mandible or open the mouth widely, such as yawning, laughing, or taking a large bite. Anterior dislocation is the most common type, in which the condylar head of the mandible dislocates out of the glenoid fossa anterior to the articular eminence of the temporal bone. These dislocations are often complicated by muscle spasm and trismus, making reduction more difficult. The emergency physician can often reduce the anterior mandibular dislocation with or without procedural sedation or local anesthesia. A variety of methods are available for closed reduction, including the classic approach and various alternatives such as the recumbent, posterior, and ipsilateral approaches, as well as the wrist pivot method, alternative manual technique, and gag reflex induction. This article will review the pathophysiology and clinical presentation of acute mandibular dislocations, as well as discuss the various closed reduction methods available for the practitioner.

Brown, R. W., M. K. Perna, et al. (2008). "Adulthood olanzapine treatment fails to alleviate decreases of ChAT and BDNF RNA expression in rats quinpirole-primed as neonates." Brain Res 1200: 66-77.

Neonatal quinpirole (dopamine D(2)/D(3) agonist) treatment to rats has been shown to increase dopamine D(2) receptor sensitivity throughout the animal's lifetime. Male and female Sprague-Dawley rats were neonatalally treated with quinpirole (1 mg/kg) from postnatal days (P) 1-21 and raised to adulthood. Beginning on P62, rats were administered the atypical antipsychotic olanzapine (2.5 mg/kg) twice daily for 28 days. Starting 1 day after the end of olanzapine treatment, animals were behaviorally tested on the place and match-to-place version of the Morris water maze (MWM) over seven consecutive days, and a yawning behavioral test was also performed to test for sensitivity of the D(2) receptor 1 day following MWM testing. Similar to results from a past study, olanzapine alleviated cognitive impairment on the MWM place version and increases in yawning produced by neonatal quinpirole treatment. Brain tissue analyses showed that neonatal quinpirole treatment resulted in a significant decrease of hipppocampal ChAT and BDNF RNA expression that were unaffected by adulthood olanzapine treatment, although adulthood olanzapine treatment produced a significant increase in cerebellar ChAT RNA expression. There were no significant effects of drug treatment on NGF RNA expression in any brain area. These results show that neonatal quinpirole treatment produced significant decreases of protein RNA expression that is specific to the hippocampus. Although olanzapine alleviated cognitive deficits produced by neonatal quinpirole treatment, it did not affect expression of proteins known to be important in cognitive performance.

Bidat, E., M. Sznajder, et al. (2008). "[A diagnostic questionnaire for the hyperventilation syndrome in children]." Rev Mal Respir 25(7): 829-38.

INTRODUCTION: Intensive efforts should be made to diagnose the hyperventilation syndrome (HVS) at an early stage as this will prevent stigmatisation and reinforcement of symptoms. It will also prevent children from undergoing unnecessary medical examinations and treatment. A diagnostic questionnaire should be useful for this purpose. METHODS: We administered a questionnaire with 16 respiratory symptoms and 23 non respiratory symptoms to 25 children with HVS alone, 20 with asthma and HVS, and two control groups: 20 children with asthma without HVS and 20 presenting with trauma. For each symptom a visual analogue scale (VAS) was completed. The symptoms for which the mean VAS values were significantly different between the children with HVS and the controls were subject to principal component analysis after varimax rotation with Kaiser normalisation. RESULTS: There was no significant difference in symptoms between HVS children with or without asthma. The five major respiratory symptoms were: throat-clearing, sniffing, difficulty in breathing in, sighing and yawning. The combined sensitivity of those symptoms was 99%, the combined specificity 24%. The five major non-respiratory symptoms were: anxiety, difficulty in going to sleep, general fatigue, abdominal pain, and joint pains. The combined sensitivity of those symptoms was 99%, the combined specificity 36%. CONCLUSIONS: We performed a simplified diagnostic questionnaire for HVS in healthy and asthmatic children and found 5 respiratory and 5 non-respiratory symptoms of significance.

Zilli, I., F. Giganti, et al. (2007). "Yawning in morning and evening types." Physiol Behav.

Yawning occurs more frequently in the early morning and in the late evening, close to sleep onset and after the awakening, and it might be linked to sleep propensity. We aimed to study yawning and its temporal distribution in morning and evening subjects who display different sleep-wake and sleepiness rhythms. Sixteen healthy young adults (8 evening-types and 8 morning-types, matched for age and gender) have been selected and instructed to keep their habitual sleep schedules and to signal every yawning occurrence for three consecutive days. Results show that evening-types yawn more frequently than morning-types, particularly during morning hours. Yawning frequency decreases across daytime in evening-types reaching its lowest level in the early evening and increases thereafter. Instead, in morning-types, yawning frequency remains quite low during daytime and increases in the evening. Moreover, both morning and evening types show a progressive increase of yawning frequency in the hours preceding sleep onset, whereas they differ after the awakening. Evening-types show a higher yawning frequency that remains quite stable in the hours following the awakening, while morning-types display a decline in yawning frequency. Our findings show that the temporal distribution of yawning frequency differs between chronotypes, supporting the hypothesis that differences in sleep-wake rhythm affect yawning, which could represent a behavioural sign of sleep propensity.

Zheng, H., K. R. Bidasee, et al. (2007). "Lack of central nitric oxide triggers erectile dysfunction in diabetes." Am J Physiol Regul Integr Comp Physiol 292(3): R1158-64.

Erectile dysfunction is a serious and common complication of diabetes mellitus. The proposed mechanisms for erectile dysfunction in diabetes include central and autonomic neuropathy, endothelial dysfunction, and smooth muscle dysfunction. The paraventricular nucleus (PVN) of the hypothalamus is known to be involved in centrally mediated penile erection. This study was designed to examine the role of nitric oxide (NO) within the central nervous system component of the behavioral responses including erection in diabetic rats. N-methyl-D-aspartic acid (NMDA)-induced erection, yawning, and stretch through the PVN can be blocked by prior administration of NO synthase (NOS) blocker, L-NMMA, in freely moving, conscious male normal rats. Four weeks after streptozotocin (STZ) and vehicle injections, NMDA-induced erection, yawning, and stretch responses through the PVN are significantly blunted in diabetic rats compared with control rats. Examination of neuronal NOS (nNOS) protein by Western blot analysis indicated a reduced amount of nNOS protein in the PVN of rats with diabetes compared with control rats. Furthermore, restoring nNOS within the PVN by gene transfer using adenoviral transfection significantly restored the erectile and yawning responses to NMDA in diabetic rats. These data demonstrate that a blunted NO mechanism within the PVN may contribute to NMDA-induced erectile dysfunction observed in diabetes mellitus.

Wicks, P. (2007). "Excessive yawning is common in the bulbar-onset form of ALS." Acta Psychiatr Scand 116(1): 76; author reply 76-7.

Walusinski, O. (2007). "Can stroke localisation be used to map out the neural network for yawning behaviour?" J Neurol Neurosurg Psychiatry 78(11): 1166.

Vinberg, M. (2007). "Attention to side effects enhances medical adherence." Acta Psychiatr Scand 115(1): 82.

Szczerbak, G., P. Nowak, et al. (2007). "Maternal Lead Exposure Produces Long-Term Enhancement of Dopaminergic Reactivity in Rat Offspring." Neurochem Res.
To determine the effect of prenatal lead exposure on brain monoaminergic systems, pregnant rats were given tap water containing 250 ppm lead acetate, for the duration of pregnancy, while tap water without lead (Pb(2+)) was substituted at birth. Control rats were derived from dams that consumed tap water during pregnancy, and had no exposure to lead afterwards. At 12 weeks after birth, Pb(2+) content of brain cortex was increased 3- to 4-fold (P < 0.05). At this time the endogenous striatal levels of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid were 19% lower in Pb(2+) exposed rats (P < 0.05), while there was no change in the striatal level of dopamine (DA), noradrenaline, 3,4-dihydroxyphenylglycol, serotonin (5-HT) and 5-hydroxyindoleacetic acid (HPLC/ED). Also there was no change in these monoamines and metabolites in the prefrontal cortex of Pb(2+) exposed rats. However, turnover of 5-HT in prefrontal cortex, as indicated by 5-hydroxytryptophan accumulation 30 min after acute treatment with the decarboxylase inhibitor NSD-1015 (100 mg/kg IP), was lower in the Pb (2+) exposed rats. In the striatum AMPH-induced (1 mg/kg IP) turnover of DA, evidenced as L-DOPA accumulation after NSD-1015, was increased to a lesser extent in the Pb(2+) exposed rats (P < 0.05). The nitric oxide synthase inhibitor 7-nitroindazole (10 mg/kg IP) attenuated the latter effect, indicating that neuronal NO mediates this AMPH effect, at least in part. Moreover, DA D(2) receptor sensitivity developed in Pb(2+) exposed rats, as evidenced by enhanced quinpirole-induced yawning activity and enhanced quinpirole-induced locomotor activity (each, P < 0.05). These findings indicate that ontogenetic exposure to lead can have consequences on monoaminergic neuronal function at an adult stage of life, generally promoting accentuated behavioral effects of direct and indirect monoaminergic agonists, and related to increased dopamine turnover in basal ganglia.

Sommet, A., M. Desplas, et al. (2007). "Drug-Induced Yawning: A Review of the French Pharmacovigilance Database." Drug Saf 30(4): 327-331.
OBJECTIVE: To review the reports with 'yawning' as an adverse drug reaction (ADR) reported into the French Pharmacovigilance Database. METHODS: All the observations with 'yawning' reported in the French Pharmacovigilance Database until December 2004 were reviewed. We recorded drug(s) involved, characteristics of patients (age, sex and underlying disease) and of ADR (seriousness, delay in occurrence, evolution, imputability). RESULTS: Twenty-eight reports were recorded between 1985 and December 2004. The sex ratio of the patients included in these reports was 1.5 and the mean age was 46.2 (2-78) years. Thirty-eight drugs were involved, mainly serotoninergic agents (serotonin reuptake inhibitors [12]), dopaminergic agents (levodopa [3], dopamine agonists [3], monoamine oxidase B inhibitor [1]), opioids (morphine [1], methadone [1], buprenorphine [1], dextromethorphan [1]), benzodiazepines (4) and sodium channel inhibitors (lidocaine [2], flecainide [1]). Four ADRs were rated 'serious' (leading to hospitalisation). Patient outcome was usually favourable after drug withdrawal. CONCLUSION: Despite its necessary methodological drawbacks (mainly under-reporting), this study reveals that several drugs may induce yawning in humans. Our work also indicates that stimulation of central dopamine or serotonin receptors elicits yawning in humans. This study underlines the role of several drugs in yawning and shows that this ADR is not systematically listed in the summary product characteristic even when it can be explained by the pharmacodynamic properties of the drugs.

Singer, O. C., M. C. Humpich, et al. (2007). "Yawning in acute anterior circulation stroke." J Neurol Neurosurg Psychiatry 78(11): 1253-4.
Pathological yawning can be a clinical sign in disorders affecting the brainstem. Here we describe seven patients with pathological yawning caused by acute middle cerebral artery stroke, indicating that pathological yawning also occurs in supratentorial stroke. We hypothesise that excessive yawning is a consequence of lesions in cortical or subcortical areas, which physiologically control diencephalic yawning centres.

Sevak, R. J., W. Koek, et al. (2007). "Insulin replacement restores the behavioral effects of quinpirole and raclopride in streptozotocin-treated rats." J Pharmacol Exp Ther 320(3): 1216-23.
Streptozotocin (STZ)-induced diabetes can modulate dopamine (DA) neurotransmission and thereby modify the behavioral effects of drugs acting on DA systems. Insulin replacement, and in some conditions repeated treatment with amphetamine, can partially restore sensitivity of STZ-treated rats to dopaminergic drugs. The present study sought to characterize the role of insulin and amphetamine in modulating the behavioral effects of drugs that selectively act on D2/D3 receptors. In control rats, quinpirole and quinelorane produced yawning, whereas raclopride and gamma-hydroxybutyric acid (GHB) produced catalepsy. Raclopride antagonized quinpirole- and quinelorane-induced yawning with similar potency. STZ treatment increased blood glucose concentration, decreased body weight, and markedly reduced sensitivity to quinpirole-induced yawning, quinelorane-induced yawning as well as to raclopride-induced catalepsy, while enhancing sensitivity to GHB-induced catalepsy. Repeated treatment with amphetamine partially restored sensitivity of STZ-treated rats to amphetamine-stimulated locomotion and also produced conditioned place preference, without affecting blood glucose and body weight changes. However, amphetamine treatment did not restore sensitivity to the behavioral effects of quinpirole, raclopride, or GHB, suggesting differential regulation of dopamine transporter activity and sensitivity of D2 receptors in hypoinsulinemic rats. Insulin replacement in STZ-treated rats normalized blood glucose and body weight changes and fully restored sensitivity to quinpirole-induced yawning, as well as to raclopride-induced catalepsy, while reducing sensitivity to GHB-induced catalepsy. Overall, these data indicate that changes in insulin status markedly affect sensitivity to the behavioral effects of dopaminergic drugs. The results underscore the importance of insulin in modulating DA neurotransmission; these effects might be especially relevant to understanding the co-morbidity of eating disorders and substance abuse.

Senju, A., M. Maeda, et al. (2007). "Absence of contagious yawning in children with autism spectrum disorder." Biol Lett.
This study is the first to report the disturbance of contagious yawning in individuals with autism spectrum disorder (ASD). Twenty-four children with ASD as well as 25 age-matched typically developing (TD) children observed video clips of either yawning or control mouth movements. Yawning video clips elicited more yawns in TD children than in children with ASD, but the frequency of yawns did not differ between groups when they observed control video clips. Moreover, TD children yawned more during or after the yawn video clips than the control video clips, but the type of video clips did not affect the amount of yawning in children with ASD. Current results suggest that contagious yawning is impaired in ASD, which may relate to their impairment in empathy. It supports the claim that contagious yawning is based on the capacity for empathy.

Rudzinska, M. and A. Szczudlik (2007). "[Apomorphine in off state--clinical experience]." Neurol Neurochir Pol 41(2 Suppl 1): S40-8.
Apomorphine, a non-ergot derivative, is a potent, directly acting dopamine receptor agonist with high affinity to D4, lower to D2, D3, D5, the lowest to D1-like dopamine receptors as well as to serotonin and adrenoreceptors. Subcutaneous apomorphine is currently used in Parkinson's disease as an add-on to levodopa therapy or monotherapy for management of sudden, unexpected and refractory to levodopa-induced off state and fluctuation in advanced stage of illness. Many clinical trials have shown markedly (about 50-72%) reduced time of off phases. Other indications include the challenge test for determining the dopaminergic responsiveness. Apomorphine is used subcutaneously either as intermittent rescue injections or continuous infusions. Several other routes - transdermal, sublingual, intranasal, rectal and intravenous infusion - have been tried. Oral administration is not recommended. Apomorphine has rapid onset of antiparkinsonian action, qualitatively comparable to that of levodopa, short duration of action and stable efficacy with usually mild adverse events similar to other dopamine agonists. Domperidone or trimethobenzamide should be introduced before starting apomorphine treatment to reduce occurrence of peripheral adverse events (nausea, vomiting, orthostatic hypotension). Dyskinesias, sleep disturbances, hallucinations, delusion, oedema and yawning can occur, but some side effects are connected only with a specific route (for example skin nodules appearing during subcutaneous administration). Despite its long history, apomorphine is registered and used in only a few countries. Apomorphine warrants wider application in treatment of advanced Parkinson disease but the high cost of the drug, the necessity of concomitant treatment for prevention of side effects and subcutaneous administration restrict its use.

Risberg-Berlin, B., R. Y. Moller, et al. (2007). "Effectiveness of olfactory rehabilitation with the nasal airflow-inducing maneuver after total laryngectomy: one-year follow-up study." Arch Otolaryngol Head Neck Surg 133(7): 650-4.
OBJECTIVE: To assess the long-term results of the nasal airflow-inducing maneuver in olfaction rehabilitation in patients who had undergone laryngectomy. DESIGN: Prospective interventional study. SETTING: University hospital. PATIENTS: Twenty-four patients who had undergone laryngectomy (21 men and 3 women; mean age, 68 years) who received olfactory rehabilitation with the nasal airflow-inducing maneuver were reevaluated 6 and 12 months after primary treatment. MAIN OUTCOME MEASURE: Olfactory function was tested by means of a semistructured interview; the Questionnaire on Olfaction, Taste and Appetite; and the Scandinavian Odor-Identification Test. Quality of life was measured with the European Organization for Research and Treatment of Cancer QLQ-C30 and QLQ-H&N35 questionnaires. Patients were categorized as smellers or nonsmellers based on results of the Scandinavian Odor-Identification Test. RESULTS: Before treatment, 10 of 24 patients (42%) were smellers and 14 (58%) were nonsmellers. At 6-month follow-up, 20 of 23 patients (87%) were smellers, whereas after 12 months, 21 of 24 patients (88%) were smellers. Long-term olfaction rehabilitation was achieved in 11 of 14 patients (79%) with anosmia, and 15 of all 24 patients (63%) could be classified as having normal olfactory capacity at the end of the study. CONCLUSION: The nasal airflow-inducing maneuver is a patient-friendly, inexpensive, and effective method for restoring the sense of smell in patients after laryngectomy, and the results persist in the long term.

Polo, P. A., R. O. Reis, et al. (2007). "Behavioral and neuropharmacological evidence that serotonin crosses the blood-brain barrier in Coturnix japonica (Galliformes; Aves)." Braz J Biol 67(1): 167-71.
This study was carried out aiming to reach behavioral and neuropharmacological evidence of the permeability of the blood-brain barrier (BBB) to serotonin systemically administered in quails. Serotonin injected by a parenteral route (250-1000 microg x kg(-1), sc) elicited a sequence of behavioral events concerned with a sleeping-like state. Sleeping-like behaviors began with feather bristling, rapid oral movements, blinking and finally crouching and closure of the eyes. Previous administration of 5-HT2C antagonist, LY53857 (3 mg x kg (-1), sc) reduced the episodes of feather bristling and rapid oral movements significantly but without altering the frequency of blinking and closure of the eyes. Treatment with the 5-HT2A/2C antagonist, ketanserin (3 mg x kg(-1), sc) did not affect any of the responses evoked by the serotonin. Quipazine (5 mg x kg(-1), sc) a 5-HT2A/2C/3 agonist induced intense hypomotility, long periods of yawning-like and sleeping-like states. Previous ketanserin suppressed gaping responses and reduced hypomotility, rapid oral movements and bristling but was

ineffective for remaining responses induced by quipazine. Results showed that unlike mammals, serotonin permeates the BBB and activates hypnogenic mechanisms in quails. Studies using serotoninergic agonist and antagonists have disclosed that among the actions of the serotonin, feather bristling, rapid oral movements and yawning-like state originated from activation of 5-HT2 receptors while blinking and closure of the eyes possibly require other subtypes of receptors.

Pan, L., X. Xia, et al. (2007). "Exposure to the phytoestrogen daidzein attenuates apomorphine-induced penile erection concomitant with plasma testosterone level reduction in dose- and time-related manner in adult rats." Urology 70(3): 613-7.
OBJECTIVES: To investigate the impact of exposure to the phytoestrogen daidzein on erectile function and sexual hormones. The negative effects of phytoestrogens on the male reproductive system, particularly on penile erection, have hardly been evaluated. METHODS: Thirty adult male Sprague-Dawley rats were equally divided into a normal control group, three experimental groups, and one positive control group. The three experimental groups were given daidzein at doses of 2, 20, and 100 mg/kg body weight daily, and the positive control group received 0.1 mg diethylstilbestrol per animal daily for 90 days. The apomorphine-induced erection test was performed 0, 30, 60, and 90 days after daidzein administration to evaluate for erectile function or dysfunction. After each test, blood samples were collected for plasma testosterone and luteinizing hormone measurement. RESULTS: High-dose daidzein (100 mg/kg) decreased erectile responses to apomorphine from the 30th day of daidzein treatment and lasted to the 90th day without significant differences compared with the diethylstilbestrol-treated rats. However, similar changes were observed in the medium-dose daidzein (20 mg/kg) group from the 60th day. Low-dose daidzein (2 mg/kg) had no significant effect on the erectile responses to apomorphine compared with the normal control group (P >0.05). The plasma testosterone and luteinizing hormone levels showed a declining trend similar to that of the apomorphine-induced erections. CONCLUSIONS: The phytoestrogen daidzein has the potential to adversely affect erectile function in a dose and time-related manner that is at least partly attributable to androgen deficiency. These findings implicate that phytoestrogens, especially isoflavones, if overconsumed for a long period, might be a novel risk factor for erectile dysfunction.

Pahwa, R., W. C. Koller, et al. (2007). "Subcutaneous apomorphine in patients with advanced Parkinson's disease: a dose-escalation study with randomized, double-blind, placebo-controlled crossover evaluation of a single dose." J Neurol Sci 258(1-2): 137-43.
OBJECTIVE: To further explore the efficacy and safety of subcutaneous apomorphine (APO) in treating off episodes in APO-naive patients with advanced Parkinson's disease (PD). METHODS: 56 patients receiving optimized oral anti-PD medication were evaluated on separate days for response to single increasing doses of APO. Acute response to oral anti-PD medication and APO dose escalation (2-10 mg) was evaluated under unblinded conditions. At the 4 mg APO dose, placebo was randomly introduced under double-blind crossover conditions. RESULTS: Mean changes from pre-dose in Unified Parkinson's Disease Rating Scale motor scores indicated significant improvement following APO 4 mg versus placebo at 20 min (p=0.0002), 40 min (p<0.0001; maximum improvement) and 90 min (p=0.0229). Improvements showed significant dose-response at 20 min, 40 min (both p<0.0001) and 90 min (p=0.0049). Adverse events were more common with APO than placebo, and also showed significant dose-response (p<0.0001). Common adverse events associated with APO included yawning, dizziness, nausea, somnolence and dyskinesias, and were generally mild to moderate. There were no significant differences between APO and placebo in the incidence of hypotension associated with a postural change from a sitting to standing position. CONCLUSIONS: Subcutaneous APO provided rapid, effective relief of off episodes associated with advanced PD.

Oshima, T., H. Utsunomiya, et al. (2007). "Identification of independent predictors for intravenous thiopental-induced yawning." J Anesth 21 (2): 131-5.
PURPOSE: To explore risk factors for the yawning response induced by the intravenous administration of thiopental during the induction of general anesthesia. METHODS: We analyzed data from a cohort of 1322 patients who underwent elective surgery under general anesthesia plus intravenous thiopental. The data collected were: (a) the patients' demographic findings (age, sex, height, weight, cigarette smoking, hypertension, and presence of cerebral lesion), and (b) anesthesia-related findings (the kind of preanesthetic medication, i.e., atropine, epidural lidocaine, priming dose of vecuronium, fentanyl, and the dose of intravenous thiopental). An association between an individual variable in the evaluation model and the likelihood of thiopental-induced yawning behavior was characterized by means of the odds ratio. Multiple logistic regression was used to examine the independent contribution of each candidate variable, while controlling for all variables. RESULTS: After the intravenous administration of thiopental, 461 patients exhibited a yawning response. The probability of this response was decreased by the prior use of intravenous fentanyl, by female sex, and by premedication with clonidine, but the probability was unaffected by premedication with hydroxyzine, by the prior use of atropine, or by the presence of hypertension or a cerebral lesion. CONCLUSION: Thiopental-induced yawning may be suppressed by female sex, prior use of intravenous fentanyl, and premedication with clonidine. These findings may allow insights into the physiologic and pharmacological aspects of yawning in humans, thereby leading to the development methods to prevent thiopental-induced yawning.

Nierenberg, A. A., J. H. Greist, et al. (2007). "Duloxetine versus escitalopram and placebo in the treatment of patients with major depressive disorder: onset of antidepressant action, a non-inferiority study." Curr Med Res Opin 23(2): 401-16.
OBJECTIVE: The goal of a non-inferiority study is to test whether a new treatment has at least as much efficacy as an established treatment. The purpose of this non-inferiority study was to compare the speed of onset of antidepressant efficacy for duloxetine (a dual serotonin and norepinephrine reuptake inhibitor) and escitalopram (a selective serotonin reuptake inhibitor). RESEARCH DESIGN AND METHODS: This was a randomized, double-blind, placebo- and active comparator-controlled study, in which patients (> or = 18 years) meeting DSM-IV criteria for Major Depressive Disorder (MDD) received duloxetine 60 mg once daily (QD; N = 273), escitalopram 10 mg QD (N = 274), or placebo (N = 137) for 8 weeks. The primary objective was to compare the onset of antidepressant efficacy, by testing the hypothesis that the percentage of duloxetine-treated patients achieving onset criteria at Week 2 was not inferior to that in the escitalopram group. MAIN OUTCOME MEASURES: Onset of efficacy was defined as a 20% decrease from baseline on the 17-item Hamilton Rating Scale for Depression (HAMD (17)) Maier subscale that was maintained or exceeded at all subsequent visits. RESULTS: Probabilities of meeting onset criteria at Week 2 for duloxetine- and escitalopram-treated patients were 42.6% versus 35.2%, respectively (treatment difference = 7.4%; 95% confidence interval, -1.3% to 16.2%; p = 0.097). Both drugs showed significant improvement compared with placebo (p < or = 0.05) on the primary efficacy measure (Maier subscale) at Week 1 and endpoint (Week 8). No differences were found between duloxetine, escitalopram, and placebo rates of remission or response at 8 weeks. Adverse events that occurred significantly more frequently among duloxetine-treated patients when compared with those receiving escitalopram were nausea, dry mouth, vomiting, yawning, and irritability. The rate of discontinuation due to adverse events did not differ significantly between treatment groups. LIMITATIONS: Given the difficulties in constructing appropriate dose comparisons, the results of this study should be interpreted specific to the doses tested and not extrapolated to the drug as a whole. This study employed a fixed-dose design; flexible-dose designs are more likely to find a difference between antidepressants and placebo. CONCLUSION: In this study, both duloxetine and escitalopram showed significantly greater improvement on the primary efficacy measure than placebo over the 8-week acute treatment period, while no differences were observed between drugs or between drugs and placebo on response and remission rates at 8 weeks. Escitalopram at a starting dose of 10 mg QD was better tolerated than duloxetine at a starting dose of 60 mg QD. This study met its pre-defined primary objective of assessing if duloxetine was non-inferior to escitalopram in antidepressant onset efficacy, and the results show that duloxetine is at least as fast as (non-inferior to) escitalopram.

Matikainen, J. and H. Elo (2007). "Does yawning increase arousal through mechanical stimulation of the carotid body?" Med Hypotheses.
Yawning is a stereotyped event that occurs in humans and animals from fish to mammals, but neither its mechanisms nor its functions are entirely known. Its widespread nature suggests that it has important physiological functions. It is associated with stretching of muscles in a large area, but the function of this stretching is understood far from completely. It has been proposed that yawning increases arousal and that it is an arousal defense reflex, whose aim is to reverse brain hypoxia. Whilst yawning has been speculated to have an important role in reversing hypoxia, there is a structure in the neck that is known to be intimately involved in the regulation of oxygen homeostasis, namely the carotid body. It senses acute changes in oxygen levels. In spite of this, a connection has never been proposed either between the carotid body and arousal, or between yawning and the carotid body. We propose that yawning stimulates mechanically the carotid body (and possibly other structures in the neck). We further propose that this stimulation gives rise to increased arousal, alertness and wakefulness and that one important physiological function of yawning is increase of arousal through this stimulation. We also propose that mechanical effects on the shunt system of the carotid body may be involved in this stimulation. Our hypothesis is supported by several facts. For example, yawning causes movements and compressions that may affect the carotid body that is situated strategically at the bifurcation of the common carotid artery. Thus, yawning may stimulate the carotid body. The carotid body is highly vascular and compressions may affect its shunt system and blood flow and for example give rise to release of hormones or other substances. Also several facts related to situations where people yawn or do not yawn support our hypothesis and are discussed. Further support comes from facts related to somnogenic substances, hormones and transmitters, and from facts related to the interconnection of homeostatic mechanisms, sleep, arousal and ventilation.

Mathew, G. A., G. Kuruvilla, et al. (2007). "Dynamic slow motion video endoscopy in eustachian tube assessment." Am J Otolaryngol 28(2): 91-7.
PURPOSE: The aim of this study was to find out if there is a correlation between dynamic video endoscopic study of eustachian tube (ET) with middle ear disease and to grade ET movements based on dynamic slow motion video endoscopy (DSVE) findings and to determine if DSVE can be used as a useful tool to evaluate tubal function. MATERIALS AND METHODS: A prospective, case control study was performed on 124 ears in 69 subjects who came to the ears, nose, and throat outpatient department. Transnasal endoscopic examination of the nasopharyngeal opening of the ET during rest, swallowing, and yawning was carried out to study its dilatory movements. RESULTS: In the control group, among the 61 ears studied, 37 ETs were found normal and 24 tubes, dysfunctional. In ears with middle ear disease (case group), 63 ETs were studied. Ten were found normal, and the remaining, dysfunctional. Ten patulous tubes were observed in this study: 3 in the control group and 7 in the case group. Tubal movements were classified into 4 grades depending on (1) appearance of tubal mucosa, (2) movements of the medial and lateral cartilaginous lamina, (3) lateral excursion and dilatory wave of the lateral pharyngeal wall, and (4) whether tubal lumen opened well or not. Upon correlation of results obtained on DSVE with middle ear disease, the P value was less than .0001, suggesting a significant relationship between the 2. Dynamic ET endoscopy findings of 121 ears (of the total 124 ears studied) were correlated with middle ear manometric studies using Mc Nemar chi(2) test. Seventy-five ears showed complete agreement, and 46 ears showed disagreement. The P value was

found to be .000, showing a strong association between the 2 tests. On correlating dynamic ET endoscopy findings in 60 of 63 ears in the case group with middle ear manometry, we noticed that 38 ears showed complete agreement and 22 ears showed disagreement. The P value was found to be .007, which again showed significant agreement between the 2 tests. CONCLUSION: Dynamic slow motion video endoscopic analysis of ET is a potentially useful tool in the quest for further understanding the pathophysiology of tubal dysfunction. We have attempted to grade ET movements based on severity of tubal pathology. We conclude that DSVE is a vital tool in diagnosing ET dysfunction in patients with middle ear disease. Additional study is required to assess the role of DSVE in predicting outcome after middle ear surgery.

Martelle, J. L., R. Claytor, et al. (2007). "Effects of Two Novel D3-Selective Compounds, NGB 2904 [N-(4-(4-(2,3-Dichlorophenyl)piperazin-1-yl)butyl)-9H-fluorene-2-carboxami de] and CJB 090 [N-(4-(4-(2,3-Dichlorophenyl)piperazin-1-yl)butyl)-4-(pyridin-2-yl)benzami de], on the Reinforcing and Discriminative Stimulus Effects of Cocaine in Rhesus Monkeys." J Pharmacol Exp Ther 321(2): 573-82.
The present study examined the effects of two novel dopamine D(3) receptor compounds, NGB 2904 [N-(4-(4-(2,3-dichlorophenyl) piperazin-1-yl)butyl)-9H-fluorene-2-carboxami de], an antagonist, and CJB 090 [N-(4-(4-(2,3-dichlorophenyl)piperazin-1-yl)butyl)-4-(pyridin-2-yl)benzami de], a partial agonist, in two models of cocaine abuse in rhesus monkeys. To establish a dose range and time course of effects, both compounds were shown to block quinpirole-induced yawning when administered i.m. 15, 30, or 120 min before quinpirole. Next, rhesus monkeys were trained to discriminate i.m. injections of saline (0.5 ml) and cocaine (0.3 mg/kg). Neither D(3) compound (0.03-3.0 mg/kg; n = 3) substituted for cocaine in any monkey. When given in combination with cocaine, CJB 090 but not NGB 2904 attenuated the discriminative stimulus effects of cocaine, shifting the cocaine dose-response curve to the right. In a separate group of monkeys, responding was maintained under a second-order schedule of either food (1.0-g pellets; n = 3) or cocaine (0.1 mg/kg/injection; n = 4) presentation. When responding was stable, a dose of NGB 2904 (1.0-5.6 mg/kg i.v.) or CJB 090 (0.3-3.0 mg/kg i.v.) was administered for 5 consecutive days, immediately before the session. CJB 090, but not NGB 2904, decreased cocaine- and food-maintained responding. These data indicate that compounds with relatively high affinity and selectivity for the D(3) receptor can attenuate the discriminative and reinforcing stimulus effects of cocaine while not producing cocaine-like effects. The present findings support the continued examination of D(3) compounds as pharmacological tools for better understanding the role of this receptor subtype in cocaine addiction and as potential lead compounds for novel therapeutic agents.

Maple, A. M., M. K. Perna, et al. (2007). "Ontogenetic quinpirole treatment produces long-lasting decreases in the expression of Rgs9, but increases Rgs17 in the striatum, nucleus accumbens and frontal cortex." Eur J Neurosci.
Ontogenetic treatment of rats with the dopamine D(2)-like receptor agonist quinpirole produces a significant increase in dopamine D(2) receptor sensitivity that persists throughout the animal's lifetime, a phenomenon known as D(2) priming. The present study was designed to investigate the effects of priming of the D(2) receptor on the expression of three different members of the regulator of G-protein signaling (RGS) family: Rgs4, Rgs9 and Rgs17. Male offspring were ontogenetically treated with quinpirole or saline from postnatal days (P) 1-21 and raised to adulthood. On approximately P65, animals were given an acute quinipirole injection (0.1 mg/kg) and the number of yawns was recorded for 1 h after the injection. Yawning has been shown to be a behavioural event mediated by the dopamine D(2)/D(3) receptor. Animals ontogenetically treated with quinpirole demonstrated a significant 2.5-fold increase in yawning as compared to controls. Rgs transcripts were analysed through in situ hybridization several weeks later. Rats ontogenetically treated with quinpirole demonstrated a significant decrease in Rgs9 expression in the frontal cortex, but a more robust decrease in the striatum and nucleus accumbens as compared to controls. Regarding Rgs17, ontogenetic quinpirole produced a modest but significant increase in expression in the same brain areas. There were no significant differences in Rgs4 expression produced by drug treatment in any of the brain regions analysed. This study demonstrates that ontogenetic quinpirole treatment, which results in priming of the D(2) receptor, results in significant decreases in Rgs9, which has been shown to regulate G-protein coupling to D(2) receptors.

Manish, M. and S. Veenu (2007). "Persistent vegetative state." Neurology 68(19): 1635.

Kocaman Akbay, B., Y. Demiraran, et al. (2007). "Use of the bispectral index to predict a positive awareness reaction to laryngeal mask airway-Fastrach insertion and intubation." Acta Anaesthesiol Scand 51(10): 1368-72.
Aim: To determine whether the bispectral index (BIS) can be monitored to predict and indicate an awareness reaction to laryngeal mask airway-Fastrach (LMA-Fastrach) insertion and intubation at BIS values between 40 and 60. Methods: Fifty-one American Society of Anesthesiologists' (ASA) class I or II status patients aged over 20 years were included in this study. Midazolam 0.1 mg/kg was given for pre-medication, 30 min before induction. For induction, a 0.1-mug/kg bolus injection of remifentanil was followed by infusion, and propofol was administered until the eyelash reflex disappeared; the infusion rate was adjusted to maintain BIS values between 40 and 60. Loss of the eyelash reflex, loss of response to verbal commands, yawning and total propofol consumption were recorded. Patients were tested for awareness twice at 1-min intervals using the isolated forearm technique. The test was considered to be positive if the patient squeezed a hand when asked; after muscle relaxation, the patient was intubated and the test was repeated. In the recovery room and ward, patients were asked whether they could recall this event. Results: Seven patients tested positive: two following LMA-Fastrach insertion and the remaining five following intubation. None of the patients had recall. Conclusion: Awareness during anaesthesia may occur at BIS levels that indicate adequate anaesthesia, but this is not associated with recall of the events later.

Horgan, D. (2007). "Antidepressant overshoot: the YES syndrome." Aust N Z J Psychiatry 41(1): 90-1.

Gutierrez-Alvarez, A. M. (2007). "Do your patients suffer from excessive yawning?" Acta Psychiatr Scand 115(1): 80-1.
OBJECTIVE: Yawning has been described in relation to drugs such as serotonin reuptake inhibitors, levodopa, dopamine agonists, MAO B inhibitor, morphine, methadone, buprenorphine, dextromethorphan, benzodiazepine, lidocaine, and flecaine. This is a report of two patients, on long-term escitalopram therapy (more than 8 weeks) with stable dosing, who presented excessive yawning. Escitalopram is widely used in major depressive disorder and generalized anxiety disorder. METHOD: A clinical description of two cases. RESULTS: Two females (62 and 59 years old, respectively) developed excessive daytime yawning. It was not associated with sedation or a feeling of needing sleep. The dosage was reduced and yawning disappeared some hours later. The patients' depression did not recur. CONCLUSION: Yawning has been described in relation to different selective serotonin reuptake inhibitors and remitted following their discontinuation; it is interesting that the reported yawning in these two cases disappeared with the reduction of dosage, rather than the interruption of treatment.

Guggisberg, A. G., J. Mathis, et al. (2007). "The functional relationship between yawning and vigilance." Behav Brain Res 179(1): 159-66.
BACKGROUND: Although yawning is a ubiquitous and phylogenetically old phenomenon, its origin and purpose remain unclear. The study aimed at testing the widely held hypothesis that yawning is triggered by drowsiness and brings about a reversal or suspension of the process of falling asleep. METHODS: Subjects complaining of excessive sleepiness were spontaneously yawning while trying to stay awake in a quiet and darkened room. Changes in their electroencephalogram (EEG) and heart rate variability (HRV) associated with yawning were compared to changes associated with isolated voluntary body movements. Special care was taken to remove eye blink- and movement-artefacts from the recorded signals. RESULTS: Yawns were preceded and followed by a significantly greater delta activity in EEG than movements ($p</=0.008$). After yawning, alpha rhythms were attenuated, decelerated, and shifted towards central brain regions ($p</=0.01$), whereas after movements, they were attenuated and accelerated ($p<0.02$). A significant transient increase of HRV occurred after the onset of yawning and movements, which was followed by a significant slow decrease peaking 17s after onset ($p<0.0001$). No difference in HRV changes was found between yawns and movements. CONCLUSIONS: Yawning occurred during periods with increased drowsiness and sleep pressure, but was not followed by a measurable increase of the arousal level of the brain. It was neither triggered nor followed by a specific autonomic activation. Our results therefore confirm that yawns occur due to sleepiness, but do not provide evidence for an arousing effect of yawning.

Giganti, F., M. J. Hayes, et al. (2007). "Yawning frequency and distribution in preterm and near term infants assessed throughout 24-h recordings." Infant Behav Dev.
Yawning has been observed in foetuses and preterm infants. The aim of this study was to assess the frequency and the 24h distribution of yawning in preterm infants. Twelve low-risk infants between 31 and 40 weeks of post-conceptional age (PCA) were continuously video-recorded for 24h in their incubator. Spontaneous yawning was defined as opening of the mouth to its full extension in a dramatic stretch movement. The results showed that the rate of yawning across the 24-h period was 1.10/h. The highest incidence of yawns was in the waking motility pattern when compared to active sleep or quiet sleep motility patterns. Between 31 and 40 weeks, yawn incidence significantly decreased mainly during the day. The marked decrease in yawn frequency with age may be related to the development of circadian and homeostatic control of sleep and wake.

Fritzen, S. A. (2007). "Strategic management of the health workforce in developing countries: what have we learned?" Hum Resour Health 5: 4.
ABSTRACT: The study of the health workforce has gained in prominence in recent years, as the dynamic interconnections between human resource issues and health system effectiveness have come into sharper focus. This paper reviews lessons relating to strategic management challenges emerging from the growing literature in this area. Workforce issues are strategic: they affect overall system performance as well as the feasibility and sustainability of health reforms. Viewing workforce issues strategically forces health authorities to confront the yawning gaps between policy and implementation in many developing countries.Lessons emerge in four areas. One concerns imbalances in workforce structure, whether from a functional specialization, geographical or facility lens. These imbalances pose a strategic challenge in that authorities must attempt to steer workforce distribution over time using a limited range of policy tools. A second group of lessons concerns the difficulties of central-level steering of the health workforce, often critically weak due to the lack of proper information systems and the complexities of public sector decentralization and service commercialization trends affecting the grassroots.A third cluster examines worker capacity and motivation, often shaped in developing countries as much by the informal norms and incentives as by formal attempts to support workers or to hold them accountable. Finally, a range of reforms centering on service contracting and improvements to human resource management are emerging. Since these have as a necessary (but not sufficient) condition some flexibility in personnel practices, recent trends towards the sharing of such functions with local authorities are promising.The paper identifies a number of current lines of productive research, focusing on the relationship between health policy reforms and the local institutional environments in which the workforce, both public and private, is deployed.

Di Martino, E. F., R. Thaden, et al. (2007). "Evaluation of Eustachian tube function by sonotubometry: results and reliability of 8 kHz signals in normal subjects." Eur Arch Otorhinolaryngol 264(3): 231-6.

Sonotubometry allows an assessment of the Eustachian tube (ET) function under physiological conditions. The reliability of the application of an 8 kHz pure-tone signal was investigated. In 40 normal subjects (80 ears) sonotubometric studies were performed with a custom-made device. ET opening was provoked by swallowing, yawning and Valsalva manoeuvre. An opening was detected in all patients but not in all manoeuvres. Four characteristic sonotubogram types were found. Most common was the spike-type (60%). The double-peak and the plateau-shaped curves occured in 17% each. The finding of an descendant curve was rare (5%). Of 623 measurements, only in 55% manouvres a positive sonotubometric result was found despite the fact that the patients reported an opening in all cases. The median opening time in dry swallowing, liquid swallowing, yawning and Valsalva was found to be 486, 355, 1,263 and 1,250 ms. A median sound increase of 16.0, 13.8, 15.0 and 15.0 dB was recorded for these manoeuvres. There was a statistic significant difference ($P < 0.02$) between the increase in sound intensity of liquid and dry swallowing. There was also a statistic significant difference found for the duration of the forced manoeuvres Valsalva and yawning as compared to dry and liquid swallowing ($P < 0.0001$). The use of an 8 kHz pure-tone signal showed a limited sensitivity for the detection of ET openings. This is mainly due to noise pollution, but also because of an altered positioning and/or dislocation of the probes and compression of the nostrils. The application of an 8 kHz signal is therefore not reliable enough for the use in practice. Further technical refinements and the use of alternative signals are necessary for a broader clinical application.

De Las Cuevas, C. and E. J. Sanz (2007). "Duloxetine-induced excessive disturbing and disabling yawning." J Clin Psychopharmacol 27(1): 106-7.

D'Andrea, G., G. P. Nordera, et al. (2007). "Biochemistry of neuromodulation in primary headaches: focus on anomalies of tyrosine metabolism." Neurol Sci 28 Suppl 2: S94-6.

Recent studies have suggested that abnormalities of dopamine and trace amines (tyramine, octopamine, and synephrine), products of tyrosine metabolism, may constitute the metabolic events that predispose to the occurrence of cluster headache (CH) and migraine attacks. This hypothesis is supported by the following evidences: the discovery of trace amine associated receptors (TAARs), expressed on the olfactory epithelium, amigdala, hypothalamus, periacqueductal gray, and the biochemical anomalies of dopamine and trace amines. The possible effects of these biochemical abnormalities on TAARs and dopamine receptors, located in different areas of CNS, may explain the behaviour (restlessness, anxiety and, at times, hypersexuality) and the autonomic signs during the painful attacks of CH, and the premonitory symptoms of migraine crisis (thirst, craving, yawning, alteration of smell, depression etc.).

Collins, G. T., A. H. Newman, et al. (2007). "Yawning and hypothermia in rats: effects of dopamine D3 and D2 agonists and antagonists." Psychopharmacology (Berl).

RATIONALE: Identification of behaviors specifically mediated by the dopamine D2 and D3 receptors would allow for the determination of in vivo receptor selectivity and aide the development of novel therapeutics for dopamine-related diseases. OBJECTIVES: These studies were aimed at evaluating the specific receptors involved in the mediation of D2/D3 agonist-induced yawning and hypothermia. MATERIALS AND METHODS: The relative potencies of a series of D2-like agonists to produce yawning and hypothermia were determined. The ability of D3-selective and D2-selective antagonists to inhibit the induction of yawning and hypothermia were assessed and a series of D2/D3 antagonists were characterized with respect to their ability to alter yawning induced by a low and high dose of PD-128,907 and sumanirole-induced hypothermia. RESULTS: D3-preferring agonists induced yawning at lower doses than those required to induce hypothermia and the D2-preferring agonist, sumanirole, induced hypothermia at lower doses than were necessary to induce yawning. The rank order of D3 selectivity was pramipexole > PD-128,907 = 7-OH-DPAT = quinpirole = quinelorane > apomorphine = U91356A. Sumanirole had only D2 agonist effects. PG01037, SB-277011A, and U99194 were all D3-selective antagonists, whereas haloperidol and L-741,626 were D2-selective antagonists and nafadotride's profile of action was more similar to the D2 antagonists than to the D3 antagonists. CONCLUSIONS: D3 and D2 receptors have specific roles in the mediation of yawning and hypothermia, respectively, and the analysis of these effects allow inferences to be made regarding the selectivity of D2/D3 agonists and antagonists with respect to their actions at D2 and D3 receptors.

Albentosa, M. J., J. J. Cooper, et al. (2007). "Evaluation of the effects of cage height and stocking density on the behaviour of laying hens in furnished cages." Br Poult Sci 48(1): 1-11.

1. Limited information is available on how changes in horizontal and vertical space within enriched or furnished layer cages (as defined by Directive 1999/74/EC) influence hen behaviour. This study evaluated the effects of varying minimum cage heights and space allowances on the behaviour of laying hens housed in furnished cages. It was conducted on two flocks of medium brown hybrid hens housed in furnished cages with access to perches and nest boxes on a semi-commercial scale at ADAS Gleadthorpe. 2. Flock 1 consisted of two layer strains (ISA Brown and Babcock 380), housed at two minimum cage heights (38 and 45 cm) and 5 stocking densities between 609 and 870 cm2/bird, with 12 replicates of each of the 20 strain/cage height/stocking density treatment combinations. Stocking density was varied by varying the number of birds per cage from 10 to 7 in standard full-width cages or housing 7 hens in a narrower cage. As a consequence stocking density, group size and trough width per bird co-varied for 4 out of 5 stocking density treatments. 3. Behaviour of flock 1 was sampled at 33 to 36, 46 and 68 weeks of age. At each age one top-tier, one middle-tier and one bottom-tier cage was sampled for each treatment. 4. Few behavioural differences due to cage treatments were detected. Hens at 870 cm2 had shorter feeding bouts than hens at 609 and 762 cm2. Yawning was more common in the cages with greater cage height. 5. Video recordings of flock 1 examined cage height effects on hens' use of vertical space and provided additional data on stretching and self-maintenance activities. No differences in behaviour between 38 and 45 cm cages were found except that scratching head was more common in cages with greater cage height. 6. Flock 2 consisted of two layer strains (Shaver Brown and Hy-Line Brown), housed at 38 and 45 cm and 609, 762 and 1016 cm2/bird, with 18 replicates of each of the 12 strain/cage height/stocking density treatment combinations. Stocking density was varied by housing 10, 8 or 6 hens in standard full-width cages. Behaviour of flock 2 was sampled at 30, 48, 60 and 67 weeks from video recordings. Three cages per treatment from middle-tiers only were sampled at each age. 7. Hens housed at 609 cm2/hen had the longest mean feeding bout, greater than for hens at 762 cm2/hen but not hens at 1016 cm2/hen. More unsuccessful attempts to reach the feeder and sideways and backwards displacements from the feeder occurred at 762 and 609 cm2/hen than at 1016 cm2/hen. A maximum of 8 hens were observed feeding synchronously. 8. These results suggest that changes in horizontal and vertical space over the ranges we studied had little effect on behaviour other than feeding behaviour. Specifying a minimum useable trough space per hen, rather than calculating feeder space from total length of feeder per cage, irrespective of accessibility, might help avoid crowding at the feeder and associated disturbance of feeding bouts.

Akerman, S. and P. J. Goadsby (2007). "Dopamine and migraine: biology and clinical implications." Cephalalgia 27(11): 1308-14.

In the last 30 years dopamine has been considered as playing a role in the pathogenesis of migraine. The literature indicates that migraineurs are hypersensitive to dopamine agonists with respect to some of the premonitory symptoms of migraine such as nausea and yawning. There are various non-specific dopamine D(2) receptor antagonists that show good clinical efficacy in migraine, and also a number of polymorphisms of dopaminergic genes related to migraine. Animal studies have also shown that dopamine receptors are present in the trigeminovascular system, the area believed to be involved in headache pain, and neuronal firing here is reduced by dopamine agonists. There appears to be little effect of dopamine on peripheral trigeminal afferents. We assess some of the limitations of the clinical studies with regard to the therapeutics, and those found in the studies that discovered differences in genetic polymorphisms in migraine, and consider the implications of this on a dopaminergic hypothesis of migraine.

Yigiter, A. B. and Z. N. Kavak (2006). "Normal standards of fetal behavior assessed by four-dimensional sonography." J Matern Fetal Neonatal Med 19(11): 707-21.

OBJECTIVE: In this prospective randomized study, fetal behavior was investigated in order to determine the standard parameters of fetal movements and facial expressions in all three trimesters of normal pregnancy. METHODS: Sixty-three pregnant women with singleton pregnancies in all trimesters were included in the investigation. Four-dimensional (4D) ultrasound was performed for each patient over a 30-minute period. Variables of maternal and fetal characteristics including gestational age, eight fetal movement patterns in the first trimester, and sixteen parameters of fetal movement and fetal facial expression patterns in the second and third trimesters were recorded for the construction of fetal neurological charts. RESULTS: In the first trimester, a tendency towards an increased frequency of fetal movement patterns with increasing gestational age was noticed. Only the startle movement pattern seemed to occur stagnantly during the first trimester ($p > 0.05$). At the beginning of the second trimester, the frequency of fetal movement patterns tended to increase. During the second and third trimester, multiple regression and polynomial regression revealed statistically significant changes in tongue expulsion ($p < 0.05$), smiling ($p < 0.05$), grimacing ($p < 0.05$), swallowing ($p < 0.05$), eye blinking ($p < 0.01$), head movements, and all hand to body contact movements ($p < 0.01$), except for head anteflexion ($p > 0.05$). There were no statistically significant changes during the second and third trimesters in mouthing, yawning, and sucking ($p > 0.05$). At the middle of the third trimester, the fetuses displayed decreasing or stagnant incidence of fetal facial expressions except for eye blinking, which showed increased frequency with increasing gestational age. A statistically significant correlation was found between all head movements and hand to body contact patterns during the second and third trimesters except for head anteflexion ($r = -0.231$; $p > 0.05$). CONCLUSIONS: The full range of quantitative fetal facial expressions and fetal movement patterns can be assessed successfully by 4D sonography. It is important to be able to assess normal fetal behavior throughout gestation to identify abnormal behavior before birth.

Yankovsky, A. E., F. Andermann, et al. (2006). "Post-ictal forceful yawning in a patient with nondominant hemisphere epilepsy." Epileptic Disord 8(1): 65-9.

Yawning has been rarely described in association with seizures and not previously documented by video-EEG. We present a 48-year-old woman with a long history of non-dominant for speech hemisphere seizures and post-ictal yawning. Yawning was irresistible, forceful and often repetitive. We reviewed the few similar epileptic cases described in the literature and discussed the possible mechanisms. [Published with video sequences].

Yan, F., S. Y. Dai, et al. (2006). "Four-dimensional sonographic assessment of fetal facial expression early in the third trimester." Int J

Gynaecol Obstet.
OBJECTIVE: To evaluate the characteristic patterns of facial expression in fetuses aged from 28 to 34 weeks using 4-dimensional (4-D) ultrasonography. METHODS: The faces of 10 healthy fetuses aged from 28 to 34 weeks were recorded continuously for 15 min with a 4-D ultrasonographic machine performing up to 25 frames per second. The occurrence rates of blinking, mouthing, yawning, tongue expulsion, smiling, scowling, and sucking were evaluated. RESULTS: Mouthing was the most frequent facial expression (median, 6.5; range, 2-19) whereas the least frequent were scowling (median, 1; range, 0-9) and sucking (median, 1; range, 0-2). Mouthing was evident in all fetuses and significantly more frequent than any other movement (P<.05). Yawning (median, 3; range, 0-6), smiling (median, 2; range, 0-9), and blinking (median, 1.5; range, 0-6) were observed in most cases. Tongue expulsion (median, 1.5; range, 0-5), scowling, and sucking were each observed in 6 cases. CONCLUSION: 4-D sonography provides a means of evaluating fetal facial expression early in the third trimester. It may be a key to predicting fetal brain function and well-being and an important modality in future fetal neurophysiologic research.

Walusinski, O. (2006). "Yawning: Unsuspected avenue for a better understanding of arousal and interoception." Med Hypotheses 67(1): 6-14.

Walusinski, O. (2006). "[Yawning: from birth to senescence]." Psychol Neuropsychiatr Vieil 4(1): 39-46.
Yawning is one of the most under-appreciated behaviors. It is a stereotyped and often repetitive motor act, characterized by gaping of the mouth accompanied by a long inspiration, a brief acme followed by a short expiration. The vigor of the act may increase arousal. Although socially offensive to many, yawns often bring pleasure to the yawner. While influenced by several neurotransmitters, yawning is strongly affected by dopamine. Dopamine activates oxytocin production in the paraventricular nucleus of the hypothalamus, oxytocin may then activate cholinergic neurotransmission in the hippocampus and the reticular formation of the brainstem. Acethylcholine induces yawning via the muscarinic receptors of effectors. Other neurotransmitters can modulate its occurence like serotonin, neuropeptides, hypocretin and sexual hormones. The decrease of yawning in the elderly suggests an associated decrease of dopaminergic activity. Yawning and stretching have related phylogenetic old origins. Ethologists agree that most vertebrates yawn. Yawning is morphologically similar in reptiles, birds, mammals and fishes. They may be ancestral vestiges surviving throughout evolution with little variation. In the human embryo, yawning occurs as early as 12 weeks after conception and remains relatively unchanged throughout life. Across the life span, night sleep undergoes several age-related modifications. Theses changes concern sleep duration and the amount of REM and NREM sleep. We can describe, for the duration of REM sleep, a curvilinear trend with a steep descending slope in the last time of fetus life and the first year of life, a plateau level across childhood and adulthood, slowly lowering until age. A parallel curve demonstrates the similarity of the evolution of yawn's frequency and the amount of REM sleep. Thus, from ontogeny, phylogeny and this modelling approach emerges a pivotal link between yawning and REM sleep. Yawning is modified in some pathologies associated with aging.

Unnikrishnan, K. P., P. K. Sinha, et al. (2006). "Mandibular dislocation from yawning during induction of anesthesia." Can J Anaesth 53(11): 1164-5.

Thacker, S. K., M. K. Perna, et al. (2006). "The effects of adulthood olanzapine treatment on cognitive performance and neurotrophic factor content in male and female rats neonatally treated with quinpirole." Eur J Neurosci 24(7): 2075-83.
Male and female Sprague-Dawley rats were administered quinpirole (1 mg/kg, i.p.) or saline once daily from postnatal day (P)1 to P21. This drug treatment has been shown to produce long-term priming of the D(2) receptor. Beginning on P62, rats were administered the atypical antipsychotic olanzapine (2.5 mg/kg) or saline twice daily (i.p.) for 28 days. One day after olanzapine treatment ceased, rats were tested on the place and match-to-place versions of the Morris water maze (MWM) for seven consecutive days. Dopamine D(2) receptor priming was verified through a yawning behavioural test, a D(2) receptor-mediated event, before olanzapine was administered as well as after olanzapine treatment and behavioural testing were complete. Results showed that neonatal quinpirole treatment induced D(2) priming that was eliminated by olanzapine treatment. On the MWM place version, D(2)-primed rats demonstrated a significant impairment that was eliminated by olanzapine treatment, but olanzapine treatment to animals neonatally treated with saline produced a significant deficit on the place version of the MWM. There were no significant deficits on the match-to-place version. Brain tissue analyses revealed that neonatal quinpirole treatment produced a significant decrease in hippocampal NGF, BDNF and ChAT that was eliminated by olanzapine treatment. Neonatal quinpirole treatment produced a significant decrease in BDNF and ChAT in the frontal cortex that was unaffected by olanzapine treatment. These results show that olanzapine eliminates D(2) receptor priming and cognitive impairment and also alleviates decreases in neurotrophins and acetylcholinergic markers produced by D(2) priming in the hippocampus.

Shalini, A. and S. Sreedharan (2006). "A complex, contagious, evolutionary habit." Ann Acad Med Singapore 35(6): 433-4.

Schoonman, G. G., D. J. Evers, et al. (2006). "The prevalence of premonitory symptoms in migraine: a questionnaire study in 461 patients." Cephalalgia 26(10): 1209-13.
Migraine attacks are often preceded by premonitory symptoms. Prevalence rates of migraine patients reporting one or more premonitory symptoms show considerable variability and rates range between 12% and 79%. Sources of variability might be differences in study population or research design. Using a questionnaire, we retrospectively studied the prevalence of 12 predefined premonitory symptoms in a clinic-based population. Of 461 migraine patients, 374 (81%) responded. At least one premonitory symptom was reported by 86.9% and 71.1% reported two or more. The most frequently reported premonitory symptoms were fatigue (46.5%), phonophobia (36.4%) and yawning (35.8%). The mean number of premonitory symptoms per person was 3.2 (+/- 2.5). Women reported 3.3 premonitory symptoms compared with 2.5 symptoms in men (P = 0.01). Age, education, migraine subtype (with or without aura) and mean attack frequency had no effect on the mean number of symptoms per individual. In conclusion, premonitory symptoms are frequently reported by migraine patients. Sensitivity and specificity of premonitory symptoms for migraine need to be assessed using prospective methods.

Sagiuchi, T., S. Tachibana, et al. (2006). "Lhermitte sign during yawning associated with congenital partial aplasia of the posterior arch of the atlas." AJNR Am J Neuroradiol 27(2): 258-60.
We describe the case of a 26-year-old man who presented with symptoms compatible with Lhermitte sign that occurred during yawning. It was associated with congenital partial aplasia of the posterior arch of the atlas. Cervical multisection-detector CT myelography during yawning showed compression of the upper cervical cord due to the inward mobility of the isolated posterior tubercle. The symptoms completely disappeared following removal of the isolated posterior tubercle.

Ronin-Walknowska, E., M. Samborska, et al. (2006). "[Anomalies of the tongue in the fetus and neonate]." Ann Acad Med Stetin 52 Suppl 3: 7-11.
This work reviews the literature on the development of the tongue and its function during fetal life. Research on fetal behavior in general and functioning of structures of the skull, face and neck during fetal life in particular was very difficult, not to say impossible, until the present era of ultrasonography with flow (color Doppler and power Doppler), as well as 3D and 4D imaging. The results of measurements of the tongue, its perimeter, length, and area in normal fetuses and in fetuses with chromosomal aberrations are discussed. Abnormalities of the tongue appear as isolated defects or in association with other genetic abnormalities. Initial ultrasonographic detection of abnormalities of the fetal tongue demands further examination with more sophisticated sonographic methods. Some researchers also advocate karyotyping. Reports are discussed on the function of the tongue, such as protrusion, licking, grooving, sucking, yawning, and swallowing, and the time during pregnancy when these functions appear concurrently with growing complexity of movements of the fetus. These functions of the tongue have been studied in normal fetuses and in those with abnormalities during fetal life, such as Rh immunization and intrauterine growth retardation. Attention should focus on the presence of fetal tumors of the tongue or floor of the oral cavity. Prenatal diagnosis of tumors of the oral cavity and throat enables treatment to be undertaken immediately after birth and during the neonatal period.

Quintela, E., J. Castillo, et al. (2006). "Premonitory and resolution symptoms in migraine: a prospective study in 100 unselected patients." Cephalalgia 26(9): 1051-60.
The nosology of migraine premonitory (PS) and resolution (RS) symptoms was studied in 100 migraineurs consulting their general physician. They were asked to fill in, for three attacks, a PS and RS questionnaire. 'True' PS/RS were those experienced the day before (or the day after) the headache had started only if they were not present in a questionnaire completed in a pain-free period. True PS and RS were experienced by 84% and 80%, respectively, of subjects for the first attack. The mean and range (per patient) of PS were 6.8 and 0-21 and of RS 4.7 and 0-15. Anxiety, phonophobia, irritability, unhappiness and yawning were the commonest PS, whereas asthenia, tiredness, somnolence and concentration difficulties were the most common RS. Gender, age and Migraine Disability Assessment scores did not influence PS and RS. Both PS and RS were more frequent in migraine with aura subjects. Patients on preventatives showed a decreased frequency of PS and, to a lesser degree, of RS. Severity of headache was associated with a higher frequency of RS. Individual RS and especially PS were quite consistent after three attacks. Almost two-thirds of the symptoms were noticed in at least two out of three attacks, while more than a half of PS and more than a quarter of RS repeated in three out of three attacks. In conclusion, around 80% of unselected migraineurs experience RS and PS. Migraine with aura and severe pain are risk factors for experiencing PS and RS, while preventatives were protective, especially for PS.

Perriol, M. P. and C. Monaca (2006). ""One person yawning sets off everyone else"." J Neurol Neurosurg Psychiatry 77(1): 3.

Paukner, A. and J. R. Anderson (2006). "Video-induced yawning in stumptail macaques (Macaca arctoides)." Biol Lett 2(1): 36-8.
This study reports the first experimental exploration of possible contagious yawning in monkeys. Twenty-two stumptail macaques (Macaca arctoides) were presented with video clips of either yawns or control mouth movements by conspecifics. At a group level, monkeys yawned significantly more often during and just after the yawn tape than the control tape. Supplementary analysis revealed that the yawn tape also elicited significantly more self-directed scratching responses than the control tape, which suggests that yawning might have been caused by tension arising from viewing the yawn tape. Understanding to what extent the observed effect resembles contagious yawning as found in humans and chimpanzees requires more detailed experimentation.

Nowak, P., L. Labus, et al. (2006). "DSP-4 prevents dopamine receptor priming by quinpirole." Pharmacol Biochem Behav.
Repeated treatments of rats with the dopamine (DA) D(2) receptor agonist quinpirole, consistently produce long-lived DA D(2) receptor supersensitization, by the process that has been termed priming. Rats so-primed in ontogeny behaviorally demonstrate adulthood enhancement of low-dose quinpirole-induced yawning. Because 1) dopaminergic neurons originate in midbrain nuclei (substantia nigra and ventral tegmental area), and 2) noradrenergic neurons originate in pontine (locus coeruleus) and medullary areas, it might be presumed that these two monoaminergic systems are independent, not interdependent. However, in the present study we demonstrate that there was an attenuation of quinpirole-enhanced yawning at 8 weeks in rats that were 1) primed by repeated neonatal quinpirole HCl treatments (50 mug/kg per day SC) during the first ten days of postnatal ontogeny, and 2) lesioned at 3 days after birth with DSP-4 (N-2-chloroethyl-N-ethyl-2-bromobenzylamine hydrochloride, 50 mg/kg SC). Dose-effect curves indicated a 23-45% reduction in yawning by DSP-4 treatment of quinpirole-primed rats, acutely treated as adults with quinpirole (25, 50, or 100 mug/kg). Effectiveness of DSP-4 is reflected by the 95% and 99% reductions in norepinephrine contents of frontal cortex and hippocampus, respectively (HPLC/ED method). The findings are supportive of a modulatory role of noradrenergic fibers on dopamine receptor priming (supersensitization) in rat brain.

Markiewicz, M. R., R. Ohrbach, et al. (2006). "Oral behaviors checklist: reliability of performance in targeted waking-state behaviors." J Orofac Pain 20(4): 306-16.
AIMS: To assess the consistency of intentional behavioral performance as an index of whether individuals understood the meanings of the behavioral terms of the Oral Behaviors Checklist, which is a self-report scale for identifying and quantifying the frequency of jaw overuse behaviors. METHODS: Surface electromyography was used to measure bilaterally the activity of the masseter, temporalis, and suprahyoid muscles (for assessment of oral behaviors) and the biceps muscles (reference task of biceps curl) in 27 temporomandibular disorder (TMD) cases and 27 controls. Subjects were asked to perform (1) biceps curls to lift 5 weights, with explanation, and (2) 10 oral behaviors (e.g., "clench", "yawn") without explanation. RESULTS: Biceps-curl performance resulted in assignments of excellent or very good for linearity-reliability based on inspection and correlation. Test-retest reliability of the 10 performed oral behaviors generally ranged from 0.6 to 0.98 for all 3 muscle groups, and many tasks had reliability coefficients comparable to those for the biceps curl. Across tasks, elevator muscle reliability of cases was 0.87, compared to 0.75 for controls; group values for opening muscles were similar. CONCLUSION: Individual subjects performed each task at a high level of consistency. Performance was not appreciably altered by being a TMD case versus a control and was not significantly different from the performance level of a reference task, indicating that each individual understood well the meaning of each oral behavior-related word.

Korkes, H., E. M. de Oliveira, et al. (2006). "Cardiac syncope induced by glossopharyngeal "neuralgia": a rare presentation." Arq Bras Cardiol 87(5): e189-91.
The first description of severe pain in the distribution of the glossopharyngeal nerve is credited to Weisenberg, in 1910, in a patient with cerebellopontine angle tumor. However, it was Harris, in 1926, who coined the term glossopharyngeal neuralgia to describe this rare condition characterized by paroxysms of excruciating pain located laterally at the back of the tongue, soft palate, throat, and lateral and posterior pharynx, radiating to the ear. Swallowing, coughing, yawning or chewing may trigger pain, which usually lasts from seconds to minutes. The association between glossopharyngeal neuralgia and syncope is very rare, being identified by brief episodes of bradycardia, asystole, and hypotension. Such an association, with this same pathophysiology, was first described by Riley et al in 1942.

Kita, I., Y. Seki, et al. (2006). "Corticotropin-releasing factor neurons in the hypothalamic paraventricular nucleus are involved in arousal/yawning response of rats." Behav Brain Res 169(1): 48-56.
Our previous studies have suggested that activation of the hypothalamic paraventricular (PVN) descending oxytocinergic projections is involved in the induction of yawning accompanied by an arousal response, but the possibility that neural systems other than the oxytocinergic system in the PVN also mediate the arousal/yawning response cannot be ruled out. We assessed the activity of corticotropin-releasing factor (CRF) neurons during yawning induced by the PVN stimulation in anesthetized, spontaneously breathing rats using double-staining for c-Fos and CRF. Yawning response was evaluated by monitoring an intercostals electromyogram as an index of inspiratory activity and a digastric electromyogram as an indicator of mouth opening. We also recorded the electrocorticogram (ECoG) to determine the arousal response during yawning. Microinjection of l-glutamate (2-5 nmol) into the PVN produced a frequent yawning accompanied by an arousal shift in the ECoG, and these behavioral effects were associated with a significant increase of c-Fos positive CRF neurons in the medial parvocellular subdivision of the PVN. In addition, a marked enhancement in the c-Fos expression was found in the both locus coeruleus (LC) and global area in the cortex when the frequency of yawning response was increased by the PVN stimulation, suggesting that the arousal response during yawning might be mediated by the activation of LC neurons. The present study suggests that an activation of CRF neurons in the PVN is responsible for the arousal response accompanied by yawning behavior.

Kita, I., Y. Yoshida, et al. (2006). "An activation of parvocellular oxytocinergic neurons in the paraventricular nucleus in oxytocin-induced yawning and penile erection." Neurosci Res 54(4): 269-75.
Intracerebroventricular (ICV) or PVN local injections of oxytocin induce yawning and penile erection, for which a positive feedback mechanism for the PVN oxytocinergic activation is suggested, but this had not been directly substantiated in vivo. We have assessed the behavioral effects and activity of oxytocinergic neurons with double-staining for c-Fos and oxytocin in the PVN after ICV administration of oxytocin in adult male rats. ICV oxytocin injections (50 and 200 ng) dose-dependently induced yawning and penile erection and significantly increased the percentage of c-Fos positive oxytocin neurons in the medial, dorsal and lateral parvocellular subdivision of the PVN. However, increases in the magnocellular portion were not significant. We also found that lithium chloride (LiCl, 0.5 and 1.0 mEq), a compound known to activate oxytocinergic neurons, also significantly increased the percentage of c-Fos positive oxytocin neurons in all PVN portions. However, LiCl did not induce yawning and penile erection, but counteracted the oxytocin-induced yawning and penile erection. These results suggest that if the activation of oxytocinergic neurons in the PVN is important for mediating oxytocin-induced yawning and penile erection, a selective activation of parvocellular oxytocinergic neurons in the PVN is likely to be involved.

Kato, T., S. Akiyama, et al. (2006). "The occurrence of spontaneous functional and nonfunctional orofacial activities in subjects without pain under laboratory conditions: a descriptive study." J Orofac Pain 20(4): 317-24.
AIMS: To assess the occurrence and the modality of spontaneous orofacial behaviors of awake healthy subjects without pain who were unaware of bruxism during wakefulness. METHODS: Sixteen asymptomatic subjects read silently for 30 minutes while polygraphic recordings, including electromyographic (EMG) activity from masticatory and leg muscles, chest respiratory movements, and the movements and sounds of larynx, were made with simultaneous audio-video monitoring. Orofacial behaviors were scored based on the polygraphic and audio-video records. The activity and duration of masseter EMG bursts were calculated for the types of orofacial behaviors. RESULTS: The number of orofacial behaviors varied between subjects; swallowing was most frequently observed. Approximately half of the orofacial behaviors occurred closely with body movements. Of all masseter EMG bursts detected, 55% were associated with functional orofacial behaviors, while 45% were regarded as nonfunctional. More than 80% of these masseter bursts lasted for less than 2 seconds, with an activity less than 20% of maximal voluntary clenching. These values did not differ between the types of associated orofacial behaviors. CONCLUSION: Although the occurrence of spontaneous orofacial motor activity is variable, asymptomatic subjects can exhibit substantial masseter bursts during wakefulness that are not associated with functional orofacial behaviors. The use of physiological and audio-video records permits spontaneous orofacial behaviors to be specifically identified, thereby allowing nonfunctional masseter EMG activity to be differentiated from functional masseter EMG activity.

Jakobovits, A. (2006). "[Paradigms of fetal ethology]." Orv Hetil 147(11): 509-15.
In utero, the fetus is protected against biological and social influences of the outside world. This circumstance offers an opportunity for sonographic investigation of inherited fetal behavior free of extraneous effects. Observation of fetal activities with ultrasound permits the recognition of certain uniform features of fetal behavior. Immediately after birth, the neonate continues repeating those activities that he/she became accustomed to in the womb. Later these become modified by environmental influences. Nonetheless, basic inherited behavioral characteristics continue to be expressed and may remain recognizable even during adulthood. Some aspects of adult behavior may derive from experience acquired during fetal life. These include the hand-face reflex, various types of facial expression, such as smiling, crying, yawning, grimaces of dissatification and desperation as well as sticking out one's tongue.

Harada, K. (2006). "Paroxetine-induced excessive yawning." Psychiatry Clin Neurosci 60(2): 260.

Gray, S. M. (2006). "Knowledge management: a core skill for surgeons who manage." Surg Clin North Am 86(1): 17-39, vii-viii.
The yawning gap between what we know and what we do has major implications for patients. By putting into practice what we know now, we will have a bigger impact on the health of individuals and populations than any drug or technology discovered in the new decade. The assumption underlying this article is that the gap can be closed by thinking, planning, analyzing, mobilizing,managing, personalizing, and using knowledge. There is, however,a risk that the attempted solution may perpetuate or aggravate the problem, and surgeons must be aware of the dangers of substituting thought for action, when knowledge management becomes an industry of its own, remote from the core activities of the organization and those who deliver them.

Graves, F. C. and K. Wallen (2006). "Androgen-induced yawning in rhesus monkey females is reversed with a nonsteroidal anti-androgen." Horm Behav 49(2): 233-6.
In the adult rhesus monkey, yawning is an androgen-dependent sexually dimorphic behavior with males yawning more frequently than do females reflecting sex differences in circulating androgens. Studies in a variety of species indicate that yawning is mediated by various neurochemicals including dopamine, serotonin, and oxytocin. In rhesus monkeys, exogenous androgen reliably induces yawning in females to male-like levels. This study investigated whether flutamide, a nonsteroidal anti-androgen, reverses yawning induced by exogenous androgen administration in adult female rhesus monkeys. Six adult female rhesus monkeys were given chronic DHT alone and in combination with daily injections of flutamide and observed for yawning behavior. Treatment with DHT alone significantly increased yawning from 0.3 yawns per 30 min at the pretreatment baseline to 4.7 yawns per 30 min. Concurrent administration of flutamide significantly reduced the rate of yawning

to 1.9 yawns per 30 min. These data indicate that flutamide is an effective tool for blocking the central effects of androgens in rhesus monkey females and that androgens regulate yawning similarly in both males and females.

Fontenot, M. B., M. N. Wilkes, et al. (2006). "Effects of Outdoor Housing on Self-Injurious and Stereotypic Behavior in Adult Male Rhesus Macaques (Macaca mulatta)." J Am Assoc Lab Anim Sci 45(5): 35-43.

We examined the effects of outdoor housing on self-injurious and stereotypic behavior in adult male rhesus macaques with a history of self-wounding that were previously singly housed indoors for at least 4 y prior to the study. Baseline behavioral observations were collected over 2.5 mo. In phase 1, animals were relocated outdoors in 1 of 2 experimental conditions, grouphoused (n = 8) or single-housed (n = 5), for 6 wk. In phase 2, group-housed animals were observed outdoors for an additional 6 wk. Behavioral observations were done using focal sampling techniques. In phase 1, rates of self-biting and self-directed stereotypies and time spent displaying idiosyncratic self-directed stereotypies decreased significantly when group- and single-housed animals were housed outdoors. Rates of yawning and scratching were significantly decreased for group- and single-housed animals and, for group-housed animals, self-grooming decreased with outdoor housing. In phase 2, rates of self-biting, time engaging in idiosyncratic self-directed stereotypies, and yawning remained significantly lower during weeks 7 through 12 (outdoor housing) compared with those under indoor housing. Rates of scratching and time spent self-grooming decreased significantly during the first 6 wk but then returned to baseline levels. Our findings suggest that self-biting and self-directed stereotypic behavior in rhesus macaques with a history of self-injurious behavior is significantly reduced by outdoor housing regardless of whether animals are socially or individually housed.

Di Martino, E. F., R. Thaden, et al. (2006). "Evaluation of Eustachian tube function by sonotubometry: results and reliability of 8 kHz signals in normal subjects." Eur Arch Otorhinolaryngol.

Sonotubometry allows an assessment of the Eustachian tube (ET) function under physiological conditions. The reliability of the application of an 8 kHz pure-tone signal was investigated. In 40 normal subjects (80 ears) sonotubometric studies were performed with a custom-made device. ET opening was provoked by swallowing, yawning and Valsalva manoeuvre. An opening was detected in all patients but not in all manoeuvres. Four characteristic sonotubogram types were found. Most common was the spike-type (60%). The double-peak and the plateau-shaped curves occured in 17% each. The finding of an descendant curve was rare (5%). Of 623 measurements, only in 55% manouvres a positive sonotubometric result was found despite the fact that the patients reported an opening in all cases. The median opening time in dry swallowing, liquid swallowing, yawning and Valsalva was found to be 486, 355, 1,263 and 1,250 ms. A median sound increase of 16.0, 13.8, 15.0 and 15.0 dB was recorded for these manoeuvres. There was a statistic significant difference ($P < 0.02$) between the increase in sound intensity of liquid and dry swallowing. There was also a statistic significant difference found for the duration of the forced manoeuvres Valsalva and yawning as compared to dry and liquid swallowing ($P < 0.0001$). The use of an 8 kHz pure-tone signal showed a limited sensitivity for the detection of ET openings. This is mainly due to noise pollution, but also because of an altered positioning and/or dislocation of the probes and compression of the nostrils. The application of an 8 kHz signal is therefore not reliable enough for the use in practice. Further technical refinements and the use of alternative signals are necessary for a broader clinical application.

Cheng, T. O. (2006). "More about yawning." Am J Cardiol 97(10): 1547-9.

Cattaneo, L., L. Cucurachi, et al. (2006). "Pathological yawning as a presenting symptom of brain stem ischaemia in two patients." J Neurol Neurosurg Psychiatry 77(1): 98-100.

Two cases of brain stem stroke involving the upper pons and the ponto-mesencephalic junction presented with transient excessive pathological yawning, associated with gait ataxia and in one subject with upper limb and facial hemiparesis. A causal relation is hypothesised between the brain stem lesion and pathological yawning, possibly related to denervation hypersensitivity of a putative brain stem yawn centre. Excessive yawning may herald brain stem ischaemia.

Brown, R. W., M. K. Perna, et al. (2006). "The effects of adulthood nicotine treatment on D2-mediated behavior and neurotrophins of rats neonatally treated with quinpirole." Synapse 59(5): 253-9.

This study was designed to analyze the effects of nicotine on yawning behavior and neurotrophin content in the hippocampus and frontal cortex of D2-receptor primed female adult Sprague-Dawley rats. Animals were neonatally treated with quinpirole, a dopamine (DA) D2/D3 agonist, from postnatal day 1-21 (P1-21) and raised to P60 and administered nicotine tartarate (0.3 mg/kg free base) or saline twice daily for 14 days. One day after nicotine treatment had ceased, the number of yawns was recorded for 1 h in response to an acute injection of quinpirole (i.p., 100 microg/kg). Yawning is a D2-receptor mediated event. D2-primed rats demonstrated a significant increase in yawning in response to acute quinpirole compared with that of controls, but nicotine did not alleviate this effect. Neonatal quinpirole treatment produced a significant decrease of nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) in the hippocampus that was alleviated by adulthood nicotine treatment. Interestingly, nicotine treatment to controls produced a significant increase of NGF in the frontal cortex, but a significant decrease of both NGF and BDNF in the hippocampus and BDNF in the frontal cortex. The decreases shown in NGF and BDNF is contrary to past findings that have shown nicotine to produce significant increases of hippocampal NGF and BDNF, but these past studies utilized male rats or mice or were performed in vitro. This study shows that nicotine has complex interactions with NGF and BDNF in D2-primed and control animals, and emphasizes the importance of gender differences when analyzing nicotine's effects on neurotrophins.

Wu, C. C., J. Y. Chen, et al. (2005). "Serotonin reuptake inhibitors attenuate morphine withdrawal syndrome in neonatal rats passively exposed to morphine." Eur J Pharmacol 512(1): 37-42.

Previous investigations had shown that inhibitor of serotonin reuptake transporter (SERT) could attenuate morphine withdrawal syndrome in adult animals. In the present study, we determined whether postnatal injection of serotonin reuptake inhibitors, fluoxetine, clomipramine, or citalopram, is able to attenuate the expression of the naloxone-precipitated morphine withdrawal syndrome in 5-day-old neonatal Sprauge-Dawley rats born to dams rat that received morphine injection since a week before mating till 5 days after delivery. Withdrawal syndrome of morphine, manifested as frequent abdominal stretching and yawning, was generated by injection of naloxone on postnatal day 5. Pre-injection with fluoxetine, clomipramine, or citalopram, significantly attenuated the naloxone-precipitated syndrome in a dose-dependent manner without apparent side effect. The rank order of inhibitory potency is citalopram=clomipramine>fluoxetine. This result suggests that inhibitor of SERT may be of potential in treating neonatal morphine withdrawal syndrome.

Woodworth, K. W. and L. G. Markwell (2005). "Bored, yawning residents falling asleep during orientation? Wake 'em up with a test!" Med Ref Serv Q 24(1): 77-91.

The librarians at the Grady Branch Library of Emory University School of Medicine describe the Ovid MEDLINE pretest given to incoming residents. The pretest is a "wake-up call" to the residents who have an inflated perception about their searching skills. This pretest gives the new residents an incentive to listen carefully to the Ovid MEDLINE presentation during the orientation of incoming residents.

Winther, B., J. M. Gwaltney, et al. (2005). "Radiopaque contrast dye in nasopharynx reaches the middle ear during swallowing and/or yawning." Acta Otolaryngol 125(6): 625-8.

Contrast dye in the nasopharynx reaches the middle ear during swallowing and yawning in normal adults. This suggests that displacement of bacteria in nasopharyngeal secretion to the middle ear may occur frequently during sleep.The middle ear is sterile under normal conditions. The purpose of this study was to examine by means of CT whether radiopaque contrast dye in the nasopharynx would reflux into the middle ear of normal adults during swallowing and/or yawning.Six normal adult volunteers were studied. Contrast dye was kept at the orifices of the Eustachian tube during swallowing and/or yawning by placing volunteers in either a head-down or lateral decubitus position. Reflux was determined by the presence of contrast dye in the middle ear on CT scanning of the temporal bone.Two of the three volunteers in each group (four out of six in total) had contrast material detected in one or both middle ear cavities.

Walusinski, O., E. Quoirin, et al. (2005). "[Parakinesia brachialis oscitans]." Rev Neurol (Paris) 161(2): 193-200.

INTRODUCTION: In some cases of hemiplegia the onset of yawning is associated with an involuntary raising of the paralyzed arm. PATIENTS AND METHOD: Four observations of this movement, which is seldom described probably because it is mostly neglected, were made in the neurology unit of the University Hospital of Poitiers. The descriptions were compared with other cases that have been published in the medical literature of the last 150 years. Cerebral imagery shows a lesion that is most often localized on the internal capsule. After comparison with experimental models in cats, it is proposed that the section of the cortico-neocerebellum tract of the extra-pyramidal system disinhibits the spino-archeocerebellum tract, enabling a motor stimulation of the arm by the lateral reticular nucleus, which harmonises central respiratory and locomotor rhythms. RESULTS AND CONCLUSION: Some subcortical structures, that are phylogenetically more ancient, thus disinhibit regained autonomy in the homeostasis process associating the massive inspiration of yawning--a form of reflex behavior that stimulates vigilance--with a motor control that is active during locomotion. For this phenomenon we coined the term "parakinesia brachialis oscitans".

Ugboko, V. I., F. O. Oginni, et al. (2005). "A survey of temporomandibular joint dislocation: aetiology, demographics, risk factors and management in 96 Nigerian cases." Int J Oral Maxillofac Surg 34(5): 499-502.

A retrospective study of 96 cases of temporomandibular joint dislocation was undertaken. Patients' ages ranged from 9 to 85 years (mean+/-SD, 35.3+/-17.4 years) and peak incidence was at 20-29 years. Mean duration was 7.9 weeks (range, 1h to 3 years). Acute, chronic and recurrent dislocations were seen in 46 (47.9%), 29 (30.2%) and 21 (21.9%) patients, respectively. Males dominated in all three categories but this was not statistically significant ($P = 0.8$). Excessive mouth opening while yawning (44 cases) was the commonest cause of dislocation, followed by road traffic accidents (13 cases). Ten patients (10.4%) had an underlying systemic disease, the commonest being epilepsy (four cases); those with acute dislocation recorded the highest incidence of underlying illness. Bilateral anterior (86 cases) dislocations were the most frequent. Of the 96 patients, 89 (92.7%) were available for treatment. Manual reduction with or without anaesthesia proved effective for 38/45 acute, 5/24 chronic and 14/20 recurrent cases. Chronic dislocations were treated mainly by surgical

osteotomy (13/24). Vertical subsigmoid and oblique ramus osteotomies were the commonest surgical techniques recorded. Treatment was satisfactory for all patients surgically handled except for one case of anterior open bite postoperatively. This study has shown that excessive mouth opening while yawning is the commonest cause of temporomandibular joint dislocation in Nigerians, and conservative approaches to management remain quite effective irrespective of the duration and clinical subtype. The best choice of surgical technique should be determined by proper clinical evaluation and the need to avoid or minimize postoperative morbidity.

Uchida, T., J. Lee, et al. (2005). "Effects of NMDA and MK-801 injected into the substantia nigra pars reticulata on jaw movements evoked by dopamine D1-/D2 receptor stimulation in the ventrolateral striatum: studies in freely moving rats." Methods Find Exp Clin Pharmacol 27(1): 31-7.

The effects of NMDA and MK-801 injected into the substantia nigra pars reticulata on jaw movements evoked by dopamine D1/D2 receptor stimulation in the ventrolateral striatum were examined in freely moving rats, by using a magnet-sensing system combined with intracerebral drug microinjection technique. Bilateral injections of a mixture of SKF 82958 (5 microg) and quinpirole (10 microg), agonist at dopamine D1 and D2 receptors respectively, into the ventrolateral striatum elicited repetitive jaw movements. Bilateral injections of NMDA (0.01 and 0.05 microg/0.2 microl in each side) into the substantia nigra pars reticulata, which alone did not produce jaw movements, reduced the repetitive jaw movements evoked by the dopamine D1/D2 receptor agonist mixture in a dose-dependent manner. Injection of the non-competitive NMDA receptor antagonist, MK-801 (0.1 and 0.5 microg/0.2 microl in each side), into the substantia nigra pars reticulata, which alone did not produce jaw movements, prevented the dopaminergic jaw movements in a dose-dependent manner. Moreover, other behaviors such as grooming, rearing, yawning, vacuous chewing, and locomotor activity that occurred after injections of the dopamine receptor agonist mixture were not significantly altered by the bilateral injections of NMDA or MK-801 into the substantia nigra pars reticulata. Given our previous results showing that both agonist and antagonist of GABA(A) receptors injected into the substantia nigra pars reticulata inhibit the jaw movements elicited by dopamine D1/D2 receptor stimulation in the ventrolateral striatum, the present results suggest that there are complex functional interactions between NMDA and GABA(A) receptors within the substantia nigra pars reticulata that may be responsible for the common profiles in the effects of NMDA and GABA(A) receptor agents.

Teichroeb, J. A., S. Marteinson, et al. (2005). "Individuals' behaviors following dye-marking in wild black-and-white colobus (Colobus vellerosus)." Am J Primatol 65(2): 197-203.

The ability to recognize individuals is a prerequisite for analyzing social relationships. We marked five adult and subadult Colobus vellerosus (three in 2002, and two in 2003) at the Boabeng Fiema Monkey Sanctuary, Ghana, to assess the feasibility of dye-marking black-and-white colobus, describe their reactions, and compare some of their behaviors with those of unmarked individuals. We used Nyanzol-D, a nontoxic black dye sprayed on the white tail (or white thigh) of the animal with a spray gun or a tree sprayer. Reactions to the marking procedure ranged from moving away and staring at the observer, without interruption in feeding (in one subject), to fleeing about 5 m away (in four subjects). In 234 hr of ad libitum observations (in 2002 and 2003), marks were scratched or otherwise were the object of attention from the bearer or other individuals on only one occasion. In 2002 we collected 22 hr of observations on the three marked monkeys and some unmarked monkeys in 10-min focal samples. Neither the marked nor the unmarked animals attended to the marks during focal samples. Marked and unmarked individuals displayed similar rates of displacement activities (autogrooming, scratching, and yawning). The proportion of scans with at least one near neighbor varied between marked and unmarked subjects, but the direction of the difference was not the same between males and females. The only aggression observed was displacements, and only in one comparison (out of four) did a difference emerge: the marked subadult male received more displacements than the unmarked males. Overall, marked and unmarked individuals did not differ consistently in our measures. Examination of the potential effects of marking should continue, since changes in pelage coloration may have longer-term social effects in species that rely largely on vision. Am. J. Primatol. 65:197-203, 2005. (c) 2005 Wiley-Liss, Inc.

Sobrian, S. K., B. L. Jones, et al. (2005). "Prenatal ethanol preferentially enhances reactivity of the dopamine D(1) but not D(2) or D(3) receptors in offspring." Neurotoxicol Teratol 27(1): 73-93.

Reports of prenatal ethanol (ETOH) effects on the dopamine system are inconsistent. In an attempt to clarify this issue, dams were given 35% ethanol-derived calories as the sole nutrient source in a liquid diet from the 10th through the 20th day of gestation (ETOH). Controls were pair-fed (PF) an isocaloric liquid diet or given ad libitum access to laboratory chow (LC). Prenatal exposure to both liquid diets reduced body weight of offspring relative to LC controls, more so for ETOH than for PF exposure. Prenatal ETOH also decreased litter size and viability, relative to both LC and PF control groups. On postnatal days 21-23, male and female offspring were given an injection of saline vehicle or one of eight specific dopamine receptor agonists or antagonists. Immediately after injection subjects were placed in individual observation cages, and over the following 30 min, eight behaviors (square entries, grooming, rearing, circling, sniffing, yawning, head and oral movements) were observed and quantified. No prenatal treatment effects on drug-induced behaviors were observed for dopamine D(2) (Apomorphine, DPAT or Quinpirole) or D(3) (PD 152255, Nafadotride, Apo or Quin effects on yawning) receptor agonists or antagonists, or for the vehicle control. In contrast, prenatal treatment effects were seen with drugs affecting the dopamine D(1) receptor. Both D(1) agonists (SKF 38393) and antagonists (SCH 23390 and high doses of spiperone) altered behaviors, especially oral and sniffing behaviors, in a manner which suggested enhanced dopamine D(1) drug sensitivity in both ETOH and PF offspring relative to LC controls. These results suggest that at this age, both sexes experience a prenatal undernutrition-linked increase in the behavioral response to dopamine D(1) agonists and antagonists, which can be intensified by gestational exposure to alcohol.

Sitzman, K. (2005). "Avoid sleepiness while driving." Home Healthc Nurse 23(4): 260.

Returning to the office after a long work day, Kristin, a hospice nurse, learns that the nighttime on-call nurse is ill. Kristin agrees to take call and hopes it will be a slow night. Now it is 2 am and Kristin has to travel to a client's home. Yawning repeatedly and driving over the rumble strip on the highway, she turns on the radio and opens the car window to the chill air, trying to shock herself into alertness.

Schurmann, M., M. D. Hesse, et al. (2005). "Yearning to yawn: the neural basis of contagious yawning." Neuroimage 24(4): 1260-4.

Yawning is contagious: Watching another person yawn may trigger us to do the same. Here we studied brain activation with functional magnetic resonance imaging (fMRI) while subjects watched videotaped yawns. Significant increases in the blood oxygen level dependent (BOLD) signal, specific to yawn viewing as contrasted to viewing non-nameable mouth movements, were observed in the right posterior superior temporal sulcus (STS) and bilaterally in the anterior STS, in agreement with the high affinity of STS to social cues. However, no additional yawn-specific activation was observed in Broca's area, the core region of the human mirror-neuron system (MNS) that matches action observation and execution. Thus, activation associated with viewing another person yawn seems to circumvent the essential parts of the MNS, in line with the nature of contagious yawns as automatically released behavioural acts-rather than truly imitated motor patterns that would require detailed action understanding. The subjects' self-reported tendency to yawn covaried negatively with activation of the left periamygdalar region, suggesting a connection between yawn contagiousness and amygdalar activation.

Platek, S. M., F. B. Mohamed, et al. (2005). "Contagious yawning and the brain." Brain Res Cogn Brain Res 23(2-3): 448-52.

Contagious yawning, the onset of a yawn triggered by seeing, hearing, reading, or thinking about another person yawn is a well-documented phenomenon. The mechanisms that drive contagious yawning are as yet unknown, but there is recent evidence of a link between contagious yawning and self-processing (S.M. Platek, S.R. Critton, T.E. Myers, G.G. Gallup Jr., Contagious yawning: the role of self-awareness and mental state attribution, Cogn. Brain Res. 17 (2003) 223-227.) that is negatively impacted by schizotypal personality traits. The neural substrates involved in contagious yawning, however, are unknown. Here, using fMRI, we show that viewing someone yawn evokes unique neural activity in the posterior cingulate and precuneus. Because of the role these areas play in self-processing (e.g., self-referential processing, theory of mind, autobiographical memory), our findings provide further support for the hypothesis that contagious yawning may be part of a neural network involved in empathy.

Ndiokwelu, E. (2005). "Bilateral dislocation of the mandible. 2 cases in a nuclear family." Odontostomatol Trop 28(112): 27-30.

Two cases of bilateral dislocation occurred in two brothers, aged 20 and 23 within a period of seventeen months. The junior one was the first victim in the month of April 1999 and the senior brother later in November 2000. The first was triggered by yawning whereas the second by vomiting. Different types of dislocation, diagnosis and management of dislocation is presented. The occurrence in two siblings raises the question of familial predisposition to dislocation.

Medrano, V., M. F. Selles-Galiana, et al. (2005). "[Yawning and temporal lobe epilepsy.]." Rev Neurol 41(1): 63-4.

Marcos, M. M., M. R. Velicia, et al. (2005). "Primary stabbing headache with buccal triggers." Eur Neurol 53(2): 91-2.

Lagares, A., P. A. Gomez, et al. (2005). "Short-lasting Unilateral Neuralgiform Headache with Conjunctival Injection and Tearing Syndrome Treated with Microvascular Decompression of the Trigeminal Nerve: Case Report." Neurosurgery 56(2): 413.

OBJECTIVE AND IMPORTANCE: Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing syndrome is a very rare disorder characterized by short-lasting neuralgiform unilateral pain affecting the orbital-periorbital area and associated with autonomic phenomena consisting mainly of conjunctival injection, tearing, and rhinorrhea. Treatment of this condition is difficult; many drugs and surgical procedures have been tried with variable results. In the literature, two cases have been described with short-term response to microvascular decompression of the trigeminal root. We present the case of a patient with short-lasting unilateral neuralgiform headache with conjunctival injection and tearing syndrome who remains asymptomatic 2 years after microvascular decompression. CLINICAL PRESENTATION: A 56-year-old woman was referred to our clinic because she had experienced pain in the distribution of the first left trigeminal branch during the previous 2 years. She experienced paroxysms lasting from a few seconds to 1 to 2 minutes superimposed over a dull sensation of pain involving the same territory. The paroxysms had no refractory period and were triggered by touching the eye or the left side of the face, chewing, yawning, washing her hair, and even by light. Although the paroxysms were triggered by light touch or chewing, she was able to talk or touch herself while having the paroxysm. During pain attacks, she experienced tearing and ipsilateral conjunctival injection, eyelid edema and rhinorrhea, as well as intense photophobia. A magnetic resonance imaging scan revealed a vascular

structure distorting and compressing the trigeminal root. INTERVENTION: The patient underwent microvascular decompression of the trigeminal root. At surgery, there was clear compression of the trigeminal root by a superior cerebellar artery loop that was resolved by interposing a Teflon patch. The patient awoke from the operation without pain, and all the accompanying signs and symptoms, such as photophobia, disappeared. The postoperative course was uneventful, and 2 years after treatment, the patient remains asymptomatic. CONCLUSION: Microvascular decompression could be an alternative therapeutic approach to this rare syndrome.

Kurjak, A., M. Stanojevic, et al. (2005). "The potential of four-dimensional (4D) ultrasonography in the assessment of fetal awareness." J Perinat Med 33(1): 46-53.

AIM: The aim of the study was to observe different expressions and movements of a fetal face during investigation of fetal behavior in the second and the third trimester of normal pregnancies, as a probable manifestation of fetal awareness. SUBJECTS AND METHODS: Over a 6-month period a study was conducted in three centers in Zagreb, Croatia and in Barcelona and Malaga, Spain. Women with singleton pregnancies (16-33 weeks) who were referred for ultrasound check-up for determination of gestational age, suspicious fetal malformations, polyhydramnios, and/or the assessment of biophysical profile or other possible pathology, were assigned to the study. After regular two-dimensional (2D) ultrasound assessment at an antenatal clinic, pregnant women were offered the possibility of undergoing 4D ultrasound examination if the fetus and the mother were considered "normal", i.e., if ultrasound and clinical assessment were uneventful. If the newborn delivered at term had 1- and 5-min Apgar scores of 7 and 10, respectively, and if the newborn was considered "term and normal" (normal spontaneous activity, normal posture and tone, and presence of some primitive reflexes) at the first and subsequent regular check-ups, the inclusion criteria were deemed to have been met. Out of 119 patients, 99 fulfilled the inclusion criteria, 40 of whom were in the second, and 59 in the third trimester of pregnancy. A Voluson 730 Expert system with a transabdominal 5-MHz transducer was used for 4D ultrasonography. After regular 2D scanning, the 4D mode was switched on, and a live 3D image was reconstructed by selecting ideal 2D mid-sagittal images of the face (the region of interest). The volume was automatically scanned every 2 s while the surface-rendered mode was switched on, and 4D images were displayed on the screen and recorded on videotape during a 30-min observation period. Movements of the following fetal face structures were analyzed: forehead, brows, nasal soft tissue and nasolabial folds, upper lip, oral cavity and tongue, lower lip and chin, eyelids and eyes, mouth and mouth angles, and facial expression. 4D ultrasonography allowed in utero observations of fetal facial expressions such as smiling, yawning, and swallowing. RESULTS: The quality of 4D depiction of fetal facial expressions increased with gestational age. The frequency of fetal facial expressions such as yawning ranged from 1 and 6 with a median of 1.5 per 30-min observation period; smiling ranged from 2 and 8 with the median of 2; tongue expulsion ranged from 2 to 6, median 3; mouth and eye squeezing ranged from 5 to 10, median 6; scowling ranged from 1 to 3, median 0.5; and isolated eye blinking ranged from 4 to 12 with a median of 5. CONCLUSIONS: Our study shows the ability of 4D sonography to depict different facial expressions and movements, which might represent fetal awareness. Nevertheless, long, precise and thorough observation of fetal faces by 4D sonography was hampered as the images were only near real-time. Thus, we were only able to study the quality and not the quantity of facial movement patterns.

Kuballa, G., P. Nowak, et al. (2005). "Central effects of nafadotride, a dopamine D(3) receptor antagonist, in rats. Comparison with haloperidol and clozapine." Pharmacol Rep 57(2): 161-9.

The aim of this study was to examine behavioral and biochemical effects of nafadotride, the new dopamine D(3) receptor antagonist, and to compare it with haloperidol (dopamine D(2) receptor antagonist) and clozapine (predominate dopamine D(4) receptor antagonist). Each drug was injected to adult male Wistar rats intraperitoneally, each at a single dose and for 14 consecutive days. Thirty minutes after single or last injection of the examined drugs, the following behavioral parameters were recorded: yawning, oral activity, locomotion, exploratory activity, catalepsy and coordination ability. By HPLC/ED methods, we determined the effects of the examined antagonists on the levels of biogenic amines in striatum and hippocampus: dopamine (DA), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 3-methoxytyramine (3-MT), 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA) and noradrenaline (NA). Additionally, DA and 5-HT synthesis rate was determined in striatum and 5-HT in hippocampus. The results of the study indicate that nafadotride, the dopamine D(3) receptor antagonist, has a behavioral and biochemical profile of action different from that of haloperidol but partially similar to that of clozapine.

Kouwen, H., F. A. van Balen, et al. (2005). "Functional tubal therapy for persistent otitis media with effusion in children: myth or evidence?" Int J Pediatr Otorhinolaryngol 69(7): 943-51.

Otitis media with effusion (OME), a form of inflammatory middle ear disease, is a common reason for young children to visit their family doctor and to have surgery. Tubal dysfunction plays a major role in the pathogenesis. In case of persistent OME, there seems to be a logical rationale for a favourable effect on the tubal dysfunction of a functional active motoric approach combined with behavioral changes (hygiene), and as a consequence for a therapeutic effect on the middle ear disease. The basic principles of this functional treatment are: active ventilation of the middle ear, correction of immature and undesirable deviant mouth habits, increasing swallowing frequency, activating jaw and palate movements, and encouraging the use of chewing gum. The bases for this functional therapy are critically analysed, and it may be concluded that all of these principles rely upon evidence based physiological mechanisms. However, the limited available clinical data from the literature are reviewed, and appear as methodologically weak. The results of an own prospective randomized pilot study comparing functional treatment with watchful waiting may be considered encouraging, since a borderline significance level was reached with a small amount of subjects.

Kasuya, Y., T. Murakami, et al. (2005). "Does yawning represent a transient arousal-shift during intravenous induction of general anesthesia?" Anesth Analg 101(2): 382-4, table of contents.

Although yawning occurs frequently during the IV induction of general anesthesia, the significance of this response remains unknown. In this study, we induced 30 surgical patients with 4 mg/kg thiopental IV, and 30 patients with 2 mg/kg propofol IV. Thereafter, the occurrence of yawning was continuously assessed, as the only clinical end-point, for 1 min. The electroencephalographic bispectral index was monitored throughout the observation period. The criterion for an arousal response was a transient increase during a continuing decrease in the bispectral index value. On the basis of this criterion, the sensitivity and specificity of the yawning response as an arousal sign were 77% and 80%, respectively. If a patient exhibited a yawning response, the chance of arousal was 84% (positive predictive value). With no yawning response, the chance of nonarousal was 71% (negative predictive value). According to simple logistic regression, the yawning response was predictive of a transient arousal-shift with an odds ratio of 13.5 (95% confidence interval: 3.8-48; $P < 0.001$). The occurrence of a yawning response during IV induction may be a clinical indicator of a transient arousal-shift during progressive loss of consciousness. IMPLICATIONS: Yawning elicited by IV anesthetic induction was related to a transient increase during the continuing decrease in the electroencephalographic bispectral index value (sensitivity and specificity, 77% and 80%, respectively). This type of yawning may be a clinical indicator of a transient arousal-shift during progressive loss of consciousness.

Heydecke, G., J. M. Thomason, et al. (2005). "The impact of conventional and implant supported prostheses on social and sexual activities in edentulous adults Results from a randomized trial 2 months after treatment." J Dent 33(8): 649-57.

OBJECTIVES: To determine the impact of mandibular two-implant overdentures or conventional complete dentures on leisure and sexual activities. METHODS: One hundred and two subjects, aged 35-65 years, received either mandibular overdentures retained by two implants (IOD; n=54) or new mandibular conventional complete dentures (CD; n=48) in a randomized controlled clinical trial. A Social Impact Questionnaire was used to assess the impact on social and sexual activity including avoiding conversation, refusing invitations, avoiding sport and feeling uneasy when kissing and in sexual relationships, and the looseness of the prostheses during such activities. Ratings were recorded on categorical scales at baseline and 2 months after treatment. Oral health related quality of life was measured with the Oral Health Impact Profile (OHIP). Between and within group comparisons were carried out using regression models. The correlation between post-treatment OHIP scores and the leisure and sexual impact items was assessed. RESULTS: Two months after delivery of the prosthesis there was significant improvements in the IOD group for looseness when eating, speaking, kissing and yawning. The IOD group reported significantly less post treatment looseness than the CD group for all parameters investigated ($p<0.0001$). IOD subjects felt less uneasy kissing and less uneasy during sexual activity than CD subjects. Correlations between the two sexual activity items (uneasiness when kissing and during sexual relations) and the OHIP scales were weak. CONCLUSIONS: Edentulism has a negative impact on social and sexual life. Mandibular overdentures provide greater improvement in of unease in intimate activities than new conventional mandibular dentures.

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Hata, T., K. Kanenishi, et al. (2005). "Real-time 3-D sonographic observation of fetal facial expression." J Obstet Gynaecol Res 31(4): 337-40.

Abstract Aim: There have been a few reports about 3-D sonographic observation of fetal movements using dynamic 3-D sonography. However, dynamic 3-D sonography is not real-time, the frame rate being in the region of 4-6 frames per second depending on the size of the

region of interest and the number of lines employed. Recently, a new faster 3-D sonography, which acquires up to 28 frames per second, has become available. Using this system, we studied a full range of fetal facial expressions during pregnancy. Methods: A total of 17 normal fetuses in 16 pregnancies (15 singletons and one twin) at 20-38 weeks' gestation was studied using a transabdominal real-time 3-D ultrasound machine. This 3-D ultrasound machine proved capable of providing continuous 3-D sonographic images every 0.05 and 0.035 s. The fetal face was monitored for 15 min for each subject. Results: Fetal eyelid movement (fetal blinking) was observed in three of 17 fetuses (17.6%). Double blinking was identified in one fetus at 38 weeks. Various types of mouth movement (yawning, a little opening, chewing, and subtle lip movement) could be observed in nine of 17 fetuses (52.9%). In the course of yawn-like opening of the mouth, tongue movements such as tongue thrust and tongue click were clearly shown in three fetuses (17.6%). A lingula movement was also identified in the course of tongue movement. Conclusion: Real-time 3-D sonography provides a novel means for evaluation of fetal movement, particularly fetal facial expression, in the second and third trimesters. Real-time 3-D sonography might be an important modality in future fetal behavior research and in evaluation of fetal well-being.

Graves, F. C. and K. Wallen (2005). "Androgen-induced yawning in rhesus monkey females is reversed with a nonsteroidal anti-androgen." Horm Behav.

In the adult rhesus monkey, yawning is an androgen-dependent sexually dimorphic behavior with males yawning more frequently than do females reflecting sex differences in circulating androgens. Studies in a variety of species indicate that yawning is mediated by various neurochemicals including dopamine, serotonin, and oxytocin. In rhesus monkeys, exogenous androgen reliably induces yawning in females to male-like levels. This study investigated whether flutamide, a nonsteroidal anti-androgen, reverses yawning induced by exogenous androgen administration in adult female rhesus monkeys. Six adult female rhesus monkeys were given chronic DHT alone and in combination with daily injections of flutamide and observed for yawning behavior. Treatment with DHT alone significantly increased yawning from 0.3 yawns per 30 min at the pretreatment baseline to 4.7 yawns per 30 min. Concurrent administration of flutamide significantly reduced the rate of yawning to 1.9 yawns per 30 min. These data indicate that flutamide is an effective tool for blocking the central effects of androgens in rhesus monkey females and that androgens regulate yawning similarly in both males and females.

Goessler, U. R., G. Hein, et al. (2005). "[Physiology, role and neuropharmacology of yawning]." Laryngorhinootologie 84(5): 345-51.

Yawning is a physiological event that can be divided into three distinct phases: a long inspiratory phase, a brief acme and a rapid exspiration. The reason for yawning is not yet well defined. However this semi-voluntary event increases vigilance and aims to alert when drowsiness occurs. Yawning may have an important role for social communication. The neuropharmacology of yawning is complex and knowledge of its mechanisms is incomplete. While under the control of several neurotransmitters, yawning is largely affected by dopamine. Dopamine may activate oxytocin production in the paraventricular nucleus of the hypothalamus, oxytocin may then activate cholinergic neurotransmission in the hippocampus, and finally acetylcholine might induce yawning via the muscarinic receptors of the effectors. In fact, this scheme is simplified. Many other molecules can modulate yawning, such as nitric oxide, glutamate, GABA, serotonin, ACTH, MSH, sexual hormones and opium derivate peptides.

Gimenez-Llort, L., T. Canete, et al. (2005). "Two distinctive apomorphine-induced phenotypes in the Roman high- and low-avoidance rats." Physiol Behav.

Strain differences in spontaneous locomotor activity and the behavioral patterns induced by dopaminergic agonists in rodents can disclose differential genetic susceptibilities to dopaminergic dysfunction (i.e. vulnerability to psychosis). Psychogenetic selection of hypoemotional Roman High-Avoidance (RHA) and hyperemotional Low-Avoidance (RLA) rats leads to divergence in dopaminergic function as well. The present study was designed to characterize their spontaneous activity and their responses to apomorphine (0.067-3 mg/kg, s.c.) as compared to those of the standard Sprague-Dawley (SD) strain. The Roman strains displayed higher spontaneous activity than SD rats and RHA exhibited the higher response to novelty which agrees with a higher sensitivity to apomorphine in this strain. The biphasic effect induced by apomorphine (locomotor inhibition and yawning at low doses but stimulation of locomotion and stereotyped behavior at higher ones) was reproduced in the standard SD strain. Low doses were less effective inducing locomotor inhibition in RHA whereas these animals were much more sensitive to high dose-induced stereotyped behavior. In contrast, RLA was characterized as a high-yawning strain and low doses of apomorphine also induced a striking motor inhibition suggesting functional enhancement of dopamine receptors mediating these behaviors. The detailed and distinctive behavioral profiles described in this work suggest between strain differences both at the presynaptic and postsynaptic dopaminergic function and may serve as paths to better specify functional mechanisms in future studies of risk of developing dopaminergic dysfunctions.

Gautam, K. (2005). "Transforming hospital board meetings: guidelines for comprehensive change." Hosp Top 83(3): 25-31.

Does the following remind you of a hospital board meeting you attended recently? The meeting starts late, the PowerPoint presentation on hospital operations is too detailed to understand, 20 minutes are spent discussing parking, one or two trustees do all the talking, others check their PDAs or scribble on the agenda, and you try to keep your mouth shut while yawning. Hospital board meetings are often described as ritualized, unfocused, rambling, mindless, and inconclusive. Experts agree that board meetings in many hospitals are dysfunctional and need restructuring (Knecht 2001; Perrine 2003; Orlikoff and Totten 2002). Recently, St. Joseph Hospital in Orange, California, employed consultants and invested much effort in making its board meetings productive (Perrine). More such endeavors are needed for better hospital governance. In the last 5 years, several books and articles have focused on reforming board meetings. In this article I draw on them to discuss key problems of board meetings and how to make the meetings more effective.

Freye, E. and J. Levy (2005). "Constitutive opioid receptor activation: a prerequisite mechanism involved in acute opioid withdrawal." Addict Biol 10(2): 131-7.

The opioid receptor antagonist naltrexone, which is used in detoxification and rehabilitation programmes in opioid addicts, can precipitate opioid withdrawal symptoms even in patients who have no opioid present. We tested the hypothesis that in order to precipitate withdrawal, opioids need to convert the inactive opioid receptor site via protein kinase C into a constitutively active form on which the antagonist precipitates withdrawal. Acute microg/kg), given for 6 days, which was followed by the antagonist naltrexone (20 microg/kg i.v.) in the awake trained canine (n = 10). Abrupt displacement of opioid binding resulted in acute withdrawal symptoms: increase in blood pressure, heart rate, increase in amplitude height of somatosensory evoked potential, reduced tolerance to colon distention and a significant increase in grading of vegetative variables (restlessness, panting, thrashing of the head, whining, yawning, gnawing, salivation and/or rhinorrhoea, mydriasis, stepping of extremities and vomiting). Following a washout period of 14 days, the same animals were given the highly specific protein kinase C inhibitor H7 (250 microg/kg) prior to the same dosages of sufentanil and naltrexone. Such pretreatment was able to either attenuate or completely abolish the acute withdrawal symptoms. The data suggest that for precipitation of withdrawal, intracellular phosphorylation is a prerequisite in order to activate the opioid mu-receptor. In such a setting, naltrexone acts like an 'inverse agonist' relative to the action of the antagonist on a non-preoccupied receptor site not being exposed previously to a potent opioid agonist.

Fontenot, M. B., E. E. Padgett, 3rd, et al. (2005). "The effects of fluoxetine and buspirone on self-injurious and stereotypic behavior in adult male rhesus macaques." Comp Med 55(1): 67-74.

The effects of two serotonergic agents--fluoxetine, a serotonin (5-HT) reuptake inhibitor, and buspirone, a 5-HT 1a agonist--on rates of self-injurious and stereotypic behavior were examined in 15 adult male Macaca mulatta. All animals received a placebo for 2 weeks followed by either buspirone or fluoxetine for 12 weeks. Behavior was monitored using a focal sampling technique throughout the study and for 2 weeks post-study. Cerebrospinal fluid (CSF) samples and body weights were obtained pre-study, at the ends of placebo and treatment phases, and post-study. Fluoxetine and buspirone were significantly effective in reducing rates of self-biting during treatment weeks 1 to 8 and self-directed stereotypic behavior during weeks 5 to 12 and post-treatment. No significant effect of either treatment on hair-plucking, stereotypic pacing, saluting, or head tossing was identified. The duration of neutral behavior increased, and rates of scratching and yawning decreased in the buspirone-treated condition. In the fluoxetine-treated condition, rates of yawning, scratching, and self-directed grooming were higher overall compared with those of buspirone-treated animals, and rates of scratching increased significantly ($P < 0.05$) in weeks 9 to 12; these findings suggest that animals in the fluoxetine-treated condition experienced higher levels of anxiety throughout the study. In both treatment conditions, concentrations of CSF 5-HIAA (5-HT metabolite) were significantly lower ($P < 0.05$) than placebo concentrations. Fluoxetine and buspirone may be efficacious for treatment of self-injurious and self-directed stereotypic behavior in macaques. Further studies are required to determine the optimal dosages and treatment length.

Feldmann, H. (2005). "[Remarks concerning the article "Physiology, role and neuropharmacology of yawning" by U.R. Goessler et al. Laryngo-Rhino-Otol 2005;84:345-351]." Laryngorhinootologie 84(8): 608-9.

Elbers, A. R., G. Koch, et al. (2005). "Performance of clinical signs in poultry for the detection of outbreaks during the avian influenza A (H7N7) epidemic in The Netherlands in 2003." Avian Pathol 34(3): 181-7.

The aim of this study was to make an inventory of the clinical signs of high-pathogenicity avian influenza (HPAI), to facilitate the development of an operational syndrome-reporting system (SRS) in The Netherlands as an early warning system for HPAI outbreaks. A total of 537 poultry flocks (240 infected and 297 non-infected) with a clinical suspicion of an infection with HPAI virus were investigated with respect to the clinical signs observed. Standardized reports were analysed with respect to observed clinical signs in the flocks. Various poultry types were distinguished. In infected commercial flocks with egg-producing chickens, the presence of increased mortality, apathy, coughing, reduction in normal vocalization, or pale eggs appeared to be overall the most sensitive indicators to detect a HPAI outbreak, matching a sensitivity of 99% with a specificity of 23%. In infected turkey flocks, the presence of apathy, decreased growth performance, reduction of normal vocalization, swollen sinuses, yawning, huddling, mucosal production from the beak, or lying down with an extended neck appeared to be overall the most sensitive indicators to detect a HPAI outbreak, matching a sensitivity of 100% with a specificity of 79%. In infected backyard/hobby flocks, increased mortality or swollen head appeared to be overall the most sensitive indicators of a HPAI outbreak, matching a sensitivity of 100% with a specificity of 26%. These results indicate that there is a solid basis for the choice of using increased mortality in the operational SRS in The Netherlands as an early warning system for HPAI outbreaks. The presence of apathy,

specifically for turkeys, should be added to the SRS as an indicator.

Diaz-Romero, M., J. A. Arias-Montano, et al. (2005). "Enhanced binding of dopamine D(1) receptors in caudate-putamen subregions in High-Yawning Sprague-Dawley rats." Synapse 56(2): 69-73.

Previous reports have shown that the inbred High-Yawning (HY) and Low-Yawning (LY) rats differ in several behavioral characteristics related to mesolimbic and nigrostriatal dopamine (DA) function. To determine if differential expression of DA receptors or DA transporter may mediate the behavioral differences in these two sublines of the Sprague-Dawley rat, we performed a quantitative autoradiography study of the DA D(1)-like, D(2)-like, and DA-transporter binding in the basal ganglia and nucleus accumbens. The results show that levels of the D(1) binding in the caudate-putamen of the HY rat were higher than in the LY animals, whereas no significant differences in the DA D(2) receptors and DA transporter were noted in these sublines. These data suggest that the differences in DA receptors in D(1) binding in HY rats may in part have contributed to the behavioral differences related to DA functions such as grooming and penile erection. Our findings are consistent with previous reports showing a decrease in the behavioral responses after systemic administration of DA agonist in LY compared to HY rats. Synapse 56:69-73, 2005. (c) 2005 Wiley-Liss, Inc.

Di Martino, E., L. E. Walther, et al. (2005). "Endoscopic examination of the eustachian tube: a step-by-step approach." Otol Neurotol 26(6): 1112-7.

OBJECTIVE: The aim of this study was to develop a step-by-step approach for endoscopic examinations of the eustachian tube on awake patients and to report anatomic and functional findings. STUDY DESIGN: Prospective study. SETTING: University hospital. PATIENTS: Convenience sample of seven individuals without a history of ear disease. INTERVENTION: Diagnostic transnasal-transpharyngeal videoendoscopy of the eustachian tube with 30- and 70-degree rigid Hopkins rod endoscopes, 2.5- and 0.8-mm, 0-degree flexible fiber endoscopes performed under local anesthesia in 12 eustachian tubes. MAIN OUTCOME MEASURES: Utility of the various endoscopes for the diagnosis in the different parts of the eustachian tube; quality of vision and the patient's comfort during the procedure. RESULTS: The 2.5-mm flexible endoscope was most useful for examination of the pharyngeal ostium and the cartilaginous lumen of the tube. The isthmus region could only be passed using an 0.8-mm fiberscope. In all cases, it was possible to insert the endoscope into the middle ear cavity. Eleven of the 12 tube examinations showed normal findings. The mobility of the tubal cartilage could be visualized with sufficient quality. In 50% of all examinations, application of local anesthesia via a tube catheter was necessary to make the procedure tolerable. CONCLUSION: The presented approach allows an assessment of both anatomic and functional changes to the eustachian tube in awake patients. The assessment of middle ear structures is limited. To ensure a comfortable and safe procedure, the use of topical anesthesia in a supine position and, in certain cases, additional anesthesia via eustachian tube catheter is recommended.

Collins, G. T., J. M. Witkin, et al. (2005). "Dopamine agonist-induced yawning in rats: a dopamine D3 receptor-mediated behavior." J Pharmacol Exp Ther 314(1): 310-9.

A specific role for the dopamine D3 receptor in behavior has yet to be elucidated. We now report that dopamine D2/D3 agonists elicit dose-dependent yawning behavior in rats, resulting in an inverted U-shaped dose-response curve. A series of experiments was directed toward the hypothesis that the induction of yawning is a D3 receptor-mediated effect, whereas the inhibition of the yawning observed at higher doses is due to competing D2 receptor activity. We compared several dopaminergic agonists with a range of in vitro D3 selectivity, including PD-128,907 [(S)-(+)-(4aR, 10bR)-3,4,4a,10b-tetrahydro-4-propyl-2H,5H-[1]benzopyrano-[4,3-b]-1,4-oxaz in-9-ol HCl], PD-128,908 [(R)-(-)-(4aS, 10bS)-3,4,4a,10b-tetrahydro-4-propyl-2H,5H-[1]benzopyrano-[4 ,3-b]-1,4-oxazin-9-ol HCl], quinelorane [(5aR-trans)-5,5a,6,7,8, 9,9a,10-octahydro-6-propylpyrido[2,3-g]quinazolin-2-amine dihydrochloride], pramipexole (N'-propyl-4,5,6,7-tetrahydrobenzothiazole-2,6-diamine), 7-OH-DPAT [(+/-)-7-hydroxy-2-dipropylaminotetralin HBr], quinpirole [trans-(-)-(4aR)-4,4a,5,6,7,8, 8a,9-octahydro-5-propyl-1H-pyrazolo[3,4-g] quinoline HCl], bromocriptine [(+)-2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl) ergotaman-3',6'-18-trione methanesulfonate], and apomorphine [(R)-(-)-5,6,6a,7-tetrahydro-6-methyl-4H-dibenzo-[de,g]quinoline-10,11-dio l HCl] with respect to their ability to induce yawning in rats. A series of D2/D3 antagonists differing in selectivity for D3 over D2 receptors were evaluated for their ability to alter the effects of the dopamine agonists. The antagonists L-741,626 (3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]methyl-1H-indole), haloperidol (4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)-1-butan one HCl), nafadotride (N-[(1-butyl-2-pyrrolidinyl) methyl]-4-cyano-1-methoxy-2-naphtha-lenecarbox amide), U99194 (2,3-dihydro-5,6-dimethoxy-N,N-dipropyl-1H-inden-2-amine maleate), SB-277011A (trans-N-[4-[2-(6-cyano-1,2,3,4-tetrahydroisoquinolin-2-yl)ethyl]cyclohexy l]-4-quinolinecarboxamide), and PG01037 (N-{4-[4-(2,3-dichlorophenyl)-piperazin-1-yl]-trans-but-2-enyl}-4-pyridine -2-yl-benzamide HCl) were used to determine effects on dose-response curves for D2/D3 agonist-induced yawning. In addition, the potential contribution of cholinergic and/or serotonergic mechanisms to the yawning response was investigated using a series of pharmacological tools including scopolamine [(a,S)-a-(hydroxymethyl)benzeneacetic acid (1a,2b,4b,5a, 7b)-9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4]-non7-yl ester hydrobromide], mianserin (1,2,3,4,10,14b-hexahydro-2-methyldibenzo[c,f]pyrazino [1,2-a]azepine HCl), and the D3-preferring antagonists nafadotride, U99194, SB-277011A, and PG01037 to differentially modulate yawning induced by PD-128,907, physostigmine [(3aS)-cis-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethylpyrrolo[2,3-b]indol-5-o l methylcarbamate hemisulfate], and N-[3-(trifluoromethyl)phenyl]piperazine HCl. The results of these experiments provide convergent evidence that dopamine D2/D3 agonist-induced yawning is a D3 agonist-mediated behavior, with subsequent inhibition of yawning being driven by competing D2 agonist activity. Thus, dopamine agonist-induced yawning may represent an in vivo method for selectively identifying D3 and D2 receptor-mediated activities.

Collins, G. T., J. M. Witkin, et al. (2005). "Dopamine Agonist-Induced Yawning in Rats: A Dopamine D3 Receptor Mediated Behavior." J Pharmacol Exp Ther.

A specific role for the dopamine D3 receptor in behavior has yet to be elucidated. We now report that dopamine D2/D3 agonists elicit dose-dependent yawning behavior in rats, resulting in an inverted U-shaped dose-response curve. A series of experiments was directed toward the hypothesis that the induction of yawning is a D3 receptor mediated effect, while the inhibition of the yawning observed at higher doses is due to competing D2 receptor activity. We compared several dopaminergic agonists with a range of in vitro D3 selectivity, including; PD-128,907, PD-128,908, quinelorane, pramipexole, 7-OH-DPAT, quinpirole, bromocriptine, and apomorphine with respect to their ability to induce yawning in rats. A series of D2/D3 antagonists differing in selectivity for D3 over D2 receptors were evaluated for their ability to alter the effects of the dopamine agonists. The antagonists L-741,626, haloperidol, nafadotride, U99194, SB-277011A, and PG01037 were used to determine effects on dose-response curves for D2/D3 agonist-induced yawning. In addition, the potential contribution of cholinergic and/or serotonergic mechanisms to the yawning response was investigated using a series of pharmacological tools including scopolamine, mianserin, and the D3-preferring antagonists; nafadotride, U99194, SB-277011A, and PG01037 to differentially modulate yawning induced by the PD-128,907, physostigmine, and TFMPP. The results of these experiments provide convergent evidence that dopamine D2/D3 agonist-induced yawning is a D3 agonist mediated behavior, with subsequent inhibition of yawning being driven by competing D2 agonist activity. Thus, dopamine agonist-induced yawning may represent an in vivo method for selectively identifying D3 and D2 receptor-mediated activities.

Chudler, E. H. and M. R. Byers (2005). "Behavioural responses following tooth injury in rats." Arch Oral Biol 50(3): 333-40.

Early changes in spontaneous behaviour (exploration, grooming, freezing, rearing, jaw motion, yawning) and body weight were measured at two and three days after pulp exposure injury and implantation of Fluorogold (FG) into molar teeth of rats. Rats with FG and injuries to three teeth gained weight less rapidly, explored less frequently and froze more often than sham-operated rats. Yawning was not observed in any rats prior to surgery and it was seen more frequently in tooth-injured rats than in sham-operated rats. These results suggest that careful observation of spontaneous behaviour after tooth injuries can be used to assess dental pain in rats and may provide behavioural markers to correlate with anatomical changes after injury. The dental nerve cell bodies that had accumulated transported FG were medium to large, and they only co-localized calcitonin gene-related peptide (CGRP) in a subset of the medium neurons. Chromatolytic or moribund FG-labelled neurons were also found.

Cheng, T. O. (2005). "Yawning for an answer." Am J Cardiol 95(3): 437.

Chen, J. J. and C. Obering (2005). "A review of intermittent subcutaneous apomorphine injections for the rescue management of motor fluctuations associated with advanced Parkinson's disease." Clin Ther 27(11): 1710-24.

BACKGROUND: As Parkinson's disease (PD) progresses,despite optimized pharmacotherapy, patients experience more frequent fluctuations between symptomatic improvement ("on" times) and the return of motor features ("off" times). Apomorphine, the first injectable dopamine agonist available in the United States, is indicated for the acute treatment of "off" episodes (eg, end-of-dose wearing-off episodes, unpredictable "on/off" episodes) in patients with advanced PD who are receiving medically optimal antiparkinsonian therapy. OBJECTIVE: This article reviews the pharmacology,clinical efficacy, and tolerability of intermittent subcutaneous apomorphine injections for the management of "off" episodes in patients with PD. METHODS: MEDLINE (1966-July 2005), the Cochrane Database of Systematic Reviews, and International Pharmaceutical Abstracts (1970-July 2005) were searched for original research and review articles published in English. The search terms were apomorphine and Parkinson's disease. The reference lists of articles were also consulted, as was selected information provided by the manufacturer of apomorphine. All relevant identified studies on intermittent subcutaneous administration of apomorphine were included in the review; trials of continuous subcutaneous infusion and non-subcutaneous administration of apomorphine were excluded. RESULTS: Intermittent subcutaneous administration of apomorphine produced consistent rescue from "of" episodes in patients with advanced PD, with a symptomatic motor improvement between the predose "off" state and postdose "on" state similar to that achieved with levodopa. The onset of effect occurred within 20 minutes, and the duration of effect was approximately 100 minutes. The therapeutic rescue dose ranged from 2 to 6 mg. During the clinical development program for subcutaneously injected apomorphine, patients required a mean of approximately 3 rescue doses per day. Common adverse effects occurring in > or =20% of patients were injection-site reaction, yawning, dyskinesias, drowsiness, nausea and vomiting, dizziness or postural dizziness, and rhinorrhea. CONCLUSIONS: The available clinical studies indicate that apomorphine is effective in providing prompt and consistent rescue from "off" episodes in patients with PD. Antiemetic prophylaxis and close medical supervision are recommended when initiating apomorphine therapy.

Cattaneo, L., L. Cucurachi, et al. (2005). "Pathological yawning as a presenting symptom of brainstem ischemia in two patients." J Neurol Neurosurg Psychiatry.

Abstract We report two cases of brainstem stroke involving the upper pons and the ponto-mesencephalic junction, presenting with transient excessive pathological yawning, associated with gait ataxia and in one subject by upper limb and facial hemiparesis. In these patients we hypothesise a causal relationship between the brainstem lesion and pathological yawning, possibly related to denervation hypersensitivity of a putative brainstem center of yawn. Excessive yawning can be a heralding sign of brainstem ischemia.

Biswas, A. K., B. L. Feldman, et al. (2005). "Myocardial ischemia as a result of severe benzodiazepine and opioid withdrawal." Clin Toxicol (Phila) 43(3): 207-9.

Long-term infusion of benzodiazepines and opioids is strongly associated with dependence and withdrawal syndromes. We report the first case of severe benzodiazepine and opioid withdrawal resulting in transient myocardial ischemia. CASE REPORT: A 6-month-old female born at 25 weeks gestation with severe opioid and benzodiazepine dependence resulting from multiple operative procedures and chronic ventilatory support was receiving continuous intravenous infusion of fentanyl and midazolam after trials of enteral methadone and diazepam had been unsuccessful due to gastric intolerance. On postoperative day 5 following Nissen fundoplication and gastrostomy tube placement, she acutely developed tachycardia, hypertension, agitation, loose stools, and yawning. Attempts to provide boluses of benzodiazepines and opioids revealed a very sluggish port in her subclavian central venous catheter. Prompt replacement of the catheter occurred without complication. After resuming infusions and providing additional sedatives and opioids, the loose stools, yawning, and agitation resolved. However, the tachycardia persisted. A 12-lead ECG was notable for significant ST depression in anterior leads. Laboratory studies revealed significantly elevated cardiac enzymes. The patient was transfused with packed red blood cells to optimize oxygen-carrying capacity. Echocardiography demonstrated a small region of dyskinetic apical endocardium. Cardiac enzymes normalized within 48 h. The ECG and echocardiographic findings fully resolved after approximately 70 h. DISCUSSION: We believe that the sluggish central venous catheter port limited delivery of the midazolam and fentanyl to our patient. The resultant tachycardia and hypertension limited diastolic filling of the coronary arteries, resulting in myocardial ischemia. As the withdrawal was treated, heart rate and blood pressure returned to baseline, myocardial perfusion normalized, and the ST depression and the cardiac enzyme values normalized. This report underscores the significant morbidity associated with withdrawal syndromes and the need to recognize withdrawal early and to treat it aggressively.

Zarrindast, M. R., M. Sahebgharani, et al. (2004). "The effect of electroconvulsive shock seizures on behaviour induced by dopaminergic agonists and on immobility in the Porsolt test." Eur Neuropsychopharmacol 14(6): 509-14.

Male, Wistar rats were given a course of eight electroconvulsive shock seizures (ECS group) or matched handling (control group). They were then tested for locomotion and rearing (7 days post-ECS), for grooming and yawning (9 days post-ECS), and for immobility in the Porsolt test (7, 14 and 21 days post-ECS). Seven days post-seizure, the ECS group showed significantly more locomotion following intraperitoneal administration of apomorphine (0.2 mg/kg), but not following injections of amphetamine (1 mg/kg). Drug-induced rearing was not different in the ECS and control animals. Nine days post-seizure, the ECS group showed significantly more grooming induced by the D-1 dopamine receptor agonist, SKF 38393 (1 mg/kg), but no difference in the yawning induced by the D-2 dopamine receptor agonist, quinpirole (0.05 mg/kg). In the Porsolt test, immobility was decreased in the ECS animals at 7 and 14, but not at 21 days post-ECS. It is concluded that ECS increases activity in the dopaminergic systems of the rat brain for at least 1-2 weeks post-seizure. The beneficial effects of electroconvulsive therapy (ECT) may relate to these dopaminergic alterations.

Zarrindast, M. R., K. Nojoomi, et al. (2004). "Nitric oxide agents and apomorphine-induced rat behaviors." Pharmacology 71(4): 169-73.

BACKGROUND: Nitric oxide (NO) may alter dopamine release in the brain. Activation of D2-dopamine receptors may suppress NO synthase, and inhibition of NO synthase prevents behaviors induced by psychostimulants. We have investigated the modulatory actions of the precursor of NO synthesis (L-arginine) and the broad-spectrum NO synthesis inhibitor NG-nitro-L-arginine methyl ester (L-NAME) on apomorphine-induced behaviors in the rat. METHODS: Apomorphine was injected subcutaneously, and behaviors induced by the drug were examined in the presence or absence of intracerebroventricular administration of L-arginine and L-NAME. RESULTS: Our data indicate that L-arginine or L-NAME treatment decreased licking and yawning, but not penile erection induced by apomorphine. CONCLUSION: Apomorphine-induced behaviors may be modulated by NO levels.

Walusinski, O. and B. L. Deputte (2004). "[The phylogeny, ethology and nosology of yawning]." Rev Neurol (Paris) 160(11): 1011-21.

Charles Darwin would have said that yawning was a useless piece of physiology. If so, then how should the survival of this very stereotyped behavior among the poikilothermal and homoeothermic vertebrates, from the basic brained reptiles to human primates, whether in the air, on the land or in the sea be understand? This issue of the ethnological, neurophysiologic and neuropsychological literature depicts yawning as being associated with an alternation of "awake-sleep" rhythms, sexuality, and nutrition, where it appears as a reference behavior of the mechanisms stimulating the state of vigilance. In pharmacology, yawning is used as an indicator of dopamine-ocytocinergic pathway activity, but in the Parkinson patient the neurologist sees it as an expression of therapeutic dopaminergic activity. J.M. Charcot and his school considered yawning as a clinical sign, long since forgotten. However, many patients complain about excessive yawning. Iatrogenic causes are the most frequent and can be found among many neurological diseases: vasovagal syncope, migraine, epilepsy, hypophyseal tumor, or stroke. Our ability to achieve motor and emotional behavior in resonance with others is deeply rooted in hominid evolution, and probably explains the strange phenomenon of contagious yawning.

Waldinger, M. D., A. H. Zwinderman, et al. (2004). "On-demand treatment of premature ejaculation with clomipramine and paroxetine: a randomized, double-blind fixed-dose study with stopwatch assessment." Eur Urol 46(4): 510-5; discussion 516.

OBJECTIVE: To investigate the degree of ejaculation delay induced by on-demand treatment with 20 mg paroxetine and 25 mg clomipramine and to assess the type and severity of non-sexual side-effects of treatment at the day of and the day after treatment with these drugs. METHOD: A randomized, double-blind, fixed-dose, on-demand study in 30 men with lifelong premature ejaculation was performed. During a 1-month baseline period and a 4-week drug treatment period patients assessed the intravaginal ejaculation latency time (IELT) at home with a stopwatch. Only men with an IELT <1 min were randomly assigned to drug treatment. Patients assessed the drug coitus interval time (DCIT) and used the UKU side effect scale questionnaire at baseline, the day of and the day after intercourse. RESULTS: On-demand treatment with 25 mg clomipramine, with a mean DCIT of 5.14 h, led to a 4.05 (95%CI: 3.26-5.02) fold-increase of the IELT. On-demand treatment with 20 mg paroxetine, with a mean DCIT of 5.39 h, led to a 1.41 (95%CI: 1.22-1.63) fold-increase of the IELT. Both drugs had a high incidence of non-sexual side effects at the coitus day and the next day. At the day of coitus paroxetine led to significant sleepiness and yawning compared to clomipramine. At the day after coitus clomipramine induced significant nausea compared to paroxetine. CONCLUSION: On-demand treatment with 25 mg clomipramine led to a clinical relevant ejaculation delay. In contrast, 20 mg paroxetine had no clinical relevant ejaculation delay in men with lifelong premature ejaculation with an IELT of less than 1 minute. Both drugs exert mostly mild yet annoying non-sexual side effects both at the coitus day and the next day.

Moore, C. T., C. G. Wilson, et al. (2004). "A GABAergic inhibitory microcircuit controlling cholinergic outflow to the airways." J Appl Physiol 96(1): 260-70.

GABA is the main inhibitory neurotransmitter that participates in the regulation of cholinergic outflow to the airways. We have tested the hypothesis that a monosynaptic GABAergic circuit modulates the output of airway-related vagal preganglionic neurons (AVPNs) in the rostral nucleus ambiguus by using a dual-labeling electron microscopic method combining immunocytochemistry for glutamic acid decarboxylase (GAD) with retrograde tracing from the trachea. We also determined the effects of blockade of GABAA receptors on airway smooth muscle tone. The results showed that retrogradely labeled AVPNs received a significant GAD-immunoreactive (GAD-IR) terminal input. Out of a pooled total of 3,161 synaptic contacts with retrogradely labeled somatic and dendritic profiles, 20.2% were GAD-IR. GAD-IR terminals formed significantly more axosomatic synapses than axodendritic synapses ($P < 0.02$). A dense population of GABAergic synaptic contacts on AVPNs provides a morphological basis for potent physiological effects of GABA on the excitability of AVPNs. GAD-IR terminals formed exclusively symmetric synaptic specializations. GAD-IR terminals were significantly larger ($P < 0.05$) in both length and width than unlabeled terminals synapsing on AVPNs. Therefore, the structural characteristics of certain nerve terminals may be closely correlated with their function. Pharmacological blockade of GABAA receptors within the rostral nucleus ambiguus increased activity of putative AVPNs and airway smooth muscle tone. We conclude that a tonically active monosynaptic GABAergic circuit utilizing symmetric synapses regulates the discharge of AVPNs.

Lutz, C., S. Tiefenbacher, et al. (2004). "Extinction deficits in male rhesus macaques with a history of self-injurious behavior." Am J Primatol 63(2): 41-8.

Self-injurious behavior (SIB) occurs in both human and nonhuman primate populations. Despite the potential for harm, SIB may persist in part because of an inability to inhibit behavior that results in wounding. A lever-pressing task was used to test the prediction that monkeys with SIB would show greater persistence in lever-pressing on extinction trials than monkeys without the disorder. The subjects were 15 individually-housed adult male rhesus macaques, 10 of which (the SIB group) had a veterinary record of self-inflicted wounding. All of the monkeys were trained to lever-press for food rewards to a criterion of 400 total responses. The test procedures consisted of five daily 30-min sessions divided into six 5-min intervals. On day 1, the subjects received continuous reinforcement. On days 2-4, testing consisted of alternating reinforced/unreinforced 5-min intervals, beginning with reinforcement. Reinforced intervals were cued with a buzzer. On day 5, the subjects received no reinforcement. The number of lever-presses and behavioral responses were recorded during each session. Saliva samples were collected for cortisol measurement before and after test sessions on days 1, 2, and 5. As predicted, monkeys with SIB lever-pressed more than controls during extinction intervals on days 2-4. There was no difference on day 1 or day 5. The frequency of scratching, yawning, and abnormal behavior increased when reinforcement was intermittent (days 2-4) or absent (day 5). Cortisol levels were highest with continuous reinforcement (day 1), and may reflect differential levels of food intake rather than stress. The presence of extinction deficits suggests that SIB may persist in some monkeys because they lack the ability to regulate the intensity of their biting behavior.

Kurjak, A., M. Stanojevic, et al. (2004). "Behavioral pattern continuity from prenatal to postnatal life--a study by four-dimensional (4D) ultrasonography." J Perinat Med 32(4): 346-53.

AIM: To investigate whether the same behavioral patterns were present pre- and postnatally, and whether there were any differences in the frequency of movements observed in fetal and in early neonatal life. SUBJECTS AND METHODS: Ten out of 37 pregnant women in the third

trimester of pregnancy (median gestational age 34 weeks, range 33 to 35 weeks) in the two-month period (from November 1st to December 31st, 2003) were enrolled in the investigation. Ten term, appropriate for gestational age newborns (seven born vaginally, three by elective SC, six girls, six first-born) and were enrolled in the study. All 4D examinations were performed on Voluson 730 (Kretztechnik, Zipt, Austria) and Acuvix (Medison, Korea) with transabdominal 5 MHz transducer. After standard assessment in 2D B-mode ultrasound, a 4D mode was switched on and live 3D image was reconstructed by selecting the ideal representative 2D image placed in the region of interest (ROI). The recordings of neonatal behavior were made on the Sony P-612 OHMPL videotape by video camera (Sony Camcoder CC DTRV 318 Hv8) and reviewed on the videocassette recorder (Sony VHS SLV-N 900). The median of newborns' age at the moment of recording was 49 hours (range 4 to 112). During the examination, newborns were lying in the bed, separated from other infants in the nursery, dressed, and lying on their backs in a supine position with unrestrained hands. The temperature in the room was 22 to 24 degrees C. The video recording was performed mainly while the children were actively awake or during alert inactivity. RESULTS: There were no movements observed in fetal life that were not present in neonatal life, while the Moro reflex was present only in neonates. The most frequent fetal and neonatal movements were scowling, eye and mouth opening, and hand to face, hand to eye and hand to head movements. Isolated blinking, mouth to eyelid movement, yawning, tongue expulsion and scowling were more frequent in neonates than in fetuses, although the difference was not statistically significant. Hand to mouth movements were more frequent in neonatal than in fetal life while all other hand movements were less frequent in neonates than in fetuses, although the differences did not reach statistical significance. Spearman rank order correlation reached statistical significance in smiling (R=0.71; t=2.91; P=0.02) and in hand to ear movement (R = 0.80; t= 3.86; P = 0.005), and was almost statistically significant in isolated eye blinking (R=0.61; t=2.17; P =0.06), while the correlations between the rest of the movements were not statistically significant. CONCLUSIONS: 4D ultrasonography is a powerful tool in the assessment of fetal behavior, and our study showed that there is a continuity from fetal to neonatal behavior, especially in terms of isolated eye blinking movements, mouth and eyelid opening, yawning, tongue expulsion, smiling, scowling and hand movements directed to other parts of the face.

Krantz, M. J., J. K. Lee, et al. (2004). "Repetitive yawning associated with cardiac tamponade." Am J Cardiol 94(5): 701-2.

Yawning occurs frequently in daily life and is often attributed to boredom and fatigue. Rarely, it may be a symptom of serious underlying medical illness, primarily involving the central nervous system. We report a case of acute cardiac tamponade resulting from a large, malignant pericardial effusion. The patient manifested striking repetitive yawning that resolved immediately after pericardial drainage. An association between repetitive yawning and acute cardiac tamponade has not been previously described.

Kostrzewa, R. M., J. P. Kostrzewa, et al. (2004). "Dopamine D2 agonist priming in intact and dopamine-lesioned rats." Neurotox Res 6(6): 457-62.

Receptor priming is a recently discovered phenomenon by which receptor agonists produce abrupt and long-lived supersensitization of receptors. Induction of dopamine (DA) D2 receptor supersensitivity by the agonist quinpirole was discovered approximately 15 years ago, and was found to occur consistently if rats were treated repeatedly at daily or weekly or monthly intervals with low or high doses of quinpirole. In this review we summarize and discuss some of the major studies that underlie DA D2 receptor supersensitivity, describe behavioral processes that are known to be altered by DA D2 receptor supersensitivity, and discuss the importance of DA innervation on expression of enhanced behaviors. DA D2 receptor supersensitivity represents one of the neural mechanisms implicated in psychiatric disorders. Also, DA D2 receptor supersensitivity and increased DA D3 receptor expression are associated with motor dyskinesias, as in L-DOPA-treated Parkinson's disease patients. An understanding of receptor priming, a knowledge of the types of behavioral expression associated with DA D2 receptor supersensitivity, and an understanding of mechanisms associated with receptor supersensitization, can lead to improvements in the treatments of psychiatric and neurological disorders.

Koller, W. and M. Stacy (2004). "Other formulations and future considerations for apomorphine for subcutaneous injection therapy." Neurology 62(6 Suppl 4): S22-6.

This manuscript reviews apomorphine administration in formulations other than intermittent bolus injection, and comments on other potential uses for this unique compound. Continuous sc apomorphine therapy has been shown to alter peak-dose dyskinesia thresholds in advancing patients, and in some instances may replace all other anti-parkinson therapies. In general continuous infusion of sc apomorphine at a rate of 4 mg/h is well tolerated, and has been postulated to be equivalent to approximately 600 mg levodopa/day. This therapy is associated with skin complications, particularly nodule formation, and focal panniculitis is seen in more than 50% of subjects. Optimal dosages for intranasal apomorphine range from 2 to 5 mg per inhalation with benefit seen at 7.5 minutes and duration of effect of 45 to 55 minutes. Side effects included nasal irritation, vestibulitis, dyskinesias, yawning, and nausea. Comparison of 3 mg sc and 30 mg sublingual apomorphine in 9 Parkinson's disease subjects in a blinded cross-over trial found that the time to peak benefit was beyond 40 minutes with sl apomorphine, compared to 21 minutes in the sc preparation. Chronic use of the sublingual formulation was associated with severe stomatitis in half the subjects, and markedly limited the treatment. Rectal administration of apomorphine has been evaluated in limited, usually post-operative settings. Administration of a 200 mg apomorphine rectal suppository resulted in an average time to benefit of 32 minutes with an average duration of 195 minutes. Sedation, nausea and faintness were reported as side effects. Although the diagnostic confirmation potential of this agent has been questioned, the drug may have an important role in evaluating the potential for benefit in the deep brain stimulation surgical setting.

Jacome, D. E. (2004). "Extracephalic yawning pain." Cephalalgia 24(5): 411-3.

The aim of this study was to report on two patients with recurrent, paroxysmal, extracephalic pain triggered by yawning. Pain with yawning may occur in several conditions (secondary yawning pain) or develop in the absence of precipitating lesions (primary yawning pain). Primary yawning pain is normally of cephalic location. Methods used were clinical neurological examinations, magnetic resonance imaging of the brain, computerized head tomography, electroencephalogram, blink reflex studies and Panorex X-ray views of the skull. The first patient had intense right shoulder pain and brief apnea for 2 years triggered by yawning. The second patient had yawning pain referred to an area of the neck where a thyroid tumour (Hurthle cell carcinoma) was later found. Neither of the two patients could precipitate their pain with imitation of yawning and neither had evidence of Eagle syndrome. Only the second patient had a history of migraine. Yawning pain may have an extratrigeminal and extracephalic distribution. It rarely serves to identify a lesion underlying the area where the pain is perceived.

Farmer, P. and N. G. Campos (2004). "Rethinking medical ethics: a view from below." Developing World Bioeth 4(1): 17-41.

In this paper, we argue that lack of access to the fruits of modern medicine and the science that informs it is an important and neglected topic within bioethics and medical ethics. This is especially clear to those working in what are now termed 'resource-poor settings'- to those working, in plain language, among populations living in dire poverty. We draw on our experience with infectious diseases in some of the poorest communities in the world to interrogate the central imperatives of bioethics and medical ethics. AIDS, tuberculosis, and malaria are the three leading infectious killers of adults in the world today. Because each disease is treatable with already available therapies, the lack of access to medical care is widely perceived in heavily disease-burdened areas as constituting an ethical and moral dilemma. In settings in which research on these diseases are conducted but there is little in the way of therapy, there is much talk of first world diagnostics and third world therapeutics. Here we call for the 'resocialising' of ethics. To resocialise medical ethics will involve using the socialising disciplines to contextualise fully ethical dilemmas in settings of poverty and, a related gambit, the systematic participation of the destitute sick. Clinical research across steep gradients also needs to be linked with the interventions that are demanded by the poor and otherwise marginalised. We conclude that medical ethics must grapple more persistently with the growing problem posed by the yawning 'outcome gap' between rich and poor.

Eguibar, J. R., M. Barajas, et al. (2004). "Genotype-dependent effect of ACTH(1-24) on grooming and yawning in two inbred strains of rats." Neuropeptides 38(5): 283-8.

It has long been known that the intracerebroventricular administration of ACTH(1-24) increases the duration of grooming episodes and the frequency of yawning in rats. The objective of this study was to investigate in what way these episodes are prolonged and whether and to what extent genotype influences such effects. We compared the effect of increasing doses of intracerebroventricular injections of ACTH(1-24) on grooming and yawning in males of two inbred strains of Sprague-Dawley rats with distinct yawning frequency, high-yawning (HY) and low-yawning (LY). In LY rats the duration of grooming episodes increased, while in HY rats grooming episodes augmented both in number and duration. In LY rats the duration of grooming components increased likewise, in HY rats however, neither the number nor the duration of the components changed. The grooming rate in both strains of rats was slowed, though more so in LY than in HY rats. Yawning increased in LY rats but not in HY rats. We conclude therefore that ACTH(1-24) increases the duration of grooming episodes by slowing the grooming rate according to genotype, and may or may not alter the frequency of yawning.

Duncan, I., P. Fourie, et al. (2004). "Imaging of carotidynia." S Afr Med J 94(12): 957-9.

de Andres, I., M. Garzon, et al. (2004). "The brain stem but not forebrain independently supports morphine tolerance and withdrawal effects in cats." Behav Brain Res 148(1-2): 133-44.

We employed polygraphic recordings and behavioral measures to study the effects of chronic morphine use upon the isolated forebrain and the decerebrate animal in cats with a midbrain transection. Cats received morphine for 12 days, and 24 h recording sessions were conducted on days 1 and 11. For the decerebrate cat, the percent time of rapid eye movement (REM) sleep was reduced during the 24 h period on both days 1 and 11. However, the values on day 11 were consistently higher than the values on day 1. Other tolerance indicators were decreases in the number of early behavioral signs and in the onset delay for REM sleep, together with an increase in onset time for motor activation. After naloxone (day 12) all cats displayed "wet shakes," tachypnea and eye squinting, as well as either pyloerection, elevated tail, salivation, licking, micturition, and yawning. In the isolated forebrain, the percent time for waking increased through the first 18 h post-morphine on both days 1 and 11. Conversely, the duration of non-REM (NREM) sleep and of drowsiness decreased. But importantly, the duration of sleep-waking states did not vary between days 11 and 1, indicating absence of tolerance. Additionally, after naloxone, the isolated forebrain entered NREM sleep, contrasting with opposite findings in intact cats. Therefore, while we could not demonstrate chronic use effects in the isolated forebrain, the decerebrate cat still displayed typical tolerance/withdrawal manifestations. This suggests that the effects of chronic opiate use are deeply seated in the brain stem, which might help understanding the ingrained nature of physical

dependence.

Brown, R. W., K. D. Thompson, et al. (2004). "Adulthood nicotine treatment alleviates behavioural impairments in rats neonatally treated with quinpirole: possible roles of acetylcholine function and neurotrophic factor expression." Eur J Neurosci 19(6): 1634-42.
Increases in dopamine D(2) receptor sensitivity are known to be common in drug abuse and neurological disorders. Past data from this laboratory have shown that long-term increases in D(2) sensitivity can be produced by quinpirole treatment (a D(2)/D(3) agonist) during early development. The present investigation was designed to test the hypothesis that nicotine administration in adulthood would reduce both cognitive and skilled reaching impairments produced by increases in D(2) sensitivity. Female Sprague-Dawley rats were treated with quinpirole (1 mg/kg) or saline from postnatal day 1 (PD 1) to PD 21. Beginning in adulthood (PD 61), rats were treated with nicotine (0.3 mg/kg free base) or saline twice daily for 14 consecutive days before behavioural testing commenced. Animals neonatally treated with quinpirole demonstrated performance deficits on the Morris water task and a skilled reaching task compared to controls. Deficits on both tasks were completely alleviated by adulthood nicotine treatment. Animals neonatally treated with quinpirole demonstrated a significant 36% decrease of ChAT in the hippocampus compared to saline controls that was partially eliminated by nicotine. Additionally, neonatal quinpirole produced a significant decrease in hippocampal NGF content compared to controls, however, nicotine failed to alleviate this decrease in NGF. The results of this investigation demonstrate that long-term increases in dopamine D(2) receptor sensitivity produce significant decreases in hippocampal cholinergic and NGF expression that may result in cognitive impairment. Nicotine alleviates both cognitive and skilled reaching impairments caused by increases in D(2) sensitivity, but the mechanism through which nicotine is acting is currently unknown.

Bowron, A. (2004). "Practical considerations in the use of apomorphine injectable." Neurology 62(6 Suppl 4): S32-6.
This manuscript provides a practical summary of guidelines for institution of apomorphine subcutaneous injectable therapy, including patient education, pre-treatment issues, dosage titration and side-effect care. The timing of each injection is crucial if an impending "off" period is to be averted. Patients need to be aware of symptoms of an approaching "off" period, and the injection should be administered at the onset or ideally, in anticipation of an "off" episode. Patients being considered for apomorphine treatment should undergo pre-treatment assessment and optimization of ongoing oral therapy prior to initiation. Education and counseling regarding the benefits of apomorphine can often alleviate this. In addition, and where available, it is beneficial to provide the patient and caregiver(s) with additional written information and videos provided by the manufacturer demonstrating the operation of the pump or pen injection systems. Once a patient has been assessed as being a suitable candidate for apomorphine, an apomorphine challenge is performed to determine responsiveness and guide appropriate dosing, establish an individual dose, and to observe for side effects, such as nausea, postural hypotension, excessive somnolence, or dyskinesia. Three days prior to the challenge, domperidone 20 mg tid or trimethobenzamide (Tigan) 300 mg tid is recommended. Potential side effects include yawning, dopaminergic side effects, such as dyskinesias, nausea, orthostatic hypotension, confusion, hallucinations, somnolence and rarely, hypersexuality or other behavioral disturbances, and skin nodule formation.

Antoniou, K., G. Papathanasiou, et al. (2004). "Individual responses to novelty predict qualitative differences in d-amphetamine-induced open field but not reward-related behaviors in rats." Neuroscience 123(3): 613-23.
Differences in the locomotor response of rats to a novel environment (high responders [HR] versus low responders [LR]) have been associated with differences in vulnerability to psychostimulants. In the present study we profiled extensively the behavioral repertoire of HR and LR rats (differentiated on the basis of vertical activity) during exposure to a novel environment and in response to d-amphetamine (d-amp; 1.5 mg/kg, i.p.). Moreover, we ascertained whether HR and LR rats differ in the rewarding effects of medial forebrain bundle electrical self-stimulation and in the ability of d-amp to increase the reinforcing efficacy of self-stimulation. Apart from rearing, HR animals displayed increased moving, sniffing, but decreased standing and yawning compared with LR. Factor analysis revealed a more complex behavioral structure consisting of locomotion, exploration, vertical activity and self-directed behavior for HR compared with LR rats. Qualitative, but not quantitative differences, between the two groups of rats in their behavioral responses to d-amp were found. In particular, a more complex profile mainly characterized by self-directed behavior, locomotion and vertical activity was manifested for HR as compared with LR rats. Baseline brain stimulation reward thresholds did not differ between the two groups of rats. Additionally, brain stimulation reward thresholds for the two groups were not differentially affected by d-amp. The above results suggest that HR and LR can be further differentiated upon exposure to a novel environment and in response to d-amp. This differentiation is primarily based on qualitative cohorts of their behavioral structure, but not on deviations in the reward processes as assessed by intracranial self-stimulation.

Anias-Calderon, J., L. Verdugo-Diaz, et al. (2004). "Adrenalectomy and dexamethasone replacement on yawning behavior." Behav Brain Res 154 (1): 255-9.
Yawning, a phylogenetic behavior, present in reptiles, birds and mammals, has been studied for several decades, but to date its physiological function is still unknown. The role of stress as well as several peptides and the hypothalamus has been studied in relation to its regulation. To date however, no studies has been carried out to determine the role of the adrenal glands. Therefore, yawning behavior was studied in adrenalectomized rats, who then received dexamethasone replacement. The results show that rats whose adrenal glands were removed stopped both spontaneous and apomorphine-induced yawning, while dexamethasone reverted this effect. The results are discussed in terms of the possible role of corticosterone on yawning behavior.

Ang, H. H., K. L. Lee, et al. (2004). "Sexual arousal in sexually sluggish old male rats after oral administration of Eurycoma longifolia Jack." J Basic Clin Physiol Pharmacol 15(3-4): 303-9.
Eurycoma longifolia Jack commonly known as Tongkat Ali in Malaysia, has been used in Malaysia to increase male virility and sexual prowess. The objective of this study is to evaluate sexual arousal in sexually sluggish old male rats, 24 months old and retired breeders, receiving 200, 400, or 800 mg/kg of various fractions of E. longifolia Jack, twice daily, for 10 days. Control rats received 3 ml/kg of normal saline. The aphrodisiac effect was monitored by the act of yawning and stretching because yawning, either alone or associated with stretching, is considered an ancestral vestige surviving throughout evolution that promotes sexual arousal. The results showed that 800 mg/kg of E. longifolia Jack increased yawning by 50% and stretching by 16.7% in sexually sluggish old male rats, by 676-719% and 31-336%, respectively, in sexually active male rats, and by 22-44% and 75-100%, respectively, in middle aged, 9 months old and retired breeders. We conclude that the results of this study support the folk use of this plant as an aphrodisiac.

Anderson, J. R., M. Myowa-Yamakoshi, et al. (2004). "Contagious yawning in chimpanzees." Proc R Soc Lond B Biol Sci 271 Suppl 6: S468-70.
Six adult female chimpanzees were shown video scenes of chimpanzees repeatedly yawning or of chimpanzees showing open-mouth facial expressions that were not yawns. Two out of the six females showed significantly higher frequencies of yawning in response to yawn videos; no chimpanzees showed the inverse. Three infant chimpanzees that accompanied their mothers did not yawn at all. These data are highly reminiscent of the contagious yawning effects reported for humans. Contagious yawning is thought to be based on the capacity for empathy. Contagious yawning in chimpanzees provides further evidence that these apes may possess advanced self-awareness and empathic abilities.

Wessells, H., V. J. Hruby, et al. (2003). "Ac-Nle-c[Asp-His-DPhe-Arg-Trp-Lys]-NH2 induces penile erection via brain and spinal melanocortin receptors." Neuroscience 118(3): 755-62.
Penile erection induced by alpha-melanocyte-stimulating hormone and melanocortin receptors (MC-R) in areas of the spinal cord and periphery has not been demonstrated. To elucidate sites of the proerectile action of melanocortin peptides, in awake male rats we administered the MC-R agonist Ac-Nle-c[Asp-His-DPhe-Arg-Trp-Lys]-NH(2) (MT-II) i.c.v., intrathecal (i.th.) and i.v. and scored penile erection and yawning. Injection of the MC-R antagonist Ac-Nle-c[Asp-His-DNal(2')-Arg-Trp-Lys]-NH(2) (SHU-9119) i.c.v. or i.th. in combination with i.th. MT-II differentiated spinal from supraspinal effects. To exclude a site of action in the penis, we recorded intracavernous pressure responses to intracavernosal injection of MT-II in the anesthetized rat.I.c.v., i.th., and i.v. MT-II induced penile erections in a dose-dependent fashion. Yawning was observed with i.c.v. and i.v. MT-II, while spinal injection did not produce this behavior. Intrathecal delivery of MT-II to the lumbosacral spinal cord was more efficacious in inducing erections than i.c.v. or i.v. administration; SHU-9119 blocked the erectile responses to i.th. MT-II when injected i.th. but not i.c.v. Intracavernosal MT-II neither increased intracavernous pressure nor augmented neurostimulated erectile responses.We confirmed the central proerectile activity of MT-II and demonstrated that in addition to a site of action in the brain, the distal spinal cord contains melanocortin receptors that can initiate penile erection independent of higher centers. These results provide new insight into the central melanocortinergic pathways that mediate penile erection and may allow for more efficacious melanotropin-based therapy for erectile dysfunction.

Wessells, H., V. J. Hruby, et al. (2003). "MT-II induces penile erection via brain and spinal mechanisms." Ann N Y Acad Sci 994: 90-5.
alpha-Melanocyte-stimulating hormone induces penile erection via melanocortin (MC) receptors in areas surrounding the third ventricle, but spinal and peripheral mechanisms have not been demonstrated. We used pharmacological strategies to localize the site of the proerectile action of the melanocortin receptor agonist MT-II. We administered MT-II intracerebroventribularly (i.c.v.), intrathecally (i.th.), and intravenously (i.v.) and scored penile erection and yawning for 90 min in awake male rats. In some animals i.c.v. or i.th. SHU-9119 was injected 10 minutes before i.c.v. and i.th. MT-II to confirm the MC receptor action of the agonist and to distinguish spinal from supraspinal effects. To exclude a site of action in the penis, we recorded intracorporal pressure responses to intracavernosal injection of MT-II in the anesthetized rat. MT-II induced penile erections in a dose-dependent fashion, with optimal response at 1 microg for both i.c.v. and i.th. routes. Supraspinal MT-II-induced erections were completely suppressed by 1 microg SHU-9119 i.c.v. Yawning was observed with i.c.v. and i.v. MT-II, whereas spinal injection did not produce this behavior. SHU-9119 blocked the erectile responses to i.th. MT-II when injected i.th. but not i.c.v. Intracavernosal MT-II neither increased intracorporal pressure nor augmented neurostimulated erectile responses. The lumbosacral spinal cord contains MC receptors that can initiate penile erection independent of higher centers. We confirmed the supraspinal proerectile action of MT-II. These results provide insight into the central melanocortinergic pathways that mediate penile erection and may allow for more efficacious melanotropin-based therapy for erectile dysfunction.

Voog, U., P. Alstergren, et al. (2003). "Impact of temporomandibular joint pain on activities of daily living in patients with rheumatoid arthritis." Acta Odontol Scand 61(5): 278-82.
The aim of this study was to investigate the impact of temporomandibular joint (TMJ) pain on daily living in patients with

rheumatoid arthritis (RA) involving the TMJ. Nineteen patients (17 F, 2 M) with a median (IQR) age of 44 (23) years were included. A scale for the influence of TMJ pain/discomfort on the activities of daily living was used. TMJ resting pain and pain upon maximum mouth opening according to a visual analog scale as well as pressure pain threshold and tenderness to digital palpation of the TMJ were assessed. Blood samples were collected to measure the level of acute phase proteins. Activities of daily living were influenced in all patients at different levels. The impact on daily living by TMJ pain/discomfort was greatest on the performance of physical exercises and jaw movements, while it was smallest on the performance of hobbies and eating. Pain during maximum mouth opening and tenderness to digital palpation were correlated to difficulties with several activities such as to yawn and open the mouth wide, while pressure pain threshold was correlated with difficulties during eating, which confirms that the pain was located in the TMJ. In conclusion, this study indicates that pain/discomfort from the TMJ in patients with RA has a significant negative impact on activities of daily living.

Vickers, S. P., L. J. Webster, et al. (2003). "Preferential effects of the cannabinoid CB1 receptor antagonist, SR 141716, on food intake and body weight gain of obese (fa/fa) compared to lean Zucker rats." Psychopharmacology (Berl) 167(1): 103-11.
RATIONALE: The selective CB(1) receptor antagonist, SR 141716, has been demonstrated to reduce food consumption in a range of animal species. OBJECTIVE: To assess the effect of chronic administration of SR 141716 on body weight and ingestive behaviour of lean and obese (fa/fa) Zucker rats. METHODS: Lean and obese Zucker rats were orally dosed with SR 141716 (3, 10, 30 mg/kg PO), sibutramine (5 mg/kg PO) or vehicle for one week. Pair-fed controls provided insight as to whether the effect of SR 141716 on body weight was attributable to drug-induced hypophagia. Subsequently, the effect of chronic oral administration of SR 141716 (1, 3, 10 mg/kg) was assessed for 28 days. At the end of this period, all animals were given vehicle for 14 days. The incidence of wet-dog shakes, yawning, scratching, and grooming behaviours, was assessed after acute administration and at weekly intervals thereafter for 4 weeks. RESULTS: SR 141716 dose-dependently decreased food intake and body weight gain in both lean and obese animals. The inhibition of food intake and body weight gain was greater in obese Zuckers than in lean Zucker controls. Changes in the body weights of pair-fed controls closely paralleled those of their drug-treated counterparts. Chronic 28-day treatment led to a maintained reduction of body weight gain. Withdrawal of SR 141716 on day 28 resulted in rebound hyperphagia and a significant weight gain. On acute administration, SR 141716 dose-dependently induced motor behaviours that showed tolerance upon repeated administration. CONCLUSION: These data indicate that chronic oral treatment with SR 141716 significantly reduces the food intake and body weight gain of obese and lean Zucker rats, an effect that is greater in obese animals and reversible upon drug withdrawal.

Topper, R., M. Mull, et al. (2003). "Involuntary stretching during yawning in patients with pyramidal tract lesions: further evidence for the existence of an independent emotional motor system." Eur J Neurol 10(5): 495-9.
A variety of associated movements have been described in patients with pyramidal tract lesions. We report three patients in whom involuntary stretching of an otherwise plegic arm could be observed during yawning. These patients had radiologically verified lesions at different levels of the pyramidal tract. As yawning and stretching are an automatic behavioural pattern in animals, it is likely that stretches during yawning in man are also an automatic motor pattern, usually inhibited in the presence of an intact corticospinal tract. The physiological function of yawning is unclear at present. Yawning might be the somatomotor manifestation of a particular emotional state characterized by boredom and fatigue. Our observation that movements of an otherwise plegic arm occur in patients with pyramidal tract lesions supports therefore the concept of an emotional motor system which has an independent input to motoneurones in the brain stem and the spinal cord.

Titze, I. R., C. C. Bergan, et al. (2003). "Source and filter adjustments affecting the perception of the vocal qualities twang and yawn." Logoped Phoniatr Vocol 28(4): 147-55.
Two vocal qualities, twang and yawn, were synthesized and rated perceptually. The stimuli consisted of synthesized vocal productions of a sentence-length utterance 'ya ya ya ya ya,' which had speech-like intonation. In a continuum transformation from normal to twang, the area in the pharynx was gradually decreased, along with vocal tract shortening and a decreased open quotient in the glottal airflow. In a continuum transformation toward yawn, the area in the pharynx was gradually increased, along with vocal tract lengthening and an increased open quotient. The normal (untransformed) vocal tract area was pre-determined by earlier studies involving MRI scans of a human subject's vocal tract. Listeners were asked to rate (on a scale from 1-10) the 'amount of twang' in one listening session and the 'amount of yawn' in another listening session. Overall, the perception of twang increased directly with pharyngeal area narrowing, vocal tract shortening, and decreased open quotient. The perception of yawn increased with pharyngeal area widening, vocal tract lengthening, and increased open quotient. Adjustments of one parameter alone yielded less significant perceptual changes than the above combinations, with open quotient showing the greatest effect in isolation. Listeners demonstrated variable perceptions in both continua with poor inter-subject, intra-subject, and inter-group reliability.

Svensson, P., B. E. Cairns, et al. (2003). "Injection of nerve growth factor into human masseter muscle evokes long-lasting mechanical allodynia and hyperalgesia." Pain 104(1-2): 241-7.
Nerve growth factor (NGF) is a neurotrophic protein with a pivotal role in development and maintenance of the nervous system on one side and inflammatory and neuropathic pain states on the other. NGF causes clear signs of behavioral hyperalgesia in animal models and following intradermal and systemic administration in humans. The present double-blinded, placebo-controlled study was designed to test quantitatively the effect and duration (1h, 1, 7, 14, 21 and 28 days) of NGF (5 microg in 0.2 ml) injected into the masseter muscle. Pressure pain thresholds (PPT) and pressure tolerance thresholds (PTOL) were used as indices of mechanical allodynia and hyperalgesia in the jaw-closing muscles. In addition, perceived pain intensity was assessed by the subjects on a 0-10 numerical rating scale (NRS) with the jaw at rest and in relation to various oral functions (chewing, yawning, talking, swallowing, drinking and smiling). Repeated measures analysis of variance (ANOVA) was used to test for significant effects. Injection of NGF into the masseter muscle was associated with significantly reduced PPT for 7 days (ANOVA: $P<0.001$) and PTOL for 1 day ($P<0.001$). Buffered isotonic saline injections into the masseter muscle also significantly lowered the PPT after 1 day but to a significantly smaller extent than the NGF injections ($P<0.001$) and isotonic saline had no significant effects on PTOL. In contrast, assessment of PPT and PTOL in the non-injected temporalis muscles demonstrated a significant increase after 14-28 days ($P<0.001$), which may have reflected an adaptation to the test procedure. NRS scores of chewing and yawning were significantly increased for 7 days following NGF injection ($P<0.001$). Systemic adverse effects were noted in one subject who reported fever and slight discomfort about 8h after the NGF injection. In conclusion, this is the first study to show that injection of NGF into the human masseter muscle causes local signs of mechanical allodynia and hyperalgesia that persist for at least 7 days as well as pain during strenuous jaw movement. The present pain model is safe and may be used to gain further insight into the neurobiological mechanisms of muscle pain and sensitization.

Sobrian, S. K., B. L. Jones, et al. (2003). "Behavioral response profiles following drug challenge with dopamine receptor subtype agonists and antagonists in developing rat." Neurotoxicol Teratol 25(3): 311-28.
As part of an investigation into the effects of gestational ethanol (ETOH) exposure on the developing dopamine (DA) system, pregnant Sprague-Dawley rats were exposed to one of three conditions: ETOH, pair-fed (PF) to the ETOH group, or ad libitum lab chow controls (LC). In this paper we report behavioral drug challenge effects for offspring of the two control groups (PF and LC). Male and female pups between postnatal days (PNDs) 21 and 23 in age were exposed to one of three intraperitoneal/subcutaneous doses of one of eight drugs chosen to assess the functional status of the DA D(1), D(2), and D(3) receptor subtype, or a saline control. Agonists were SKF 38393, apomorphine (APO), quinpirole (QUIN), and 7-hydroxy-N,N-di-n-propyl-2-amino-tetralin [7-OH-DPAT (DPAT)]; antagonists were spiperone (SPIP), SCH 23390, and two recently developed D(3) antagonists nafadotride (NAF) and PD 152255. Immediately following drug injection, pups were placed in observation cages, where eight behaviors (square entries, grooming, circling, rearing, sniffing, head and oral movements, and yawning) were scored at 3-min intervals for 30 min. Classic behavioral profiles were generally obtained for the high-dose mixed agonists APO, DPAT, and QUIN, which potently increased square entries, rearing, and sniffing, while reducing grooming and head movements. However, low-dose APO had no effect on behavior. The D(1) agonist, SKF 38393, had a strikingly different behavioral profile; it had no effect on square entries at any dose, while increasing grooming and sniffing at the medium dose. The D(1) antagonist, SCH 23390, profoundly decreased all behaviors except oral and head movements, especially at high doses. In contrast, the effects of the D(2) antagonist, SPIP, were limited to increasing sniffing at the medium dose. The two putative D(3) antagonists, NAF and PD 152255, presented strikingly different profiles. NAF induced a pattern of behavioral suppression that resembled the profile of high-dose SCH, while high-dose PD 152255 stimulated behavior. The failure of low-dose APO to have any effect on behavior suggests that the D(2) autoreceptor is not functional in preweanling rats. This hypothesis is further supported by the lack of behavioral suppression seen with low-dose QUIN and DPAT. Failure of NAF to produce behavioral activation at low doses and the stimulatory effects seen with PD 152255 suggests that either the D(3) autoreceptor, the postsynaptic D(3) receptor, or both are not fully functional at this age as well.

Seki, Y., Y. Nakatani, et al. (2003). "Light induces cortical activation and yawning in rats." Behav Brain Res 140(1-2): 65-73.
We examined the effects of light stimulation on cortical activation and yawning response in anesthetized, spontaneously breathing rats. Cortical activation was assessed by means of an electrocorticogram (ECoG) and yawning response was evaluated by monitoring an intercostal electromyogram as an index of inspiratory activity and a digastric electromyogram as an indicator of mouth opening. Light stimulation elicited an arousal shift in the ECoG to faster rhythms. This arousal response was followed by a single large inspiration with mouth opening, i.e. a yawning response. Higher light intensity significantly reduced the onset latency of the arousal/yawning response. Pretreatment with pyrilamine, an H1-histamine receptor antagonist, injected into the lateral ventricle blocked both the cortical activation and the yawning response induced by light stimulation, suggesting a role of brain histaminergic neurotransmission in modulating the light-induced arousal/yawning responses.

Platek, S. M., S. R. Critton, et al. (2003). "Contagious yawning: the role of self-awareness and mental state attribution." Brain Res Cogn Brain Res 17(2): 223-7.
Contagious yawning is a common, but poorly understood phenomenon. We hypothesized that contagious yawning is part of a more general phenomenon known as mental state attribution (i.e. the ability to inferentially model the mental states of others). To test this hypothesis we compared susceptibility to contagiously yawn with performance on a self-face recognition task, several theory of mind stories, and on a

measure of schizotypal personality traits. Consistent with the hypothesis, susceptibility to contagiously yawn was positively related to performance on self-face recognition and faux pas theory of mind stories, and negatively related to schizotypal personality traits. These data suggest that contagious yawning may be associated with empathic aspects of mental state attribution and are negatively affected by increases in schizotypal personality traits much like other self-processing related tasks.

Pae, C. U., J. J. Kim, et al. (2003). "Injured temporomandibular joint associated with fluoxetine-monotherapy-induced repeated yawning." Gen Hosp Psychiatry 25(3): 217-8.

Nasello, A. G., A. S. Sassatani, et al. (2003). "Modulation by sudden darkness of apomorphine-induced behavioral responses." Physiol Behav 78(4-5): 521-8.

Sudden darkness increases motor activity and decreases anxiety. In the present study, we focused on the role of dopaminergic mechanisms involved in the effects of sudden darkness. The influence of sudden darkness on the behavioral effects of low (0.05 and 0.1 mg/kg) and high (0.25, 0.45 and 0.6 mg/kg) doses of apomorphine (APO) was tested. We assayed the effects of low APO doses on yawning-penile erection syndrome (YES; 0.05 and 0.1 mg/kg) and on motor activity (0.05 mg/kg), and the effects of high APO doses on motor activity (0.25 mg/kg) and stereotyped behavior (0.45 mg/kg and 0.6 mg/kg). Spontaneous total and genital grooming of male and female rats were also recorded. Sudden darkness modified some spontaneous behaviors and also modulated several APO-induced behavioral effects. It increased spontaneous total grooming and genital grooming in male rats but had no effect on these parameters in female rats. These results show sexual dimorphism for total and genital grooming in both control and sudden darkness conditions. APO was able to induce YES in a dose-dependent manner. Sudden darkness decreased yawning elicited by both 0.05 and 0.1 mg/kg of the drug. No other parameter of YES was modified. In the open-field test, sudden darkness increased total locomotion and rearing and decreased immobility duration. APO at a dose of 0.05 mg/kg had the opposite effect on these parameters under light conditions; none of them were modified by sudden darkness. Animals treated with APO at 0.25 mg/kg, a dose that augmented total locomotion and rearing and diminished immobility duration, were clearly divided into two groups according to their responses, i.e., hypo- and hyper-responsive rats. Sudden darkness improved total locomotion and rearing, reduced immobility duration and total grooming in the hyporesponsive group, and showed no effects on the hyper-responsive group. Sudden darkness caused no modifications of stereotyped behavior. These results may be due to a sudden darkness-induced physiological release of dopamine that diminishes pre-synaptic responses to APO and increases low-intensity post-synaptic responses such as motor activity without modifying high-intensity post-synaptic responses such as stereotyped behavior.

Muchnik, S., S. Finkielman, et al. (2003). "[Yawning and temporal lobe epilepsy]." Medicina (B Aires) 63(2): 137-9.

Temporal lobe epilepsy is a partial epileptic disorder in which mesial structures are responsible for the principal ictal symptoms. Its characteristic feature is the recurrence of simple and complex partial seizures, associated with postictal confusion and amnesia of the event. The facilitating effect of NREM sleep on the propagation of the seizure, as well as the sleep abnormalities provoked by epilepsy were evident in our two patients. Yawning is a physiological reflex induced by arousal and drowsiness and may appear in different neurological conditions. Its relation with epilepsy of limbic origin has been rarely reported. We describe in a 95 year old male patient, the occurrence of yawning followed by complex partial seizure during a state of drowsiness. His EEG showed independent bilateral interictal foci of temporal sharp waves and after being medicated with carbamazepine 400 mg/day, the episode did not recur. Another patient, a 17 year old female, displayed complex partial seizures and secondarily generalized seizures with yawning during the posictal period, after naps. The EEG was normal and her polysomnography showed bilateral synchronous temporal spikes and slow waves with secondarily generalization during stage 2 of NREM sleep that produce paroxysmal microarousals and increased stages 1 and 2 of NREM sleep and REM sleep diminished. After being medicated with divalproex sodium 750 mg/day, she suffered no further seizures. Temporal lobe epilepsy, sleep-wake cycles and yawning seem not only to share the same anatomic structures but also the same neurochemical mechanisms. The fact that endogenous opiods are considered as part of a protective system that stop and prevent seizures may allow us to postulate that yawning would be the expression of the endogenous opiods induced mechanisms that stop and prevent the recurrence of the temporal lobe epilepsy. Another hypothesis may be that this is only a particular form of temporal lobe epilepsy.

Muchnik, S., S. Finkielman, et al. (2003). "[Yawning]." Medicina (B Aires) 63(3): 229-32.

Yawning is a normal reflex triggered by arousal, drowsiness, boredom, hunger and emotional conditions and it is associated to several neurological diseases and drug abuse. Its wide presence in the phylogenetic vertebrate scale and even in human fetuses as young as 12 weeks directed the search for the common anatomic and biochemical mechanisms involved. The demonstration that yawning is not connected with high CO2 or low O2 blood levels left aside a prevalent metabolic hypothesis. Its close relationship with the sleep-wake cycle, specially in moments previous to falling asleep and after awaking has been related to changes in personal situation and activity. A single component of this reflex which is to be found exclusively in humans, is the fact that yawning is contagious. Thus, it is considered a component of the adaptative mechanism that is part of the surveillance reflex, becoming a significant paralinguistic evolutive expression aimed at protection and social cohesion. The common anatomical structures and neurochemical systems taking part in yawning, the sleep-wake cycle and the temporal lobe epilepsy may imply that yawning results from a set of protective systems induced by endogenous opiods which intervene in the inhibition and prevention of the temporal lobe epileptic seizures.

Malik, R., P. Zunino, et al. (2003). "Complete heart block associated with lupus in a dog." Aust Vet J 81(7): 398-401.

A 5-year-old Poodle-cross was initially presented for exercise intolerance and difficulty in chewing and yawning. Some months later it acutely developed lethargy referable to complete heart block. Further investigations before and after permanent pacemaker implantation demonstrated Coombs-positive immune-mediated haemolytic anaemia, presumptive masticatory myositis and hypoadrenocorticism, suggesting the possibility of multisystem auto-immune disease. A diagnosis of systemic lupus erythematosus (SLE) was made based on these findings and a positive anti-nuclear antibody titre. It was thought that immune-mediated destruction of cardiac conduction tissues was responsible for the development of atrioventricular conduction block. Glucocorticoid deficiency was corrected using cortisone replacement therapy. SLE was controlled successfully for 10 months using azathioprine monotherapy until signs, subsequently shown to be due to subacute bacterial endocarditis, resulted in the death of the patient. Lupus should be considered as a potential underlying aetiology in dogs that develop heart block.

Lindner, M. D., D. B. Hodges, Jr., et al. (2003). "An assessment of the effects of serotonin 6 (5-HT6) receptor antagonists in rodent models of learning." J Pharmacol Exp Ther 307(2): 682-91.

Antagonists of serotonin 6 (5-HT6) receptors have been reported to enhance cognition in animal models of learning, although this finding has not been universal. We have assessed the therapeutic potential of the specific 5-HT6 receptor antagonists 4-amino-N-(2,6-bis-methylamino-pyrimidin-4-yl)-benzenesulfonamide (Ro 04-6790) and 5-chloro-N-(4-methoxy-3-piperazin-1-yl-phenyl)-3-methyl-2-benzothiophenesulfonamide (SB-271046) in rodent models of cognitive function. Although mice express the 5-HT6 receptor and the function of this receptor has been investigated in mice, all reports of activity with 5-HT6 receptor antagonists have used rat models. In the present study, receptor binding revealed that the pharmacological properties of the mouse receptor are different from the rat and human receptor: Ro 04-6790 does not bind to the mouse 5-HT6 receptor, so all in vivo testing included in the present report was conducted in rats. We replicated previous reports that 5-HT6 receptor antagonists produce a stretching syndrome previously shown to be mediated through cholinergic mechanisms, but Ro 04-6790 and SB-271046 failed to attenuate scopolamine-induced deficits in a test of contextual fear conditioning. We also failed to replicate the significant effects reported previously in both an autoshaping task and in a version of the Morris water maze. The results of our experiments are not consistent with previous reports that suggested that 5-HT6 antagonists might have therapeutic potential for cognitive disorders.

Kurjak, A., G. Azumendi, et al. (2003). "Fetal hand movements and facial expression in normal pregnancy studied by four-dimensional sonography." J Perinat Med 31(6): 496-508.

AIM: To evaluate the developmental pattern of fetal hand movements and facial activity and expression during the second and third trimester of pregnancy by four-dimensional ultrasound (4D-US). SUBJECTS AND METHODS: A total of 25 fetuses in uncomplicated pregnancies were analyzed; 15 fetuses at 13 to 16 weeks and 10 fetuses at 30 to 33 weeks of gestation were studied with abdominal 4D-US. After standard assessment in two dimensional (2D) real-time B mode, a 4D mode was switched on. Further examination lasted a maximum of 15 minutes. RESULTS: Isolated hand movement and subtypes of hand movements were easily recognized by 4D-US. The sub-types of hand to head movement are: hand to head, hand to mouth, hand near mouth, hand to face, hand near face, hand to eye and hand to ear. All subtypes of hand to head movement can be seen from 13 weeks of gestation, with fluctuating incidence. Facial activities and different forms of expression are easily recognized by 4D-US. Among these, two types can be easily differentiated: smiling and scowling. CONCLUSIONS: 4D-US is superior over real-time two-dimensional ultrasound (2D-US) for qualitative, but inferior for quantitative analysis of hand movements. Thus 4D-US makes it possible to determine exactly the direction of the fetal hand, but the exact number of each type of hand movements can still not be determined. 4D-US is superior over two- and three-dimensional sonography in the evaluation of complex facial activity and expression. Among facial activities observed by 4D-US, simultaneous eyelid and mouthing movements dominate between 30 and 33 weeks of gestation. Pure mouth movements such as mouth opening, tongue expulsion, yawning and pouting are present, but at a significantly lower incidence. Facial expressions such as smiling and scowling can be precisely observed using 4D-US.

Krasnianski, M., C. Gaul, et al. (2003). "Yawning despite trismus in a patient with locked-in syndrome caused by a thrombosed megadolichobasilar artery." Clin Neurol Neurosurg 106(1): 44-6.

We report a 62-year-old woman with a locked-in syndrome with bilateral masticatory spasms and persistent trismus, who was still able to yawn. A vascular malformation of the basilar artery-megadolichobasilar artery (fusiform aneurysm, vertebrobasilar dolichoectasia) was determined to be the underlying cause of this rare combination of symptoms. A thrombus in the megadolichobasilaris as well as an almost total pontine infarction were demonstrated on CT- and MRI-scans. Thus, trismus may be associated with locked-in syndrome due to megadolichobasilar artery thrombus, although yawning is still possible.

Holditch-Davis, D., D. H. Brandon, et al. (2003). "Development of behaviors in preterm infants: relation to sleeping and waking." Nurs Res

52(5): 307-17.
BACKGROUND: Although nurse clinicians and researchers use infant behaviors to indicate the responses of preterm infant to stimulation, little is known about how the biological factors of development, sleeping and waking states, infant characteristics, and infant illness severity affect preterm infant behaviors. OBJECTIVE: This study examined the development of eight infant behaviors over the preterm period and determined the relation of these behaviors to sleeping and waking and to infant characteristics and illness severity. METHODS: Seventy-one preterm infants were observed once per week from 7:00 p.m. to 11:00 p.m. from the time they were no longer critical until term or discharge. The occurrence of four sleep-wake states and eight behaviors were recorded every 10 seconds during the observations. RESULTS: Negative facial expressions increased over the preterm period; sighs, startle/jerks, jitters, and the likelihood of having hiccups decreased. Infant characteristics had only minor effects: boys had more negative facial expressions, and longer mechanical ventilation was associated with more sighs and jitters. All behaviors showed state-related differences in frequency. In addition, only startle/jerks and jitters showed the same developmental patterns within each state. CONCLUSIONS: Significant development of infant behaviors occurs over the preterm period but involves changes not only in the absolute percentage of each behavior but also in the percentages within each sleeping and waking state. Thus, preterm infant behaviors cannot be used clinically for assessment without consideration of the state in which they occur.

Grabczewska, Z., Z. Orzalkiewicz, et al. (2003). "[Yawning as a prodromal sign of vaso-vagal reaction]." Pol Merkuriusz Lek 14(79): 94.

Giffin, N. J., L. Ruggiero, et al. (2003). "Premonitory symptoms in migraine: an electronic diary study." Neurology 60(6): 935-40.
BACKGROUND: Migraine is frequently associated with nonheadache symptoms before, during, and after the headache. Premonitory symptoms occurring before the attack have not been rigorously studied. Should these symptoms accurately predict headache, there are considerable implications for the pathophysiology and management of migraine. METHODS: Electronic diaries were used in a 3-month multicenter study to record nonheadache symptoms before, during, and after migraine. The authors recruited subjects who reported nonheadache symptoms in at least two of three attacks that they believed predicted headache. Symptoms were entered in the diaries by patient initiation and through prompted entries at random times daily. Entries could not be altered retrospectively. Data recorded included nonheadache symptoms occurring during all three phases of the migraine, prediction of the attack from premonitory symptoms, general state of health, and action taken to prevent the headache. RESULTS: One hundred twenty patients were recruited: 97 provided usable data. Patients correctly predicted migraine headaches from 72% of diary entries with premonitory symptoms. A range of cognitive and physical symptoms was reported at a similar rate through all three phases of the migraine. The most common premonitory symptoms were feeling tired and weary (72% of attacks with warning features), having difficulty concentrating (51%), and a stiff neck (50%). Subjects who functioned poorly in the premonitory phase were the most likely to correctly predict headache. CONCLUSIONS: Using an electronic diary system, the authors show that migraineurs who report premonitory symptoms can accurately predict the full-blown headache.

Ficca, G. and P. Salzarulo (2003). "[Yawning: a facial signal]." Kos(212): 22-5.

Eguibar, J. R., J. C. Romero-Carbente, et al. (2003). "Behavioral differences between selectively bred rats: D1 versus D2 receptors in yawning and grooming." Pharmacol Biochem Behav 74(4): 827-32.
We used SKF 38393 and quinpirole for determining whether activation of D(1) and D(2) receptors, respectively, is involved in behaviors of rats selectively bred for high or low rates of yawning. After injection of SKF 38393, yawning diminished more markedly in high-yawning (HY) than in low-yawning (LY) rats, whereas this drug increased the number and duration of grooming episodes similarly in both strains. After injection of quinpirole, yawning increased more markedly in HY than in LY rats, whereas this drug decreased the number and duration of grooming episodes similarly in both rat strains. After coadministration of SKF 38393 and quinpirole, yawning increased similarly in both rat strains, whereas the combination of drugs failed to reliably affect grooming behavior. We interpret our findings as indicating that D(2) receptors are more important than D(1) receptors for differences in yawning behavior between HY and LY rats.

Derouesne, C. (2003). "[Theory of mind, empathy and...yawning]." Psychol Neuropsychiatr Vieil 1(4): 286-7.

da Silva, G. E., M. S. Fernandes, et al. (2003). "Potentiation of penile erection and yawning responses to apomorphine by cannabinoid receptor antagonist in rats." Neurosci Lett 349(1): 49-52.
The effect of systemic administration of the cannabinoid antagonist SR 141716A (N-(piperidin-1-yl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazole-3-carboxyamide) on penile erection and yawning induced by apomorphine was investigated in rats. SR 141716A (2 mg/kg, i.p.) administered 40 min before apomorphine (40 and 80 microg/kg, s.c.) increased the number of penile erection and yawning responses. The administration of cannabinoid agonist Delta9-tetrahydrocannabinol (1.25 mg/kg, i.p.) 15 min before apomorphine (40 and 80 microg/kg, s.c.) did not affect penile erection, however it decreased yawning. The present results provide additional evidence that cannabinoid agonists interfere with dopaminergic systems and that SR 141716A together with a dopaminergic agonist could be useful to potentiate dopaminergic activity.

Choy, C. K., P. Cho, et al. (2003). "Reflex tear ascorbate in Hong Kong Chinese subjects: method comparison and biological variation." Optom Vis Sci 80(9): 632-6.
BACKGROUND: Tear ascorbate is important for corneal health. A rapid and simple method for measurement of ascorbate in tears is needed, and adequate knowledge of physiological variation of tear ascorbate is important to facilitate comparative studies of the effect of, for example, contact lens wear and environmental conditions and stresses. However, there are currently no data on physiological variation of tear ascorbate. This study validated a simple and speedy method for tear ascorbate and investigated between-eye and between-day variation in tear ascorbate in healthy young adults. METHODS: Yawn-induced reflex tears were collected from 32 healthy Hong Kong Chinese subjects and measured by both high-performance liquid chromatography (HPLC) and by an enzyme-linked colorimetric method known as FRASC (total ferric reducing (antioxidant) activity and ascorbate concentration measurement). For between-eye variation, yawn reflex tears were collected from each eye of the same 32 healthy subjects, and ascorbate was measured using HPLC; in a separate experiment for between-day variation, tears were collected on two separate days from 14 subjects, and ascorbate was measured by FRASC. RESULTS: Both HPLC and FRASC showed high precision, and results obtained using FRASC were not statistically different from those using HPLC; mean +/- SD were, respectively, 18.5 +/- 4.4 microM and 18.5 +/- 4.8 microM for HPLC and FRASC methods ($p = 0.943$). No significant between-eye difference in tear ascorbate was found ($p = 0.386$), and no significant between-day variation was found overall: mean +/- SD ascorbate was 20.0 +/- 6.2 microM on day 1 and 19.3 +/- 6.8 microM on day 2 ($p = 0.772$). However, between-day variation was large in seven of 14 subjects. CONCLUSION: FRASC is an acceptable alternative to HPLC for measurement of tear ascorbate. Tears for ascorbate investigation can be collected from either eye or, if necessary, from both eyes and pooled. However, tear ascorbate may vary widely from day to day in the same individual. The reasons for this variation require further study but may relate to differences in ascorbate supply or demand within the precorneal tear layer.

Chen, J. C., P. L. Tao, et al. (2003). "Endomorphin-1 and -2 induce naloxone-precipitated withdrawal syndromes in rats." Peptides 24(3): 477-81.
In 1997, endomorphin-1 (EM-1) and -2 (EM-2) were identified as the most specific endogenous mu-opioid ligands. These two peptides have shown analgesic effects and many other opioid functions. In the present study, we attempt to investigate the possible ability of endomorphins to induce naloxone-precipitated withdrawal in comparison with that induced by morphine. Using the previously established scoring system in rats, 12 withdrawal signs (chewing, sniffing, grooming, wet-dog shakes, stretching, yawning, rearing, jumping, teeth grinding, ptosis, diarrhea, and penile erection) were observed and scored following naloxone (4 mg/kg, i.p.) challenge. Compared with the sham control, EM-1 and EM-2 (20 microg, i.c.v., b.i.d. for 5 days) both produced significant naloxone-induced withdrawal syndromes with similar severity to that induced by the same dose of morphine. There was no significant difference between EM-1, EM-2, and morphine-treated group for naloxone-induced withdrawal signs, except for grooming. EM-1 and EM-2 induced more grooming than that caused by morphine. Although EM-1 and EM-2 both led to the withdrawal, they displayed different potency for certain signs and suggest their distinct regulations. The present results indicate EM-1 and EM-2 could initiate certain mechanism involved opiate dependence.

Yap, A. U., E. K. Chua, et al. (2002). "Clinical TMD, pain-related disability and psychological status of TMD patients." J Oral Rehabil 29 (4): 374-80.
This study investigated the clinical temporomandibular disorders (TMD), pain-related disability and psychological status of TMD patients using a computerized on-line TMD diagnostic system (NUS TMD v1.1). A total of 107 patients (32 male, 75 female) referred to the TMD clinics at the National Dental Centre and National University Hospital participated in this study. The mean age of the predominantly Chinese population (82.2%) was 30.8 years (range from 12 to 64 years). The history questionnaire and clinical examination were input directly into computers by patients and clinicians. A 'Summary of Findings' was then immediately generated by the program based on Axis I and II rules. The data was subsequently exported to SPSS for statistical analysis. About 20.6% of the patients had myofascial pain but only 7.5% experienced limited mandibular opening associated with myofascial pain. The majority of patients (> 80%) did not suffer from disc displacements (right and left joints). The frequency of arthralgia was also low (right joint 8.4%; left joint 7.5%) and only one patient had osteoarthosis of the TMJ. About 78.5% of the patients had low disability with almost equal distribution between low and high intensity pain, 27.1% of the patients were moderately depressed and 11.2% had severe depression. No significant difference in limitations related mandibular functioning scores was observed between normal/depressed patients and between patients with the different graded chronic pain severity classification. The three most frequent jaw disabilities were: eating hard foods (77.6%), yawning (75.7%) and chewing (64.5%). NUS TMD v1.1 is an extremely useful tool in the diagnosis/research of clinical TMD.

Walusinski, O. and B. L. Deputte (2002). "[Yawn: from ethology to clinical medicine]." Rev Prat 52(18): 1981-3.

Valdes-Cruz, A., V. M. Magdaleno-Madrigal, et al. (2002). "Chronic stimulation of the cat vagus nerve: effect on sleep and behavior." Prog Neuropsychopharmacol Biol Psychiatry 26(1): 113-8.
The effect of electrical vagus nerve stimulation (VNS) on sleep and behavior was analyzed in freely moving cats. Eight cats were

prepared for 23-h sleep recordings. The left vagus nerve of four of them was stimulated during 1 min, five times at 1-h intervals, for 5 days. The VNS induces: ipsilateral myosis, blinking, licking, abdominal contractions, upward gaze, swallowing, and eventually yawning and compulsive eating, as well as an increase of ponto-geniculate-occipital (PGO) wave density and of the number of stages and total amount of rapid eye movement (REM) sleep. Besides, there was a sudden transition from waking stage to REM sleep. The present results suggest that VNS modifies sleep in the cat. This effect could be explained by an activation of the areas involved in the physiological mechanisms of sleep.

Simon, H. B. (2002). "On call. I'm a 62-year-old man in good health. I take Zocor for my cholesterol as well as a baby aspirin and several vitamins every day. My problem may seem silly, but it's really a nuisance: uncontrollable yawning. Do you have any idea why I yawn so much or what I can do about it?" Harv Mens Health Watch 6(9): 8.

Seki, Y., I. Sato-Suzuki, et al. (2002). "Yawning/cortical activation induced by microinjection of histamine into the paraventricular nucleus of the rat." Behav Brain Res 134(1-2): 75-82.
The effects of microinjection of histamine into the paraventricular nucleus (PVN) of the hypothalamus on yawning responses were investigated in anesthetized, spontaneously breathing rats. Yawning responses were evaluated by monitoring the intercostal electromyogram (EMG) as an index of inspiratory activity and digastric EMG as an indicator of mouth opening. We also recorded the electrocorticogram (ECoG) to determine the arousal response during yawning. Autonomic function was evaluated by measuring blood pressure and heart rate. Microinjection of histamine into the medial parvocellular subdivision (mp) of the PVN elicited a yawning response, i.e. a single large inspiration with mouth opening, and an arousal shift in ECoG to lower voltage and faster rhythms. Microinjection of HTMT dimaleate, an H1 receptor agonist, into the PVN also caused the yawning/arousal response. Pretreatment with pyrilamine, an H1 receptor antagonist, inhibited the histamine induced yawning behavior. These data demonstrate that a histamine receptive site for triggering yawning/arousal responses exists in the PVN, and suggest that these responses are mediated by activation of H1 receptor within the PVN.

Schiller, F. (2002). "Yawning?" J Hist Neurosci 11(4): 392-401.
Since antiquity yawning has attracted a moderate interest among philosophers, psychologists, physiologists, as well as educators, moralists and physicians. Organisms from birds to men and from the womb to the deathbed were found to be displaying it. While sometimes satisfying to the producer, its display is offensive to the lay observer. Hippocrates had it on his lists of useful 'natures.' Aristotle dropped a few words on the matter. Boerhaave elevated its function to the intellect of animals. Haller has commented on its relation to the acoustic system, blood-flow, and baby sleep. Darwin mentioned it in connection with emotional behavior. Some modern authors praised its beneficial effects on respiration and smell. In the 1960s, Ashley Montagu tried to correct the contemporary failure to explain the behavior by the fact of raised CO2 and arterial compression. It also interested some neurologists, especially in its association with the encephalitis lethargica in the 1920s, with 'spasmodic yawning,' with epilepsy, not to speak of hysteria. As to boredom or its stimulus, a 40-page dissertation survives from the court of Frederick the Great of the 18th century condemning idleness, a subject that also inspired Blaise Pascal and William James. But in the Hindu world, public yawning was a religious offense.

Sato-Suzuki, I., I. Kita, et al. (2002). "Cortical arousal induced by microinjection of orexins into the paraventricular nucleus of the rat." Behav Brain Res 128(2): 169-77.
Orexin-A is a neuropeptide which has been suggested to be involved in sleep and arousal mechanisms. Orexin-A, for example, stimulates arousal when administrated intracerebroventricularly to rats. We attempted to identify specific neural sites of orexin-A and orexin-B action. Orexin-A and orexin-B were microinjected into the medial parvocellular subdivision of the paraventricular nucleus (PVN) in anesthetized, spontaneously breathing rats, and cortical arousal and yawning responses were assessed. Cortical arousal responses were monitored with the electrocorticogram (ECoG), and yawning responses were evaluated by monitoring intercostal electromyograms as an index of inspiratory activity and digastric electromyograms as an indicator of mouth opening. We also measured blood pressure and heart rate during yawning responses, since yawning is accompanied by changes in autonomic activity. Microinjection of orexin-A into the PVN elicited an arousal shift in the ECoG to lower voltage and faster rhythms. This cortical arousal response was followed by a single large inspiration with mouth opening, i.e. a yawning response. On the other hand, microinjection of orexin-B into the PVN elicited an arousal shift in the ECoG without yawning responses. These results demonstrate that an orexin receptive site for triggering arousal/yawning responses exists in the PVN, and suggest that the PVN is involved in arousal mechanisms.

Plyashkevich, Y. G. and G. G. Barsegyan (2002). "Delayed effects of 1,2-epoxypropyltrimethylammonium chloride on behavioral reactions in rats." Bull Exp Biol Med 133(1): 51-3.
We studied immediate and delayed effects of intraventricular injection of 1,2-epoxypropyltrimethylammonium chloride on behavioral reactions in rats. Apomorphine-induced yawning increased and orientation and exploratory activity was improved 144 h postinjection, which indicates activation of the brain dopaminergic system during this period.

Ottani, A., F. Ferrari, et al. (2002). "Neuroleptic-like profile of the cannabinoid agonist, HU 210, on rodent behavioural models." Prog Neuropsychopharmacol Biol Psychiatry 26(1): 91-6.
(1) The present study was performed to assess the effects exerted by the cannabinoid (CB) agonist, (-)11-hydroxy-delta8-tetrahydrocannabinol-dymethylheptyl (HU 210; 12.5-50 microg/kg ip), on rodent behavioural tests involving dopamine (DA) transmission; in comparison, the DA D2 antagonist, S(-)-3-chloro-5-ethyl-N-[(1-ethyl-2-pyrrolidinyl)methyl]-6-hydroxy-2-metho xy-benzamide hydrochloride ((-) eticlopride; 50 microg/kg sc), was used. (2) In rats, HU 210, at all doses, potently antagonized penile erection (PE) and stretching-yawning (SY) typically elicited by the DA D2/D3 agonists, 6-allyl-2-amino-5,6,7,8-tetrahydro-4H-thiazolo-[4,5-d]-azepine (B-HT 920) and +/-7-hydroxy-N,N-di-n-propylaminotetralin hydrobromide (7-OH-DPAT) both at 100 pg/kg ip. (3) In nonreserpinized mice, HU 210 impaired motor ability assessed by means of a motor test battery, and B-HT 920 (1 mg/kg ip) worsened the phenomenon. (4) In reserpinized mice, HU 210 at 50 microg/kg counteracted the amelioration exerted by B-HT 920 (1 mg/kg ip) on reserpine-induced akinesia. (5) As all these effects were similarly displayed by (-)eticlopride (50 microg/kg sc), our data suggest a neuroleptic-like profile of acute HU 210 in animal behavioural tests.

Nakamura-Palacios, E. M., O. F. Amodeo Bueno, et al. (2002). "Acute or chronic effects of cannabinoids on spontaneous or pharmacologically induced yawning in rats." Pharmacol Biochem Behav 74(1): 205-12.
Yawning is a reflex or event that is not fully understood. It is controlled by many neurotransmitters and neuropeptides and can be induced pharmacologically by cholinergic or dopaminergic agonists. Amongst their many actions, cannabinoids acting on cannabinoid (CB(1) or CB(2)) receptors can alter cholinergic and/or dopaminergic activity. This study examined the effects of Delta(8)-tetrahydrocannabinol (Delta (8)-THC) administered acutely (2.5 mg/kg intraperitoneally [ip], 15 min before test) or chronically (5 mg/kg for 30 days followed by 24 h or 7 days of discontinuation) on yawning induced by pilocarpine, a cholinergic agonist (0, 1, 2, 4 or 8 mg/kg ip), or apomorphine, a dopaminergic agonist (0, 20, 40 or 80 microg/kg subcutaneously [sc]). Acute effects of different doses of Delta(9)-tetrahydrocannabinol (Delta(9)-THC: 0, 0.5, 1.25 or 2.5 mg/kg ip) on yawning induced by pilocarpine (2 mg/kg ip) or apomorphine (40 microg/kg sc) were also investigated. Both pilocarpine and apomorphine produced yawning in a dose-related manner. Acute administration of Delta(8)-THC and Delta(9)-THC significantly reduced yawning induced by both pilocarpine and apomorphine. Chronic administration of Delta(8)-THC did not change yawning induced by either agonist 24 h or 7 days after discontinuation of Delta(8)-THC. However, a high frequency of spontaneous yawning was observed 7 days after Delta(8)-THC discontinuation. These results suggest that cannabinoid agonists inhibited yawning induced by cholinergic or dopaminergic agonists. In addition, the increased frequency of spontaneous yawning following cessation of chronic administration of a cannabinoid agonist may be of importance as a withdrawal sign for these drugs.

Moyaho, A. and J. Valencia (2002). "Grooming and yawning trace adjustment to unfamiliar environments in laboratory Sprague-Dawley rats (Rattus norvegicus)." J Comp Psychol 116(3): 263-9.
The authors studied grooming and yawning caused by mild stress in laboratory Sprague-Dawley rats (Rattus norvegicus). Two groups received 3 and 6 sequences of 5 foot shocks at random intervals (RI) and fixed intervals (FI), respectively. A 3rd group was not shocked (NS). The groups were exposed for 60 min twice. Grooming did not differ among groups, but yawning diminished with RI. Yawning increased and grooming decreased with the 2nd exposure, except in RI in which grooming increased. In NS and FI, grooming prevailed during the first 20 and 30 min, respectively, whereas yawning dominated the remainder of the time. In RI, grooming occurred more than yawning. An upward shift on this scale causes grooming to substitute yawning, whereas a downward shift causes the reverse effect.

Melis, M. R. and A. Argiolas (2002). "Reduction of drug-induced yawning and penile erection and of noncontact erections in male rats by the activation of GABAA receptors in the paraventricular nucleus: involvement of nitric oxide." Eur J Neurosci 15(5): 852-60.
The effect of muscimol, a GABAA receptor agonist, injected into the paraventricular nucleus (PVN) of the hypothalamus on drug-induced (apomorphine, oxytocin and NMDA) yawning and penile erection, and on the increase in the concentration of NO2- and NO3- occurring in the paraventricular dialysate in these experimental conditions, was studied in male rats. Muscimol (50, 100 and 200 ng) reduced, in a dose-dependent manner, penile erection and yawning induced by apomorphine (50 ng), oxytocin (30 ng) and NMDA (50 ng) delivered into the PVN. The reduction of penile erection and yawning was parallel to a reduction of the concomitant NO2- and NO3- increase that occurs in the paraventricular dialysate in this experimental condition. In contrast, baclofen (200 ng), a GABAB receptor agonist, was ineffective. The muscimol effects on drug-induced penile erection, yawning and NO2- increase were prevented by the prior administration of bicuculline (250 ng into the paraventricular nucleus). Muscimol (200 ng) but not baclofen (200 ng), injected into the PVN, reduced both noncontact erections in male rats placed in the presence of an inaccessible receptive female, and also the NO2- increase that occurs in the paraventricular dialysate in this experimental condition. As found with drug-induced penile erection, the muscimol reduction of noncontact erections and of NO2- increase was prevented by bicuculline. The present results show that the activation of GABAA receptors in the PVN reduces yawning and penile erection induced by drugs or physiological stimuli by reducing the increase in NO activity that occurs in this hypothalamic nucleus in these experimental conditions.

McGauran, A. (2002). "A yawning gap. Senior house officers, the weary foot-soldiers of the NHS, stand to benefit from an overhaul of their

training." Health Serv J 112(5821): 8-9.

Marchese, G., S. Ruiu, et al. (2002). "Carmoxirole is able to reduce amisulpride-induced hyperprolactinemia without affecting its central effect." Eur J Pharmacol 447(1): 109-14.
Prolactin blood level and apomorphine-induced yawning were studied in rats treated with the substituted benzamide amisulpride in association with bromocriptine or carmoxirole; two dopamine D(2) receptor agonists with high or low propensity to cross the brain-blood barrier, respectively. Administration of amisulpride produced a maximum increase in rat serum prolactin level (315+/-18%) vs. vehicle-treated animals (ED(50)=0.25+/-0.017 mg/kg, s.c.). The concurrent administration of carmoxirole or bromocriptine completely reversed the hyperprolactinemia induced by amisulpride (0.5 mg/kg, s.c.) (ID(50)=14.9+/-0.8 mg/kg and 0.81+/-0.03 mg/kg, respectively). Carmoxirole (15 mg/kg, i.p.) did not affect yawning induced by apomorphine (0.08 mg/kg, s.c.) nor amisulpride (0.5 mg/kg, s.c.) blockade of apomorphine-induced yawning. Conversely, a significant increase in the number of yawns was observed when bromocriptine (0.8 mg/kg, i.p.) was associated with apomorphine in the absence or presence of amisulpride. These results suggested that a peripheral dopamine D(2) receptor agonists could be a useful tool in alleviating amisulpride-induced hyperprolactinemia without possibly affecting its central effect.

Lum, L. M., M. B. Connolly, et al. (2002). "Hyperventilation-induced high-amplitude rhythmic slowing with altered awareness: a video-EEG comparison with absence seizures." Epilepsia 43(11): 1372-8.
PURPOSE: Hyperventilation-induced high-amplitude rhythmic slowing (HIHARS) in children may be associated with clinical episodes of altered awareness. The presence of automatisms has been proposed as a distinguishing feature that helps to differentiate absence seizures from nonepileptic causes of decreased responsiveness. This retrospective, controlled, video-EEG study compared the clinical characteristics of episodes of HIHARS with loss of awareness with those of absence seizures. METHODS: The database of a tertiary Children's Hospital was searched for patients studied between April 1993 and April 1997 who had at least one episode of HIHARS with loss of awareness. The absence control group was obtained by selecting the next patient, after an HIHARS study subject, who met the following criteria: (a) had at least one absence seizure occurred during hyperventilation in the EEG recording, and (b) had a diagnosis of idiopathic generalized epilepsy. The video-EEG and medical histories of all patients were reviewed and summarized. RESULTS: We reviewed video-EEG recordings of 77 episodes of HIHARS with loss of awareness from 22 children and 107 absence seizures during hyperventilation from 22 children. Eye opening and eyelid flutter were seen more frequently in absence seizures, whereas fidgeting, smiling, and yawning occurred more frequently during HIHARS episodes. Arrest of activity, staring, and oral and manual automatisms were observed in both groups. CONCLUSIONS: Automatisms are common in both HIHARS and absence seizures. Yawning, smiling, and particularly fidgeting occur more commonly and eye opening and eyelid flutter less commonly in HIHARS. However, episodes of HIHARS with loss of awareness clinically mimic absence seizures, and these conditions can be distinguished reliably only by EEG.

Kim, D. W., H. Y. Kil, et al. (2002). "Relationship between clinical endpoints for induction of anesthesia and bispectral index and effect-site concentration values." J Clin Anesth 14(4): 241-5.
STUDY OBJECTIVE: To assess the relationship between clinical endpoints for induction of anesthesia and the electroencephalographic (EEG) bispectral index (BIS) and effect-site concentration (C(E)) values when using a target-controlled infusion (TCI) of either thiopental sodium or propofol, by hypothesizing that yawning may be a useful alternative to other commonly used clinical signs for determining loss of consciousness. DESIGN: Randomized observational clinical study. SETTING: Operating room of a university-based hospital.PATIENTS: 60 healthy adult patients (aged 20-50 yrs) scheduled for elective surgery with general anesthesia. INTERVENTIONS: During a TCI of propofol (n = 30) or thiopental (n = 30), clinical endpoints for loss of verbal responsiveness (LOV), loss-of-eyelash reflex (LOE), occurrence of yawning, and apnea were assessed at 15-second intervals. In addition, BIS and C(E) values were recorded at each of the endpoints. MEASUREMENTS AND MAIN RESULTS: In both anesthetic groups, the sequence of occurrence of the clinical endpoints was similar, namely LOV, LOE, yawning, and, lastly, apnea. Compared with LOV and LOE, yawning was associated with lower BIS and higher C(E) values with both anesthetics. The frequency of yawning was higher with thiopental than propofol (83% vs. 63%, respectively). However, the frequency of apnea was higher with propofol than thiopental (77% vs. 53%, respectively). CONCLUSION: The correlation of the clinical endpoints with BIS and C(E) values was highest for LOV. Yawning was as unreliable as LOE for determining the onset of unconsciousness during induction of anesthesia. This clinical sign failed to be observed in 17% and 37% of patients induced with thiopental and propofol, respectively.

Hilgers, F. J., H. A. Jansen, et al. (2002). "Long-term results of olfaction rehabilitation using the nasal airflow-inducing ("polite yawning") maneuver after total laryngectomy." Arch Otolaryngol Head Neck Surg 128(6): 648-54.
OBJECTIVES: To study the long-term results of the nasal airflow-inducing maneuver (NAIM) as an olfaction rehabilitation tool after laryngectomy and to investigate the effectiveness of a new, simpler odor detection test (ODT) called the smell disk test (SDT), or Zurcher Geruchstest. DESIGN: Intervention study. SETTINGS: National cancer center. PATIENTS: Forty-one laryngectomees who received olfaction rehabilitation training with the NAIM 4 months to 2 years earlier. This so-called polite yawning maneuver creates an "underpressure" in the oral cavity, which, in turn, generates a nasal airflow that enables odor molecules to again reach the olfactory epithelium. MAIN OUTCOME MEASURES: Olfaction acuity testing with a standard ODT, along with a questionnaire, providing a subjective olfaction score (present odor perception scale [POPS]), and the SDT, as well as assessment of the patients' correct execution of the NAIM by speech-language pathologists on video recordings made during odor testing and long-term assessment of olfaction acuity. RESULTS: The correlation between the previously used ODT-POPS combination and the SDT was kappa = 0.56 (P<.001). Based on these results, we preferred to use the much simpler SDT instead of the laborious combination of the ODT-POPS. Based on the SDT results, 19 (46%) of the 41 laryngectomees were "smellers" and could be considered normosmic. There was a significant relationship (P =.03) between the patient's correct execution of the NAIM and whether or not the laryngectomee was a smeller according to the SDT. CONCLUSIONS: The effectiveness of the NAIM, or so-called polite yawning technique, for the rehabilitation of olfaction in individuals who have undergone total laryngectomy was reconfirmed. Long-term olfaction rehabilitation was achieved in about 50% of the patients, but more intensified training may be needed to increase the percentage of successfully rehabilitated individuals. The SDT is an effective and simple test for the assessment of olfaction acuity after laryngectomy.

Gugle, M. M. (2002). "Etiology, pathogenesis and treatment of habitual dislocations of the T.M. Joints [original work]." Indian J Dent Res 13(2): 88-94.
Definite treatment of any pathological condition, is based on the understanding of its correct pathogenesis and etiology. Without this basic understanding correct and lasting treatment is not possible. When there is no knowledge of exact pathogenesis and etiology, various theories and treatments are suggested by various workers. This is what exactly happened in the case of habitual dislocations of the T.M. Joints. This in term has happened because the dental surgeons and so called oral surgeons, never expanded their vision, beyond their restricted field of 20 deciduous teeth and 32 permanent teeth. Lack of understanding of basic physiological functions, of various tissues in the body and their effects on various systems as a whole was neglected. For this study four patients were selected from many, who could visit my clinic regularly and co-operate to follow all the instructions over a period of at least 5 years. The analysis of their symptoms and signs, had a different story to tell than what was described in the literature so far.

Guardia, J., M. Casas, et al. (2002). "The apomorphine test: a biological marker for heroin dependence disorder?" Addict Biol 7(4): 421-6.
This experimental study was conducted in the inpatient detoxification addictive behavior unit of the Sant Pau Hospital in Barcelona and included 22 healthy subjects (HS) and 42 intravenous heroin-dependent subjects (HDS). Apomorphine-induced yawning rates were investigated in three different groups; heroin-dependent patients stabilized on d-propoxiphene, heroin-dependent patients recently withdrawn from d-propoxiphene and normal controls. Yawning responses were recorded continuously by independent observers for periods of 45 minutes following administration of low doses of subcutaneous apomorphine and NaCl. The lowest subcutaneous apomorphine dose able to induce a significantly higher number of yawning responses in HS was 0.005 mg/kg. The yawning responses induced by this dose in HDS were also significantly higher than those induced by placebo. When comparing the number of yawning responses between the study groups, differences were observed only between HDS and HS and no effect of gender was obtained. The apomorphine test may be useful in assessing central dopamine system alterations associated with chronic heroin consumption and could be a stable and reliable biological marker of heroin-dependence disorders.

Graves, F. C., K. Wallen, et al. (2002). "Opioids and attachment in rhesus macaque (Macaca mulatta) abusive mothers." Behav Neurosci 116(3): 489-93.
This study investigated the role of the endogenous opioid system in maternal and affiliative behavior of group-living rhesus macaque (Macaca mulatta) mothers with a history of abusive parenting. Eighteen mothers received an injection of the opioid antagonist naltrexone or saline for 5 days per week for the first 4 weeks of the infant's life. After treatment, mother-infant pairs were focally observed. Naltrexone did not significantly affect infant abuse or other measures of maternal behavior. Naltrexone increased the amount of grooming received by mothers from other group members and reduced the mothers' rate of displacement activities such as scratching, yawning, and self-grooming. These results concur with previous primate studies in suggesting that opioids mediate the rewarding effects of receiving grooming and affect anxiety-related behaviors.

Gowing, L., R. Ali, et al. (2002). "Buprenorphine for the management of opioid withdrawal." Cochrane Database Syst Rev(2): CD002025.
BACKGROUND: Managed withdrawal (detoxification) is a necessary step prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system. OBJECTIVES: To assess the effectiveness of interventions involving the short-term use of buprenorphine to manage the acute phase of opioid withdrawal. SEARCH STRATEGY: Multiple electronic databases were searched using a strategy designed to retrieve references broadly addressing the management of opioid withdrawal. Reference lists of retrieved studies, reviews and conference abstracts were handsearched. SELECTION CRITERIA: Randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies that compared different buprenorphine regimes, or that compared buprenorphine with another form of treatment (or placebo) to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent. DATA COLLECTION AND ANALYSIS: Potentially relevant studies were assessed for inclusion by one reviewer. Inclusion decisions were confirmed by consultation between reviewers. One reviewer undertook data extraction with the process confirmed by consultation between all three reviewers. MAIN RESULTS: Six studies (5 RCTs and 1

controlled prospective study), involving 357 participants, met the criteria for inclusion in the review. Four studies compared buprenorphine with clonidine. All found withdrawal to be less severe in the buprenorphine treatment group. In three of these studies all participants were withdrawing from heroin. Participants in one study were withdrawing from methadone (10mg/day). Aches, restlessness, yawning, mydriasis, tremor, insomnia, nausea and mild anxiety were reported as being experienced by some participants. Rates of completion of withdrawal ranged from 65% to 100%. None of the studies included in the review reported adverse effects. However a single-group study which therefore did not meet the inclusion criteria, reported the occurrence in some participants of headaches, sedation, nausea, constipation, anxiety, dizziness and itchiness, particularly in the first 2-3 days of treatment. In one of the six studies, and in two studies that did not meet the inclusion criteria, treatment was provided on an outpatient basis. REVIEWER'S CONCLUSIONS: Buprenorphine has potential as a medication to ameliorate the signs and symptoms of withdrawal from heroin, and possibly methadone, but many aspects of treatment protocol and relative effectiveness need to be investigated further.

Giganti, F., M. J. Hayes, et al. (2002). "Yawning and behavioral states in premature infants." Dev Psychobiol 41(3): 289-96.
Low risk, premature infants between 30 to 35 weeks post-conceptual age (PCA) residing in an neonatal intensive care unit environment were observed in the home incubator for spontaneous yawning from 2400 to 0500 hr. Videorecordings were analyzed for the behavioral states of quiet sleep (QS), active sleep (AS), wake (W), and drowse (D) in 3-min epochs as well as the contextual behaviors before and after yawn events using a 1-min window. Yawning periods predicted higher levels of motoric activation than nonyawn periods. Sequence analysis of preceding and following states with or without yawns were examined for stability or change. All states with or without yawn events had state stability for the preceding and following epochs, with two exceptions: 1) D state with yawning was associated with state change in the preceding 3-min epoch (most often W), and 2) D state without yawning was associated with state change in the following epoch (W or AS). Yawns were not present in QS. The results suggest that yawning is associated with increased behavioral arousal that is not state-specific. However, yawning in D state predicts state transitions in the preceding, but not the following, epoch. It is proposed that D may be an unstable state that becomes more stable when yawning is present.

Ferrari, F., A. Ottani, et al. (2002). "Influence of sildenafil on central dopamine-mediated behaviour in male rats." Life Sci 70(13): 1501-8.
Two experiments were performed to evaluate the effects of sildenafil on spontaneous or dopamine agonist-induced behaviour in male rats. Data obtained in experiment 1 show that oral administration of the drug, at 1 mg/kg, significantly increased the occurrence of penile erections, anogenital self-grooming and homosexual mounting in grouped sexually-experienced, but not inexperienced, animals. In experiment 2, pre-treatment with sildenafil (0.5, 1 or 10 mg/kg) dose-dependently modified several behavioural signs, centrally evoked by the D2/D3 dopamine agonists, 7-OH-DPAT or B-HT 920 (both at 0.1 mg/kg), in experimentally naive male rats. While sildenafil at 1 mg/kg significantly increased the number of penile erection and stretching-yawning episodes induced by 7-OH-DPAT or B-HT 920, at 10 mg/kg it elicited low stereotyped behaviour, antagonizing stretching-yawning and sedation in 7-OH-DPAT treated rats. Discussion centres on the modulatory activity of sildenafil on central dopaminergic pathways and, possibly, on nitric oxide production.

Diaz-Romero, M., J. R. Eguibar, et al. (2002). "Bombesin decreases yawning in a high-yawning subline of Sprague-Dawley rats." Pharmacol Biochem Behav 71(1-2): 103-9.
This study analysed the effect of the intracerebroventricular administration of bombesin (BN) at doses of 0.001, 0.005, 0.1 and 1.0 microg/2 microl on yawning, grooming and other behavioral correlates in two inbred strains of male rats. These were selected for high-yawning (HY) and low-yawning (LY) frequency, a difference that correlates with novelty-induced grooming. Grooming increased with BN in a strain-specific manner, and yawning decreased in HY rats. Principal component analysis (PCA) showed that rats' behaviors changed from yawning to grooming with BN. Such change differed between the strains. While the first principal component was dominated by grooming in both strains, the second principal component was dominated by stretching and penile erections in HY rats, and by scratching in LY rats. While LY rats spent more time in scratching both within and outside grooming bouts, HY rats tended to favour the latter category. An increment in mean duration of grooming bouts characterized the effect of the highest dose. These findings show that BN inhibits yawning and increases grooming, suggesting that this peptide enhances the initial response to novel environments. The study shows the importance of combining studies on inbred strains with appropriate multivariate methods to separate drug-induced behavioral patterns.

Avidan, A. (2002). "Dislocation of the temporomandibular joint due to forceful yawning during induction with propofol." J Clin Anesth 14(2): 159-60.

Abou-Jaoude, E. S., M. Brooks, et al. (2002). "Spontaneous wound dehiscence after removal of single continuous penetrating keratoplasty suture." Ophthalmology 109(7): 1291-6; discussion 1297.
PURPOSE: To determine the incidence and complications of spontaneous wound dehiscence after removal of a single continuous penetrating keratoplasty (PK) suture. DESIGN: Retrospective consecutive, noncomparative interventional case series. METHODS: Retrospective review of 324 consecutive continuous suture PKs performed between 1992 and 1999. RESULTS: Sixty-nine (21.3%) of 324 PKs reviewed had the continuous suture removed. The average interval for suture removal after PK was 24.5 +/- 15 months (range, 2.8-63.3 months). Five of the 69 eyes (7.2%) developed spontaneous wound dehiscence without direct eye trauma. In the five eyes that developed wound dehiscence, the continuous suture was removed at 24.6 +/- 10.3 months (range, 14-42 months). Dehiscence occurred at 11.6 +/- 6.5 (range, 3-18) days after suture removal. Significant history associated with wound dehiscence included coughing, yawning, falling without trauma to the eye, and spontaneous wound separation. The reasons for suture removal were astigmatism in four of five (80%) patients and a broken suture in one of the five patients. In four of five (80%) patients, the location of wound dehiscence correlated with the steep axis of corneal keratometry before suture removal. Surgical intervention preserved the presuture removal best-corrected visual acuity in four of the five eyes. No eyes with an intact suture spontaneously dehisced. CONCLUSIONS: The rate of spontaneous wound dehiscence after removal of a continuous suture in our series was 7.2%. All spontaneous dehiscences occurred within 2 weeks after suture removal. Older patients, who had PK for corneal edema with postoperative astigmatism and have been using corticosteroids drops for prolonged periods of time, are at higher risk of wound dehiscence. Patients should be monitored closely during the first 2 weeks after removal of a continuous suture for signs of wound separation, especially when suture removal is performed for astigmatism. Patients should be cautioned about the risk and symptoms of wound dehiscence before suture removal to facilitate early recognition and intervention for preservation of best visual potential.

Yap, A. U., K. B. Tan, et al. (2001). "On-line computerized diagnosis of pain-related disability and psychological status of TMD patients: a pilot study." J Oral Rehabil 28(1): 78-87.
Temporomandibular disorders (TMD) is a collective term embracing a number of clinical problems, which involve the masticatory musculature, the temporomandibular joint or both. Virtually all theories dealing with the aetiology and treatment of TMD have recognized the importance of psychological factors. This paper reports the development of a computerized on-line program (NUS TMD v1.1) for the diagnosis of pain-related disability and psychological status of TMD patients based on Axis II of the research diagnostic criteria (RDC)/TMD (Dworkin, S.F. & LeResche, L. 1992. Journal of Craniomandibular Disorders: Facial Oral Pain, 6, 301), which was developed to redress the lack of diagnostic criteria in TMD research. Methods adopted by RDC/TMD for use in assessing Axis II status include a seven-item questionnaire for grading chronic pain severity, the Symptom Checklist 90 Revised (SCL-90-R) and a jaw disability checklist. A pilot study, based on 37 new TMD patient records, was conducted to study the pain-related disability and psychological status of TMD patients using this newly developed program. The mean age of the predominantly Chinese population (86.5%) was 32.19 years (range 20-72 years) with a sex distribution of 24 females and 13 males. Most patients (78%) had low disability, with 12 patients having low intensity and 17 patients having high intensity pain. Approximately 73% of the sample population were moderately or severely depressed. Patients that were moderately and severely depressed had significantly higher scores for limitation related to mandibular functioning than normal patients. The three most frequent jaw disabilities were: eating hard foods (84%), yawning (78%) and chewing (65%).

Poe, D. S., A. Abou-Halawa, et al. (2001). "Analysis of the dysfunctional eustachian tube by video endoscopy." Otol Neurotol 22(5): 590-5.
OBJECTIVE: Human eustachian tubes with known pathologic conditions of the ear were inspected endoscopically, and video recordings were made for slow-motion analysis of the pathophysiologic changes. SETTING: Ambulatory office in a tertiary referral center. SUBJECTS: Forty-four adults with 64 ears having pathologic conditions. INTERVENTIONS: Transnasal endoscopic examination of the nasopharyngeal opening of the eustachian tube during rest, swallowing, and yawning to study the dilatory movements of the eustachian tube. MAIN OUTCOME MEASURES: Slow-motion video analysis of the dilatory movements of the eustachian tube. RESULTS: Sixty-four ears and eustachian tubes with pathologic changes were studied. Tubal function was graded on (1) the extent of lateral excursion and progression of dilatory wave as estimates of tensor veli palatini and dilator tube muscle function, reduced function being observed in 43 tubes; (2) the degree of mucosal disease, which was significant in 48 tubes; (3) obstructive mucosal changes, which were present in 15 tubes; (4) ease and frequency of tubal dilation with maneuvers-26 tubes opened moderately, 21 opened minimally, and 11 were unable to open; and (5) patulous tubes-all 6 clinically patulous tubes showed concavities in the superior third of the tube, which is convex in normal subjects. All tubes with active pathologic conditions of the ear (otitis media with effusion, tympanic membrane retraction, draining ear, cholesteatoma) had significant abnormalities. A correlation could not be made between the severity of middle ear disease and the severity of observed eustachian tube dysfunction. CONCLUSIONS: Slow-motion endoscopic video analysis is a potentially useful technique in classifying types of pathologic changes in the eustachian tube. Additional studies of dysfunctional tubes are needed to predict outcomes in operative ear cases and to design intratubal therapy for chronically dysfunctional tubes.

Ogura, H., T. Kosasa, et al. (2001). "Central and peripheral activity of cholinesterase inhibitors as revealed by yawning and fasciculation in rats." Eur J Pharmacol 415(2-3): 157-64.
This study was designed to investigate the central and peripheral activity profile of cholinesterase inhibitors in rats. Intravenous injection of cholinesterase inhibitors caused fasciculation, a fine involuntary muscular movement. This peripheral cholinergic sign was tightly correlated with in vitro anti-acetylcholinesterase activity by cholinesterase inhibitors, suggesting that fasciculation is a valid index of peripheral cholinergic activation. Yawning, used as a marker of central cholinergic activation, was also monitored. E2030 (3-(2-(1-(1,3-dioxolan-2-ylmethyl)-4-piperidyl)ethyl)-2H-3,4-dihydro-1,3-b enzoxazin-2,4-dione hydrochloride) elicited yawning at more than 4 mg/kg,

while fasciculation was significantly intensified only at a dose of 16 mg/kg. Donepezil and tacrine induced both yawning and fasciculation at doses greater than 4 mg/kg, whereas physostigmine induced both behaviors at a dose of 8 mg/kg and above. Finally, ipidacrine elicited yawning at a dose of 16 mg/kg and fasciculation at doses greater than 8 mg/kg. Thus, all putative centrally acting cholinesterase inhibitors elicited yawning. TAK-147 (3-[1-(phenylmethyl)-4-piperidinyl]-1-(2,3,4,5-tetrahydro-1H-benzazepin-8- yl)-1-propanone fumarate) did not significantly elicit yawning at doses under 16 mg/kg, but elicited fasciculation at a dose of more than 4 mg/kg. Distigmine, a peripherally acting cholinesterase inhibitor, evoked fasciculations, but not yawning. When mild to moderate fasciculation was evoked, donepezil and E2030 elicited more than nine yawns over 30 min, while the other cholinesterase inhibitors elicited approximately five yawns at most during this period. These results indicated that E2030 and donepezil exhibited the most marked preferential central cholinergic activity, relative to peripheral activity, among cholinesterase inhibitors tested. Scopolamine, a centrally acting antimuscarinic drug, completely inhibited E2030-induced yawning, while peripherally acting methylscopolamine did not. Haloperidol, a dopamine receptor antagonist, partially blocked E2030-induced yawning, but did not block donepezil-induced yawning. These results suggest that central cholinergic and, in part, dopaminergic mechanisms are involved in E2030-induced yawning.

Nowak, P., R. Brus, et al. (2001). "Amphetamine-induced enhancement of neostriatal in vivo microdialysate dopamine content in rats, quinpirole-primed as neonates." Pol J Pharmacol 53(4): 319-29.

Amphetamine (AMPH)-induced sensitization of central dopamine (DA) receptors, produced by repeated AMPH treatments, is associated with increased AMPH-induced DA release in the rat forebrain. However, for DA receptor sensitization produced by repeated DA receptor agonist treatments, the effects on forebrain DA release are not known. The objective of our study was to determine this. DA receptor sensitization was produced by administering the DA D2 agonist quinpirole (50 microg/kg/day) to rats, from the 1st to 11th days after birth - a process known as 'priming'. When these rats were tested at 3 months, DA receptor sensitization was manifested as increased quinpirole-induced yawning. We also found that AMPH (1.0 mg/kg, ip) acutely induced a 5-fold greater increase in DA content in the neostriatal in vivo microdialysate of these quinpirole-primed rats (vs. controls), accompanied by a reduction in dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) levels in the microdialysate. Conversely, an acute injection of quinpirole x HCl (100 microg/kg, ip) reduced the microdialysate contents of DA, DOPAC and HVA to comparable levels in quinpirole-primed and control rats. Therefore, we can conclude that long-lived DA receptor sensitization, produced by repeated DA D2 agonist treatments in ontogeny, is associated with enhanced AMPH-induced DA release in the neostriatum in adulthood, but is not accompanied by evident alteration in quinpirole-induced DA release.

Nassif, N. J. and Y. F. Talic (2001). "Classic symptoms in temporomandibular disorder patients: a comparative study." Cranio 19(1): 33-41.

Numerous symptoms have been reported in the literature associated with temporomandibular disorders (TMD). However, it has not been stated what TMD symptoms are the most important and consistent and in turn, can be referred to as the gold standard or classic symptoms. The purpose of this study was: 1. To review the literature regarding TMD symptoms; 2. To compare so-called classic TMD symptoms with the symptoms of patients diagnosed as having TMD. Out of 52 consecutive patients, 40 were diagnosed as having TMD and were selected for this study. Forty non-TMD subjects served as a control group. A total range of subjective symptoms, from a self-administered TMD history form, was collected, but only so-called classic or the most common TMD symptoms were reported in this study. Results revealed that the major complaints of the TMD patients, including headaches, were similar to the suggested classic TMD symptoms derived from the literature.

Muller, E. and M. P. Rios Calvo (2001). "Pain and dental implantology: sensory quantification and affective aspects. Part I: At the private dental office." Implant Dent 10(1): 14-22.

After an extensive review of the dental literature, few articles were found related to pain and implantology. Management of orofacial pain has traditionally been a difficult challenge for the dental-medical profession. Patients may be afraid of dental pain, particularly in cases of dental implantology. Therefore, a study to obtain more conclusive data was developed. Taking into account that the perception of pain and the threshold of pain vary among individuals, a 2-year clinical study was established in private practice utilizing a verbal method (double-blind). The study was used to quantify sensory and affective aspects of pain associated with dental implantology on 75 patients in a private dental office. All of the implants were placed by the same clinician. Data were recorded following a Pain Data Sheet designed for this particular study. The aim of this study was to obtain different aspects of data as follows: 1) Fear of the dentist and fear of dental implant procedures utilizing a descriptive scale of 1 to 10, with 1 indicative of no fear. 2) Dental areas and ridges: Dental pain, pain in edentulous areas, and pain in the implanted area utilizing a scale of 0 to 8, with 0 indicative of no pain. 3) Function and pain: during mastication, swallowing, speech, yawning, opening, closing, and lateral excursions and indication of cervical pain or back pain, each calibrated by the presence or absence of pain. 4) Palpation and pain of the temporomandibular joint, the temporal muscle, the area of the pterygoid muscles, masseter muscle, and sternocleidomastoid muscle, all calibrated on the indication of presence or absence of pain. 5) Others: ear pain, neuralgia, headaches, edema, and hematoma, calibrated on the basis of presence or absence. The aforementioned factors were evaluated immediately before surgery and after surgery, at 24 hours, and during a follow up for a period of 2 years at intervals of 1 week; 1, 2, 3, 4, and 6 months; and 1 and 2 years after surgery. Also recorded were the uses of presurgical and postsurgical medication at the first and second surgical phases, age, sex, buccal opening, number and position of implants, previous dental experiences, and the psychological preparation for dental implant treatment. The results of the statistical analysis indicate no correlation between pain and dental implantology procedures, in a private dental practice, at the level of significance of P > .001.

Mancuso, F., R. Porta, et al. (2001). "Substance P and its transglutaminase-synthesized spermine derivative elicit yawning behavior via nitric oxide in rats." Peptides 22(9): 1453-7.

Previously, we showed that intranigrostriatal injection of substance P (SP) cause behavioral changes in rats. Those effects, such as locomotion and food intake, resulted related to catecholamines release modulated by nitric oxide [18]. Here we report that intranigrostriatal injection of SP elicited yawning in rats. Moreover, since in previous studies we demonstrated that transglutaminase-synthesized gamma-(glutamyl5)spermine derivative of SP (Spm-SP) could be a useful tool in differentiating NK1 receptors [5,19,26], we reports the effects of injecting the selective septide-sensitive NK1 receptor agonist Spm-SP into the nigrostriatal region of the rat brain on yawning. The administration of L-N(omega)-nitroarginine methyl ester, a NO-synthase inhibitor, stereospecifically reduced in a dose related manner both SP and Spm-SP-induced yawning. In contrast, L-arginine pretreatment prevented the effect of NO-synthase inhibitor. Moreover, the NK1 antagonist RP,67580 blocked yawning behavior induced by both SP and Spm-SP, whereas the pretreatment with systemic reserpine determined its increase. The administration of NO-synthase inhibitor resulted ineffective in reducing SP and Spm-SP-induced yawns in reserpinized rats. Finally, yawns elicited by SP or Spm-SP were blocked when rats were treated with scopolamine but not with methylscopolamine.These results indicate that yawning induced in rats by SP injection is dependent upon endogenous dopamine levels in brain nigrostriatal area. Moreover, we demonstrate, by using Spm-SP, that septide-sensitive NK1 receptor are specifically involved in yawning behavior.

Jacome, D. E. (2001). "Compulsive yawning as migraine premonitory symptom." Cephalalgia 21(5): 623-5.

Jacome, D. E. (2001). "Primary yawning headache." Cephalalgia 21(6): 697-9.

To describe three patients with recurrent severe paroxysmal headache precipitated by yawning. Pain elicited by yawning is a well-recognized clinical phenomenon in patients with cranial neuralgia, temporomandibular joint dysfunction syndrome and Eagle syndrome. Clinical history, neurological and oral examinations, brain magnetic resonance imaging (MRI), cranial nerve electrophysiological testing and skull X-rays are reported. In all the patients pain was induced by yawning; in the third patient pain was also triggered by eructation. None had history of migraine. Facial gestures and forceful opening of the mouth did not reproduce the pain. The first patient had retroauricular pain, simvastatin-induced myopathy and subclinical axonal peripheral neuropathy; the second patient had a post-viral benign sensory neuropathy; and the third had retroauricular and facial pain and no underlying neurological illness. Cranial nerve testing and MRI of the brain were normal except for a coincidentally found pituitary adenoma on the first patient. Headache or cranial pain with yawning may occur in patients with no apparent cause (primary yawning headache). It is a chronic, benign condition that requires no specific treatment but needs to be distinguished from secondary yawning headache, of greater clinical relevance.

Hanning, C. D. (2001). "Yawning." Sleep Med Rev 5(5): 411.

Dewey, R. B., Jr., J. T. Hutton, et al. (2001). "A randomized, double-blind, placebo-controlled trial of subcutaneously injected apomorphine for parkinsonian off-state events." Arch Neurol 58(9): 1385-92.

OBJECTIVE: To assess the safety and efficacy of subcutaneous apomorphine hydrochloride administration for off-state (poor motor function) periods in patients with Parkinson disease with motor fluctuations under both inpatient titration and outpatient therapeutic conditions. PATIENTS AND METHODS: Twenty-nine patients had advanced Parkinson disease with 2 hours or more off time despite aggressive oral therapy. Patients randomly received titrated doses of subcutaneous apomorphine hydrochloride (2-10 mg, n = 20) or pH-matched vehicle placebo (n = 9) during an inpatient and 1-month outpatient phase. A change in the United Parkinson Disease Rating Scale motor score 20 minutes after inpatient dosing during a practically defined off-state event and the percentage of injections successfully aborting off-state events were the primary inpatient and outpatient efficacy factors. RESULTS: The average (SEM) levodopa equivalent dose of apomorphine hydrochloride was 5.4 +/- 0.5 mg and the mean placebo dose was 1.0 mL. Mean inpatient United Parkinson Disease Rating Scale motor scores were reduced by 23.9 and 0.1 points (62% and 1%) by apomorphine treatment and placebo, respectively (P<.001). The mean percentage of outpatient injections resulting in successful abortion of off-state events was 95% for apomorphine and 23% for placebo (P<.001). Inpatient response was significantly correlated with and predictive of outpatient efficacy (P<.001). The levodopa dose was not predictive of the apomorphine dose requirement. Frequent adverse events included dyskinesia, yawning, and injection site reactions. CONCLUSION: Apomorphine by intermittent subcutaneous injection is effective and safe for outpatient use to reverse off-state events that occur despite optimized oral therapy.

Daquin, G., J. Micallef, et al. (2001). "Yawning." Sleep Med Rev 5(4): 299-312.

YAWNING IS A COMMON PHYSIOLOGICAL EVENT THAT CAN BE DIVIDED INTO THREE DISTINCT PHASES: a long inspiratory phase, a brief acme and a rapid expiration. The aim of yawning is not yet well defined. However this semi-voluntary event increases vigilance and aims to alert when drowsiness occurs. Yawning probably has an important role for social communication as well. Yawning can be responsible for pain, luxation or

even transient ischaemic attack. Abnormal yawning is present in various pathologies: migraine, Parkinson's disease, tumours, psychiatric diseases, infections or iatrogenic pathologies. The neuro-pharmacology of yawning is complex and knowledge of its mechanisms is incomplete. While under the control of several neurotransmitters, yawning is largely affected by dopamine. Dopamine may activate oxytocin production in the paraventricular nucleus of the hypothalamus. Oxytocin may then activate cholinergic transmission in the hippocampus and, finally, acetylcholine might induce yawning via the muscarinic receptors of the effectors. This is an over-simplification; many other molecules can modulate yawning, such as nitric oxide, glutamate, GABA, serotonin, ACTH, MSH, sexual hormones and opium derivate peptides. Dopamine involvement in yawning could have practical applications in the study of new drugs or the exploration of neurological diseases such as migraine or psychosis. 2001 Harcourt Publishers Ltd

Dalessio, D. J. (2001). "Relief of cluster headache and cranial neuralgias. Promising prophylactic and symptomatic treatments." Postgrad Med 109(1): 69-72, 75-8.

When a patient presents with persistently unilateral head or face pain, cluster headache and trigeminal neuralgia should be considered. Diagnosis is based on the patient's history; anatomical studies are performed only to rule out problems other than tumor or stroke. A patient who presents with pain in the pharynx, tonsils, and ear--particularly if it is initiated by swallowing, yawning, or eating--may have glossopharyngeal neuralgia. Treatment with carbamazepine is indicated; if the patient does not respond to this drug, the diagnosis is doubtful. Several effective treatments are available for these conditions. Oxygen, drug therapy, or surgery may be indicated depending on the course of the disease.

Coupar, I. M. and B. L. Tran (2001). "Withdrawal and bidirectional cross-withdrawal responses in rats treated with adenosine agonists and morphine." Life Sci 69(7): 779-90.

The aim of this study was to investigate whether the A1/A2 receptor agonist, 5'-N-ethylcarboxamidoadenosine (NECA), and the selective A1 agonist, N6-cyclopentyladenosine (CPA), induced physical dependence by quantifying specific antagonist-precipitated withdrawal syndromes in conscious rats. In addition, the presence of bidirectional cross-withdrawal was also investigated. The agonists were administered s.c. to groups of rats at 12 h intervals. Antagonists were administered s.c., 12 hours after the last dose, followed by observation and measurement of faecal output for 20 min. NECA (4 x 0.03 mg kg(-1), s.c) and CPA (4 x 0.03, 0.1 and 0.3 mg kg(-1), s.c.) induced physical dependence, as shown by the expression of a significant withdrawal syndrome when challenged with the adenosine A1/A2 receptor antagonist, 3,7-dimethyl-1-propargylxanthine (DMPX, 0.1 mg kg(-1), s.c.) and the A1 antagonist, 8-cyclopentyl-1,3-dipropylxanthine (CPDPX, 0.1 mg kg(-1), s.c.) respectively. The syndromes consisted of teeth chattering and shaking behaviours shown to occur in morphine-dependent animals withdrawn with naloxone viz, paw, body and 'wet-dog' shakes, but with the additional behaviours of head shaking and yawning. In further contrast to the opiate withdrawal syndrome, no diarrhoea occurred in the groups of animals treated with adenosine agonists and withdrawn with their respective antagonists. Bidirectional cross-withdrawal syndromes were also revealed when naloxone (3 mg kg (-1), s.c.) was administered to adenosine agonist pre-treated rats and adenosine antagonists were given to morphine pre-treated rats. This study provides further information illustrating that close links exist between the adenosine and opiate systems.

Choy, C. K., P. Cho, et al. (2001). "Water-soluble antioxidants in human tears: effect of the collection method." Invest Ophthalmol Vis Sci 42(13): 3130-4.

PURPOSE: To resolve differences in published data on tear antioxidant levels by comparing the concentration of water-soluble antioxidants in human reflex tears collected by capillary tube and by the Schirmer strip collection method and in basal and reflex tears collected using the Schirmer strip method. METHODS: Yawn-induced reflex tears (collected simultaneously by capillary tubes and by Schirmer strips) and basal tears (by Schirmer strips and using local anesthetic) were collected from 12 healthy subjects. Tear cysteine, ascorbate, glutathione, urate, and tyrosine were measured by high-performance liquid chromatography within a few minutes of collection. RESULTS: Cysteine, ascorbate, glutathione, and tyrosine were 5 to 10 times higher ($P < 0.01$) in both reflex and basal tears collected by Schirmer strip compared with reflex tears collected by capillary tube from the same subject. Urate levels were slightly but nonsignificantly higher in Schirmer strip samples ($P > 0.05$). CONCLUSIONS: The conflict in published data on tear antioxidants is caused by differences in collection methods. With the exception of urate, antioxidants accumulate to very high levels in corneal cells. Spuriously high antioxidant levels in tears collected using Schirmer strips, therefore, are most probably caused by contamination with intracellular constituents. The capillary tube collection method is proposed as the method of choice for reflex tear collection for biochemical studies. This less-invasive method facilitates the evaluation of tear antioxidant levels as a biomonitoring tool for corneal health. Although moderately increased antioxidant levels may be beneficial, the authors hypothesize that marked increases may indicate damage to the ocular surface.

Zafar, H., E. Nordh, et al. (2000). "Temporal coordination between mandibular and head-neck movements during jaw opening-closing tasks in man." Arch Oral Biol 45(8): 675-82.

Previous finding of concomitant mandibular and head movements during jaw function suggest a functional relation between the human jaw and neck regions. This study examined the temporal coordination between mandibular and head-neck movements during maximal jaw opening-closing tasks, at fast and slow speed. Twenty-four healthy individuals, median age 25 years, participated in the study. They were seated with firm back support but without head-neck support. Mandibular and head movements were simultaneously monitored by a wireless optoelectronic system for three-dimensional movement recording. The timing of head movement in relation to mandibular movement was estimated at defined time-points (start, peak, end and maximum velocity of movement), and during the entire course of the jaw-opening and jaw-closing phases. The results showed that the head in general started to move simultaneously with or before the mandible, reached the peak position simultaneously with, before or after the mandible, and reached the end position after the mandible. A higher degree of temporal coordination was found for fast speed at the start and the peak positions. The head most often attained maximum velocity after the mandible, and mostly lagged behind the mandible during the entire jaw-opening and -closing phases. These findings support the notion of a functional linkage between the human temporomandibular and craniocervical regions. They suggest that "functional jaw movements" comprise concomitant mandibular and head-neck movements which involve the temporomandibular, the atlanto-occipital and the cervical spine joints, and are caused by jointly activated jaw and neck muscles. It is proposed that these jaw and neck muscle actions, particularly at fast speed, are elicited and synchronized by preprogrammed neural command(s) common to both the jaw and the neck motor systems. From the present results and previous observations of concurrent jaw and head movement during fetal yawning, we suggest that these motor programmes are innate.

Zafar, H. (2000). "Integrated jaw and neck function in man. Studies of mandibular and head-neck movements during jaw opening-closing tasks." Swed Dent J Suppl(143): 1-41.

This investigation was undertaken to test the hypothesis of a functional relationship between the human temporomandibular and craniocervical regions. Mandibular and head-neck movements were simultaneously recorded in healthy young adults using a wireless optoelectronic system for three dimensional movement recording. The subjects were seated in an upright position without head support and were instructed to perform maximal jaw opening-closing movements at fast and slow speed. As a basis, a study was undertaken to develop a method for recording and analysis of mandibular and head-neck movements during natural jaw function. A consistent finding was parallel and coordinated head-neck movements during both fast and slow jaw opening-closing movements. The head in general started to move simultaneously with or before the mandible at the initiation of jaw opening. Most often, the head attained maximum velocity after the mandible. A high degree of spatiotemporal consistency of mandibular and head-neck movement trajectories was found in successive recording sessions. The head movement amplitude and the temporal coordination between mandibular and head-neck movements were speed related but not the movement trajectory patterns. Examination of individuals suffering from temporomandibular disorders and whiplash associated disorders (WAD) showed, compared with healthy subjects, smaller amplitudes, a diverse pattern of temporal coordination but a similar high degree of spatiotemporal consistency for mandibular and head-neck movements. In conclusion, the results suggest the following: A functional linkage exists between the human temporomandibular and craniocervical regions. Head movements are an integral part of natural jaw opening-closing. "Functional jaw movements" comprise concomitant mandibular and head-neck movements which involve the temporomandibular, the atlanto-occipital and the cervical spine joints, caused by jointly activated jaw and neck muscles. Jaw and neck muscle actions are elicited and synchronised by neural commands in common for both the jaw and the neck motor systems. These commands are preprogrammed, particularly at fast speed. In the light of previous observations of concurrent jaw and head movements during foetal yawning, it is suggested that these motor programs are innate. Neural processes underlying integrated jaw and neck function are invariant both in short- and long-term perspectives. Integrated jaw and neck function seems to be crucial for maintaining optimal orientation of the gape in natural jaw function. Injury to the head-neck, leading to WAD may derange integrated jaw-neck motor control and compromise natural jaw function.

Williams, D. R. (2000). "The yawning reflex: an upper motor neuron sign in amyotrophic lateral sclerosis." Neurology 55(10): 1592-3.

Wessells, H., D. Gralnek, et al. (2000). "Effect of an alpha-melanocyte stimulating hormone analog on penile erection and sexual desire in men with organic erectile dysfunction." Urology 56(4): 641-6.

OBJECTIVES: To assess the safety, erectogenic properties, and effect on sexual desire of Melanotan II, a synthetic melanotropic initiator of erection, in men with erectile dysfunction and organic risk factors. METHODS: Ten subjects were enrolled in a double-blind, placebo-controlled, crossover study. Melanotan II (0.025 mg/kg) and vehicle were each administered twice by subcutaneous injection; real-time RigiScan monitoring and a visual analog were used to quantify the erections during a 6-hour period. The level of sexual desire and side effects were recorded with a questionnaire. RESULTS: Melanotan II initiated subjectively reported erections in 12 of 19 injections versus only 1 of 21 doses of placebo. The mean rigidity score of the responders was 6.9 on a scale of 0 to 10. The mean duration of tip rigidity greater than 80% was 45.3 minutes with Melanotan II versus 1.9 for placebo ($P = 0.047$). The level of sexual desire after injection was significantly higher after Melanotan II administration than after placebo. Nausea and stretching/yawning occurred more frequently with Melanotan II, and 4 of 19 injections were associated with severe nausea. CONCLUSIONS: The erectogenic properties of Melanotan II are not limited to cases of psychogenic erectile dysfunction; men with a variety of organic risk factors developed penile erections. The finding of increased sexual desire warrants further investigation of centrally acting agents on disorders of sexual desire.

Wessells, H., N. Levine, et al. (2000). "Melanocortin receptor agonists, penile erection, and sexual motivation: human studies with Melanotan II." Int J Impot Res 12 Suppl 4: S74-9.

We review our experience with Melanotan II, a non-selective melanocortin receptor agonist, in human subjects with erectile dysfunction (ED). Melanotan II was administered to 20 men with psychogenic and organic ED using a double-blind placebo-controlled crossover design. Penile rigidity was monitored for 6 h using RigiScan. Level of sexual desire and side effects were reported with a questionnaire. In the absence of sexual stimulation, Melanotan II led to penile erection in 17 of 20 men. Subjects experienced a mean of 41 min Rigiscan tip rigidity>80%. Increased sexual desire was reported after 13/19 (68%) doses of Melanotan II vs 4/21 (19%) of placebo (P<0.01). Nausea and yawning were frequently reported side effects due to Melanotan II; at a dose of 0.025 mg/kg, 12.9% of subjects had severe nausea. We conclude that Melanotan II is a potent initiator of penile erection in men with erectile dysfunction. Our findings warrant further investigation of melanocortin agonists and antagonists on penile erection. International Journal of Impotence Research (2000) 12, Suppl 4, S74-S79.

Sharifzadeh, M., E. K. Firooz, et al. (2000). "Effects of different periods of lithium pretreatment and aminoglycoside antibiotics on apomorphine-induced yawning in rats." Pharmacol Toxicol 87(2): 84-8.

Interactive effects of intracerebroventricular administration of the aminoglycoside antibiotics, amikacin and gentamicin, and different duration of lithium pretreatment on apomorphine-induced yawning were investigated in male rats. The study was designed to investigate whether the hypothesis that the aminoglycoside antibiotics, amikacin and gentamicin, via their effects on phosphoinositide pathways and calcium channel might influence dopaminergic mechanisms as manifested in the yawning effect. Lithium is known to interact with phosphoinositide metabolism and was also tested after chronic studies on the apomorphine yawning model. Subcutaneous administration of apomorphine (0.1, 0.2 and 0.4 mg/kg) to rats induced yawning in a biphasic manner. However the maximum response was obtained by 0.2 mg/kg of the drug. Intracerebroventricular administration of aminoglycoside antibiotics amikacin (25 microg/rat) increased and gentamicin (10 and 20 microg/rat) decreased apomorphine-induced yawning. Pretreatment of animals with lithium (600 mg/l) in drinking water for 7, 14 and 21 days reduced yawning induced by apomorphine. Administration of lithium for 28 days did not induce any significant effect on yawning response. Amikacin and gentamicin function via the same mechanism on phosphoinositide cascade. Since amikacin and gentamicin did not affect the yawning response similarly, they apparently do not involve inositol trisphosphate level in the alterations of dopaminergic-induced yawning. Probably, the effect of lithium pretreatment on the number of yawns is also time-dependent and some tolerance to the inhibitory effect of lithium might occur after 28 days' treatment.

Sanchez, M. S., M. E. Celis, et al. (2000). "Evidence that alpha-MSH induced grooming is not primarily mediated by any of the cloned melanocortin receptors." Neuropeptides 34(2): 77-82.

It is well established that melanocortic peptides, such as melanocyte-stimulating hormone (MSH) and adrenocorticotropin, induce grooming behavior. The MC3 and MC4 receptors are the MC receptors which are most abundantly expressed in the brain. gamma-MSH, a peptide with preference to the MC3 receptor, however, does not induce grooming. Recent studies have shown that MC4 receptor antagonists are very effective in inhibiting alpha-MSH induced grooming. These data have indicated that grooming behavior in rodents may be mediated by the MC4 receptor. In this study we investigated if the recently developed MC1 receptor selective agonist MS05 was able to induce grooming in comparison with alpha-MSH. The results show that MS05 is effective in inducing grooming after either intracerebroventricular or ventral tegmental area administration in rats. Central administration of either MS05 or alpha-MSH besides grooming also induced stretching, yawning, rearing and locomotion. The results indicate that the earlier hypothesis that the MC4 receptor is the main mediator of grooming behavior has to be modified. Moreover, as this behaviour does not pharmacologically correlate to the profile of any of the five cloned MC receptors, we suggest that alpha-MSH induced grooming may not primarily be mediated by any of these receptors.

Rosaria Melis, M., M. S. Spano, et al. (2000). "Activation of gamma-aminobutyric acid(A) receptors in the paraventricular nucleus of the hypothalamus reduces apomorphine-, N-methyl-D-aspartic acid- and oxytocin-induced penile erection and yawning in male rats." Neurosci Lett 281(2-3): 127-30.

The effect of muscimol and baclofen injected into the paraventricular nucleus of the hypothalamus on penile erection and yawning induced by apomorphine, oxytocin and N-methyl-D-aspartic acid (NMDA) was studied in male rats. Muscimol (20-200 ng), but not baclofen (200 ng), injected into the paraventricular nucleus of the hypothalamus 10 min before apomorphine (50 ng), oxytocin (10 ng) or NMDA (50 ng) reduced penile erection and yawning induced by the above compounds given into the paraventricular nucleus. Bicuculline (250 ng) injected into the paraventricular nucleus 5 min before muscimol (100 ng) prevented the inhibitory effect of muscimol on penile erection and yawning induced by apomorphine, oxytocin and NMDA. The present results show that gamma-aminobutyric acid (GABA) inhibits penile erection and yawning by acting on GABA(A) receptors in the paraventricular nucleus of the hypothalamus.

Poe, D. S., I. Pyykko, et al. (2000). "Analysis of eustachian tube function by video endoscopy." Am J Otol 21(5): 602-7.

OBJECTIVE: Human eustachian tubes (ET) were inspected in vivo endoscopically, and video recordings were made for careful slow-motion analysis of normal physiologic function. SETTING: Ambulatory office in a tertiary referral center. SUBJECTS: Thirty-four adults, 17 with no history of ET dysfunction (2 of whom had tympanic membrane perforations), 17 with known ET dysfunction. INTERVENTIONS: Transnasal endoscopic examination of the nasopharyngeal opening of the eustachian tube during rest, swallowing, and yawning. MAIN OUTCOME MEASURES: Video analysis of ET opening movements. RESULTS: Normal ETs had four consistent sequential movements: (1) palatal elevation causing passive, then active, rotation of the medial cartilaginous lamina; (2) lateral excursion of the lateral pharyngeal wall; (3) dilation of the lumen, caused primarily by tensor veli palatini muscle movement beginning distally and inferiorly, then opening proximally and superiorly; and (4) opening of the tubal valve at the isthmus caused by dilator tubae muscle contraction. Dysfunctional ETs had intraluminal edema, polyps, or minimal muscle movement. CONCLUSIONS: Slow-motion endoscopic video analysis may be a useful new technique for the study of eustachian tube physiology. Consistent muscle movement patterns were demonstrated in normal subjects but were absent in abnormal subjects. More studies of normal and abnormal patterns are needed to establish useful clinical correlates.

Ouagazzal, A. M. and I. Creese (2000). "Intra-accumbens infusion of D(3) receptor agonists reduces spontaneous and dopamine-induced locomotion." Pharmacol Biochem Behav 67(3): 637-45.

The present study investigated whether PD 128907 and 7-OH-DPAT, described as preferential dopamine (DA) D(3) receptor agonists, produce hypolocomotion by acting at postsynaptic dopaminergic receptors within the nucleus accumbens. Bilateral infusion of PD 128907 (1.5 and 3 microg/0.5 microl) induced a dose-dependent hypolocomotion, whereas its enantiomer, PD 128908, was inactive. Local infusion of 7-OH-DPAT and the preferential DA autoreceptor agonist, B-HT 920, at the same dose range also decreased spontaneous locomotion. In addition, both drugs induced yawning with B-HT 920 producing the greatest effect. In the second experiment, the ability of these agonists to reduce the locomotor activity induced by intra-accumbens injection of DA (10 microg/0.5 microl) was studied. Pretreatment with either PD 128907 or 7-OH-DPAT (3 microg) reduced DA-induced hyperactivity. Local infusion of B-HT 920 (3 microg) failed to antagonise the locomotor effects of DA. Altogether these findings suggest that PD 128907 and 7-OH-DPAT induce hypolocomotion by acting in part at postsynaptic DA receptors. The possible role of D(2) and/or D(3) receptors in the mediation of these effects is discussed.

Oswiecimska, J., R. Brus, et al. (2000). "7-OH-DPAT, unlike quinpirole, does not prime a yawning response in rats." Pharmacol Biochem Behav 67(1): 11-5.

Repeated treatment in ontogeny with the dopamine (DA) D(2)/D(3) receptor agonist quinpirole is associated with enhanced quinpirole-induced yawning and other behaviors such as vacuous chewing, vertical jumping, and antinociception. To determine if the reputedly DA D(3) agonist (+/-)-2-(dipropylamino)-7-hydroxy-1,2,3, 4-tetrahydronaphthalene (7-OH-DPAT) would prime for yawning in a manner analogous to that for quinpirole, rats were treated for the first 11 days after birth with an equimolar dose of either quinpirole or 7-OH-DPAT (195.4 nmol/kg/day) and tested for agonist-induced yawning in adulthood. While enhanced quinpirole-induced and 7-OH-DPAT-induced yawning was observed in quinpirole-primed rats, acute treatments with quinpirole and 7-OH-DPAT did not produce an enhanced yawing response in 7-OH-DPAT-"primed" rats. Our findings indicate that 7-OH-DPAT, unlike quinpirole, does not prime for quinpirole- or 7-OH-DPAT-induced yawning in rats.

Murray, G. D. (2000). "Promoting good research practice." Stat Methods Med Res 9(1): 17-24.

Embarking on a new millennium provides the stimulus both to take stock and also to look forward. In the field of medical statistics there is much to make us feel proud and excited. Rapid methodological developments together with parallel developments in computer technology have enormously expanded our statistical repertoire. At the same time, the high profile attained by the evidence-based medicine movement means that the importance of our discipline is recognized more widely then ever before. However, any medical statistician who is involved in medical publishing, or who is even a regular reader of the medical literature, must be aware of the yawning chasm between what is recognized as good statistical practice and what is actually published. Poor study design, inappropriate analysis and selective reporting are commonplace. In my opinion the most important challenge currently facing our profession is the task of bridging this chasm.

Minagar, A. and W. A. Sheremata (2000). "Glossopharyngeal neuralgia and MS." Neurology 54(6): 1368-70.

Glossopharyngeal neuralgia (GPN) is characterized by a severe lancing pain in the posterior pharynx, tonsillar fossa, and base of the tongue. It is induced frequently by swallowing and yawning. GPN has not been described previously in MS patients. The authors report four MS patients with GPN. Three responded to carbamazepine and one resolved during treatment with adrenocorticotrophin hormone (ACTH) and cyclophosphamide. Withdrawal of carbamazepine after 1 week in one patient resulted in recurrence of pain. GPN may be associated with MS and responds to carbamazepine.

Millan, M. J., A. Dekeyne, et al. (2000). "S33084, a novel, potent, selective, and competitive antagonist at dopamine D(3)-receptors: II. Functional and behavioral profile compared with GR218,231 and L741,626." J Pharmacol Exp Ther 293(3): 1063-73.

The selective dopamine D(3)-receptor antagonist S33084 dose dependently attenuated induction of hypothermia by 7-hydroxy-2-dipropylaminotetralin (7-OH-DPAT) and PD128,907. S33084 also dose dependently reduced 7-OH-DPAT-induced penile erections (PEs) but had little effect on 7-OH-DPAT-induced yawning and hypophagia, and it did not block contralateral rotation elicited by the preferential D(3) agonist quinpirole in unilateral substantia nigra-lesioned rats. In models of potential antipsychotic activity, S33084 had little effect on conditioned avoidance behavior and the locomotor response to amphetamine and cocaine in rats, and weakly inhibited apomorphine-induced climbing in mice. Moreover, S33084 was inactive in models of potential extrapyramidal activity in rats: induction of catalepsy and prolactin

secretion and inhibition of methylphenidate-induced gnawing. Another selective D(3) antagonist, GR218,231, mimicked S33084 in inhibiting 7-OH-DPAT-induced PEs and hypothermia but neither hypophagia nor yawning behavior. Similarly, it was inactive in models of potential antipsychotic and extrapyramidal activity. In distinction to S33084 and GR218,231, the preferential D(2) antagonist L741,626 inhibited all responses elicited by 7-OH-DPAT. Furthermore, it displayed robust activity in models of antipsychotic and, at slightly higher doses, extrapyramidal activity. In summary, S33084 was inactive in models of potential antipsychotic and extrapyramidal activity and failed to modify spontaneous locomotor behavior. Furthermore, it did not affect hypophagia or yawns, but attenuated hypothermia and PEs, elicited by 7-OH-DPAT. This profile was shared by GR218,231, whereas L741,626 was effective in all models. Thus, D(2)-receptors are principally involved in these paradigms, although D(3)-receptors may contribute to induction of hypothermia and PEs. S33084 should comprise a useful tool for further exploration of the pathophysiological significance of D(3)- versus D(2)-receptors.

Melis, M. R., S. Succu, et al. (2000). "EP 60761 and EP 50885, two hexarelin analogues, induce penile erection in rats." Eur J Pharmacol 404 (1-2): 137-43.

The effect of hexarelin and four related peptide analogues, EP 40904, EP 40737, EP 50885 and EP 60761, injected into the paraventricular nucleus of the hypothalamus of male rats in doses between 2 and 2000 ng on spontaneous penile erection was studied. Of these peptides, EP 60761 and EP 50885, but not hexarelin, EP 40904 or EP 40737, increased dose-dependently the number of spontaneous penile erections. EP 60761 was active already at the dose of 20 ng, which induced the sexual response in 70% of the treated rats. The maximal response was induced by 200 ng of the peptide. EP 50885 was less potent than EP 60761, with 1000 ng being the minimal effective dose and 2000 ng as the dose required to induce the maximal response. At the doses used, both peptides also increased slightly the number of spontaneous yawning episodes. EP 60761- and EP 50885-induced penile erection was prevented by the oxytocin receptor antagonist [d(CH(2))(5) Tyr(Me)(2)-Orn(8)]vasotocin (0.1-1 microg) given intracerebroventricularly (i.c.v.), but not into the paraventricular nucleus (0.1-1 microg), by the competitive nitric oxide (NO) inhibitor N(G)-nitro-L-arginine methyl ester (L-NAME) given either into the paraventricular nucleus (10-20 microg) or i.c.v. (75-150 microg), by the N-type Ca(2+) channel blocker omega-conotoxin-GVIA (2-5 ng) or by the opiate morphine (1-10 microg), but not by the dopamine receptor antagonist (Z)-4-[3-[2-(trifluoromethyl)-9H-thioxanthen-9-ylidene]propyl]-1-p ipe razine-ethanol (cis-flupenthixol) (10 microg) or by the N-methyl-D-aspartic acid (NMDA) receptor antagonist (5R, 10S)-(+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5, 10-imine ((+)-MK-801) (1 microg), all given into the paraventricular nucleus before either peptide. The present results show that EP 60761 and EP 50885 induced penile erection by increasing central oxytocin transmission, possibly by activating NO synthase in the cell bodies of oxytocinergic neurons located in the paraventricular nucleus that control penile erection.

Meissner, W., U. Schmidt, et al. (2000). "Oral naloxone reverses opioid-associated constipation." Pain 84(1): 105-9.

Opioid-related constipation is one of the most frequent side effects of chronic pain treatment. Enteral administration of naloxone blocks opioid action at the intestinal receptor level but has low systemic bioavailability due to marked hepatic first-pass metabolism. The aim of this study was to examine the effects of oral naloxone on opioid-associated constipation in an intraindividually controlled manner. Twenty-two chronic pain patients with oral opioid treatment and constipation were enrolled in this study. Constipation was defined as lack of laxation and/or necessity of laxative therapy in at least 3 out of 6 days. Laxation and laxative use were monitored for the first 6 days without intervention ('control period'). Then, oral naloxone was started and titrated individually between 3x3 to 3x12 mg/day depending on laxation and withdrawal symptoms. After the 4-day titration period, patients were observed for further 6 days ('naloxone period'). The Wilcoxon signed rank test was used to compare number of days with laxation and laxative therapy in the two study periods. Of the 22 patients studied, five patients did not reach the 'naloxone period' due to death, operation, systemic opioid withdrawal symptoms, or therapy-resistant vomiting. In the 6 day 'naloxone' compared to the 'control period', the mean number of days with laxation increased from 2.1 to 3.5 (P<0.01) and the number of days with laxative medication decreased from 6 to 3.8 (P<0.01). The mean naloxone dose in the 'naloxone period' was 17.5 mg/day. The mean pain intensity did not differ between these two periods. Moderate side effects of short duration were observed in four patients following naloxone single dose administrations between 6 and 20 mg, resulting in yawning, sweating, and shivering. Most of the patients reported mild or moderate abdominal propulsions and/or abdominal cramps shortly after naloxone administration. All side effects terminated after 0.5-6 h. This controlled study demonstrates that orally administered naloxone improves symptoms of opioid associated constipation and reduces laxative use. To prevent systemic withdrawal signs, therapy should be started with low doses and patients carefully monitored during titration.

Lal, S., Y. Tesfaye, et al. (2000). "Effect of time-of-day on the yawning response to apomorphine in normal subjects." Neuropsychobiology 41 (4): 178-80.

The yawning response to the dopamine (DA) receptor agonist apomorphine HCl (Apo, 7 microg/kg s.c.) and placebo (physiological saline) were examined in two groups of normal men. One group (n = 11) was investigated in the morning and the other group (n = 16) in the afternoon. The frequency of yawning was polygraphically monitored for 60 min following injection. Apo increased yawning compared with placebo when given in the morning (p < 0.02), but not when given in the afternoon. Yawning frequency was increased after both Apo (p < 0.01) and placebo (p < 0.025) when given in the morning compared with responses in the afternoon. These results suggest that yawning frequency with both Apo and placebo is influenced by time of day, possibly as a result of diurnal variation in DA receptor sensitivity.

Kita, I., I. Sato-Suzuki, et al. (2000). "Yawning responses induced by local hypoxia in the paraventricular nucleus of the rat." Behav Brain Res 117(1-2): 119-26.

Yawing was induced by microinjections of L-glutamate, cyanide and a nitric oxide-releasing compound (NOC12) into the paraventricular nucleus of the hypothalamus (PVN) in anesthetized, spontaneously breathing rats. To evaluate physiological aspects of yawning, we monitored intercostal electromyogram (EMG) as an index of inspiratory activity, digastric EMG, blood pressure and electrocorticogram (ECoG). Microinjection of L-glutamate in the medial parvocellular subdivision (mp) elicited a stereotyped yawning response, i.e. an initial depressor response and an arousal shift in ECoG followed by a single large inspiration with mouth opening. The same sequential events were observed during spontaneous yawning, indicating that the mp is responsible for triggering yawning. Microinjection of cyanide into the mp caused the same yawning responses as the ones elicited by microinjection of L-glutamate, suggesting that the mp is sensitive to chemical hypoxia or ischemia within the PVN. Microinjection of NOC12 into the mp elicited a single large inspiration with a variable onset delay, suggesting that diffusible nitric oxide (NO) within the mp may act as a paracrine agent to cause a yawning response. We hypothesize that the mp of the PVN contains an oxygen sensor that causes a yawning response.

Hilgers, F. J., F. S. van Dam, et al. (2000). "Rehabilitation of olfaction after laryngectomy by means of a nasal airflow-inducing maneuver: the "polite yawning" technique." Arch Otolaryngol Head Neck Surg 126(6): 726-32.

OBJECTIVE: To develop a nasal airflow-inducing maneuver and apply it in the olfactory rehabilitation of patients who have undergone laryngectomy. DESIGN: Intervention study; before-and-after trial. SETTING: National cancer center. PATIENTS: Forty-four patients who underwent laryngectomy; 34 men and 10 women; mean age, 64 years (range, 42-80 years); mean time since surgery, 6 years (range, 8 months to 18 years). INTERVENTION: In a prospective clinical intervention study, we assessed the effectiveness of a nasal airflow-inducing maneuver ("polite yawning," ie, yawning with closed lips). Speech therapists trained the patients in the maneuver, and its effectiveness in inducing nasal airflow was checked with digital and water manometers. MAIN OUTCOME MEASURES: Olfactory acuity was assessed before and after the intervention by means of an odor detection test and a structured questionnaire concerning olfaction, taste, and appetite. Patients were categorized as "smellers" and "nonsmellers" on the basis of the results of the odor detection test and the present odor perception scale derived from the questionnaire. RESULTS: The nasal airflow-inducing maneuver could be taught to all patients, mostly in only one 30-minute therapy session. Fifteen of the 33 patients in the pretreatment nonsmeller category converted to smellers, for a success rate of 46% (P<. 001). CONCLUSION: The nasal airflow-inducing maneuver (the "polite yawning" technique) allowed almost half of the patients to recover their sense of smell.

Gowing, L., R. Ali, et al. (2000). "Buprenorphine for the management of opioid withdrawal." Cochrane Database Syst Rev(3): CD002025.

BACKGROUND: Managed withdrawal, or detoxification, is not in itself a treatment for opioid dependence, but it is a required first step for many forms of longer-term treatment. It may also represent the end point of an extensive period of treatment such as methadone maintenance. As such, managed withdrawal is an essential component of an effective treatment system. This review is one of a series that aims to assess the evidence as to the effectiveness of the variety of approaches to managing opioid withdrawal. OBJECTIVES: To assess the effectiveness of interventions involving the short-term use of buprenorphine to manage the acute phase of opioid withdrawal. SEARCH STRATEGY: Multiple electronic databases, including Medline, Embase, Psychlit, Australian Medical Index and Current Contents, were searched using a strategy designed to retrieve references broadly addressing the management of opioid withdrawal. Reference lists of retrieved studies, reviews and conference abstracts were handsearched. SELECTION CRITERIA: We included randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies comparing buprenorphine (treatment 10 days or less) with another form of treatment. Studies were required to provide detailed information on the type and dose of drugs used and the characteristics of patients treated. Studies were also required to provide information on the nature of withdrawal signs and symptoms experienced, the occurrence of adverse effects OR rates of completion of the withdrawal episode. DATA COLLECTION AND ANALYSIS: Potentially relevant studies were assessed for inclusion by one reviewer (LG). Inclusion decisions were confirmed by consultation between reviewers. Included studies were assessed by all reviewers. One reviewer (LG) undertook data extraction with the process confirmed by consultation between all three reviewers. MAIN RESULTS: Five studies met the criteria for inclusion in the review. No data tables are included in this review and no meta-analysis has been undertaken because of differences in treatment regimes and the assessment of outcomes in these studies. Four studies compared buprenorphine with clonidine. All found withdrawal to be less severe in the buprenorphine treatment group. In three of these studies all participants were withdrawing from heroin. Participants in one study were withdrawing from methadone, with doses reduced to 10mg/day prior to treatment with buprenorphine. Three of the studies commented on residual symptoms experienced by participants treated with buprenorphine to manage heroin withdrawal. Aches, restlessness, yawning, mydriasis, tremor, insomnia, nausea and mild anxiety were reported as being experienced by some participants. Rates of completion of withdrawal were able to be calculated for all studies included in the review but the definition of completion varied between studies. Rates ranged from 65% to 100%. None of the studies included in the review reported adverse effects. However, approximately approximately Lintzeris 1999a approximately approximately (a single-group study which therefore did not meet the inclusion criteria) reported 50% of participants withdrawing from heroin experienced headaches, 28% sedation, 21% nausea, 21% constipation,

21% anxiety, 17% dizziness and 17% itchiness during withdrawal. These adverse effects were most common in the first 2-3 days of treatment and then subsided. In four of the five studies treatment was undertaken on an inpatient basis. Only approximately approximately O'Connor 1997 approximately approximately provided outpatient treatment. However, two studies that did not meet the inclusion criteria (approximately approximately Diamant 1998 approximately approximately and approximately approximately Lintzeris 1999a approximately approximately) also provided outpatient treatment. The findings of these studies support the feasibility of heroin withdrawal being managed with buprenorphine on an outpatient basis

Fanciullacci, M., M. Alessandri, et al. (2000). "Dopamine involvement in the migraine attack." Funct Neurol 15 Suppl 3: 171-81.
Clinical evidence and recent genetic findings seem to indicate an involvement of dopamine in the pathophysiology of the migraine attack. Prodromal symptomatology (mood changes, yawning, drowsiness, food craving), accompanying symptoms (nausea, vomiting, hypotension) and postdromal symptoms (mood changes, drowsiness, tiredness) may be related to dopaminergic activation. The dopaminergic system could also play a role in the headache phase, either by taking part in nociception mechanisms, or by regulating cerebral blood flow. A body of pharmacological findings seems to support this involvement. Migraine patients, between attacks, show a higher responsiveness to acute administration of dopaminergic agents. Apomorphine administration induces in migraineurs more yawns as well other dopaminergic symptoms e.g. nausea, vomiting, dizziness. Migraine has been associated with hypotension and, occasionally, with syncope. Bromocriptine causes severe orthostatic syndrome in migraine patients. Both piribedil and apomorphine markedly increase cerebral blood flow of migraine patients, thus indicating enhanced responsiveness of dopamine receptors which are involved in cerebral blood flow regulation. Interictal dopaminergic hypersensitivity has also been demonstrated by means of neuroendocrine tests. Altered dopaminergic control of prolactin secretion exists in migrainous women. L-deprenyl, a MAO-B inhibitor, is significantly more effective in reducing prolactin levels in migraineurs than in controls. Taken together, these findings support the view that hypersensitivity of peripheral and central dopaminergic receptors is a specific migraine trait. Finally, a high density of lymphocytic D5 receptors has been found in migraine sufferers, thus suggesting their upregulation. Therefore, the hypothesis that dopaminergic activation is a primary pathophysiological component in certain subtypes of migraine, namely those characterised by marked dopaminergic symptomatology, has been advanced. From this perspective, a blockade of dopaminergic hyperresponsive receptors can be considered as a rationale for the therapy of migraine.

Clifford, J. J. and J. L. Waddington (2000). "Topographically based search for an "Ethogram" among a series of novel D(4) dopamine receptor agonists and antagonists." Neuropsychopharmacology 22(5): 538-44.
The effects of three selective D(4) antagonists [CP-293,019, L-745, 870, and Ro 61-6270] and two putative selective D(4) agonists [CP-226,269 and PD 168077] were compared with those of the generic D(2)-like [D(2L/S),D(3), D(4)] antagonist haloperidol to identify any characteristic "ethogram," in terms of individual topographies of behavior within the natural rodent repertoire, as evaluated using ethologically based approaches. Among the D(4) antagonists, neither L-745,870 (0.0016-1.0 mg/kg) nor Ro 61-6270 (0.2-25.0 mg/kg) influenced any behavior; whereas, CP-293,019 (0.2-25.0 mg/kg) induced episodes of nonstereotyped sniffing, sifting, and vacuous chewing; there were no consistent effects on responsivity to the D(2)-like agonist RU 24213. Among the putative D(4) agonists, CP-226, 269 (0.2-25.0 mg/kg) failed to influence any behavior; whereas, PD 168077 (0.2-25.0 mg/kg) induced nonstereotyped shuffling locomotion with uncoordinated movements, jerking, and yawning, which were insensitive to antagonism by CP-293,019, L-745,870, or haloperidol. These findings fail to indicate any "ethogram" for selective manipulation of D(4) receptor function at the level of the interaction between motoric and psychological processes in sculpting behavioral topography over habituation of exploration through to quiescence and focus attention on social, cognitive, or other levels of examination.

Canales, J. J. and S. D. Iversen (2000). "Dynamic dopamine receptor interactions in the core and shell of nucleus accumbens differentially coordinate the expression of unconditioned motor behaviors." Synapse 36(4): 297-306.
Many neurochemical and behavioral functions mediated by dopamine require the dynamic interaction between dopamine receptors. We examined the behavioral effects evoked by microinjections of drugs with relative selectivity for specific dopamine receptors into the nucleus accumbens (Acb). The results showed that, at behaviorally inactive doses, the dopamine D1-class receptor agonist SKF 38393 switched the behavioral profile induced by injections of the dopamine D2-class receptor agonist quinpirole into the Acb, from sedation, yawning, and motor inhibition to hyperactive-like behavior. Further, the effects of injections of the dopamine D2-class receptor agonist (+)-PD 128907 into the shell of Acb, including suppression of rearing, locomotion, and grooming, and induction of oral dyskinesia, yawning, and sedation, could not be distinguished from those elicited by (+)-PD 128907 following infusions into the core of Acb. However, the behavioral effects elicited by coadministration of SKF 38393 and (+)-PD 128907 into the core or the shell of Acb showed a striking anatomical specificity. The infusion of SKF 38393 plus (+)-PD 128907 into the core, but not into the shell, of Acb modified the pattern of responses induced by (+)-PD 128907, inducing behavioral hyperactivity. These results suggest critical differences in the functional interaction between dopamine receptors in the core and the shell of the Acb and reveal a mechanism of behavioral switching in the core of Acb by virtue of which dopamine D1-class receptors regulate the transition from states of behavioral suppression to states of heightened psychomotor arousal.

Canales, J. J. and S. D. Iversen (2000). "Psychomotor-activating effects mediated by dopamine D(2) and D(3) receptors in the nucleus accumbens." Pharmacol Biochem Behav 67(1): 161-8.
The contribution made by specific dopamine receptor subtypes to the induction of motor behaviors has not been firmly established. Here, we first characterized the behavioral effects induced by a D(2)-class receptor agonist, bromocriptine, following injections into the nucleus accumbens (Acb). Bromocriptine showed an atypical D(2)-class receptor agonist profile, having no observable effect on a range of motor behaviors. However, when coadministered with the D(1)-class receptor agonist SKF 38393, bromocriptine showed a typical D(2)-class receptor agonist profile, enhancing locomotor activity and suppressing spontaneous yawning. We then administered the dopamine receptor antagonists L-741626 and nafadotride, which possess relative selectivity for D(2) and D(3) receptors, respectively, prior to injections of dopamine agonists into the Acb. Nafadotride significantly reduced the locomotor-enhancing effects elicited by the coadministration of SKF 38393 and the D(2)-class receptor agonist (+)-PD 128907 into the Acb, and also attenuated the effects induced by the combination of SKF 38393 and bromocriptine, although not significantly so. L-741626 mildly attenuated the locomotor effects elicited by both drug combinations. Taken together, these results suggest that both D(2) and D(3) receptors in the Acb contribute to the expression of heightened psychomotor activation.

Brumback, R. A. (2000). "Weinberg's syndrome: a disorder of attention and behavior problems needing further research." J Child Neurol 15(7): 478-80.
A subset of inattentive children have an underlying problem in sustaining wakefulness ("vigilance"). This disorder of vigilance, termed Weinberg's syndrome, is characterized by difficulty in maintaining wakefulness and alertness as evidenced by (among other symptoms) motor restlessness (fidgeting and moving about, yawning and stretching, talkativeness) and complaints of tiredness. During tasks requiring concentration (continuous mental activity) such as reading, children with Weinberg's syndrome will daydream, lose interest, complain of boredom, and become increasingly restless. Napping, while infrequent, usually is not refreshing. A distinct personality described by family members and friends as kind, affectionate, compassionate, or "angelic" also seems to characterize this condition. Weinberg's syndrome has a familial pattern suggesting autosomal-dominant inheritance. Additional neurophysiologic, pharmacotherapeutic, epidemiologic, and genetic studies will be necessary for a full understanding of Weinberg's syndrome.

Brien, S. E., E. Wilson, et al. (2000). "The conditioned response erection (CRE)--a new approach to modelling erectile responses in the rat." Int J Impot Res 12(2): 91-6.
Several animal models are currently used in erectile (dys)function research; these models fail to account for the conditions involving the more spontaneous erections in humans. Recently, we observed an increase in the number of 'spontaneously' occurring erections in rats with previous exposure to apomorphine (APO), a centrally acting drug that initiates penile erections and yawns. Based on this observation, we designed a series of experiments to characterize the development of enhanced, non-apomorphine-induced erections or 'spontaneous' erectile responses to vehicle administration in rats with previous exposure to APO. We further examined the effects of castration on these conditioned erections. Naive (ie never received APO) rats were administered vehicle (1 ml/kg saline) to determine the frequency of baseline erections and yawns. An alternating series of APO (80 microg/kg s.c.) and vehicle administrations were performed over several days and subsequent erectile and yawning responses were recorded. Following 3 sets of 3 APO administrations (with vehicle administered between sets), and the 3rd vehicle administration, these rats were then surgically castrated and allowed 30 days to recover. Following this, APO was administered 3 times to determine erectile and yawning responses post-castration, followed by vehicle administration to determine the effects of castration on conditioned APO responses. The major findings were: (1) that although naive rats had a basal spontaneous erectile response (0.75 +/- 0.88; 4 of 8 rats with at least one erection), repetitive administration (up to 22 treatments) of the central initiator apomorphine significantly increased the number of erections (1.8 +/- 0.7; 7 of 8 rats with at least one erection) and yawning (2.5 +/- 2.47) responses to vehicle administration; and (2) both spontaneous yawning and erectile responses were found to be androgen dependent since castration dramatically lowered the number of erections (0.13 +/- 0.35; 1 of 8 rats with at least one erection) and yawns (0). Therefore, this method of producing erections without a pharmacological manipulation provides an additional animal model which can be used in conjunction with the APO-induced erections in characterizing the physiology and pathophysiology of erectile function in conscious rats.

Billeth, R., E. Jorgler, et al. (2000). "[Bilateral anterior operculum syndrome]." Nervenarzt 71(8): 651-4.
Characteristically, patients with anterior operculum syndrome (AOS), also known as Marie-Foix-Chavany syndrome cannot perform voluntary movements of the face, jaw, tongue, and pharynx. As a result, they are unable to speak, swallow, grimace, smile, or carry out any other voluntary facial masticatory or linguopharyngeal movement. At the same time, involuntary movements of the aforementioned muscles are fully preserved. Laughing, yawning, and coughing, as well as mimicking movements accompanying emotions, eye closure during sleep, or the blink reflex are unaffected. The pathoanatomic substrate of this voluntary-involuntary dissociation is a bilateral lesion of the frontoparietal operculum usually caused by ischemic strokes. The prognosis is usually poor, especially concerning the ability to speak and eat. The name Marie-Foix-Chavany for this syndrome is fully established, although the characteristic voluntary-involuntary dissociation is not mentioned in the original French publication of 1926. We present a case and discuss clinical features, pathophysiology, and differential

diagnosis of AOS. In a 7-year follow-up, we observed better functional outcome than is commonly described in the literature.

Beltramo, M., F. R. de Fonseca, et al. (2000). "Reversal of dopamine D(2) receptor responses by an anandamide transport inhibitor." J Neurosci 20(9): 3401-7.
We characterized the pharmacological properties of the anandamide transport inhibitor N-(4-hydroxyphenyl)-arachidonamide (AM404) in rats and investigated the effects of this drug on behavioral responses associated with activation of dopamine D(2) family receptors. Rat brain slices accumulated [(3)H]anandamide via a high-affinity transport mechanism that was blocked by AM404. When administered alone in vivo, AM404 caused a mild and slow-developing hypokinesia that was significant 60 min after intracerebroventricular injection of the drug and was reversed by the CB1 cannabinoid receptor antagonist SR141716A. AM404 produced no significant catalepsy or analgesia, two typical effects of direct-acting cannabinoid agonists. However, AM404 prevented the stereotypic yawning produced by systemic administration of a low dose of apomorphine, an effect that was dose-dependent and blocked by SR141716A. Furthermore, AM404 reduced the stimulation of motor behaviors elicited by the selective D(2) family receptor agonist quinpirole. Finally, AM404 reduced hyperactivity in juvenile spontaneously hypertensive rats, a putative model of attention deficit hyperactivity disorder. The results support a primary role of the endocannabinoid system in the regulation of psychomotor activity and point to anandamide transport as a potential target for neuropsychiatric medicines.

Beale, M. D. and T. M. Murphree (2000). "Excessive yawning and SSRI therapy." Int J Neuropsychopharmacol 3(3): 275-276.
As we become more experienced with the long-term use of selective serotonin reuptake inhibitors (SSRIs), more subtle side-effects may become evident. Clinicians may be aware of yawning as a side-effect of antidepressant therapy, however sparse literature exists on the topic. We present two cases in which excessive daytime yawning was associated with SSRI treatment.

Argiolas, A., M. R. Melis, et al. (2000). "ACTH- and alpha-MSH-induced grooming, stretching, yawning and penile erection in male rats: site of action in the brain and role of melanocortin receptors." Brain Res Bull 51(5): 425-31.
The effect of adrenocorticotropin (ACTH)(1-24) and alpha-melanocyte stimulating hormone (alpha-MSH) on grooming, stretching, yawning and penile erection was studied after injection into different brain areas. Both peptides induce the above responses when injected into the hypothalamic periventricular region of the third ventricle. This region includes the paraventricular nucleus, the dorsomedial nucleus, the ventromedial nucleus and the anterior hypothalamic area. The minimal effective dose of both peptides was 0.5 microg and the maximal effect was seen with 2 microg, the highest dose tested. Irrespective of the injection site, grooming started 5-7 min after injection of either peptide, while stretching, yawning and penile erection started only after 15-35 min and lasted for 90-120 min. In contrast both peptides were ineffective when injected into the preoptic area, the caudate nucleus or the CA1 field of the hippocampus. Grooming, stretching and yawning, but not penile erection, were prevented by cyclic[AcCys(11), D-Nal(14), Cys(18), AspNH(2)(22)]-beta-MSH (11-22) (HS014), a selective melanocortin 4 receptor antagonist, injected into the same periventricular area 10 min before of ACTH(1-24) or alpha-MSH. The results show that ACTH(1-24) and alpha-MSH act in the hypothalamic periventricular region to induce the above responses and that grooming, stretching and yawning, but not penile erection, are mediated by melanocortin 4 receptors.

Anupama and P. Ravindra (2000). "Value-added food: single cell protein." Biotechnol Adv 18(6): 459-79.
The alarming rate of population growth has increased the demand for food production in third-world countries leading to a yawning gap in demand and supply. This has led to an increase in the number of hungry and chronically malnourished people. This situation has created a demand for the formulation of innovative and alternative proteinaceous food sources. Single cell protein (SCP) production is a major step in this direction. SCP is the protein extracted from cultivated microbial biomass. It can be used for protein supplementation of a staple diet by replacing costly conventional sources like soymeal and fishmeal to alleviate the problem of protein scarcity. Moreover, bioconversion of agricultural and industrial wastes to protein-rich food and fodder stocks has an additional benefit of making the final product cheaper. This would also offset the negative cost value of wastes used as substrate to yield SCP. Further, it would make food production less dependent upon land and relieve the pressure on agriculture. This article reviews diversified aspects of SCP as an alternative protein-supplementing source. Various potential strains and substrates that could be utilized for SCP production are described. Nutritive value and removal of nucleic acids and toxins from SCP as a protein-supplementing source are discussed. New processes need to be exploited to improve yield. In that direction the solid state fermentation (SSF) method and its advantages for SCP production are highlighted.

Zarrindast, M. R., S. Fazli-Tabai, et al. (1999). "Influence of different adrenoceptor agonists and antagonists on physostigmine-induced yawning in rats." Pharmacol Biochem Behav 62(1): 1-5.
In the present study, effects of adrenoceptor agonists and antagonists on physostigmine-induced yawning was investigated. Intraperitoneal (i.p.) injection of different doses of physostigmine (0.03, 0.05, 0.1, and 0.2 mg/kg) induced yawning in rats. The maximum response was obtained by 0.2 mg/kg of the drug. The alpha1-adrenoceptor agonist, phenylephrine, and the alpha2-adrenoceptor agonist, clonidine, decreased yawning induced by physostigmine. Prazosin and higher doses of phenoxybenzamine reduced the inhibitory effect of phenylephrine. Higher doses of yohimbine also reduced the clonidine response. The adrenoceptor antagonists, prazosin, phenoxybenzamine, and propranolol, did not significantly alter the physostigmine response. However, yohimbine, or lower doses of prazosin, decreased the physostigmine response. It may be concluded that alpha1- and alpha2-adrenoceptor stimulation decreases the physostigmine-induced yawning behavior in rats.

Tizabi, Y., R. L. Copeland, Jr., et al. (1999). "Nicotine blocks quinpirole-induced behavior in rats: psychiatric implications." Psychopharmacology (Berl) 145(4): 433-41.
RATIONALE AND OBJECTIVES: Because of known and imputed roles of dopaminergic and nicotinic cholinergic systems in a variety of neurological and neuropsychiatric disorders, combined neurochemical and behavioral methods assessments were made to study the intermodulatory roles of these neurochemical systems. Methods: Rats were treated daily during postnatal ontogeny with the dopamine D2/D) agonist, quinpirole (QNP) HCl (1.0 mg/kg/day), for the first 3 weeks from birth. This priming process replicated previous findings of behavioral sensitization, manifested as hyperlocomotion, increased paw treading with jumping, and increased yawning. RESULTS: All effects were partially or totally blocked by acute treatment with nicotine (0.3 mg/kg, i.p.). The effects of nicotine, in turn, were partially or totally blocked by the nicotinic antagonist, mecamylamine (1.0 mg/kg, i.p.). In concert with these behavioral actions, QNP-primed rats displayed greater binding of [3H]cytisine in midbrain and cerebellum and greater [125I]alpha-bungarotoxin binding in hippocampus and striatum. CONCLUSIONS: Accordingly, these selective ligands for alpha4beta2 and alpha7 nicotinic receptors, respectively, demonstrate that nicotinic receptors are altered by dopamine D2/D3 agonist treatment of rats with primed dopamine receptors. We propose that nicotinic agonists may have a therapeutic benefit in behavioral disorders brought about by central dopaminergic imbalance.

Sandyk, R. (1999). "Treatment with AC pulsed electromagnetic fields improves olfactory function in Parkinson's disease." Int J Neurosci 97 (3-4): 225-33.
Olfactory dysfunction is a common symptom of Parkinson's disease (PD). It may manifest in the early stages of the disease and infrequently may even antedate the onset of motor symptoms. The cause of olfactory dysfunction in PD remains unknown. Pathological changes characteristic of PD (i.e., Lewy bodies) have been demonstrated in the olfactory bulb which contains a large population of dopaminergic neurons involved in olfactory information processing. Since dopaminergic drugs do not affect olfactory threshold in PD patients, it has been suggested that olfactory dysfunction in these patients is not dependent on dopamine deficiency. I present two fully medicated Parkinsonian patients with long standing history of olfactory dysfunction in whom recovery of smell occurred during therapeutic transcranial application of AC pulsed electromagnetic fields (EMFs) in the picotesla flux density. In both patients improvement of smell during administration of EMFs occurred in conjunction with recurrent episodes of yawning. The temporal association between recovery of smell and yawning behavior is remarkable since yawning is mediated by activation of a subpopulation of striatal and limbic postsynaptic dopamine D2 receptors induced by increased synaptic dopamine release. A high density of dopamine D2 receptors is present in the olfactory bulb and tract. Degeneration of olfactory dopaminergic neurons may lead to upregulation (i.e., supersensitivity) of postsynaptic dopamine D2 receptors. Presumably, small amounts of dopamine released into the synapses of the olfactory bulb during magnetic stimulation may cause activation of these supersensitive receptors resulting in enhanced sense of smell. Interestingly, in both patients enhancement of smell perception occurred only during administration of EMFs of 7 Hz frequency implying that the release of dopamine and activation of dopamine D2 receptors in the olfactory bulb was partly frequency dependent. In fact, weak magnetic fields have been found to cause interaction with biological systems only within narrow frequency ranges (i.e., frequency windows) and the existence of such frequency ranges has been explained on the basis of the cyclotron resonance model.

Sandyk, R. (1999). "AC pulsed electromagnetic fields-induced sexual arousal and penile erections in Parkinson's disease." Int J Neurosci 99 (1-4): 139-49.
Sexual dysfunction is common in patients with Parkinson's disease (PD) since brain dopaminergic mechanisms are involved in the regulation of sexual behavior. Activation of dopamine D2 receptor sites, with resultant release of oxytocin from the paraventricular nucleus (PVN) of the hypothalamus, induces sexual arousal and erectile responses in experimental animals and humans. In Parkinsonian patients subcutaneous administration of apomorphine, a dopamine D2 receptor agonist, induces sexual arousal and penile erections. It has been suggested that the therapeutic efficacy of transcranial administration of AC pulsed electromagnetic fields (EMFs) in the picotesla flux density in PD involves the activation of dopamine D2 receptor sites which are the principal site of action of dopaminergic pharmacotherapy in PD. Here, 1 report 2 elderly male PD patients who experienced sexual dysfunction which was recalcitrant to treatment with anti Parkinsonian agents including selegiline, levodopa and tolcapone. However, brief transcranial administrations of AC pulsed EMFs in the picotesla flux density induced in these patients sexual arousal and spontaneous nocturnal erections. These findings support the notion that central activation of dopamine D2 receptor sites is associated with the therapeutic efficacy of AC pulsed EMFs in PD. In addition, since the right hemisphere is dominant for sexual activity, partly because of a dopaminergic bias of this hemisphere, these findings suggest that right hemispheric activation in response to administration of AC pulsed EMFs was associated in these patient with improved sexual functions.

Sandyk, R. (1999). "Yawning and stretching induced by transcranial application of AC pulsed electromagnetic fields in Parkinson's disease."

Int J Neurosci 97(1-2): 139-45.
Yawning is considered a brainstem regulated behavior which is associated with changes in arousal and activity levels. Yawning and stretching are dopamine (DA) mediated behaviors and pharmacological studies indicate that these behaviors are associated with increased DA release coupled with stimulation of postsynaptic DA-D2 receptors. Despite their relation to the dopaminergic system, yawning and stretching are poorly documented in untreated or treated patients with Parkinson's disease (PD). A 49 year old fully medicated female patient with juvenile onset PD is presented in whom recurrent episodes of yawning and stretching developed during transcranial administration of AC pulsed electromagnetic fields (EM Fs) of picotesla flux density. These episodes have not been observed previously in this or other patients during treatment with levodopa or DA receptor agonists or in unmedicated PD patients during treatment with AC pulsed EMFs. It is suggested that yawning and stretching behavior resulted in this patient from a synergistic interaction between EMFs and DA derived from levodopa supplementation with EMFs possibly facilitating the release of DA and simultaneously activating postsynaptic DA-D2 receptors in the nigrostriatal dopaminergic pathways. In addition, it is postulated that the release of ACTH/MSH peptides from peptidergic neurons in the brain upon stimulation of the DA-D2 receptors reinforced the yawning and stretching behavior.

Queiroz, C. M. and R. Frussa-Filho (1999). "Effects of buspirone on an animal model of tardive dyskinesia." Prog Neuropsychopharmacol Biol Psychiatry 23(8): 1405-18.
1. The effects of buspirone were studied on an animal model of tardive dyskinesia, i.e., the quantification of orofacial dyskinesia in rats repeatedly treated with reserpine. 2. Rats were co-treated with saline [SAL] or buspirone [BUS] (3.0 mg/kg, i.p., twice daily) and vehicle [VEH] or reserpine [RES] (0.1 mg/kg, s.c., once every other day) for 19 days. On the day 20, the animals were observed for quantification of the behavioral parameters of orofacial dyskinesia: tongue protrusion and vacuous chewing movements frequencies and duration of twitching of the facial musculature. 3. Rats of the SAL + RES group exhibited a significant increase in the three behavioral parameters of orofacial dyskinesia relative to the rats of the SAL + VEH group. However, animals of the BUS + RES group showed only an increased frequency of vacuous chewing movements when compared to animals of the SAL + VEH group. In addition, the duration of the facial twitching was significantly decreased in the BUS + RES group in relation to rats of the SAL + RES group. There were no significant differences in the orofacial parameters between the BUS + VEH and the SAL + VEH groups. 4. Because it was also verified that chronic buspirone treatment was able to increase apomorphine-induced yawning behavior, the possibility is raised that buspirone attenuates reserpine-induced orofacial dyskinesia through the development of dopamine autoreceptor supersensitivity.

Petrikovsky, B., G. Kaplan, et al. (1999). "Fetal yawning activity in normal and high-risk fetuses: a preliminary observation." Ultrasound Obstet Gynecol 13(2): 127-30.
OBJECTIVE: To study yawning activity in healthy fetuses and in fetuses at high risk. METHODS: Yawning activity was studied in 16 healthy and 22 high-risk fetuses. Studies were performed in the postprandial state at 09.00 and 12.00 in a quiet room with the woman in the lateral recumbent position. All ultrasound examinations were performed using a 3.5-MHz Acuson 128 PX curvilinear probe. Fetal lips, mouth, tongue, pharynx, larynx, trachea and esophagus were surveyed in serial coronal and sagittal planes. All fetal mouthing movements were analyzed by a review of the videotape in slow motion. RESULTS: In both normal and high-risk fetuses, yawning was represented by isolated mouthing movements and consisted of slow opening of the mouth with simultaneous downward movements of the tongue. This phase occupied 50-75% of the yawning cycle. After reaching its maximum opening, the mouth remained wide open for 2-8 s and returned to its resting position within seconds. Growth-restricted fetuses demonstrated yawning patterns consisting of isolated yawns similar to those seen in healthy fetuses. Unusual bursts of fetal yawning activity were recorded in anemic fetuses. CONCLUSION: Yawning activity in anemic fetuses may represent a compensatory process to increase venous return to the heart.

O'Sullivan, J. D., A. J. Lees, et al. (1999). "Yawning in Parkinson's disease." Neurology 52(2): 428.

Melis, M. R. and A. Argiolas (1999). "Yawning: role of hypothalamic paraventricular nitric oxide." Zhongguo Yao Li Xue Bao 20(9): 778-88.
Yawning is a phylogenetically old, stereotyped event that occurs alone or associated with stretching and/or penile erection in humans, in animals from reptiles to birds and mammals, under different conditions. Several neurotransmitters and neuropeptides are involved in its control at the central level. One of these at the level of the paraventricular hypothalamic nucleus (PVHN) is nitric oxide (NO). First, NO synthase inhibitors injected into this hypothalamic nucleus prevent yawning induced by dopamine agonists, oxytocin or N-methyl-D-aspartic acid (NMDA), which induce yawning by activating PVHN oxytocinergic neurons projecting to extra-hypothalamic brain areas. The inhibitory effect of NO synthase inhibitors was not observed when these compounds were given concomitantly with L-arginine, the precursor of NO. Second, dopamine agonists, NMDA and oxytocin given at doses that induce yawning, increase NO production in the PVHN, as determined by in vivo microdialysis. Conversely, the opiate morphine, which prevents yawning induced by dopamine agonists, oxytocin and NMDA, also prevents the increase in the paraventricular NO production induced by these compounds. Third, NO donors, such as nitroglycerin, sodium nitroprusside and hydroxylamine, induce yawning when injected into the PVHN apparently by activating oxytocinergic transmission. Since guanylate cyclase inhibitors and NO scavengers (hemoglobin) injected into the PVHN do not prevent drug-induced yawning, nor 8-Br-cGMP injected into the PVHN induces this behavioral response, it is likely that NO acts as an intracellular rather than an intercellular modulator inside the PVHN oxytocinergic neurons in which NO is formed to facilitate the expression of this phylogenetically old event by guanylate cyclase-independent mechanisms.

Leonhardt, M., M. Abele, et al. (1999). "Pathological yawning (chasm) associated with periodic leg movements in sleep: cure by levodopa." J Neurol 246(7): 621-2.

Laurent-Vannier, A., G. Fadda, et al. (1999). "[Foix-Chavany-Marie syndrome in a child caused by a head trauma]." Rev Neurol (Paris) 155(5): 387-90.
We report the case of a traumatic Foix-Chavany-Marie syndrome (SFMC) which is the cortico-subcortical type of suprabulbar palsy. A 10-year-old boy was brain injured in a traffic accident in August 1996. He was found comatous (initial GCS = 6) without any focal neurological deficit. The hemodynamic situation was stable even though he presented two wounds of the scalp and a hemoperitoneum that required intensive perfusions. The initial CT scan elicited a frontal fracture, ischemo hemorrhagic lesions of the right frontopolar and anterior temporal cortex. On the second day, he developed on the left side a subdural collection and a extradural hematoma which was surgically withdrawn. The comatous state ended on the ninth day. On examination, The child was awake and alert, able to understand spoken and written language but unable to speak. There was masticatory diplegia: the mouth was half open, the patient was drooling, chewing was impossible. The most striking feature was the automatic voluntary dissociation which might be observed on laughing, crying and yawning. The patient was unable to initiate swallowing but reflex swallowing was preserved once food was placed into the pharynx. The child had a deficit of voluntary control of muscles supplied by nerves V, VI, IX, X, XI. These clinical features are the hallmarks of SFMC. The first case was reported in 1837 by Magnus. The syndrome was described by Foix Chavany et Marie in 1926, and called SFMC by Weller (1993). His literature review of 62 SFMC allowed the differentiation of five clinical types: the classical and most common form associated with cerebrovascular disease, a subacute form caused by central nervous system infections, a developmental form, a reversible form in children with epilepsy and a rare type associated with neurodegenerative disorders. Bilateral opercular lesions was confirmed in 31 of 41 patients who had CT or MRI performed, and by necropsy in 7 of 10 patients. As previously reported, the outcome was poor for this boy who recovered very limited orofacial motor abilities. The medical functional readaptation was long et tedious and took in consideration the fact that the speech disturbance was anarthria and not an aphasic or an apraxic one and the age of onset of this acute acquired syndrome.

Kropmans, T. J., P. U. Dijkstra, et al. (1999). "The smallest detectable difference of mandibular function impairment in patients with a painfully restricted temporomandibular joint." J Dent Res 78(8): 1445-9.
Mandibular functions such as speech, laughing, yawning, mastication, and taking a large bite may be impaired if temporomandibular disorders exist. The Mandibular Function Impairement Questionnaire is a validated instrument that scores perceived difficulty of representative mandibular functions in relation to jaw complaints. However, the reliability of the Mandibular Function Impairment Questionnaire has never been adequately tested. Generalizability and decision studies are currently proposed to assess the reliability of a measurement device. The smallest detectable difference is the smallest statistically significant amount of change to be detected with a measurement device. The purpose of this study was to assess the reliability of the Mandibular Function Impairement Questionnaire in terms of the smallest detectable difference. Twenty-five consecutive patients with painfully restricted temporomandibular joints completed the Mandibular Function Impairement Questionnaire on two separate measurement days, one week apart, using two consecutive sessions per day. Spearman's r was calculated for test-retest reliability. Variance components such as patients, measurement days, repetitions, and all their interactions were analyzed in the generalizability study. In the decision study, the smallest detectable difference was calculated for different days and repetitions. Spearman's r varied from 0.69 to 0.96. The between-patient variance and the error variance contributed 81% and 19% to total variance, respectively. The Mandibular Function Impairment Questionnaire is a reliable instrument for the assessment of mandibular function impairment. The minimal amount of change to be detected is 14 units on a scale of 0 to 68. Reliability in terms of the smallest detectable difference increases if the measurement is repeated twice on two separate days: The smallest detectable difference improves to 10 units.

Hipolide, D. C., L. L. Lobo, et al. (1999). "Treatment with dexamethasone alters yawning behavior induced by cholinergic but not dopaminergic agonist." Physiol Behav 65(4-5): 829-32.
Because stressful manipulations have been reported to modify drug-induced yawning, the present study investigated the effects of single and repeated treatment with a synthetic glucocorticoid, dexamethasone (DEXA) on apomorphine- and pilocarpine-induced yawning in male rats. Neither single nor repeated treatment with DEXA altered apomorphine-induced yawning. Single administration of DEXA, however, resulted in an increased number of yawns induced by pilocarpine. Conversely, repeated administration of DEXA led to a decreased number of yawns induced by pilocarpine. In conclusion, the present findings show that dopaminergic and cholinergic are distinctly altered by DEXA, in terms of yawning behavior when animals received DEXA.

Herbert, A. and J. A. Smith (1999). "Cervical intraepithelial neoplasia grade III (CIN III) and invasive cervical carcinoma: the yawning gap

revisited and the treatment of risk." Cytopathology 10(3): 161-70.
In a 3-year study of the population of Southampton and south-west Hampshire there were 10 times as many cases of CIN III compared with invasive squamous carcinoma (700 compared with 70). The peak incidence of CIN III per 1000 screened women years was in those aged 25-29 years, which was 20 years earlier than the peak incidence of invasive cervical cancer per 1000 women years at risk. Ninety percent of CIN III was diagnosed in women under 50 years. There were 14 cases of cervical glandular intraepithelial neoplasia grade III (CGIN III), three coexisting with CIN III, all in women aged under 50 years: the gap between intraepithelial and invasive lesions was not seen for glandular neoplasia. Although referral was for at least moderate dyskaryosis in 86.8% of women with CIN III or CGIN III, most had been screened previously, either having had mild abnormalities requiring repeat cytology (39.8%) or negative cytology (34.5%). Only 12 women aged > or = 50 years had previous negative cytology: 21.4% compared with 35.6% of women aged < 50 years (P = 0.034). The results of this study suggest that the best opportunity for preventing invasive squamous cell carcinoma lies in screening women aged 20-39 years when the incidence of CIN III in the screened population is highest and before the peak incidence of invasive disease. The results also indicate the importance of repeated screening and follow up of minor cytological abnormalities in the detection of CIN III. The benefit of screening must be regarded as a treatment of risk, since it is almost certain that a high proportion of CIN III regresses or persists unchanged.

Fernandez-Guardiola, A., A. Martinez, et al. (1999). "Vagus nerve prolonged stimulation in cats: effects on epileptogenesis (amygdala electrical kindling): behavioral and electrographic changes." Epilepsia 40(7): 822-9.
PURPOSE: To analyze the effect of prolonged (daily) electrical vagus nerve stimulation (VNS) on daily amygdaloid kindling (AK) in freely moving cats. METHODS: Fifteen adult male cats were implanted in both temporal lobe amygdalae, both lateral geniculate bodies, and prefrontal cortices. A bipolar hook (5-mm separation) stainless steel electrode also was implanted in the unsectioned left vagus nerve. AK only was performed on five of the cats as a control. The remaining 10 cats were recorded under the following experimental conditions: VNS (1.2-2.0 mA, 0.5-ms pulses, 30 Hz) for 1 min along with AK (1-s train, 1-ms pulses, 60 Hz, 300-600 microA), followed by VNS alone for 1 min, four times between 11:00 a.m. and 2 p.m. At different times, VNS was arrested, and AK was continued until stage VI kindling was reached. RESULTS: The behavioral changes evoked by VNS were as follows: left miosis, blinking, licking, abdominal contractions, swallowing, and eventually yawning, meowing, upward gaze, and short head movements. Compulsive eating also was present with a variable latency. Outstanding polygraphic changes consisted of augmentation of eye movements and visual evoked potentials while the animal was awake and quiet, with immobility and upward gaze. An increase of the pontogeniculooccipital (PGO) wave density in rapid eye movement (REM) sleep also was noticeable. AK was completed (to stage VI) in the control animals without a vagus nerve implantation in 23.4+/-3.7 trials. In animals with VNS, the AK was significantly delayed, remaining for a long time in the behavioral stages I-III and showing a reduction of afterdischarge duration and frequency. Stage VI was never reached despite 50 AK trials, except when the vagus nerve electrodes were accidentally broken or vagal stimulation was intentionally arrested. Under these circumstances, 24.4+/-8.16 AK trials alone were necessary to reach stage VI of kindling. CONCLUSIONS: Our results indicate that left, electrical VNS interferes with AK epileptogenesis. This anticonvulsant effect could be related to the increase of REM sleep.

Evidente, V. G. and K. G. Hardy (1999). "Yawning in Parkinson's disease." Neurology 52(2): 428.

Eaton, G. G., J. M. Worlein, et al. (1999). "Self-injurious behavior is decreased by cyproterone acetate in adult male rhesus (Macaca mulatta)." Horm Behav 35(2): 195-203.
Self-injurious behavior (SIB) presents a serious problem in laboratory macaques that cannot be socially housed for scientific reasons and among institutionalized children and adults where it is often associated with different forms of brain dysfunction. We have experienced limited success in reducing SIB in macaques by enhancing their environment with enrichment devices. Psychotropic drugs also help, but problems are associated with their use. Because sexual and aggressive behavioral problems in men have been treated with progestational drugs, we tested the efficacy of cyproterone acetate (CA, 5-10 mg/kg/week) on reducing SIB in 8 singly housed, adult male rhesus macaques. The main findings were: (1) SIB and other atypical behaviors were significantly reduced during CA treatment; (2) serum testosterone was significantly reduced during CA treatment; (3) cerebral spinal fluid (CSF) levels of 5HIAA and HVA, metabolites of serotonin and dopamine, respectively, declined significantly during CA treatment; (4) the duration of SIB positively correlated with levels of 5HIAA in CSF; but (5) sperm counts were not reduced during treatment. Thus, CA was a partially effective treatment (3 months) for adult male macaques whose behavioral problems include SIB. In summary, CA reduced SIB, overall aggression, serum testosterone, CSF 5HIAA, and CSF HVA. We hypothesized that the progestin activity of CA represses the hypothalamic gonadal axis and decreases testosterone, which in turn decreases SIB. In addition, we speculate that the decrease in 5HIAA and HVA in CSF may have been caused by progestins decreasing the activity of MAO. Therefore, the reduction of SIB may also be related to an increase in the availability of active monoamines in the CNS.

de Wied, D. (1999). "Behavioral pharmacology of neuropeptides related to melanocortins and the neurohypophyseal hormones." Eur J Pharmacol 375(1-3): 1-11.
Neuropeptides are peptides which affect the nervous system. They are derived from large precursor molecules. These are converted to neurohormones, neuropeptides of the "first generation", which can be further converted to neuropeptides of the "second generation". This review is a brief survey of the nervous system effects of neuropeptides derived from pro-opiomelanocortin (POMC) and the neurohypophyseal hormones. Processing of these molecules results in neuropeptides of the first and second generation which have similar, different, more selective or even opposite effects. Among those are effects on learning and memory processes, grooming, stretching and yawning, social, sexual and rewarded behavior, aging and nerve regeneration, thermoregulation, pain, sensitivity to seizures, and cardiovascular control. Results of animal studies as well as those of clinical studies suggest that these neuropeptides may be beneficial in aging, neuropathy, memory disturbances and schizophrenia. Most of these nervous system effects in animal studies were found before receptors in the nervous system for the various neuropeptides were detected. G-protein-coupled receptors for the neuropeptides of the "first generation", i.e., melanocortin receptors, opioid receptors, and neurohypophyseal hormone receptors have been found, in contrast to the receptors for neuropeptides of the "second generation", although there are indications that G-protein coupled receptors for these may be present in the brain.

Colosimo, C. and F. E. Pontieri (1999). "Yawning in Parkinson's disease." Neurology 52(2): 428.

Chen, K. K., J. Y. Chan, et al. (1999). "Dopaminergic neurotransmission at the paraventricular nucleus of hypothalamus in central regulation of penile erection in the rat." J Urol 162(1): 237-42.
PURPOSE: To investigate whether the paraventricular nucleus of hypothalamus (PVN) is involved in the central regulation of apomorphine-induced penile erection in the rat, and to decipher dopamine receptor subtypes in the PVN that are involved in apomorphine-induced penile erection. MATERIALS AND METHODS: Male adult Sprague-Dawley rats (200 to 300 gm.) anesthetized with pentobarbital sodium were used. The intracavernous pressure (ICP), recorded along with systemic and mean arterial pressure (SAP, MAP) as well as heart rate (HR), was measured via a 26-gauge needle inserted into one corpus cavernosum. The PVN was activated by stereotaxically delivered apomorphine hydrochloride (0.1 nmol./100 nl.). Injection of saline into PVN served as a vehicle control. To investigate the participation of dopamine receptor subtypes in the PVN on apomorphine-induced penile erection, D1 or D2 receptor antagonist, SCH-23390 (100 pmol./100 nl.) or sulpiride (100 pmol./100 nl.) respectively, was administered into the PVN prior to subcutaneous application of apomorphine (80 microg./kg.). The effects on ICP of microinjection of D1, D2 or D3 receptor agonist, SKF-38393 (200 pmol./100 nl.), lisuride (200 pmol./100 nl.) or 7-hydroxy-DPAT (200 pmol./100 nl.) respectively, into the PVN were also evaluated. RESULTS: The mean resting ICP was 5.2+/-0.4 mm. Hg. Upon administration of apomorphine into the PVN, there was a significant increase in ICP that peaked at 50.7+/-5.3 mm. Hg and persisted for 45.2 +/-18.0 minutes after an onset latency of 677.7+/-311.6 seconds. Yawning and teeth gnashing were also observed in most of animals during the period of ICP increase. There was no significant change in SAP, MAP or HR. In addition, there was no elevation in ICP after administration of saline to the PVN or direct injection of apomorphine into the cavernous tissue. Microinjection of D1 or D2 receptor antagonist into the PVN blocked the increase in ICP after subcutaneous administration ofapomorphine. Direct application of D2, but not D1 or D3 receptor agonist into the PVN, on the other hand, increased the ICP. CONCLUSIONS: Our results demonstrate that application of apomorphine to the paraventricular nucleus of hypothalamus elicited penile erection in the rat. Such an increase in ICP to apomorphine was due mainly to activation of the D2 receptor subtype in the PVN. These observations indicate that PVN may be involved in the central regulation of apomorphine-induced penile erection in the rat.

Castles, D. L., A. Whiten, et al. (1999). "Social anxiety, relationships and self-directed behaviour among wild female olive baboons." Anim Behav 58(6): 1207-1215.
Self-directed behaviour (SDB) can be used as a behavioural indicator of stress and anxiety in nonhuman primates (Maestripieri et al. 1992, Animal Behaviour, 44, 967-979). We investigated the effect of nearest neighbours' relative dominance status on the SDB of sexually mature female olive baboons, Papio anubis. When the animal nearest to (within 5 m of) a female was a dominant individual, SDB rates (a combined measure of self-scratching, self-grooming, self-touching, body shaking and yawning) increased by ca. 40% over those observed when the nearest neighbour was a subordinate. The results indicate that (1) SDB can be used as a measure of uncertainty during the social interactions of cercopithecine primates and (2) as there was considerable variation in SDB response according to the nature of the dominant individual, SDB can be used to assess relationship security (i.e. the perceived predictability of a relationship for one partner). Finally, in combination with measures of affiliation rate, SDB may provide insight into relationship value. Copyright 1999 The Association for the Study of Animal Behaviour.

Bentley, J. C., A. Bourson, et al. (1999). "Investigation of stretching behaviour induced by the selective 5-HT6 receptor antagonist, Ro 04-6790, in rats." Br J Pharmacol 126(7): 1537-42.
1. The present study examined the effects of the selective 5-HT6 receptor antagonist 4-amino-N-(2, 6 bis-methylamino-pyrimidin-4-yl)-benzene sulphonamide (Ro 04-6790) on locomotor activity and unconditioned behaviour in male Sprague Dawley rats (230-300 g). 2. In non-quantified behavioural observations, animals treated with Ro 04-6790 (3, 10 or 30 mg kg(-1), i.p) showed no overt behavioural signs except a dose-dependent reduction in locomotor activity and a behavioural syndrome of stretching, yawning and chewing. The latter behaviour was most pronounced between 30 and 90 min following the administration of Ro 04-6790. 3. Detailed analysis of the stretching and yawning behaviour

showed that Ro 04-6790 (3, 10 or 30 mg kg(-1), i.p.) dose-dependently induced stretching. The number of stretches observed following treatment with either Ro 04-6790 (10 mg kg(-1) i.p.) or Ro-04-6790 (30 mg kg(-1), i.p.) was significantly greater than that observed in saline-treated rats. The yawning behaviour, however, was not dose-dependent nor was the number of yawns in any of the drug treated groups significantly greater than in those treated with saline. 4. Pretreatment (30 min) with the non-selective muscarinic antagonists scopolamine (0.1, 0.3 or 1 mg kg(-1), i.p.) and atropine (0.3, 1 or 3 mg kg(-1), s.c.) but not methylatropine (1, 3 or 10 mg kg(-1), s.c) significantly inhibited stretching induced by Ro 04-6790 (30 mg kg(-1), i.p.). 5. The dopamine D2-like receptor antagonist, haloperidol (0.03, 0.1 or 0.3 mg kg(-1), s.c.) given at the same time as Ro 04-6790 (30 mg kg(-1), i.p.) had no effect on the stretching induced by the 5-HT6 antagonist. 6. These data suggest that systemic injection of the 5-HT6 antagonist, Ro 04-6790, produces a stretching behaviour that appears to be mediated by an increase in cholinergic neurotransmission in the CNS and which could be a useful functional correlate for 5-HT6 receptor blockade. There is no evidence for dopamine D2-like receptor involvement in this behaviour.

Asencio, M., B. Delaquerriere, et al. (1999). "Biochemical and behavioral effects of boldine and glaucine on dopamine systems." Pharmacol Biochem Behav 62(1): 7-13.

The aporphine alkaloids boldine and glaucine have been reported to show "neuroleptic-like" actions in mice, suggesting that they may act as dopamine antagonists. We have found that in vitro boldine displaces specific striatal [3H]-SCH 23390 binding with IC50 = 0.4 microM and [3H]-raclopride binding with IC50 = 0.5 microM, while the affinities of glaucine at the same sites are an order of magnitude lower. In vivo, however, 40 mg/kg boldine (i.p.) did not modify specific striatal [3H]-raclopride binding and only decreased [3H]-SCH 23390 binding by 25%. On the other hand, 40 mg/kg glaucine (i.p.) displaced both radioligands by about 50%. Behaviors (climbing, sniffing, grooming) elicited in mice by apomorphine (0.75 mg/kg s.c.) were not modified by boldine at doses up to 40 mg/kg (i.p.) but were almost completely abolished by 40 mg/kg glaucine (i.p.). In the apomorphine-induced (0.1 mg/kg s.c.) rat yawning and penile erection model, boldine and glaucine appeared to be similarly effective, inhibiting both behaviors by more than 50% at 40 mg/kg (i.p.). Boldine and glaucine, injected i.p. at doses up to 40 mg/kg, were poor modifiers of dopamine metabolism in mouse and rat striatum. These data suggest that boldine does not display effective central dopaminergic antagonist activities in vivo in spite of its good binding affinity at D1- and D2-like receptors, and that glaucine, although less effective in vitro, does appear to exhibit some antidopaminergic properties in vivo.

(1999). "[Antihistaminics for urticaria. Scratching or yawning--alternatives of the past]." MMW Fortschr Med 141(44): 65.

Wessells, H., K. Fuciarelli, et al. (1998). "Synthetic melanotropic peptide initiates erections in men with psychogenic erectile dysfunction: double-blind, placebo controlled crossover study." J Urol 160(2): 389-93.

PURPOSE: We evaluated the erectogenic properties of a new cyclic alpha-melanocyte-stimulating hormone analogue, Melanotan-II, to treat men with psychogenic erectile dysfunction. MATERIALS AND METHODS: Ten men with erectile dysfunction of no known organic cause were entered in a double-blind, placebo controlled crossover study in which the erectogenic properties of Melanotan-II and a vehicle placebo were compared using real-time RigiScan monitoring. The presence, duration and rigidity of erections were recorded during a 6-hour period. RESULTS: In 8 of 10 men treated with Melanotan-II clinically apparent erections developed. Mean duration of tip rigidity greater than 80% was 38.0 minutes with Melanotan-II and 3.0 with placebo (p=0.0045). Transient side effects of nausea, stretching and yawning, and decreased appetite were reported more frequently after injections of Melanotan-II than placebo but none required treatment. CONCLUSIONS: Melanotan-II is a potent initiator of erections in men with psychogenic erectile dysfunction and has manageable side effects at a dose of 0.025 mg./kg.

Vergoni, A. V., A. Bertolini, et al. (1998). "Differential influence of a selective melanocortin MC4 receptor antagonist (HS014) on melanocortin-induced behavioral effects in rats." Eur J Pharmacol 362(2-3): 95-101.

We injected i.c.v. the natural agonist alpha-MSH (melanocyte-stimulating hormone) and the first selective melanocortin MC4 receptor antagonist HS014 (cyclic [AcCys11, D-Nal14, Cys18, Asp-NH(2)22]-beta-MSH(11-22) in rats and scored a number of behavioral effects which have been related to the melanocortic peptides. The results showed that HS014 (5 microg/rat) completely blocked alpha-MSH (3 and 5 microg/rat)-induced grooming, yawning and stretching. Penile erections induced by alpha-MSH were, however, only partially blocked by HS014. Injections of alpha-MSH decreased food intake in food-deprived rats, whereas HS014 increased food intake. When the peptides were given together, the food intake was similar to that of saline treated controls. Locomotion/exploration and resting were not influenced by either peptide. Our data show that exogenous beta-MSH decreases food intake, and that an endogenous central melanocortinergic inhibitory tone on feeding prevails which can be blocked with HS014, leading to an increase in food intake. Our data also provide evidence that grooming, stretching and yawning in rats may be mediated by the melanocortin MC4 receptor, whereas penile erections might perhaps be mediated by some other melanocortin receptor.

Succu, S., M. S. Spano, et al. (1998). "Different effects of omega-conotoxin on penile erection, yawning and paraventricular nitric oxide in male rats." Eur J Pharmacol 359(1): 19-26.

A dose of apomorphine or oxytocin that induces penile erection and yawning increases nitric oxide production in the paraventricular nucleus of the hypothalamus, as determined by the increase in NO2- and NO3- concentration induced by these substances in the paraventricular dialysate obtained from male rats. All the above responses were prevented by a dose of omega-conotoxin-GVIA as low as 5 ng. This potent inhibitor of N-type Ca2+ channels was injected into the paraventricular nucleus 15 min before apomorphine (50 ng) or oxytocin (10 ng). In contrast, omega-conotoxin was ineffective when the above responses were induced by N-methyl-D-aspartic acid (50 ng). The peptide toxin (5 ng) was also ineffective on the penile erection and yawning induced by the nitric oxide donors sodium nitroprusside (50 microg) or hydroxylamine (50 microg), injected into the paraventricular nucleus. The present results suggest that omega-conotoxin-sensitive Ca2+ channels are involved in the activation of nitric oxide synthase, penile erection and yawning induced by apomorphine and oxytocin, but not by N-methyl-D-aspartic acid, at the paraventricular level.

Stangerup, S. E., O. Tjernstrom, et al. (1998). "Point prevalence of barotitis in children and adults after flight, and effect of autoinflation." Aviat Space Environ Med 69(1): 45-9.

The most common cause of barotitis is pressure changes during descent in aviation. Equilibration is normally achieved by swallowing, jaw movements, yawning, or chewing, but some have to perform a Valsalva maneuver several times during descent and even by these means some fail. The aim of the study was to estimate the point prevalence of barotrauma in children and adults after flight, and to test the effect of an autoinflation device (Otovent), in improving negative middle ear pressure after flight. Questionnaires and Otovent, were distributed to all air passengers in eight incoming flights. The questionnaires inquired about nasal allergy, nasal congestion, previous and actual ear pain, use of decongestants and experience of inflating the Otovent set during descent. After flight, the passengers were offered an ear examination including otoscopy and tympanometry both before and after a Valsalva maneuver, as well as after Otovent inflation. Otoscopic signs of barotitis were found in 10% of the adults and in 22% of the children. Negative middle ear pressure of more than 10 hPa after landing was found in 20% of the adults and in 40% of the children. The Valsalva maneuver normalized the pressure in 46% of the adults and in 33% of the children. Of the adults, 73%, and of the children, 69% with an unsuccessful Valsalva maneuver could improve or normalize the middle ear pressure by inflating the Otovent set. In conclusion, we recommend autoinflation using the Otovent set to air passengers with problems clearing the ears during flight.

Sleight, A. J., F. G. Boess, et al. (1998). "Characterization of Ro 04-6790 and Ro 63-0563: potent and selective antagonists at human and rat 5-HT6 receptors." Br J Pharmacol 124(3): 556-62.

1. This study describes the in vitro characterization of two potent and selective 5-HT6 receptor antagonists at the rat and human recombinant 5-HT6 receptor. 2. In binding assays with [3H]-LSD, 4-amino-N-(2,6 bis-methylamino-pyrimidin-4-yl)-benzene sulphonamide (Ro 04-6790) and 4-amino-N-(2,6 bis-methylamino-pyridin-4-yl)-benzene sulphonamide (Ro 63-0563) had mean pKi values +/-s.e.mean at the rat 5-HT6 receptor of 7.35+/-0.04 and 7.83+/-0.01, respectively and pKi values at the human 5-HT6 receptor of 7.26+/-0.06 and 7.91+/-0.02, respectively. 3 .Both compounds were found to be over 100 fold selective for the 5-HT6 receptor compared to 23 (Ro 04-6790) and 69 (Ro 63-0563) other receptor binding sites. 4. In functional studies, neither compound had any significant effect on basal levels of cyclicAMP accumulation in Hela cells stably expressing the human 5-HT6 receptor, suggesting that the compounds are neither agonists nor inverse agonists at the 5-HT6 receptor. However, both Ro 04-6790 and Ro 63-0563 behaved as competitive antagonists with mean +/-s.e.mean pA2 values of 6.75+/-0.07 and 7.10+/-0.09, respectively. 5. In rats habituated to observation cages, Ro 04-6790 produced a behavioural syndrome similar to that seen following treatment with antisense oligonucleotides designed to reduce the expression of 5-HT6 receptors. This behavioural syndrome consisted of stretching, yawning and chewing. 6. Ro 04-6790 and Ro 63-0563 represent valuable pharmacological tools for the identification of 5-HT6 receptors in natural tissues and the study of their physiological function.

Sato-Suzuki, I., I. Kita, et al. (1998). "Stereotyped yawning responses induced by electrical and chemical stimulation of paraventricular nucleus of the rat." J Neurophysiol 80(5): 2765-75.

Yawning was evoked by electrical or chemical stimulation in the paraventricular nucleus (PVN) of anesthetized, spontaneously breathing rats. To evaluate physiological aspects of yawning, we monitored polygraphic measures as follows; a coordinated motor pattern of yawning was assessed by monitoring breathing [intercostal electromyogram (EMG)], mouth opening (digastric EMG), and stretching of the trunk (back EMG). We also recorded blood pressure (BP), heart rate, and the electrocorticogram (ECoG) to evaluate autonomic function and arousal responses during yawning. A stereotyped yawning response was reproducibly evoked by electrical stimulation or microinjection of -glutamate or NOC-7, a nitric oxide (NO)-releasing compound, into the PVN. The stereotyped yawning response consisted of two sequential events, an initial response represented a depressor response and an arousal shift in the ECoG to lower voltage and faster rhythms. These initial changes were followed by a yawning behavior characterized by a single large inspiration with mouth opening and stretching of the trunk. A similar sequence of events occurred during spontaneous yawning; a fall in BP and ECoG arousal preceded a yawning behavior. An increase in the frequency of spontaneous yawns was also observed after microinjection of -glutamate or NOC-7 into the PVN. Intravenous administration of NG-monomethyl--arginine, an inhibitor of nitric oxide synthase (NOS), prevented the stereotyped yawning response evoked by chemical stimulation of the PVN. Histological examination revealed that effective sites for the yawning responses were located in the medial part of the rostral PVN, the site of parvocellular and magnocellular neurons. NADPH-diaphorase histochemistry showed the existence of NOS-containing cells in yawning-evoked sites of the PVN. In summary, the sequential events of yawning may be generated by NOS-containing parvocellular

neurons in the medial part of the rostral PVN projecting to the lower brain stem.

Sandyk, R. (1998). "Yawning and stretching--a behavioral syndrome associated with transcranial application of electromagnetic fields in multiple sclerosis." Int J Neurosci 95(1-2): 107-13.

Intracerebral administration of adrenocorticotropic hormone (ACTH) elicits in experimental animals a yawning stretching behavior which is believed to reflect an arousal response mediated through the septohippocampal cholinergic neurons. A surge in plasma ACTH levels at night and just prior to awakening from sleep is also associated in humans with yawning and stretching behavior. Recurrent episodes of uncontrollable yawning and body stretching, identical to those observed upon awakening from physiological sleep, occur in a subset of patients with multiple sclerosis (MS) during transcranial therapeutic application of AC pulsed electromagnetic fields of picotesla flux density. This behavioral response has been observed exclusively in young female patients who are fully ambulatory with a relapsing remitting course of the disease who also demonstrate a distinctly favorable therapeutic response to magnetic stimulation. ACTH is employed for the treatment of MS due to its immunomodulatory effects and a surge in its release in response to AC pulsed magnetic stimulation could explain some of the mechanism by which these fields improve symptoms of the disease.

Rimondini, R., S. Ferre, et al. (1998). "Differential effects of selective adenosine A1 and A2A receptor agonists on dopamine receptor agonist-induced behavioural responses in rats." Eur J Pharmacol 347(2-3): 153-8.

The effects of the systemic (i.p.) administration of the selective adenosine A1 receptor agonist N6-cyclopentyladenosine (CPA) and the selective adenosine A2A receptor agonist sodium 2-p-carboxyethyl)phenylamino-5'-N-carboxamidoadenosine (CGS 21680) on different dopamine receptor agonist-induced behaviours were studied in the male rat. CGS 21680 (1 micromol/kg), but not CPA, was found to counteract the stereotypies induced by the non-selective dopamine receptor agonist apomorphine (0.25 mg/kg s.c.). Low doses of CGS 21680 (0.1 micromol/kg) and high doses of CPA (3 micromol/kg) counteracted yawning induced by the dopamine D2 selective agonist quinpirole (0.05 mg/kg). On the other hand, low doses of CPA (0.3 micromol/kg) antagonized grooming induced by the selective dopamine D1 receptor-selective agonist SKF 38393 (10 mg/kg i.p.), while CGS 21680 was ineffective. These results are consistent with the proposed existence of a selective antagonistic modulation of dopamine D1 and D2 receptors by adenosine A1 and A2A receptors, respectively. The ability of CGS 21680 to counteract apomorphine-induced stereotypies is weaker compared to its previously reported antagonistic effect of amphetamine-induced motor activity. This supports the hypothesis that adenosine A2A receptor agonists may be potential antipsychotic drugs with a low potential for extrapyramidal side effects.

Protais, P., M. Lesourd, et al. (1998). "Similar pharmacological properties of 8-OH-DPAT and alnespirone (S 20499) at dopamine receptors: comparison with buspirone." Eur J Pharmacol 352(2-3): 179-87.

Alnespirone (S 20499) has previously been described as a potential anxiolytic drug that acts by stimulation of 5-HT1A receptors. Some data suggest that alnespirone might also be a weak dopamine D2 receptor agonist: it displays moderate affinity for dopamine D2 receptors in vitro and it inhibits prolactin release and induces yawning in rats. In order to test for possible interactions of alnespirone with dopamine receptors in vivo, we studied the changes of in vivo striatal [3H]SCH 23390 (R(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1H-3-benza zepine) and [3H]raclopride binding following the injection of a tracer dose of either tritiated ligand (4 microCi) in mice treated with increasing doses of alnespirone (5, 10, 20 and 40 mg/kg, i.p.) and, in the same animals, the changes in the levels of dopamine, 5-hydroxytryptamine (5-HT) and their metabolites 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA) and 5-hydroxyindolacetic acid (5-HIAA). These changes were compared with those produced by increasing doses of the reference 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-2-(di-n-propylamino)tetralin, 0.25, 1 and 4 mg/kg, i.p.) or buspirone (5 and 20 mg/kg, i.p.). Decreased in vivo striatal [3H]SCH 23390 specific binding was observed in mice treated with 5, 10 and 40 mg/kg alnespirone. In contrast, increased in vivo striatal [3H]raclopride specific binding was observed in mice treated with 5 and 20 mg/kg alnespirone. In these animals, the striatal 5-HIAA/5-HT ratio was decreased by 5 to 40 mg/kg alnespirone, whereas the striatal HVA/DA ratio was unaffected at all tested doses of alnespirone. Similarly, 8-OH-DPAT decreased specific in vivo striatal [3H]SCH 23390 binding at 0.25, 1 and 4 mg/kg, and increased in vivo specific striatal [3H]raclopride binding at 1 and 4 mg/kg. In the same animals, all tested doses of 8-OH-DPAT decreased the striatal 5-HIAA/5-HT ratio but did not modify the striatal HVA/dopamine ratio. Buspirone (5 and 20 mg/kg) completely inhibited in vivo specific striatal [3H]raclopride binding and increased the striatal HVA/DA ratio but did not modify the striatal 5-HIAA/5-HT ratio, whereas apomorphine (3 mg/kg) decreased both in vivo specific striatal [3H]SCH 23390 and [3H]raclopride binding as well as the striatal HVA/DA and 5-HIAA/5-HT ratios. Finally, increasing doses of alnespirone or 8-OH-DPAT weakly increased sniffing induced by apomorphine (0.75 mg/kg, s.c.) in mice and decreased grooming induced by the dopamine D1 receptor agonist SK&F 39393 ((+/-)-1-phenyl-2,3,4,5-tetrahydro-(1H)-3-benzazepine-7,8-diol, 1.87 mg/kg, s.c.), whereas buspirone decreased both apomorphine-induced sniffing and SK&F 39393-induced grooming. These results indicate that alnespirone and 8-OH-DPAT have a similar profile and do not seem to interact directly with dopamine receptors. The results also suggest that the stimulation of 5-HT1A receptors by either alnespirone or 8-OH-DPAT modulates the availability of striatal [3H]SCH 23390 and [3H] raclopride binding sites and possibly the functioning of striatal dopamine D1 and D2 receptors in opposite directions.

Poggioli, R., R. Arletti, et al. (1998). "Diabetic rats are unresponsive to the penile erection-inducing effect of intracerebroventriculary injected adrenocorticotropin." Neuropeptides 32(2): 151-5.

The penile erection-inducing effect of intracerebroventricularly (i.c.v.) injected adrenocorticotropin-(1-24) [ACTH-(1-24)] (4 or 10 microg/animal) was almost completely absent in diabetic rats, either 8 days or 2 months after streptozotocin administration. The other behavioral symptoms (stretching, yawning, excessive grooming) were unevenly affected: stretching was significantly reduced either in early or in long-standing diabetes; yawning was practically absent in early diabetes and significantly reduced at the highest dose of ACTH-(1-24) in long-standing diabetes; grooming was reduced only at the highest dose of ACTH-(1-24), both in early and in long-standing diabetes. The fact that ACTH-induced penile erections (a centrally mediated effect) are practically absent even a few days after streptozotocin injection suggests that diabetes mellitus-induced penile dysfunction occurs, at least in part, through central mechanisms, and is not solely the consequence of peripheral nerve and vascular lesions.

Pandita, R. K., A. Nylen, et al. (1998). "Oxytocin-induced stimulation and inhibition of bladder activity in normal, conscious rats--influence of nitric oxide synthase inhibition." Neuroscience 85(4): 1113-9.

The role of the oxytocin-containing projections to the autonomic nuclei of the spinal cord for lower urinary tract function has not been clarified. The hypothesis was tested that oxytocin acts as a mediator of bladder contraction at the spinal cord level. In conscious female rats undergoing continuous cystometry, intrathecal oxytocin (30 ng approximately 30 pmoles) significantly increased micturition pressure ($P<0.001$), and decreased bladder capacity ($P<0.01$) and micturition volume ($P<0.01$). Residual volume increased ($P<0.05$), and so did the amplitude and frequency of non-voiding contractions ($P<0.01$). Immediately after administration of oxytocin, the animals showed frequent stretching movements and yawning, and they licked their tails. The effects of oxytocin were dose-dependent; high concentrations (100 ng) were ineffective. Intra-arterial injection of oxytocin (30 ng) near the bladder had no effect. In isolated detrusor strips, oxytocin caused a concentration-dependent contraction; the concentration response curve was concentration-dependently shifted to the right by the oxytocin antagonist, 1-deamino, 2-D-Tyr(OEt), 4-Thr, 8-Orn-OT. Intrathecal injection of the antagonist (500 ng), had per se no effect on micturition. However, when the antagonist was given intrathecally 4-5 min prior to intrathecal oxytocin (30 ng), the effects of oxytocin were reduced or completely prevented. When given after intrathecal administration of the nitric oxide synthase inhibitor, N(omega)-nitro-L-arginine methyl ester, intrathecal oxytocin (30 ng) abolished micturition within 5-7 min; all animals developed overflow incontinence, and paralysis of the hindlimbs. These results suggests that in the rat, oxytocin, released from descending pathways, may act as a modulator of the micturition reflex at the spinal level, and that it may interact with nitric oxide. The physiological implications of the findings remain to be established.

Liu, Y. C., B. D. Sachs, et al. (1998). "Sexual behavior in male rats after radiofrequency or dopamine-depleting lesions in nucleus accumbens." Pharmacol Biochem Behav 60(2): 585-92.

Considerable neurochemical evidence links dopamine (DA) in nucleus accumbens (NAcc) to male sexual behavior. The present experiments were conducted to extend this information to the male's sexual response to remote stimuli from estrous female (noncontact erection; NCE). Male rats were tested for copulation and NCE after either 6-hydroxydopamine (6-OHDA) or radiofrequency (RF) lesions in NAcc). Males with an average 78% depletion of DA in NAcc had a lower incidence of NCE, longer latency to display NCE, and fewer erections. DA-depleted males also had less locomotor activity after injections of d-amphetamine, and reductions in apomorphine-induced yawning, but a normal incidence of penile erection. Males with RF lesions of the NAcc had longer NCE latencies. All males copulated to ejaculation after either 6-OHDA or RF lesions with little or no deficit, although the 6-OHDA-treated males had longer intromission latencies. The NCE deficit supports the hypothesized role of NAcc DA in arousal processes in responding to remote cues from estrous females. The minimal effect of lesions on copulation suggests that the presence of additional proximal stimulation during copulation may overcome the deficits induced by DA depletions or lesions in NAcc.

Khroyan, T. V., D. A. Baker, et al. (1998). "Differential effects of 7-OH-DPAT on amphetamine-induced stereotypy and conditioned place preference." Psychopharmacology (Berl) 139(4): 332-41.

Low doses of the dopamine D3-preferring agonist 7-hydroxy-N,N-di-n-propyl-2-aminotetralin (7-OH-DPAT) produce a behavioral profile that is opposite to that produced by the psychomotor stimulants cocaine and amphetamine. For example, low doses of 7-OH-DPAT produce conditioned place aversion and hypolocomotion, whereas psychomotor stimulants produce conditioned place preference (CPP) and hyperlocomotion. In experiment 1, the effects of low doses of 7-OH-DPAT (0.01-0.1 mg/kg) on d-amphetamine-induced (1 mg/kg) motor behaviors and CPP were assessed. In experiment 2, the effects of 0.1 mg/kg 7-OH-DPAT on d-amphetamine (0-10 mg/kg) dose-response curves for the same behaviors were examined. During conditioning, drug injections were paired with a distinct compartment, whereas saline injections were paired with another compartment. Locomotion and headbobbing were measured following acute and repeated drug administration during conditioning and place conditioning was assessed 24 h following the last conditioning day. In experiment 1, d-amphetamine-induced locomotion was dose-dependently decreased by 7-OH-DPAT following repeated administration, which was probably due to the emergence of headbobbing, a behavior not observed with d-amphetamine alone. d-Amphetamine-CPP was not altered by co-administration of 0-0.03 mg/kg 7-OH-DPAT, but was attenuated by co-administration of 0.1 mg/kg 7-OH-DPAT. In experiment 2, 7-OH-DPAT co-administered with low doses of d-amphetamine (0-0.5 mg/kg) produced

a decrease in locomotion following acute administration. However, 7-OH-DPAT produced sensitization of locomotion at the 0.5 mg/kg dose of d-amphetamine and an increase in headbobbing at the 0.5-10 mg/kg doses of d-amphetamine following repeated administration. In contrast, d-amphetamine-CPP was attenuated by co-administration of 7-OH-DPAT. These findings suggest that 0.1 mg/kg 7-OH-DPAT attenuates the reinforcing effects of d-amphetamine despite enhancing stereotypic behaviors.

Ignat'ev, D. A., V. V. Vorob'ev, et al. (1998). "Effects of a number of short peptides isolated from the brain of the hibernating ground squirrel on the EEG and behavior in rats." Neurosci Behav Physiol 28(2): 158-66.

Intracerebroventricular administration of the peptides kyotorphin (Tyr-Arg), neokyotorphin (Thr-Ser-Lys-Tyr-Arg), and Asp-Tyr at doses of 4 and 8 micrograms altered the behavior of rats in a manner similar to that seen after similar administration of brain fractions from hibernating ground squirrels (Citellus undulatus), which contained these peptides; there were increases in orientational reactions, increases in the frequency of stereotypical scratching movements, grooming, yawning, hiccuping, and sneezing. Animals became drowsy after 15-20 min. Peptides and brain fractions also had similar effects on the EEG of rats. Brain fractions reduced theta and alpha rhythms and enhanced delta and beta frequencies. Increases in delta waves were seen with all peptides (a 4-microgram dose of kyotorphin produced alternating increases and reductions in the delta rhythm). Inhibition of theta and alpha rhythms after administration of Asp-Tyr and kyotorphin was more transient than after brain fractions. Increases in beta frequencies were seen only after administration of 8 micrograms of Asp-Tyr, the smaller dose not producing this effect.

Goren, J. L. and J. H. Friedman (1998). "Yawning as an aura for an L-dopa-induced "on" in Parkinson's disease." Neurology 50(3): 823.

Ghazi-Khansari, M., N. Rezvani, et al. (1998). "Effects of lead exposure on licking and yawning behaviour in rats." Pharmacol Toxicol 83(3): 120-4.

In the present study, effects of lead exposure on licking and yawning behaviour have been studied. The dopaminergic receptor agonist, apomorphine (0.15, 0.25 and 0.5 mg/kg), induced dose-dependent licking in rats. The maximum response was obtained with 0.5 mg/kg of the apomorphine. Lead acetate (0.05%) exposure significantly increased apomorphine-induced licking. Yawning induced by the D2 dopaminergic agonist, bromocriptine (2, 3, 4, 8 mg/kg), and the cholinergic drug, physostigmine (0.1 or 0.3 mg/kg), was significantly decreased by lead acetate (0.05%) exposure. It may be concluded that the behaviour induced by dopaminergic or cholinergic agents can be affected by lead subchronic exposure.

Garcia de Mateos-Verchere, J., J. Leprince, et al. (1998). "The octadecaneuropeptide ODN inhibits apomorphine-induced yawning in rats." Eur J Pharmacol 357(2-3): 121-6.

High concentrations of diazepam-binding inhibitor (DBI) have been detected in brain areas containing dopaminergic cell bodies and nerve terminals. In the present study, we have investigated the effect of a proteolytic fragment of DBI, the octadecaneuropeptide ODN, on apomorphine-induced yawning in Sprague-Dawley rats. Injection of graded doses of ODN (12.5 to 100 ng i.c.v.) caused a dose-dependent inhibition of apomorphine-induced yawning and penile erections. At a dose of 100 ng, intracerebroventricularly administered ODN was able to inhibit, during more than 3 h, the apomorphine-evoked yawning. ODN also inhibited pilocarpine-induced yawning. Apomorphine induces a bell-shaped dose-dependent effect on yawning with a maximum response at the dose of 100 microg/kg and a much lower effect at a dose of 200 microg/kg. Injection (i.c.v.) of 100 ng ODN markedly attenuated the number of yawns induced by 100 microg/kg apomorphine but partially restored the yawning behavior in rats treated with a 200 microg/kg dose of apomorphine. At doses of 0.5 or 5 mg/kg s.c., diazepam did not modify the inhibitory effect of ODN on the apomorphine-induced yawning. Taken together, the present data suggest that ODN inhibits yawning downstream dopaminergic as well as cholinergic synapses involved in yawning. In addition, the effect of ODN cannot be ascribed to an inverse agonistic activity on central-type benzodiazepine receptors.

Del Zompo, M., A. Cherchi, et al. (1998). "Association between dopamine receptor genes and migraine without aura in a Sardinian sample." Neurology 51(3): 781-6.

BACKGROUND: Migraine seems to be caused by a combination of environmental and genetic factors. Clinical and pharmacologic evidence supports the hypothesis that dopaminergic transmission is involved in the pathogenesis of migraine. OBJECTIVE: The current report concerns a genetic study to test the involvement of genes for dopamine (DA) receptors D2 (DRD2), D3 (DRD3), and D4 (DRD4) in migraine without aura, particularly in a subgroup with enhanced DA sensitivity. METHODS: For the first time, a family-based association method--the Transmission Disequilibrium Test (TDT)--was used to examine an isolated population, such as Sardinians. We studied 50 nuclear families of patients affected by migraine without aura. The subgroup of dopaminergic migraineurs was selected based on the presence of both nausea and yawning immediately before or during the pain phase of migraine. RESULTS: No association was detected using the TDT between DRD3, DRD4, and migraine without aura either in the overall sample or in the subgroup. No difference was observed in DRD2 allelic distribution in the overall sample, although the allelic distribution at the DRD2 locus differed significantly in the subgroup of dopaminergic migraineurs (p = 0.004). Allele 1 of the TG dinucleotide intronic noncoding polymorphism of the DRD2 locus was the individual allele that appeared to be in disequilibrium with migraine without aura (p = 0.02). CONCLUSIONS: Our data suggest that a genetic approach could be useful in providing molecular support to the hypothesis that hypersensitivity of the dopaminergic system may represent the pathophysiologic basis of migraine, at least in a subgroup of patients.

Canales, J. J. and S. D. Iversen (1998). "Behavioural topography in the striatum: differential effects of quinpirole and D-amphetamine microinjections." Eur J Pharmacol 362(2-3): 111-9.

Behavioural evidence has accumulated that supports the hypothesis that specific territories of the striatum contribute differentially to the control of motor behaviours. The present experiments compare the behavioural effects of microinjections of amphetamine (20 microg/0.5 microl) with those elicited by the D2-class dopamine receptor agonist quinpirole (3 microg/0.5 microl) following direct microinjection into three anatomically distinct sectors of the striatum: the nucleus accumbens, the ventrolateral striatum and the anterodorsal striatum. Our findings demonstrate that site-specific behavioural responses are induced by microinjections of amphetamine, but not of quinpirole, into the striatum. Our results suggest that widespread areas of the striatum are implicated in the induction of a syndrome of sedation, yawning and motor inhibition, observed readily following microinjections of quinpirole into the striatum. This evidence supports both homogeneity and segregation of function in the striatum at the behavioural level. Further, the results suggest that the elicitation of site-specific action sequences at the level of the striatum seems to require cooperative interactions between D1-class and D2-class dopamine receptors.

Atallah, M. M., A. Hoeft, et al. (1998). "Does spinal anesthesia affect cerebral oxygenation during transurethral prostatectomy?" Reg Anesth Pain Med 23(2): 119-25.

BACKGROUND AND OBJECTIVES: Transurethral resection of the prostate (TURP) is associated with the unique complication of transurethral resection of prostate syndrome (TURS), which is attributed to the absorption of irrigating fluid. This study was initiated to investigate the effects of spinal anesthesia and TURP on cerebral oxygen balance. METHODS: Thirty patients scheduled for TURP were included. Jugular bulb oxygen saturation (SjbO2) was measured via retrograde cannulation of jugular venous bulb. Spinal anesthesia was initiated by 3 mL hyperbaric 0.5% bupivacaine injected at L3-L4 in the sitting position, producing a block to the T10 dermatome. Hemodynamic measurements and arterial and jugular bulb blood gasometry were performed before and after spinal anesthesia, throughout surgery, and during the postoperative period. RESULTS: A significant decrease of cerebral perfusion pressure after spinal anesthesia was accompanied by a significant decrease of SjbO2 below a preoperative value of 61% +/- 1. Eight patients developed yawning, irritability, restlessness, and nausea toward the end of surgery, and these were considered to be early signs of TURS. These patients demonstrated SjbO2 below 55% and 50% in 63% and 42% of respective data set points. CONCLUSION: The neurologic symptoms in patients undergoing TURP during spinal anesthesia might not only be caused by absorption of irrigating fluid but also by impairment of cerebral oxygenation.

Argiolas, A. and M. R. Melis (1998). "The neuropharmacology of yawning." Eur J Pharmacol 343(1): 1-16.

Yawning is a phylogenetically old, stereotyped event that occurs alone or associated with stretching and/or penile erection in humans and in animals from reptiles to birds and mammals under different conditions. Although its physiological function is still unknown, yawning is under the control of several neurotransmitters and neuropeptides at the central level as this short overview of the literature on the neurochemistry of yawning shows. Among these substances, the best known are dopamine, excitatory amino acids, acetylcholine, serotonin, nitric oxide, adrenocorticotropic hormone-related peptides and oxytocin, that facilitate yawning and opioid peptides that inhibit this behavioral response. Some of the above compounds interact in the paraventricular nucleus of the hypothalamus to control yawning. This hypothalamic nucleus contains the cell bodies of oxytocinergic neurons projecting to extra-hypothalamic brain areas that play a key role in the expression of this behavioral event. When activated by dopamine, excitatory amino acids and oxytocin itself, these neurons facilitate yawning by releasing oxytocin at sites distant form the paraventricular nucleus, i.e. the hippocampus, the pons and/or the medulla oblongata. Conversely, activation of these neurons by dopamine, oxytocin or excitatory amino acids, is antagonized by opioid peptides, that, in turn, prevent the yawning response. The activation and inhibition, respectively of these oxytocinergic neurons is related to a concomitant increase and decrease, respectively, of paraventricular nitric oxide synthase activity. However, other neuronal systems in addition to the central paraventricular oxytocinergic neurons are involved in the control of yawning, since they do not seem to be involved in the expression of yawning induced by the stimulation of acetylcholine or serotoninergic receptors, nor by adrenocorticotropic hormone (ACTH) and related peptides. Nitric oxide is also involved in the induction of yawning by the latter compounds and neuronal links, for instance between dopamine and acetylcholine and dopamine and serotonin, seem to be involved in the yawning response. Finally, other neurotransmitters, i.e. gamma-aminobutyric acid (GABA) and noradrenaline, and neuropeptides, i.e. neurotensin and luteinizing hormone-releasing hormone (LH-RH), influence this behavioral response. In conclusion, in spite of some recent progress, little is known of, and more has to be done to identify, the neurochemical mechanisms underlying yawning at the central level.

Antoniou, K., Z. Papadopoulou-Daifotis, et al. (1998). "Differential alterations in basal and D-amphetamine-induced behavioural pattern following 6-OHDA or ibotenic acid lesions into the dorsal striatum." Behav Brain Res 97(1-2): 13-28.

It is well known that the corpus striatum is related to the sterotyped activation induced by several psychostimulants. In this study

we analyzed the effects of 6-OHDA, in comparison with those of ibotenic acid lesions, into the dorsal striatum, on the behavioural pattern induced by saline or D-amphetamine treatment. A computerized technique for recording the animal motor activity was developed in order to define in a detailed way the behavioural profile in lesioned and sham-operated rats induced by the saline or D-amphetamine treatment. A 6-OHDA lesion into the dorsal striatum modified the basal behavioural pattern which was mainly characterized by reduced motor activation while ibotenic acid lesion affected the structure of the basal behavioral pattern. D-Amphetamine administration in 6-OHDA lesioned rats induced a behavioural stimulation, but a decreased motor and stereotyped activation was observed compared to the sham-operated animals treated with D-amphetamine. In contrast, D-amphetamine administration in the ibotenic acid-lesioned rats induced a motor and stereotyped activity which was not reduced compared to that seen after D-amphetamine treatment in sham-operated rats. These results suggest that these two types of lesion induced differential effects on the behavioural pattern either after saline or after D-amphetamine administration. Dopaminergic neurotransmission in the dorsal striatum plays a permissive role on the emergence of the behavioural responses, while the dorsal striatum circuitry plays a crucial role on the organization of the behavioural pattern. In addition, dopaminergic activity in this structure serves a primary control in the D-amphetamine-elicited motor activation or stereotypy, while the striatal structure is involved in the shaping of the D-amphetamine behavioural pattern.

Wong, K. Y., K. C. Ngan, et al. (1997). "Sphenoidal sinus mucocoele and yawning after radiation treatment for nasopharyngeal carcinoma." Clin Oncol (R Coll Radiol) 9(6): 415-7.

The long term complications of radiotherapy in treating patients with nasopharyngeal carcinoma (NPC) are well recognized. Among these, neurological and endocrinological complications are usually considered to be more clinically important. On the other hand, postirradiation sinusitis is often neglected or overlooked because symptoms are usually non-specific or not clinically disturbing. This leads to the under-reporting of this complication. We report the case history of a patient with NPC who developed recurrent and debilitating bouts of yawning attacks 13 years after radiotherapy. The attacks were thought to be due to the compression of the hypothalamus by a large mucocoele in the sphenoidal sinus, which was successfully managed by surgical drainage.

Veenema, H. C., B. M. Spruijt, et al. (1997). "Aging, dominance history, and social behavior in Java-monkeys (Macaca fascicularis)." Neurobiol Aging 18(5): 509-15.

The aim of this study was to investigate the influence of the dominance history of socially housed Java-monkeys on the aging process. In monkeys, social subordinance is generally associated with elevated levels of cortisol, which, in turn, have been suggested to influence cognitive decline. As cognitive skills are necessary for successful social life, we investigated the effect of old age in relation to the dominance history of the animals on their social behavior by comparing old females with their younger daughters. Old age, especially in combination with a history of low rank, led to a withdrawal from social interactions with unfamiliar animals and to a decrease in amounts of aggression received. Still, however, old animals showed an increase in behaviors associated with arousal. A reduced ability to deal with complex social interactions, caused by a decline in information processing abilities, is suggested as an explanation for these results.

Smith, H. P., D. E. Nichols, et al. (1997). "Locomotor inhibition, yawning and vacuous chewing induced by a novel dopamine D2 post-synaptic receptor agonist." Eur J Pharmacol 323(1): 27-36.

The N-n-propyl analog of dihydrexidine ((+/-)-trans-10, 11-dihydroxy-5,6,6a,7,8,12b-hexahydrobenzo[a]phenanthridine) is a dopamine receptor agonist with high affinity for dopamine D2 and D3 receptors (K0.5 = 26 and 5 nM, respectively). Members of the hexahydrobenzo[a] phenanthridine structural class are atypical because they display high intrinsic activity at post-synaptic dopamine D2 receptors, but low intrinsic activity at dopamine D2 autoreceptors. The present study examined the effects of (+/-)-N-n-propyl-dihydrexidine on unconditioned behaviors in rats. The most striking results observed were large, dose-dependent decreases in locomotor activity (e.g., locomotor inhibition), and increases in vacuous chewing; yawning was also increased at the highest dose of (+/-)-N-n-propyl-dihydrexidine. The locomotor inhibition and yawning induced by (+/-)-N-n-propyl-dihydrexidine were blocked by pre-treatment with (-)-remoxipride (S(-)-3-bromo-N-((1-ethyl-2-pyrrolidinyl)-methyl)-2, 6-dimethoxybenzamide), a dopamine D2 receptor antagonist, but not by the dopamine D1 receptor antagonist (+)-SCH23390 (R(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1 H-3-benzazepine). Vacuous chewing was decreased by both (-)-remoxipride and (+)-SCH23390. These data support the hypothesis that a subpopulation of post-synaptic dopamine D2 receptors has a critical role in decreases in locomotor activity and induction of vacuous chewing and yawning.

Sharifzadeh, M., M. Abdollahi, et al. (1997). "Alterations of physostigmine-induced yawning by chronic lithium administration in rats." Pharmacol Toxicol 81(4): 159-63.

The effect of chronic lithium pretreatment on physostigmine-induced yawning was investigated in male rats. Intraperitoneal administration of physostigmine to rats induced yawning in a biphasic manner. However the maximum response was obtained by 0.2 mg/kg of the drug. Intracerebroventricular administrations of a putative M1 and M2 muscarinic receptor antagonists, pirenzepine and methoctramine decreased physostigmine-induced yawning. Intraperitoneal administration of a non-selective muscarinic receptor antagonist, atropine, also decreased the physostigmine-induced yawning significantly. Chronic lithium pretreatment (30 days) reduced yawning induced by physostigmine. The inhibitory effect of pirenzepine, methoctramine and atropine on physostigmine-induced yawning increased in rats pretreated with chronic lithium. These findings indicate that yawning is induced by a central cholinergic mechanism and that chronic pretreatment of lithium may interact with the cholinergic-induced behaviour.

Scatton, B., Y. Claustre, et al. (1997). "Amisulpride: from animal pharmacology to therapeutic action." Int Clin Psychopharmacol 12 Suppl 2: S29-36.

Amisulpride is a benzamide derivative with a unique neurochemical and psychopharmacological profile. This compound has selective affinity for human dopamine D3 and D2 receptor subtypes in vitro (binding constant, K approximately 3 nmol/l) and blocks functional responses mediated by these receptors. In ex vivo binding studies, amisulpride is twice as selective for D3 as for D2 receptors. At low doses, it preferentially blocks presynaptic dopamine autoreceptors (increase in dopamine release in vivo in the rat olfactory tubercle, 50% effective dose, ED50 3.7 mg/kg), while postsynaptic dopamine receptor antagonism is apparent at higher doses (decrease in striatal acetylcholine levels, ED50 approximately 60 mg/kg). Anisulpride preferentially stimulates dopamine synthesis and displaces 3H-raclopride binding in vivo in the limbic system rather than the striatum. It antagonizes apomorphine-induced hypothermia in mice and amphetamine-induced hypermotility in rats at low doses (ED50 2-3 mg/kg), blocks apomorphine-induced climbing and spontaneous grooming in mice, blocks apomorphine-induced gnawing in rats at higher doses (ED50 19-115 mg/kg) and does not induce catalepsy at 100 mg/kg. The preferential antagonism by amisulpride of presynaptic D2/D3 receptors is reflected behaviourally in the potent blockade of apomorphine-induced effects mediated by dopamine autoreceptors (yawning and hypomotility: ED50 0.2 and 0.3 mg/kg, respectively) compared with those medicated by postsynaptic D2 receptors (e.g. gnawing: ED50 115 mg/kg). Moreover, low doses of amisulpride induce prohedonic (potentiation of food-induced place preference) effects in rats. The atypical neurochemical and psychopharmacological profiles of amisulpride may explain its therapeutic efficacy on both positive and negative symptoms of schizophrenia.

Sato, F., H. Aoki, et al. (1997). "Suppressive effects of chronic hyperprolactinemia on penile erection and yawning following administration of apomorphine to pituitary-transplanted rats." J Androl 18(1): 21-5.

Recent studies showed in vivo and in vitro that acutely introduced prolactin (PRL) excess was capable of diminishing penile erectile function independently of the LH-testosterone (T) dynamics. In the present investigation, we examined if such independent suppressive effects can be demonstrated in the pituitary-transplant rat model with chronically elevated serum PRL. We also compared the effects of pituitary transplantation and castration on the level of erectile activity. Rats were made hyperprolactinemic by homologous transplantation of three anterior pituitaries underneath the kidney capsules, with the eutopic pituitaries left in situ. Before and 3, 5, and 8 weeks after transplant or sham surgeries, 80 micrograms/kg s.c. injection of apomorphine was given as an inducer of erection. This was followed by 30-minute observation periods during which the numbers of erections and yawning were recorded. Similar experiments were also performed with castrated rats without transplanted pituitaries. In the transplanted rats plasma PRL was markedly elevated (51.4 +/- 3.7 ng/ml) and was significantly ($P < 0.001$) higher than the values in the sham group (6.0 +/- 2.7 ng/ml). In contrast, plasma T was not different ($P > 0.05$) between the two groups. The castrated rats showed very low plasma T (0.17 +/- 0.01 ng/ml, $P < 0.05$ compared to the sham group) and normal PRL ($P > 0.05$). The numbers of both erection and yawning were significantly ($P < 0.05$-0.01) less in the transplant than in the sham group 8 weeks after surgeries. Castrated rats showed a significant reduction ($P < 0.05$) only in the numbers of erection. These results indicated that the pituitary transplantation with chronic excess of PRL and castration with T deficiency caused roughly comparable degrees of suppression of penile erectile activity through mechanisms presumably independent from one another in the rat.

Sandyk, R. (1997). "The biological significance of yawning elicited by application of electromagnetic fields in multiple sclerosis." Int J Neurosci 89(1-2): 53-60.

Rajakumar, N., L. Laurier, et al. (1997). "Effects of intrastriatal infusion of D2 receptor antisense oligonucleotide on apomorphine-induced behaviors in the rat." Synapse 26(3): 199-208.

An antisense oligonucleotide strategy was employed to specifically deplete postsynaptic striatal D2 receptors in order to determine the possible role of presynaptic D2 autoreceptors in mediating behavioral responses induced by low doses of apomorphine. A phosphorothioate-modified antisense oligonucleotide complementary to the first 19 bases of the coding region of D2 receptor mRNA, a scrambled sequence comprising the same bases, or saline was infused bilaterally into the striatum of adult rats, twice daily for 2 days via indwelling cannulae. After an interval of 8-12 h, rats were habituated and challenged with high (300 micrograms/kg; subcutaneous) or low (50 micrograms/kg; s.c.) doses of apomorphine or its vehicle (0.1% ascorbic acid). Yawning, vacuous chewing mouth movements, hypoexploration, and penile grooming induced by low-dose apomorphine were unaffected by antisense infusion into the striatum, whereas stereotypic sniffing following high-dose apomorphine was markedly suppressed. Intrastriatal infusion of antisense resulted in significantly diminished [3H]-raclopride binding, while binding of [3H]-SCH 23390 (D1 receptors) and [3H]-WIN 35428 (dopamine transporter) was unchanged. D2 mRNA levels determined by quantitative in situ hybridization were normal in the striatum and the substantia nigra. Our results confirm that stereotypic sniffing is mediated via postsynaptic D2 receptors in the striatum, and favor the notion that behavioral responses induced by low doses of apomorphine are mediated by presynaptic D2 autoreceptors.

Phillips-Bute, B. G. and J. D. Lane (1997). "Caffeine withdrawal symptoms following brief caffeine deprivation." Physiol Behav 63(1): 35-9.
The effects of short-term caffeine deprivation on mood, withdrawal symptoms and psychomotor performance were studied in habitual coffee drinkers. Thirty-one male and female coffee drinkers were tested twice at midday (1130 to 1330 h) 4 h after double-blind administration of 250 mg of caffeine or placebo. Mood and withdrawal symptoms reports were collected by questionnaires. Psychomotor performance was tested with a brief computerized test battery, and causal blood pressure was measured. Caffeine deprivation was associated with decreased vigor and increased fatigue and with symptoms including sleepiness and yawning. Blood pressure was lower by 5-6 mm Hg. No changes in psychomotor performance were observed. Even short periods of caffeine deprivation, equivalent in length to missing regular morning coffee, can produce noticeable unpleasant caffeine withdrawal symptoms in habitual coffee drinkers. Such symptoms may be common side effects of habitual caffeine consumption that contribute to the maintenance of this behavior.

Perrault, G., R. Depoortere, et al. (1997). "Psychopharmacological profile of amisulpride: an antipsychotic drug with presynaptic D2/D3 dopamine receptor antagonist activity and limbic selectivity." J Pharmacol Exp Ther 280(1): 73-82.
Amisulpride, a benzamide derivative, is an antipsychotic drug with a pharmacological profile distinct from that of classical neuroleptics such as haloperidol and from that of another benzamide, remoxipride. In mice, amisulpride antagonized hypothermia induced by apomorphine, quinpirole or (+/-) 7-hydroxy-2-(di-n-propylamino)-tetralin, an effect involving D2/D3 receptors, at similar doses (ED50 approximately 2 mg/kg i.p.), which were much lower than doses that blocked apomorphine-induced climbing, an effect involving postsynaptic D2 and D1 receptor activation (ED50 = 21 mg/kg i.p.). Much higher doses (ED50 = 54 mg/kg i.p.) of amisulpride were needed to block grooming behavior observed after a short period in water, a D1 receptor-mediated behavior. In rats, amisulpride preferentially inhibited effects produced by low doses of apomorphine (hypomotility and yawning), related to stimulation of presynaptic D2/D3 dopamine autoreceptors (ED50 = 0.3 and 0.19 mg/kg i.p.). By contrast, amisulpride antagonized apomorphine-induced hypermotility, a postsynaptic dopamine receptor-mediated effect, at a much higher dose (ED50 = 30 mg/kg i.p.). Amisulpride (100 mg/kg i.p.) only partially inhibited apomorphine-induced stereotypies (gnawing) and had no effect on stereotypies induced by d-amphetamine. However, d-amphetamine-induced hyperactivity was antagonized by doses of amisulpride as low as 3 mg/kg i.p., which may indicate selectivity of this drug for limbic dopaminergic mechanisms. In addition, in contrast to haloperidol or remoxipride, which produced catalepsy at doses 2 or 3 times higher than those that antagonized stereotypies induced by apomorphine, amisulpride did not induce catalepsy up to a dose of 100 mg/kg i.p., which occupies 80% of striatal D2 receptors. This pharmacological profile of amisulpride, characterized by a preferential blockade of effects involving presynaptic mechanisms and limbic structures, may explain the clinical efficacy of this drug against both negative and positive symptoms of schizophrenia and its low propensity to produce extrapyramidal side effects.

Peroutka, S. J. (1997). "Dopamine and migraine." Neurology 49(3): 650-6.
This review summarizes a growing body of biological, pharmacologic, and genetic data that support a role for dopamine in the pathophysiology of certain subtypes of migraine. Most migraine symptoms can be induced by dopaminergic stimulation. Moreover, there is dopamine receptor hypersensitivity in migraineurs, as demonstrated by the induction of yawning, nausea, vomiting, hypotension, and other symptoms of a migraine attack by dopaminergic agonists at doses that do not affect nonmigraineurs. Conversely, dopamine receptor antagonists are effective therapeutic agents in migraine. Recent genetic data suggest that molecular variations within dopamine receptor genes play a modifying role in the pathophysiology of migraine with aura. Therefore, modulation of dopaminergic neurotransmission should be considered in the therapeutic management of migraine.

Melis, M. R., S. Succu, et al. (1997). "Oxytocin increases nitric oxide production in the paraventricular nucleus of the hypothalamus of male rats: correlation with penile erection and yawning." Regul Pept 69(2): 105-11.
A dose of oxytocin (50 ng i.c.v.) that induces penile erection and yawning, increased the concentration of NO2- from 0.98 +/- 0.29 to 4.2 +/- 0.79 microM and of NO3- from 5.6 +/- 0.33 to 12.03 +/- 0.99 microM in the dialysate from the paraventricular nucleus of the hypothalamus of male rats, as measured by in vivo microdialysis. NO2- concentration was also increased by [Thr4, Gly7]-oxytocin (100 ng i.c.v. and oxytocin(8) (1 microgram i.c.v.) which also induced penile erection and yawning, but not by oxytocin(1-6) (1 microgram i.c.v.) or oxytocin (7-9) 1 microgram i.c.v.), which were unable to induce these behavioral responses. The oxytocin effect on NO2 concentration, penile erection and yawning was prevented by the oxytocin receptor antagonist. d(CH2)5,Tyr(Me)-Orn8-vasotocin (1 microgram i.e.v.) or by the nitric oxide synthase inhibitor, NG-nitro-1-arginine methyl ester (200 micrograms i.c.v.), but not by the dopamine receptor antagonist, haloperidol (0.5 mg/kg i.p.). The nitric oxide scavenger, hemoglobin (200 micrograms i.c.v.), prevented oxytocin-induced NO2- concentration increase, but was unable to prevent penile erection and yawning. Methylene blue (300 micrograms i.c.v.) an inhibitor of guanylate cyclase, was ineffective on oxytocin-induced NO2- concentration increase, but prevented the behavioral responses. The results suggest that oxytocin induces penile erection and yawning by increasing nitric oxide synthase activity in the cell bodies of oxytocinergic neurons projecting to extra-hypothalamic brain areas and mediating the behavioral responses.

Melis, M. R., S. Succu, et al. (1997). "Prevention by morphine of apomorphine- and oxytocin-induced penile erection and yawning: involvement of nitric oxide." Naunyn Schmiedebergs Arch Pharmacol 355(5): 595-600.
The possible involvement of nitric oxide in the prevention by morphine of apomorphine- and oxytocin-induced penile erection and yawning was investigated by measuring the concentration of NO2- and NO3- in the dialysate obtained with a vertical microdialysis probe implanted in the paraventricular nucleus of the hypothalamus of male rats. Either apomorphine (80 micrograms/kg s.c.) or oxytocin (30 ng i.c.v.) increased significantly basal NO2- and NO3- concentration in the paraventricular dialysate, penile erection and yawning. Morphine (1.5 and 10 mg/kg i.p.) prevented dose-dependently either apomorphine or oxytocin responses when given 15 min before apomorphine or oxytocin. Prevention by morphine of apomorphine and oxytocin responses was abolished by naloxone (3 mg/kg i.p.) given 15 min before morphine. Morphine prevented apomorphine and oxytocin responses also when given in the lateral ventricles or directly in the paraventricular nucleus. In contrast, the selective agonist of the kappa opioid receptor subtype U-69,593 was found to be ineffective. The present results confirm previous findings showing that morphine acts through mu receptors in the paraventricular nucleus to prevent apomorphine and oxytocin-induced penile erection and yawning and suggest that this morphine effect is mediated by a decreased activity of nitric oxide in the paraventricular nucleus of the hypothalamus.

Melis, M. R., S. Succu, et al. (1997). "N-methyl-D-aspartic acid-induced penile erection and yawning: role of hypothalamic paraventricular nitric oxide." Eur J Pharmacol 328(2-3): 115-23.
A dose of N-methyl-D-aspartic acid (NMDA, 50 ng) that induces penile erection and yawning when injected into the paraventricular nucleus of the hypothalamus, increased the concentration of NO2- from 1.10 +/- 0.28 microM to 7.32 +/- 1.12 microM and of NO3 from 4.96 +/- 0.69 microM to 10.5 +/- 1.61 microM in the paraventricular dialysate obtained from male rats by in vivo microdialysis. NO2- concentration was not increased by (+/-)-alpha-(amino)-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA, 100 ng) or by trans-(+/-)-1-amino-1,3-cyclopentanedicarboxylic acid (ACPD) (100 ng), which were unable to induce these behavioral responses. N-Methyl-D-aspartic acid effect on NO2- concentration, penile erection and yawning was prevented by dizolcipine (MK-801) (10-100 ng) or by the nitric oxide synthase inhibitor N(G)-nitro-L-arginine methyl ester (20 microg), but not by the oxytocin receptor antagonist [d(CH2)5,Tyr(Me)2,Orn8]vasotocin (100 ng), or by the guanylate cyclase inhibitor methylene blue (20 microg) given in the paraventricular nucleus 15 min before N-methyl-D-aspartic acid or by the dopamine receptor antagonist haloperidol (0.5 mg/kg) given intraperitoneally 30 min before N-methyl-D-aspartic acid. In contrast, the nitric oxide scavenger hemoglobin (20 microg) given in the paraventricular nucleus prevented N-methyl-D-aspartic acid-induced NO2- concentration increase, but was unable to prevent penile erection and yawning. The results suggest that N-methyl-D-aspartic acid induces penile erection and yawning by increasing nitric oxide synthase activity in the paraventricular nucleus of the hypothalamus, possibly in the cell bodies of oxytocinergic neurons projecting to extra-hypothalamic brain areas and mediating these behavioral responses.

Melis, M. R. and A. Argiolas (1997). "Role of central nitric oxide in the control of penile erection and yawning." Prog Neuropsychopharmacol Biol Psychiatry 21(6): 899-922.
1. Recent experimental evidence has shown that nitric oxide (NO) plays an important role in the expression of penile erection and yawning and that this molecule has to be added to the list of the best known neurotransmitters and neuropeptides involved in this symptomatology. 2. This was first suggested by the ability of NO synthase inhibitors injected in the lateral ventricles (i.c.v.) or in the paraventricular nucleus of the hypothalamus (PVN) to prevent these behavioral responses induced by dopamine agonists, oxytocin and NMDA. The inhibitory effect of NO synthase inhibitors was not observed when these compounds were injected concomitantly with L-arginine, the precursor of NO. Most important, this hypothalamic nucleus is one of the richest brain areas of NO synthase and also the brain site where dopamine, NMDA and oxytocin act to induce penile erection and yawning by activating central NO synthase containing oxytocinergic neurons. 3. NO synthase inhibitors given i.c.v. but not in the PVN prevent also penile erection and yawning induced by ACTH and serotonin1c agonists, which induce these responses by acting with mechanisms unrelated to oxytocinergic transmission. 4. Dopamine agonists, NMDA and oxytocin increase NO production in the PVN at doses that induce penile erection and yawning, as determined by measuring the concentration of NO2- and NO3- in the dialyzate obtained with a vertical probe implanted in the PVN by in vivo microdialysis. 5. NO donors, such as nitroglycerin, sodium nitroprusside and hydroxylamine, induce penile erection and yawning indistinguishable from those induced by oxytocin, dopamine agonists or NMDA when injected in the PVN. The NO donor response was prevented by the i.c.v. injection of the oxytocin receptor antagonist d(CH2)5-Tyr (Me)-Orn8-vasotocin, indicating that these compounds also induce penile erection and yawning by activating oxytocinergic transmission. 6. Finally, guanylate cyclase inhibitors (i.e. methylene blue and LY 83583) and hemoglobin injected in the PVN do not prevent drug-induced penile erection and yawning, nor 8-Br-cGMP injected in the PVN induces these behavioral responses suggesting that the mechanism by means of which endogenous or NO donor-derived NO facilitates oxytocinergic transmission to induce penile erection and yawning is not related to the activation of guanylate cyclase. Furthermore, since hemoglobin, in spite of its ability to prevent drug-induced NO production in the PVN, does not prevent penile erection and yawning, it is likely that NO acts as an intracellular rather than an intercellular modulator in the PVN neurons in which is formed to facilitate the expression of these behavioral responses.

Melis, M. R., S. Succu, et al. (1997). "Prevention by morphine of N-methyl-D-aspartic acid-induced penile erection and yawning: involvement of nitric oxide." Brain Res Bull 44(6): 689-94.

The effect of morphine on the increase of NO2- and NO3- concentration in the dialysate obtained with a microdialysis probe implanted in the paraventricular nucleus of the hypothalamus, and penile erection and yawning induced by N-methyl-D-aspartic acid (NMDA) was studied in male rats. NMDA (50 ng) injected in the paraventricular nucleus of the hypothalamus, induced penile erection and yawning and increased NO2- from 1.10 +/- 0.28 microM to 7.30 +/- 1.10 microM and NO3- from 5.05 +/- 0.71 microM to 11.03 +/- 1.61 microM. Morphine (1-10 microg), but not U-69,593 (10 microg), a selective agonist of the kappa opiate receptor subtype, prevented in a dose-dependent manner NMDA-induced increase in NO2- and NO3- concentration when injected in the paraventricular nucleus 15 min before NMDA. Morphine prevention of NMDA-induced NO2- and NO3- increase was related to a concomitant decrease in the number of penile erection and yawning episodes induced by the excitatory amino acid. Morphine effect was not observed in male rats treated with the opiate receptor antagonist naloxone (10 microg) microinjected in the paraventricular nucleus 15 min before morphine. The present results suggest that morphine prevents an NMDA-induced increase in paraventricular NO production, penile erection, and yawning by inhibiting NO synthase activity in the paraventricular nucleus of the hypothalamus through the stimulation of opioid receptors of the micro subtype.

McManus, B., P. Devine, et al. (1997). "A fetal yawn?" N Engl J Med 336(18): 1329-30.

Khroyan, T. V., R. A. Fuchs, et al. (1997). "Effects of D3-preferring agonists 7-OH-PIPAT and PD-128,907 on motor behaviors and place conditioning." Behav Pharmacol 8(1): 65-74.

Dose-dependent effects of 7-OH-PIPAT and PD-128,907 on motor behaviors and place conditioning were examined in rats. Four 2-day conditioning trials were conducted over 8 consecutive days. On one day of each trial, animals received an injection of either saline, one of six doses of 7-OH-PIPAT (0.01-10.0 mg/kg), or one of five doses of PD-128,907 (0.01-1.0 mg/kg), and were placed into a distinct compartment for 40 min. On the other day, animals received an injection of saline and were placed into a different compartment for 40 min. Locomotion, sniffing, and yawning were measured following the first and last drug injections. Place conditioning was assessed the day following the last conditioning trial. None of the doses of 7-OH-PIPAT or 0-0.3 mg/kg PD-128,907 produced place conditioning. However, 1 mg/kg PD-128,907 produced conditioned place preference (CPP). Across doses, both 7-OH-PIPAT and PD-128,907 produced a U-shaped change in sniffing and locomotion and an inverted U-shaped change in yawning. Across time, lower doses produced a decrease in sniffing and locomotion and an increase in yawning that were evident immediately, whereas higher doses produced a biphasic change in that there was an initial decrease followed by an increase in sniffing and locomotion. Behaviors produced by both low and high doses were sensitized following repeated administration. PD-128,907 produced CPP and was more potent than 7-OH-PIPAT in altering motor behaviors, possibly due to its greater selectivity for the D3 receptor.

Ferrari, F. and D. Giuliani (1997). "Involvement of dopamine D2 receptors in the effect of cocaine on sexual behaviour and stretching-yawning of male rats." Neuropharmacology 36(6): 769-77.

The effect of cocaine (7.5, 15 and 30 mg/kg) administered in acute or subchronic mode, on the mating behaviour of sexually active male rats varied in a dose- and mode-dependent manner. Regardless of mode of treatment, 30 mg/kg markedly impaired the rats copulatory ability and impairment continued for a week after suspension of subchronic treatment. An acute dose of 15 mg/kg reduced intromission frequency, while in subchronic mode it also reduced ejaculation latency. Mount frequency was increased by 7.5 and 15 mg/kg, but only on first injection. In the case of sexually-naive male rats, acute administration of cocaine (3-30 mg/kg) stimulated penile erections at 7.5 mg/kg and motor hyperactivity at all doses. (-) Eticlopride (0.025 and 0.05 mg/kg), a DA D2 antagonist, counteracted cocaine-induced motor hyperactivity but not penile erection, which it enhanced. (-) Eticlopride at the same doses also antagonized cocaine potentiation of lisuride (0.2 mg/kg)-induced behavioural effects. When male rats treated with subchronic cocaine (15 mg/kg) were injected with the DA D2 agonist SND 919 (0.1 mg/kg), they displayed a more marked stretching-yawning behaviour than control animals receiving SND 919 at the same dose. The involvement of DA D2 receptors in cocaine-induced effects is suggested.

Fanibunda, K. and D. J. Lovelock (1997). "Calcified stylohyoid ligament: unusual pressure symptoms." Dentomaxillofac Radiol 26(4): 249-51.

Two previously unreported clinical features, namely obstruction of the submandibular salivary gland and discomfort on yawning, were encountered in a 42-year-old male with gross calcification of the stylohyoid ligament. The diagnosis was confirmed on clinical grounds, routine radiography, sialography and CT scanning.

Eguibar, J. R. and A. Moyaho (1997). "Inhibition of grooming by pilocarpine differs in high- and low-yawning sublines of Sprague-Dawley rats." Pharmacol Biochem Behav 58(2): 317-22.

A comparative study of the effect of pilocarpine, a muscarinic receptor agonist, on grooming, scored during 45 min via a time-sampling procedure, was carried out on two sublines of male rats selectively bred for high-(HY) and low-yawning (LY) frequency. In one condition, we introduced rats in a novel cage and observed them immediately after receiving an I.P. injection of pilocarpine (0.5-3.75 mg/Kg) or an equivalent volume of saline. Besides grooming, the occurrence of yawns was continuously recorded. In the other condition, we immersed rats in water for 60 s, then they received an I.P. injection of pilocarpine (3.75 mg/Kg) or an equivalent volume of saline and we placed them in an open field, in which we recorded the number of crossed squares. Grooming scores were significantly higher in the condition after water immersion than in the novel situation; in both conditions HY had a grooming response higher than that of LY rats. Pilocarpine produced a dose-dependent inhibition of novelty-induced grooming in HY rats, whereas LY grooming was reduced only with the highest dose. In contrast, yawning increased in a dose-dependent manner with HY rats curve over that of LY animals, except for the highest dose. Pilocarpine inhibited water immersion-induced grooming in both sublines of rats, but it did not reduce grooming as much as it did in the novel condition. Pilocarpine affected distinctly each of the components of grooming, without inhibiting animals locomotor activity. The results indicate that HY rats also have a higher number of grooms than LY rats, and because grooming and yawning can appear after stressful circumstances, HY rats may be used to study the role that both behaviors could have in counteracting the effects of stress. Similarly, HY animals might be utilized to study the underlying neurochemical mechanisms of grooming. This study also indicates that the cholinergic systems exert an inhibitory influence on grooming which contrasts with the excitatory effect on yawning.

Cohen, K. P., W. M. Ladd, et al. (1997). "Comparison of impedance and inductance ventilation sensors on adults during breathing, motion, and simulated airway obstruction." IEEE Trans Biomed Eng 44(7): 555-66.

The goal of this study was to compare the relative performance of two noninvasive ventilation sensing technologies on adults during artifacts. We recorded changes in transthoracic impedance and cross-sectional area of the abdomen (abd) and rib cage (rc) using impedance pneumography (IP) and respiratory inductance plethysmography (RIP) on ten adult subjects during natural breathing, motion artifact, simulated airway obstruction, yawning, snoring, apnea, and coughing. We used a pneumotachometer to measure air flow and tidal volume as the standard. We calibrated all sensors during natural breathing, and performed measurements during all maneuvers without changing the calibration parameters. No sensor provided the most-accurate measure of tidal volume for all maneuvers. Overall, the combination of inductance sensors [RIP(sum)] calibrated during an isovolume maneuver had a bias (weighted mean difference) as low or lower than all individual sensors and all combinations of sensors. The IP(rc) sensor had a bias as low or lower than any individual sensor. The cross-correlation coefficient between sensors was high during natural breathing, but decreased during artifacts. The cross correlation between sensor pairs was lower during artifacts without breathing than it was during maneuvers with breathing for four different sensor combinations. We tested a simple breath-detection algorithm on all sensors and found that RIP(sum) resulted in the fewest number of false breath detections, with sensitivity of 90.8% and positive predictivity of 93.6%.

Cerbo, R., P. Barbanti, et al. (1997). "Dopamine hypersensitivity in migraine: role of the apomorphine test." Clin Neuropharmacol 20(1): 36-41.

We investigated the effects of apomorphine administration at two different doses (2-10 micrograms/kg, s.c.) in 35 migraineurs in headache-free period and in 20 age-matched healthy control subjects, with and without pretreatment with domperidone. Neither patients or controls complained of headache at either dose, whereas at the dose of 10 micrograms/kg migraineurs showed a statistically significant higher incidence of dopaminergic symptoms (nausea, vomiting, drowsiness, yawning, dizziness, sweating) than controls. Furthermore, symptoms due to postsynaptic dopamine receptors activation (i.e., nausea and vomiting) only appeared in migraineurs. No symptom, however, resembled those characterizing a spontaneous migraine attack. In conclusion, migraineurs show a lower threshold for dopamine receptor activation than normal subjects.

Camarini, R. and M. A. Benedito (1997). "Rapid eye movement (REM) sleep deprivation reduces rat frontal cortex acetylcholinesterase (EC 3.1.1.7) activity." Braz J Med Biol Res 30(5): 641-7.

Rapid eye movement (REM) sleep deprivation induces several behavioral changes. Among these, a decrease in yawning behavior produced by low doses of cholinergic agonists is observed which indicates a change in brain cholinergic neurotransmission after REM sleep deprivation. Acetylcholinesterase (Achase) controls acetylcholine (Ach) availability in the synaptic cleft. Therefore, altered Achase activity may lead to a change in Ach availability at the receptor level which, in turn, may result in modification of cholinergic neurotransmission. To determine if REM sleep deprivation would change the activity of Achase, male Wistar rats, 3 months old, weighing 250-300 g, were deprived of REM sleep for 96 h by the flower-pot technique (N = 12). Two additional groups, a home-cage control (N = 6) and a large platform control (N = 6), were also used. Achase was measured in the frontal cortex using two different methods to obtain the enzyme activity. One method consisted of the obtention of total (900 g supernatant), membrane-bound (100,000 g pellet) and soluble (100,000 g supernatant) Achase, and the other method consisted of the obtention of a fraction (40,000 g pellet) enriched in synaptic membrane-bound enzyme. In both preparations, REM sleep deprivation induced a significant decrease in rat frontal cortex Achase activity when compared to both home-cage and large platform controls. REM sleep deprivation induced a significant decrease of 16% in the membrane-bound Achase activity (nmol thiocholine formed min-1 mg protein-1) in the 100,000 g pellet enzyme preparation (home-cage group 152.1 +/- 5.7, large platform group 152.7 +/- 24.9 and REM sleep-deprived group 127.9 +/- 13.8). There was no difference in the soluble enzyme activity. REM sleep deprivation also induced a significant decrease of 20% in the enriched synaptic membrane-bound Achase activity (home-cage group 126.4 +/- 21.5, large platform group 127.8 +/- 20.4, REM sleep-deprived group 102.8 +/- 14.2). Our results suggest that REM sleep deprivation changes Ach availability at the level of its receptors through a decrease in Achase activity.

Brus, R., R. Szkilnik, et al. (1997). "Nitro-l-arginine attenuates SKF 38393-induced oral activity in neonatal 6-hydroxydopamine-lesioned rats." Acta Neurobiol Exp (Wars) 57(4): 283-7.

Nitric oxide (NO) in brain has been implicated in neuronal regulatory processes and in neuropathologies. Previously we showed that NO modified quinpirole-induced yawning, a behavioral measure of dopamine (DA) D3 receptor activation in rats. The aim of this study was to characterize the effect of nitro-L-arginine methyl ester HCl (NAME) and L-arginine HCl on reactivity of rats to the DA D1 receptor agonist SKF 38393 and DA D1 antagonist SCH 23390 in intact and neonatal 6-hydroxydopamine (6-OHDA)-lesioned rats (134 micrograms of base ICV at 3rd day after birth). L-arginine HCl (300 mg/kg i.p.) increased the oral activity response in 6-OHDA-lesioned rats, like SKF 38393, and induced catalepsy in intact control rats, like SCH 23390. In contrast, NAME had no effect on oral activity or catalepsy, but fully attenuated SKF 38393-induced oral activity. These findings indicate that L-arginine HCl has no apparent effect at the DA D1 receptor, but that NAME is effective in attenuating a DA D1 agonist-induced effect. Consequently NO may be an intracellular second messenger for supersensitized receptors associated with DA D1 agonist-induced oral activity.

Aureli, F. and F. B. de Waal (1997). "Inhibition of social behavior in chimpanzees under high-density conditions." Am J Primatol 41(3): 213-28.

This is the first study to investigate the short-term effects of high population density on captive chimpanzees (Pan troglodytes). Subjects of the study were 45 chimpanzees living in five different groups at the Yerkes Regional Primate Research Center. The groups were observed under two conditions: 1) when they had access to both the indoor and outdoor sections of their enclosures; 2) during cold days when they were locked into the indoor runs, which reduced the available space by more than half. Under the high-density condition, allogrooming and submissive greetings decreased, but juvenile play increased. Remarkably, the rate of various forms of agonistic behavior, such as aggression, bluff charge, bluff display, and hooting, occurred less frequently under the high-density condition. This general decrease in adult social activity, including agonistic behavior, can be interpreted as an inhibition strategy to reduce opportunities for conflict when interindividual distances are reduced. This strategy is probably effective only in the short run, however. Behavioral indicators of anxiety, such as rough scratching and yawning, showed elevated rates, suggesting increased social tension under the high-density condition.

Zumpe, D., A. N. Clancy, et al. (1996). "Behavioral responses to Depo-Provera, Fadrozole, and estradiol in castrated, testosterone-treated cynomolgus monkeys (Macaca fascicularis): the involvement of progestin receptors." Physiol Behav 60(2): 531-40.

Sexual motivation and behavior decreased in male cynomolgus monkeys given either Depo-Provera (medroxyprogesterone acetate, MPA), which reduces androgen uptake by brain, or the nonsteroidal aromatase inhibitor, Fadrozole, which virtually eliminates the conversion of testosterone (T) to estradiol (E2) in brain. This suggested that both unchanged T and E2 are important for the control of male primate sexual behavior, but combined treatment with MPA and Fadrozole did not have the anticipated summatory effects in intact males: the behavioral decrements when MPA-treated males were given Fadrozole were about half those observed when Fadrozole was given alone. The present study tested the hypothesis that Fadrozole suppressed the behavioral effects of MPA by preventing the induction by E2 of progestin receptors in the brain to which MPA binds. Eight castrated, T-treated males were each tested with an estrogenized female i) during baseline, ii) during MPA treatment, iii) during treatment with MPA and Fadrozole together, and iv) with E2 treatment added to condition (iii) (256 1-h behavior tests). All dosages were those used in previous studies. Sexual motivation, as reflected in mounting attempts and mounting attempt latencies, was further diminished by E2 treatment in males receiving both MPA and Fadrozole, but ejaculatory activity was not changed. Immunocytochemistry demonstrated that the distributions of progestin and androgen receptors were little affected by MPA treatment, and that progestin receptor immunoreactivity was almost completely abolished in the brains of males receiving both MPA and Fadrozole but present in those receiving additional E2 treatment, findings that supported the hypothesis.

Wielosz, M. and H. Szymczyk (1996). "Yawning induced by apomorphine, physostigmine or pilocarpine is inhibited by electroconvulsive shock (ECS)." Acta Physiol Hung 84(4): 473-5.

Single and repeated ECS decrease sensitivity of dopamine D2 and acetylcholine receptors as measured by yawning behavior. This reduced sensitivity is dependent from the number of applied shocks, since effects of repeated ECS disappear 5 days after the last shock but effect of single ECS disappear 24 h after the shock.

Sleight, A. J., F. J. Monsma, Jr., et al. (1996). "Effects of altered 5-ht6 expression in the rat: functional studies using antisense oligonucleotides." Behav Brain Res 73(1-2): 245-8.

The purpose of the present study was to determine whether the 5-ht6 receptor is functionally expressed in the rat brain by blocking its translation from mRNA with treatments of phosphorothioate antisense oligonucleotides. Rats were treated with either saline, antisense (AO) or scrambled oligonucleotides (SO) for 4 days. Treatment with AO reduced the number of [3H]LSD binding sites in the frontal lobes by 30% but had no significant effect on the number of 5-HT1A and 5-HT2A receptor binding sites in the cortex of the rats. A behavioural syndrome of yawning, stretching and chewing, however, was observed in AO treated rats but not in any of the other treatment groups. This AO-specific behaviour had returned to normal 5 days after cessation of the oligodeoxynucleotide treatment. These data suggest that the 5-ht6 receptor has a physiological function in the rat brain where it appears to be under the tonic control of endogenous 5-HT.

Shvartz, E. (1996). "Endurance fitness and orthostatic tolerance." Aviat Space Environ Med 67(10): 935-9.

BACKGROUND: Several lower body negative pressure studies conducted in recent years have suggested that aerobically fit individuals have poo-orthostatic tolerance (OT). HYPOTHESIS: There will be significant differences between OT of highly fit endurance runners and unfit individuals. METHODS: Subjects were 17 men and 17 women aged 29-42 yr who were administered two orthostatic tests (20 min standing) before, and 5 min following a VO2max test. There were 6 men and 6 women who were highly trained endurance runners with VO2max of 63 and 50 ml.kg-1.min-1 for the men and women, respectively; 6 men and 6 women had average fitness (VO2max of 40 and 32 ml.kg-1.min-1, respectively), and the remaining 5 men and 6 women had poor fitness (VO2max of 32 and 26 ml.kg-1.min-1, respectively). RESULTS: The trained men and women showed good OT before and after exercise, which was characterized by very low orthostatic heart rates (54 and 64 bpm before, 70 and 75 bpm after exercise, for the men and women, respectively); relatively large pulse pressures (PP); and a lack of any adverse subjective reactions. The untrained subjects' orthostatic heart rates were 30-40 bpm higher than in the trained subjects, (18 bpm higher after, vs. before exercise) their PP was narrower, and there were 7 cases of orthostatic weakness (dizziness, yawning) and 8 fainting episodes. (6 cases before, 9 cases after exercise). CONCLUSIONS: Aerobically fit individuals have good OT while unfit individuals show poor OT. Since the maintenance of good OT is important in the Space Shuttle flights, endurance training enhances crew/vehicle safety.

Sandyk, R. (1996). "Effects of picotesla flux electromagnetic fields on dopaminergic transmission in Tourette's syndrome." Int J Neurosci 84 (1-4): 187-94.

Tourette's syndrome (TS), a chronic familial neuropsychiatric disorder of unknown etiology, is characterized clinically by the presence of motor and vocal tics that wax and wane in severity over the time and by the occurrence of a variety of neurobehavioral disorders. It is believed that the tics of TS result from increased dopamine (DA) activity caused by postsynaptic DA receptor supersensitivity. The synthesis and release of DA is regulated presynaptically by a specific class of DA D2 receptors, termed autoreceptors activation of which causes inhibition of DA synthesis and release. In experimental animals and humans administration of small doses of apomorphine, a DA D2 autoreceptor agonist, produces yawning. Recurrent episodes of yawning followed by increased motor tic activity was observed in two patients with TS during exposure to brief, extracranial applications of picotesla flux electromagnetic fields (EMFs). On the basis of these observations it is suggested that recurrent episodes of yawning in response to application of EMFs was induced by activation of presynaptic DA D2 autoreceptors while further exposure to these EMFs caused excessive stimulation of postsynaptic DA D2 receptors resulting in exacerbation of the tics. Thus, the dual effects of picotesla flux EMFs on the DA D2 autoreceptor and the postsynaptic receptor resemble the biphasic pharmacological and behavioral properties of apomorphine, a DA agonist which activates the autoreceptors in low doses while in higher doses causes stimulation of the postsynaptic receptors producing exacerbation of symptoms of TS. These findings demonstrate that picotesla flux EMFs applied extracerebrally may influence nigrostriatal DA transmission at pre- and postsynaptic DA D2 receptor sites.

Sandyk, R. (1996). "Bidirectional effect of electromagnetic fields on ketanserin-induced yawning in patients with multiple sclerosis: the role of melatonin." Int J Neurosci 85(1-2): 93-9.

5-HT2 receptors regulate sleep including yawning behavior. Ritanserin, a selective 5-HT2A receptor antagonist, increases the duration of slow wave in rats and humans. This effect is more pronounced during the light period when melatonin plasma levels are low; melatonin inhibits the sleep effects of ritanserin. These findings indicate that melatonin co-determines the effects of ritanserin on sleep. In a cohort of multiple sclerosis (MS) patients ketanserin, a selective 5-HT2A receptor antagonist, induces recurrent yawning particularly when administered in daytime. The frequency of yawning induced by the drug was modified by AC pulsed picotesla flux electromagnetic fields (EMFs) which affect melatonin secretion. Two MS patients are presented in whom the frequency of ketanserin-induced yawning was altered in opposite directions by these EMFs. The first patient, a 50 year old woman with a remitting-relapsing course, developed recurrent yawning and sleepiness after administration of ketanserin (10 mg, PO). Yawning was decreased dramatically during application of EMFs but was unaffected by a placebo EMFs treatment. The second patient, a 35 year old man with a chronic progressive course, manifested a single and brief yawn after administration of an equal dose of ketanserin. Yawning was increased dramatically during application of EMFs while remaining unchanged during a placebo EMFs treatment. These observations demonstrate a bidirectional effect of picotesla flux EMFs on ketanserin-induced yawning which may be related to differences in daytime melatonin plasma levels among MS patients. If validated by estimations of melatonin plasma levels in a larger cohort of patients the information derived from the effects of picotesla EMFs on ketanserin-induced yawning could be used to: (a) assess pineal melatonin functions in patients with MS; (b) indicate differences in pineal functions between male and female MS patients; and (c) indicate a relationship between plasma melatonin levels and the fatigue of MS.

Riley, D. E. (1996). "Paroxysmal kinesigenic dystonia associated with a medullary lesion." Mov Disord 11(6): 738-40.

A 67-year-old man experienced the abrupt onset of intermittent spasms of tightening of his throat muscles and elevation of his tongue to the roof of his mouth. These were precipitated by initiating movements, either of his mouth (eating, drinking, speaking, yawning) or of his whole body (arising from bed or a chair, lifting heavy weights). Episodes occurred six to 20 times per day, lasted 10-30 s, then resolved spontaneously. Two years later, results of his general neurological examination, including speech, were normal. Several spasms were

provoked by arising from a seated or supine position or by drinking. Objectively, there was a strained dysphonia accompanied by palpable hardening of the supralaryngeal muscles. Each episode resolved within 15 s. Magnetic resonance imaging (MRI) showed evidence of a remote hemorrhage in the medulla. No abnormal blood vessels were seen. Phenytoin 300 mg/day abolished the spasms within days. Decreasing the dose to 200 mg/day months later led to a partial return of symptoms. Relief has persisted for 3 years. This patient has paroxysmal kinesigenic dystonia (PKD) of structures (pharynx, larynx, tongue) innervated by lower cranial motor nerves and a medullary lesion on MRI. PKD has been associated with focal lesions at all levels of the central nervous system (CNS), although never before in the medulla. PKD seems to be a nonspecific phenomenon of the CNS in reaction to injury.

Postert, T., D. Pohlau, et al. (1996). "Pathological yawning as a symptom of multiple sclerosis." J Neurol 243(3): 300-1.

Poe, G. R., M. P. Kristensen, et al. (1996). "Hippocampal activity during transient respiratory events in the freely behaving cat." Neuroscience 72(1): 39-48.

We measured dorsal hippocampal activity accompanying sighs and apnea using reflectance imaging and electrophysiologic measures in freely behaving cats. Reflected 660-nm light from a 1-mm2 area of CA1 was captured during sighs and apnea at 25 Hz through a coherent image conduit coupled to a charge coupled device camera. Sighs and apnea frequently coincided with state transitions. Thus, state transitions without apnea or sighs were separately assessed to control for state-related activity changes. All dorsal hippocampal sites showed discrete regions of activation and inactivation during transient respiratory events. Imaged hippocampal activity increased 1-3 s before the enhanced inspiratory effort associated with sighs, and before resumption of breathing after apnea. State transitions lacking sighs and apnea did not elicit analogous optical activity patterns. The suprasylvian cortex, a control for site, showed no significant overall reflectance changes during phasic respiratory events, and no discrete regions of activation or inactivation. Spectral estimates of hippocampal electroencephalographic activity from 0-12 Hz showed significantly increased power at 3-4 Hz rhythmical slow activity before sighs and apnea, and increased 5-6 Hz rhythmical slow activity power during apnea, before resumption of breathing. Imaged activity and broadband hippocampal electroencephalogram power decreased during sighs. We propose that increased hippocampal activity before sigh onset and apnea termination indicates a role for the hippocampus in initiating inspiratory effort during transient respiratory events.

Piepponen, T. P., J. Katajamaki, et al. (1996). "Behavioural and neurochemical sensitization of morphine-withdrawn rats to quinpirole." Pharmacol Biochem Behav 54(4): 787-92.

The sensitivity of dopamine D2-like receptors in morphine-withdrawn rats was studied using the selective agonist quinpirole. Morphine was administered twice daily increasing the daily dose from 20 to 50 mg/kg during 7 days. Twenty-four hours after the last morphine administration the rats were given quinpirole (0.01-1 mg/kg) and their behavior was assessed. Withdrawal from repeated morphine treatment enhanced yawning behavior and penile erections induced by small doses (0.01-0.1 mg/kg) as well as the intensity of stereotypy induced by a large dose (1.0 mg/kg) of quinpirole. In the morphine-withdrawn rats the dose of 1 mg/kg of quinpirole caused less yawning than in the control rats, whereas the number of erections induced by this dose was enhanced as compared with the control animals. In the control rats, the striatal and limbic concentrations of dopamine metabolites, 3,4-dihydroxphenylacetic acid (DOPAC), and homovanillic acid (HVA), were not clearly affected by the smallest dose of quinpirole. However, the small dose of quinpirole (0.01 mg/kg) significantly reduced the levels of DOPAC and HVA in the striatum and limbic forebrain of the rats withdrawn from morphine either for 24 or 48 h. These findings indicate that withdrawal from repeated morphine treatment enhances the sensitivity of dopamine D2-like receptors.

Perrault, G., H. Schoemaker, et al. (1996). "[The place of amisulpride in the atypical neuroleptic class]." Encephale 22 Spec No 2: 3-8.

Amisulpride is a benzamide derivative which displays a pharmacological profile distinct from that of classical neuroleptics such as haloperidol. In vitro, amisulpride selectively binds to dopamine (DA) receptors and is devoid of any affinity for serotonergic, alpha-adrenergic, histaminergic or muscarinic receptors. It has high and equal affinities for human D2 and D3 receptors, without affinity for D1 and D4 receptors. In vivo, in rats, amisulpride preferentially blocked D2 and D3 receptors localized in limbic structures in comparison with receptors found in the striatum. In addition, amisulpride selectively blocked presynaptic DA receptors. Thus, amisulpride antagonized apomorphine-induced effects (yawning, hypomotility) related to presynaptic DA receptor stimulation at very low doses (ED50 = 0.3-1 mg/kg, ip) compared to those needed to inhibit hypermotility and gnawing (60-80 mg/kg, ip) which involve post-synaptic DA receptor stimulation. The high affinity of amisulpride for D2 and D3 receptors, and its high degree of limbic selectivity may explain the lack of catalepsy in rats and the low incidence of neurological side effects in clinical studies. The enhancement of DA function produced by its selective presynaptic receptor DA blockade may account for the clinical efficacy of amisulpride against negative symptoms of schizophrenia.

Melis, M. R., S. Succu, et al. (1996). "Dopamine agonists increase nitric oxide production in the paraventricular nucleus of the hypothalamus: correlation with penile erection and yawning." Eur J Neurosci 8(10): 2056-63.

A low dose of apomorphine (80 micrograms/kg s.c.), a mixed D1/D2 agonist that induces penile erection and yawning, increased the concentration of NO2-from 1.12 +/- 0.45 microM to 3.8 +/- 0.75 microM and NO3-from 5.53 +/- 0.82 to 11.25 +/- 2.30 microM in the dialysate collected from the paraventricular nucleus of the hypothalamus of male rats by in vivo microdialysis. The NO2-concentration was also increased by LY 171555 (50 micrograms/kg s.c.), a D2 agonist that induces penile erection and yawning, but not by SKF 38393 (5 mg/kg s.c.), a D1 agonist with no effect on these responses. Conversely, apomorphine's effect on NO2-was prevented by haloperidol (0.5 mg/kg i.p.), a mixed D1/D2 antagonist and L-sulpiride (25 mg/kg i.p.), a D2 antagonist, but not by the D1 agonist SCH 23390 (50 micrograms/kg s.c.), although all three compounds prevented penile erection and yawning. The apomorphine effect on NO2-, penile erection and yawning was also prevented by the nitric oxide synthase inhibitor NG-nitro-L-arginine methyl ester (200 micrograms i.c.v.). The nitric oxide scavenger haemoglobin (200 micrograms i.c.v.) also prevented the NO2-increase, but was ineffective against penile erection and yawning. In contrast, the oxytocin antagonist d(CH2)5Tyr(Me)-Orn8-vasotocin (1 microgram i.c.v.) and the guanylate cyclase inhibitor methylene blue (300 micrograms i.c.v.) had no effect on the NO2-increase, but did prevent the behavioural responses. We infer from this that dopamine agonists induce penile erection and yawning by acting on D2 receptors that increase nitric oxide synthase activity in the cell bodies of paraventricular oxytocinergic neurons projecting to extra-hypothalamic brain areas.

Masuzaki, H., M. Masuzaki, et al. (1996). "Color Doppler imaging of fetal yawning." Ultrasound Obstet Gynecol 8(5): 355-6.

Kurashima, M., M. Domae, et al. (1996). "Inhibitory effects of putative dopamine D3 receptor agonists, 7-OH-DPAT and quinpirole, on prolactin secretion in rats." Pharmacol Biochem Behav 53(2): 379-83.

The present experiments were performed to investigate effects of (+/-)-2-(dipropylamino)-7-hydroxy-1,2,3,4-tetrahydronaphthalene (7-OH-DPAT) or quinpirole (LY 171555), putative dopamine (DA) D3 receptor agonists, on serum prolactin levels in male rats. Basal prolactin levels were reduced dose-dependently by SC administration of 7-OH-DPAT or quinpirole at respective doses of 10-100 micrograms/kg and 25-250 micrograms/kg. Daily treatment with estradiol, 35 micrograms/kg/day for 3 days, increased serum prolactin levels to fourfold higher levels than those of nonprimed rats. Intraperitoneal injection of alpha-methyl-p-tyrosine (alpha-MT), 300 mg/kg, also increased serum prolactin levels. 7-OH-DPAT or quinpirole at a dose of 50 micrograms/kg caused a marked reduction in serum prolactin levels in both the estradiol- and alpha-MT-induced hyperprolactinemia. The 7-OH-DPAT- and quinpirole-induced decreases in serum prolactin levels were antagonized by the administration of the DA D2 receptor antagonist, spiperone, at 0.5 mg/kg. The results indicate that 7-OH-DPAT and quinpirole decrease prolactin levels in rats by stimulation of the D2 receptor.

Kimura, H., K. Yamada, et al. (1996). "Involvement of catecholamine receptor activities in modulating the incidence of yawning in rats." Pharmacol Biochem Behav 53(4): 1017-21.

Possible involvement of catecholamine receptor activities in modulating the incidence of yawning, which involves activation of dopaminergic-cholinergic linked neuronal mechanism, was investigated in rats. Subcutaneous injection of talipexole (B-HT 920), a selective dopamine D2-receptor-agonist, elicited yawning behavior. This behavior was increased by prazosin and bunazosin, alpha 1-adrenoceptor antagonists, and by pindolol, a beta-adrenoceptor antagonist. The yawning induced by physostigmine, an anticholinesterase agent, and pilocarpine, a direct muscarinic receptor agonist, was increased by pindolol, but was unaffected by prazosin and bunazosin. In addition, the yawning induced by the dopaminergic agonists, but not by the cholinergic agonists, was markedly suppressed by ST587, an alpha 1-adrenoceptor agonist. All the yawning responses to dopaminergic and cholinergic agents were reduced not only by scopolamine, a muscarinic receptor antagonist, but also by idazoxan, rauwolscine, and yohimbine, alpha 2-adrenoceptor antagonists. The results suggest that catecholamine receptor activities seem to play different roles in inhibitory modulation of the occurrence of yawning caused by dopaminergic and cholinergic stimulation.

Ignat'ev, D. A., V. V. Vorob'ev, et al. (1996). "[The effect of short peptides isolated from the brain of a hibernating suslik on the rat EEG and behavior]." Zh Vyssh Nerv Deiat Im I P Pavlova 46(6): 1049-58.

The intracerebroventricular injection of the peptides kyotorphin (KT), newkyotorphin (NKT), and Aps-Tyr (BS) changed rat behaviour. There was an increase in the rate of exploratory reactions, rearing, grooming, stereotypic scratching movements, yawning, stretching, hiccupping, sneezing. Similar effects had been earlier observed in rats after administration of the fraction (F, 1-10 kD) from the brain of hibernating ground squirrels in which the studied peptides were found. The EEG effects depended on a peptide dose. As in the case of F injection, KT in the dose of 4 mcg suppressed the theta- and alpha-rhythms, KT injection in the dose of 8 mcg produced similar effect within the first minutes. Then it was substituted for an enhancement of the delta-, theta-, and alpha-rhythms while the beta-activity was suppressed. The effects of BS (4 mcg) and KT (mcg) were similar, however, increase in the BS dose to 8 mcg resulted in an enhancement of the beta-activity as in the case of F injection. The NKT effects also consisted in delta-enhancement and beta-suppression, but, in contrast to KT, the theta- and alpha-suppression was short-term, delayed and occurred only after the peptide injection in the dose of 8 mcg.

Giuliani, D. and F. Ferrari (1996). "Differential behavioral response to dopamine D2 agonists by sexually naive, sexually active, and sexually inactive male rats." Behav Neurosci 110(4): 802-8.

This study was performed with male rats categorized as sexually naive (SN), sexually active (SA), or sexually inactive (SI). In a first experiment the effects of dopamine (DA) D2 agonist SND 919 (0.05, 1, and 10 mg/kg) on the copulatory behavior of SN, SA and SI rats

were assessed. In a second experiment the DA D2 agonist B-HT 920 (0.2 mg/kg) was used, and examination was limited to SN and SA rats. The effects exerted on stretching-yawning, penile erection, and sedation by the same compounds at the same doses in these three rat categories were also investigated. The main findings were that SND 919 and B-HT 920 facilitated ejaculation in SA rats, and that the rats that were different as regards level of sexual activity exhibited different behavioral responses to the two DA agonists.

Furukawa, T. (1996). "Yawning behavior for preclinical drug evaluation." Methods Find Exp Clin Pharmacol 18(2): 141-55.

Fundaro, A. (1996). "Chronic nimodipine and yawning behavior in grouped or individually housed rats." Prog Neuropsychopharmacol Biol Psychiatry 20(1): 121-7.

1. The effects of a chronic administration (around 30 mg/ kg/day) of the dihydropyridine calcium antagonist nimodipine, on apomorphine induced yawning behaviour of grouped or individual housed rats, were studied. 2. Nimodipine treatment had no effect in grouped rats. 3. Individually housed animals gave a significant lower number of yawns in respect to grouped controls: this difference disappeared in isolated, nimodipine treated, group. 4. The results show the ability of nimodipine to restore a depressed behavioural performance.

Fujikawa, M., M. Nagashima, et al. (1996). "Partial agonistic effects of OPC-14597, a potential antipsychotic agent, on yawning behavior in rats." Pharmacol Biochem Behav 53(4): 903-9.

The present experiments were performed to examine the behavioral effects of OPC-14597, which acts on dopamine receptors in rats. OPC-14597 administered subcutaneously (SC) at doses of 0.1-5 mg/kg elicited yawning, as did OPC-4392 (0.5-2 mg/kg, SC) and (-)-3-PPP (2.5-10 mg/kg, SC). These yawning responses were blocked by intraperitoneal (IP) pretreatment with haloperidol (0.5 mg/kg) but were increased by pindolol (20 mg/kg, IP) or reserpine (5 mg/kg, IP), which per se did not elicit yawning. The yawning induced by talipexole, a selective dopamine D2 receptor agonist, was inhibited by OPC-14597 (0.5-5 mg/kg, SC) and (-)-3-PPP (10 mg/kg, SC). Apomorphine (0.5 mg/kg, SC), a dopamine D1/D2 receptor agonist, elicited stereotypy such as sniffing and licking but OPC-14597 (5-20 mg/kg, SC) did not induce this behavior. The stereotypy induced by apomorphine was inhibited not only by haloperidol (0.5 mg/kg, IP) and (-)-3-PPP (10 mg/kg, SC) but also by OPC-14597 (5-20 mg/kg, SC), without being affected by OPC-4392 (2 mg/kg, SC). In 6-hydroxydopamine (6-OHDA)-treated rats, apomorphine (0.5 mg/kg, SC) elicited rotation behavior whereas OPC-14597, OPC-4392 and (-)-3-PPP did not produce this behavior. These findings suggest that OPC-14597 provokes yawning without causing stereotypy and rotation but markedly antagonizes the talipexole-induced yawning and apomorphine-induced stereotypy, and that OPC-14597 thus exerts partial agonistic effects on yawning behavior but antagonistic effects on stereotypy in rats.

Fujikawa, M., K. Yamada, et al. (1996). "The new muscarinic M1-receptor agonist YM796 evokes yawning and increases oxytocin secretion from the posterior pituitary gland in rats." Pharmacol Biochem Behav 55(1): 55-60.

The present experiments were performed to examine the effects of a new muscarinic M1-receptor agonist, (-)-YM796 ((-)-S-2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4.5]decane L-tartrate monohydrate), on yawning and oxytocin secretion from the posterior pituitary gland in rats YM796, at doses of 2.5-50 mg/kg (SC), elicited yawning. The yawning response was markedly increased by pretreatment with a beta-adrenoceptor antagonist, pindolol (20 mg/kg, IP), which per se did not elicit yawning. The yawning induced by YM796 (10 mg/kg, SC) in combination with pindolol (20 mg/kg, IP) was inhibited by scopolamine (0.5 mg/kg, SC), a muscarinic receptor antagonist, and pirenzcpine (300 micrograms/ rat, ICV) and EEDQ (N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline) (5 mg/kg, IP), muscarinic M1-receptor antagonists, but not by spiperone (0.5 mg/kg, SC), a dopamine D2-receptor antagonist, 4-DAMP (4-diphenylacetoxy-N-methylpiperidine methiodide) (100 micrograms/rat, ICV), a muscarinic M3-receptor antagonist, and [d(CH2)5, Tyr(Mc)2, Orn8]-vasotocin (100 ng/rat, ICV), an oxytocin receptor antagonist. YM796 at 2.5-50 mg/kg (SC) did not exert an action on prolactin levels but increased oxytocin secretion from the posterior pituitary gland in rats. This augmentation of oxytocin secretion by YM796 was inhibited by scopolamine (0.5 mg/kg, SC) and pirenzepine (3 mg/kg, SC), but not by mecamylamine (1 mg/kg, IP), a nicotinic receptor antagonist. The present findings obtained with YM796 suggest that the muscarinic M2-receptor stimulation participates in causing yawning behavior and oxytocin secretion in rats.

Ferrari, F. and D. Giuliani (1996). "Behavioral effects induced by the dopamine D3 agonist 7-OH-DPAT in sexually-active and -inactive male rats." Neuropharmacology 35(3): 279-84.

The present study investigates the effects induced by the putative DA D3 agonist 7-OH-DPAT (0.1 and 1 mg/kg, s.c.) on: (1) the sexual behavior of male rats, categorized on the basis of seven consecutive mating pre-tests as sexually-active (SA) and sexually-inactive (SI); and (2) stretching-yawning, penile erection, sedation and stereotyped behavior of the same animals. The data obtained show that 7-OH-DPAT at both doses modifies the copulatory pattern of SA rats, facilitating ejaculation mechanisms, but fails to increase the sexual drive of the animals as is evident from the ineffectiveness in SI rats. The second major finding is that the two groups of rats, which are markedly different as regards sexual typology, exhibit different behavioral responses to 7-OH-DPAT.

Egerman, R. S. and D. S. Emerson (1996). "Images in clinical medicine. A fetal yawn." N Engl J Med 335(20): 1497.

Dorr, R. T., R. Lines, et al. (1996). "Evaluation of melanotan-II, a superpotent cyclic melanotropic peptide in a pilot phase-I clinical study." Life Sci 58(20): 1777-84.

A pilot phase I study was conducted with a cyclic heptapeptide analog of alpha-melanocyte stimulating hormone (alpha-MSH). The lactam-bridged molecule, called Melanotan-II (MT-II), has the structure Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10 alpha-MSH4-10-NH2 (MT-II) and has superpotent melanotropic activity in vitro. A single-blind, alternating day (saline or MT-II), placebo-controlled trial was conducted in 3 normal male volunteers at the starting dose of 0.01 mg/kg of MT-II. Subcutaneous injections of MT-II or saline were given daily (Monday-Friday) for 2 consecutive weeks. Two subjects were escalated by 0.005 mg/kg increments to 0.03 mg/kg and one to 0.025 mg/kg. The 0.03 mg/kg dose produced Grade II somnolence and fatigue in one of two subjects (WHO standards). Mild nausea, not requiring antiemetic treatment, was reported at most MT-II dose levels. A stretching and yawning complex appeared to correlate with the onset of spontaneous, penile erections which were intermittently experienced for 1-5 hours after MT-II dosing, depending on the MT-II dose. Two subjects had increased pigmentation in the face, upper body and buttock, as measured by quantitative reflectance and by visual perception 1 week after MT-II dosing ended. These results demonstrate that MT-II has tanning activity in humans given only 5 low doses every other day by subcutaneous injection. The recommended single MT-II dose for future Phase I studies is 0.025 mg/kg/day.

Brus, R., R. Szkilnik, et al. (1996). "Nitric oxide (NO) and central dopamine (DA) D3 receptor reactivity to quinpirole in rats." Acta Neurobiol Exp (Wars) 56(1): 15-9.

Nitric oxide (NO) has been implicated in large number of pathologies and in normal physiological function of the brain. The aim of this study was to recognize the effect of Nitro-L-Arginine Methyl Ester.HCl (NAME) and L-Arginine Ethyl Ester.HCl (ARGININE) on reactivity of the central DA D3 receptor to agonist (Quinpirole) in rats. For this reason we have been used specific behavioural procedure such yawning behaviour which is mediated via central DA D3 receptors. Experiments were perform in adult male Wistar rats treated daily with quinpirole (0.05 mg/kg IP) or vehicle (0.9% NaCl) for the first 11 days from birth to obtain of the central D3 receptor supersensitivity. NAME and ARGININE in different way modified response of the central DA receptor to quinpirole estimated by means yawning behavioural procedure.

Bristow, L. J., G. P. Cook, et al. (1996). "The behavioural and neurochemical profile of the putative dopamine D3 receptor agonist, (+)-PD 128907, in the rat." Neuropharmacology 35(3): 285-94.

The functional relevance of the dopamine D3 receptor is still unresolved, largely because of the absence of selective D3 receptor ligands. In the present study we have examined the in vivo profile of (+)-PD 128907, a potent and functionally selective D3 receptor agonist. Low doses of (+)-PD 128907 reduced spontaneous locomotor activity in the rat (ED50 = 13 +/- 3 micrograms/kg, s.c.) a response which was comparable with the non-selective D2,3 receptor agonist apomorphine (ED50 = 13 +/- 1.6 micrograms/kg, s.c.). In addition (+)-PD 128907 impaired prepulse inhibition of the acoustic startle response, with significant effects observed at doses of 30 micrograms/kg when appropriate prepulse intensities were used. Higher doses reversed gamma-butyrolactone-induced catecholamine synthesis (ED50 = 95 +/- 22 and 207 +/- 37 micrograms/kg in accumbens and striatum respectively) and induced yawning (100-300 micrograms/kg), penile grooming (30-1000 micrograms/kg) and sniffing (> or = 300 micrograms/kg) although doses 3- to 10-fold greater than apomorphine were required to produce maximal effects. In contrast to apomorphine, however, (+)-PD 128907 failed to induce intense stereotyped licking and biting in the rat. In view of the potency and selectivity of (+)-PD 128907 for the D3 receptor, a role in the control of locomotor activity is suggested. In addition, the observation that (+)-PD 128907 disrupts prepulse inhibition, a phenomenon which is also impaired in schizophrenic subjects, may indicate the pathological importance of this receptor subtype.

Baenninger, R., S. Binkley, et al. (1996). "Field observations of yawning and activity in humans." Physiol Behav 59(3): 421-5.

Rates of wrist activity and yawning were recorded continuously for 7-15 days in adult human male and female subjects. In the 15 min following 747 yawns wrist motion increased reliably in all subject records. The data were consistent with an hypothesis that yawning is predictive of an increase in activity level. In a second study, data from daily logs kept by 45 subjects confirmed previous findings that yawning frequency is unrelated to prior amount of sleep, or to times of awaking or retiring. More yawning occurred during the week than during weekends.

Askenasy, J. J. and N. Askenasy (1996). "Inhibition of muscle sympathetic nerve activity during yawning." Clin Auton Res 6(4): 237-9.

Yawning is a complex event that depends largely on the autonomic nervous system. Microneurographic techniques were used to study the mechanism involved in yawning. A series of spontaneous yawns displayed by a healthy 39-year-old male offered us the opportunity to study the muscle sympathetic nerve activity (MSNA) during this phenomenon. It was found that 2 s of yawning inhibited the MSNA recorded at the right peroneal nerve in the lateral knee area, while 3 s of slow expiration succeeding a yawn provoked an MSNA discharge. Blood pressure decreased with each slow expiration by 5-6 mmHg, and increased again with the renewed MSNA discharge. We conclude that yawning is associated with a sympathetic suppression that favours a parasympathetic dominance, as indicated by the MSNA and the decrease in blood pressure. The slow expiration following a yawn is associated with a sympathetic activation marked by an MSNA discharge and an increase in blood pressure.

Zarrindast, M. R., R. Adeli, et al. (1995). "Effects of adenosine receptor agonists and antagonists on physostigmine-induced yawning." Eur J Pharmacol 276(1-2): 3-7.
The effect of adenosine receptor agonists and antagonists on physostigmine-induced yawning was investigated in intact or cannulated rats. Intraperitoneal (i.p.) or intracerebroventricular (i.c.v.) administration of physostigmine to rats induced yawning dose dependently. I.p. or i.c.v. treatment of the animals with atropine, theophylline, 5-N-ethylcarboxamidoadenosine (NECA) or N6-cyclohexyladenosine reduced the yawning induced by i.p. injection of physostigmine. I.p. administration of theophylline decreased the yawning induced by i.c.v. injection of physostigmine. The inhibitory action of N6-cyclohexyladenosine (i.p.) also was decreased by 8-phenyltheophylline (i.p.) pretreatment. It is concluded that yawning induced by a central cholinergic mechanism and a central adenosine mechanism interacts with the cholinergic-induced behaviour.

Zarrindast, M. R., F. Fatehi, et al. (1995). "Effects of adenosine agents on apomorphine-induced yawning in rats." Psychopharmacology (Berl) 122(3): 292-6.
In the present work, adenosine agonists and antagonists on apomorphine-induced yawning in rats was investigated. Subcutaneous (SC) injection of apomorphine (0.02, 0.05 and 0.1 mg/kg) induced dose-dependent yawning behaviour in rats. Intracerebroventricular (ICV) administration of different doses of the drug (1, 3, 5 micrograms/rat) also caused a dose-related yawning. ICV administration of the adenosine receptor agonists 5-N-ethylcarboxamidoadenosine (NECA) and N6-cyclohexyladenosine (CHA) decreased apomorphine-induced yawning. The response induced by the adenosine agonists was reduced by 8-phenyladenosine (8-PT) pretreatment. The yawning induced by SC and ICV administration of apomorphine was decreased by ICV or IP injection of theophylline, respectively. It is concluded that at least A1 adenosine receptors may exert negative influence on the apomorphine-induced yawning. However, the exact mechanism(s) of adenosine receptors in this behaviour remain to be established.

Zarrindast, M. R., V. Toloui, et al. (1995). "Effects of GABAergic drugs on physostigmine-induced yawning in rats." Psychopharmacology (Berl) 122(3): 297-300.
In the present work the effects of GABA agonists and antagonists on yawning induced by physostigmine have been studied. Intraperitoneally (IP) injection of physostigmine (0.05-0.3 mg/kg) induced dose-related yawning in rats. The maximum yawning response was observed with 0.2 mg/kg of the drug. The GABA agonists muscimol (1-4 mg/kg) and baclofen (0.125-1 mg/kg) decreased yawning induced by physostigmine (0.2 mg/kg) dose dependently. Combination of both GABA agonists elicited greater inhibition of yawning. The GABA-A antagonists bicuculline or picrotoxin but not the GABA-B antagonist phaclofen reduced the inhibitory response induced by muscimol, whereas phaclofen but not bicuculline or picrotoxin reduced baclofen's inhibitory effect. Administration of bicuculline, picrotoxin or phaclofen also decreased the yawning induced by physostigmine. However, when the GABA-A and GABA-B antagonists were employed in combination, the inhibitory responses of both drugs were lost. It is concluded that GABA-A and/or GABA-B receptor stimulation may inhibit physostigmine-induced yawning.

Vergoni, A. V., M. Sandrini, et al. (1995). "Opening of brain potassium-channels inhibits the ACTH-induced behavioral syndrome in the male rat." Neurosci Lett 188(1): 29-32.
In adult male rats, the intracerebroventricular (i.c.v.) injection of pinacidil, a potassium channel opener, at the doses of 100, 200 or 300 micrograms/rat, dose-dependently reduced the display of the most typical behavioral symptoms (excessive grooming, stretching, yawning, penile erections) induced by the i.c.v. administration of ACTH-(1-24) (4 micrograms/rat). These data indicate that the complex mechanism of the melanocortin-induced behavioral syndrome involves closure of potassium channels in target neurons, and provide further experimental support to the idea that melanocortins are functional antagonists of opioids.

van den Buuse, M. (1995). "Differential effects of quinelorane and pergolide on behaviour, blood pressure, and body temperature of spontaneously hypertensive rats and Wistar-Kyoto rats." Pharmacol Biochem Behav 50(3): 389-97.
The systemic administration of the dopamine agonists quinelorane or pergolide to Wistar-Kyoto rats (WKY) induced a significant increase of locomotor activity at higher doses. In spontaneously hypertensive rats, these compounds induced a significant hypoactivity at low doses, but only a modest, and late, increase in locomotor activity at higher doses. Quinelorane was more potent than pergolide on locomotor activity. In WKY and SHR, which had unilateral lesions of the nigrostriatal dopamine system, quinelorane and pergolide induced similar dose-dependent contralateral turning that, in the case of pergolide, was significantly greater in SHR than in WKY. Both quinelorane and pergolide induced yawning similarly in WKY and SHR, and quinelorane was more potent than pergolide. The intravenous administration of quinelorane induced an immediate and dose-dependent increase in blood pressure in WKY and SHR, which could be completely prevented by pretreating the rats with the dopamine antagonist haloperidol. Pergolide similarly caused a rise in blood pressure in WKY and SHR, but its effect could only partially be blocked by haloperidol. The subcutaneous injection of quinelorane or pergolide induced similar dose-dependent hypothermia in WKY. Pergolide also caused a decrease of body temperature in SHR, but quinelorane had little effect in this strain. These results show differences in the effects of quinelorane and pergolide between various experimental test situations and between WKY and SHR. These differences may be related to the involvement of dopamine receptor subtypes and to the previously described changes in central dopaminergic activity in SHR.

Tufik, S., C. de Luca Nathan, et al. (1995). "Effects of stress on drug-induced yawning: constant vs. intermittent stress." Physiol Behav 58 (1): 181-4.
Effects of stress on drug-induced yawning: Constant vs. intermittent stress. PHYSIOL BEHAV 58(1) 181-184, 1995.--Experiment 1 tested whether chronic exposure to immobilization, foot shock or forced swimming would result in suppression of apomorphine-, pilocarpine-, and physostigmine-induced yawning. Immobilization caused suppression of yawning, whereas foot shock and swimming resulted in increased number of yawns. Since interstressor interval was long in the two latter stressors, animals could have recovered and the increase in yawning could be due to the last (acute) exposure to stress. In Experiment 2 we recorded the number of yawns induced by pilocarpine in animals exposed to 1 h of swimming or foot shock. No differences between control and acutely stressed animals were detected. These results suggest that yawning is differently altered by constant and intermittent stressors (i.e., diminished by constant and increased by intermittent stress).

Tang, A. H. and C. S. Himes (1995). "Apomorphine produced more yawning in Sprague-Dawley rats than in F344 rats: a pharmacological study." Eur J Pharmacol 284(1-2): 13-8.
Apomorphine induced yawning in both Sprague-Dawley and F344 rats in the same dose range, but F344 rats emitted only about 1/4 as many yawns as did Sprague-Dawley rats. At higher doses, rats of both strains exhibited stereotypic behavior with a comparable intensity. Pretreatment with either SCH 23390 [R(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine-7-o l] or pindolol increased apomorphine-induced yawning further in Sprague-Dawley rats, but had little effect on the low yawning score produced by apomorphine in F344 rats. The low yawning response to apomorphine in F344 rats is, therefore, not due to a high baseline dopaminergic or adrenergic activity. Apomorphine-induced yawning in F344 rats was increased after an acute injection of physostigmine, or 24 h after an injection of reserpine. It is postulated that a low baseline cholinergic activity in F344 rats may be responsible, in part, for their lower yawning response to dopaminergic receptor stimulation.

Takeuchi, Y., T. Kikusui, et al. (1995). "Changes in the behavioral parameters following the lipopolysaccharide administration in goats." J Vet Med Sci 57(6): 1041-4.
The present study was aimed at the establishment of an experimental model for the numerical assessment of sick animal behavior. Four goats were given bolus injections of 200 ng/kg of lipopolysaccharide (LPS) or vehicle (0 hr) under non-restrained conditions, and observed for behavioral changes and clinical symptoms during the period between -1 and 10 hr. The apparent clinical symptoms of miosis and shivering were observed during the period from 39.5 +/- 3.1 to 296.5 +/- 9.9 min and from 46.0 +/- 2.3 to 251.0 +/- 15.5 min after the LPS administration, respectively. As to the general behaviors, the total length for standing and sternum lying during the period from 0 to 5 hr after LPS administration showed no change, however, that for feeding and rumination, and the cumulative number of grooming episode were significantly reduced as compared to the control period. On the other hand, the cumulative numbers of urination, defecation and yawning showed a tendency to increase but not significantly. These results suggest that stereotyped behavioral responses, which are typically seen in acute phase of sickness, can be transiently induced in goats by treating them with LPS.

Taha, S. A., A. M. Ageel, et al. (1995). "Effect of (-)-cathinone, a psychoactive alkaloid from khat (Catha edulis Forsk.) and caffeine on sexual behaviour in rats." Pharmacol Res 31(5): 299-303.
The effect of (-)-cathinone, caffeine and their combinations was studied on the sexual behaviour of male rats. Male sexual activities were assessed by recording the erectile responses (grooming of genitalis, yawning/stretching and homosexual mounting), in the absence of females. The copulatory behaviour was observed by caging males with receptive females brought into oestrus with s.c. injection of oestradiol benzoate and progesterone. The copulatory pattern of male rats (mounting, intromissions, ejaculations and refractory period) was recorded. The oral treatment of cathinone (5 mg kg-1 day-1), caffeine (50 mg kg-1 day-1) and their combinations for 15 days increased arousal (motivation) in male rats as evidenced by increased mounting performance and anogenital investigatory behaviour. However, erectile and ejaculatory responses, measured in the present study, showed no stimulant effect. It is conceivable from the present results that cathinone, the psychostimulant constituent of khat modified masculine pattern behaviour and caffeine also changed the effect of cathinone when administered concomitantly. However, our data provide no evidence that cathinone could be considered as an aphrodisiac.

Sepulveda, W. and M. Mangiamarchi (1995). "Fetal yawning." Ultrasound Obstet Gynecol 5(1): 57-9.
Incidental fetal yawning movements can rarely be observed during real-time ultrasonographic examination. In this report we document repetitive fetal yawning movements in a 27-week fetus over a 7-min period. Each episode lasted for 4-6 s, and the intervals between them varied from 21 to 195 s. This case demonstrated that fetal yawning, a complex involuntary behavioral reflex, is present in its full extent during the second half of pregnancy.

Sandyk, R. (1995). "Cholinergic mechanisms in Gilles de la Tourette's syndrome." Int J Neurosci 81(1-2): 95-100.
Gilles de la Tourette syndrome (GTS), a chronic, familial, neuropsychiatric disorder of unknown etiology, is characterized

clinically by the presence of motor and vocal tics that wax and wane in severity over time and by the occurrence of a variety of neurobehavioral disturbances including hyperactivity, self-mutilatory behavior, obsessive compulsive behavior, learning disabilities, and conduct disorder. Pharmacological studies suggest that the tics of GTS result from dysfunction of monoaminergic systems, more specifically from increased dopaminergic activity due to postsynaptic dopamine receptor supersensitivity. However, given that striatal dopaminergic and cholinergic systems exhibit reciprocal antagonism in other movement disorders such as Parkinsonism and chorea, it is conceivable that the cholinergic system is implicated in the disease. In the present communication it is proposed that: (a) the emergence of motor and vocal tics in GTS is associated with increased central cholinergic activity; (b) cholinergic overactivity is involved in the manifestation of other symptoms in GTS including depression, sleep disorders, motion sickness, pain, sensory tics, and the waxing and waning course of the disease; (c) abnormalities of the cholinergic system support previous evidence linking GTS with delayed cerebral maturation in a subset of young patients; and (d) drugs which stimulate cholinergic receptors may exacerbate symptoms of GTS, and as with dopamine agonists, should be avoided in patients with GTS.

Rauca, C. and H. Schroder (1995). "Effect of BCH 325 (Pro-D-Phe-Pro-Gly) on central dopaminergic functions." Peptides 16(4): 635-40.
Three behavioral models were used to characterize the pharmacological action of BCH 325 on central dopaminergic transmission. The effect of acute SC treatment with BCH 325 upon dopaminergic mechanisms affecting motor activity was studied on the climbing behavior of mice. It was shown that the beta-casomorphin analogue evoked a dose-dependent increase in apomorphine (APO)-induced hypoactivity that was reversed by sulpiride (SULP). In in vitro studies on slices of nucleus accumbens of mice it could be demonstrated that 10(-6) M APO caused a reduction of K(+)-stimulated [14C]dopamine (DA) release that was potentiated following simultaneous incubation with 10(-6) M BCH 325. To prove a postsynaptic influence in D1 receptor-mediated behavior pattern, the action of BCH 325 was studied on bromocriptine (BROMO)-evoked yawning behavior of rats after pretreatment with reserpine (RES) or saline. The peptide could not influence the BROMO yawning after saline administration, but it was able to normalize the number of yawns, which were reduced after RES. To investigate the effect of BCH 325 on postsynaptic D2 receptors, jerking behavior on RES-pretreated rats after a high dose of BROMO was used. Following RES pretreatment only, the number of BROMO-induced jerks was decreased by treatment of rats with 0.5 mumol/kg BCH 325. In contrast, the jerking behavior was enhanced by 0.5 mumol/kg BCH 325 in rats that were additionally treated with alpha-methyl-p-tyrosine (MPT). In biochemical studies on slices of the nucleus accumbens of mice, the in vivo pretreatment with RES caused a reduction of K(+)-stimulated [14C]DA release that was blocked by the SC administration of 0.5 mumol/kg BCH 325.(ABSTRACT TRUNCATED AT 250 WORDS)

Protais, P., M. Windsor, et al. (1995). "Post-synaptic 5-HT1A receptor involvement in yawning and penile erections induced by apomorphine, physostigmine and mCPP in rats." Psychopharmacology (Berl) 120(4): 376-83.
Apomorphine and mCPP induced yawning associated with penile erections in rats, whereas physostigmine induced only yawns. Apomorphine-induced yawning and penile erections were antagonized by low doses of raclopride, whereas physostigmine-induced yawning and mCPP-induced effects were only partly inhibited at high doses of raclopride. Scopolamine as well as clozapine antagonized yawning and penile erections induced by apomorphine, mCPP and physostigmine. Similarly, the 5-HT1A agonists 8-OH-DPAT and S 14506 inhibited yawning and penile erections induced by apomorphine, mCPP and physostigmine, and at similar doses induced lower lip retraction and hyperreactivity to handling. The beta/5-HT1A antagonist tertatolol reversed the inhibitory effects of 8-OH-DPAT and S 14506 on drug-induced yawning and penile erections and increased apomorphine- and physostigmine-induced yawn frequency but not penile erection frequency. Like tertatolol, propranolol increased apomorphine- and physostigmine-induced yawn frequency, whereas ICI 118551 increased only physostigmine-induced yawning. 8-OH-DPAT- and S 14506-induced lower lip retraction and hyperreactivity to handling were also significantly antagonized by tertatolol. Finally, p-chlorophenylalanine pretreatment produced about 95% depletion in 5-HT in hypothalamus, hippocampus, striatum and frontal cortex and modified neither the responses of the inducing drugs nor the inhibitory effects of 8-OH-DPAT and S 14506 on drug-induced yawning and penile erections.(ABSTRACT TRUNCATED AT 250 WORDS)

Poggioli, R., A. Benelli, et al. (1995). "Nitric oxide is involved in the ACTH-induced behavioral syndrome." Peptides 16(7): 1263-8.
In many animal species, the ICV injection of ACTH and of several shorter sequences of the ACTH molecule (melanocortin peptides) induces a peculiar behavioral syndrome mainly characterized by excessive grooming and by repeated acts of stretching and yawning. In adult males, spontaneous penile erections with ejaculation are also induced. We have studied the effect of NO synthase inhibition on this behavioral syndrome. The IP injection of the NO synthase inhibitor L-NG-nitroarginine methyl ester (NAME) significantly prevented--at the doses of 50 and 100 mg/kg--all the behavioral symptoms induced by the ICV administration of ACTH(1-24) (4 micrograms/rat). On the other hand, the ICV injection of NAME (up to 300 micrograms/rat) had no influence on the ACTH-induced excessive grooming and stretching, while significantly inhibited the display of yawnings and penile erections. These data indicate that brain NO synthase is involved in the mechanism of ACTH-induced yawning and penile erections, whereas peripheral NO synthase is involved in the induction of stretching and grooming.

Plummer, J. L., G. K. Gourlay, et al. (1995). "Behavioural effects of norpethidine, a metabolite of pethidine, in rats." Toxicology 95(1-3): 37-44.
This study investigated behavioural effects of the toxic pethidine metabolite, norpethidine, in rats and its interactions with reserpine, apomorphine and physostigmine. Following intraperitoneal administration, brain concentrations of norpethidine reached a plateau after 20-40 min and remained elevated for 2 h. In the dose range 0.06-0.18 mmol/kg, norpethidine induced myoclonic jerks, a characteristic splayed posture, and episodes of exaggerated shivering. Forward locomotion, grooming, yawning and rearing were suppressed. Seizures and reverse locomotion occurred occasionally. Administration of reserpine 1 h prior to norpethidine, or of apomorphine or physostigmine 15 min after norpethidine, did not alter the norpethidine-induced behaviours; neither did norpethidine block the effects of apomorphine or physostigmine. The characteristic profile of behaviours induced by norpethidine make this toxicant readily amenable to animal studies. Our results indicate that its mechanism of action is unlikely to involve dopaminergic or cholinergic pathways.

Nasello, A. G., C. A. Tieppo, et al. (1995). "Apomorphine-induced yawning in the rat: influence of fasting and time of day." Physiol Behav 57(5): 967-71.
Yawning behavior is an experimental tool to study physiological responses, to elucidate the mechanisms of action of some drugs and hormones, and it is also a paradigm for some diseases and for dopamine (DA) agonists' clinical use. In this study, the effects of 24- and 48-h fasting as well as the influence of the light-dark cycle on apomorphine (APO)-induced yawning were evaluated. Initially, control and 48-h-fasted adult male rats were tested for yawning induced by APO (50, 100, 150 micrograms/kg, SC). The most effective dose tested was 100 micrograms/kg. Fasting significantly lowered yawning in all doses tested. Comparison between 24- and 48-h-fasted rats for APO (100 micrograms/kg)-induced yawning showed no significant difference between groups. Ad lib-fed groups were tested for APO (100 micrograms/kg)-induced yawning in both the light and in the dark phases of the cycle. Total number of yawnings increased significantly in the dark period. The present data show that fasting reduces and dark period increases APO-induced yawning in rats, suggesting that these conditions modulate the expression of this behavior.

Naish, J. (1995). "A yawning gulf between educationalists and nursing managers." Nurs Manag (Harrow) 2(4): 3.

Minematsu, N. (1995). "[Behavioral effects of chronic apomorphine, and D-1/D-2 dopamine receptor activities in rats]." Nihon Shinkei Seishin Yakurigaku Zasshi 15(3): 247-52.
The present study was conducted to investigate the effects of chronic treatment with apomorphine on yawning and stereotyped behaviors induced by apomorphine, and catalepic responses induced by haloperidol. Rats received apomorphine (1 mg/kg, sc), a direct dopamine D1/D2 agonist, or vehicle once a day for 21 days. The chronic treatment with apomorphine shifted to the right the dose response curve of yawning to administration of apomorphine, which preferentially activates presynaptic dopamine D-2 receptors (auto receptors) at low doses. Haloperidol (0.5 mg/kg, ip)-induced catalepsy mediated by the inhibition of postsynaptic D-2 receptors was unaltered. A subsequent challenge dose of apomorphine (5 mg/kg, ip) produced oral stereotyped behaviors such as sniffing, licking and biting in the vehicle-treated rats. Chronic apomorphine treatment produced significant enhancement of sniffing alone, which may be behavioral sensitization to apomorphine, and, in contrast, attenuated licking and biting, which depend on D-2 receptor activities. These phenomena lasted for at least 30 days. Sniffing might involve relatively increased stimulation of D-1 receptors, as compared with licking and biting. These results suggest that chronic apomorphine reduces presynaptic dopamine D-2 receptor activity, and as a consequence may induce long-lasting postsynaptic dopamine receptor (mainly D-1 receptor) activation.

Melis, M. R., R. Stancampiano, et al. (1995). "Nitroglycerin-induced penile erection and yawning in male rats: mechanism of action in the brain." Brain Res Bull 36(6): 527-31.
The effect of the central administration of nitroglycerin, a potent organic nitrate vasodilator, on penile erection and yawning was studied in male rats. When given intracerebroventricularly (ICV), nitroglycerin (33-99 micrograms) induced the above responses dose-dependently. The minimal effective dose was 33 micrograms, which was active in 60% of the rats. Nitroglycerin (1.65-6.6 micrograms) induced penile erection and yawning also when injected in the paraventricular nucleus of the hypothalamus. Nitroglycerin responses were prevented by methylene blue (200-400 micrograms ICV), by d(CH2)5Tyr(Me)2-Orn8-vasotocin (0.5-1 micrograms ICV) but not hemoglobin (100-200 micrograms ICV). In contrast methylene blue (10-20 micrograms), d(CH2)5Tyr(Me)2-Orn8-vasotocin (0.05-0.1 microgram) and hemoglobin (10-20 micrograms) were ineffective when injected in the paraventricular nucleus. Systemic haloperidol (0.5-1 mg/kg IP) was also ineffective. The results suggest that nitroglycerin induces penile erection and yawning by activating brain oxytocinergic transmission through the formation of nitric oxide in the paraventricular nucleus of the hypothalamus.

Melis, M. R., R. Stancampiano, et al. (1995). "Role of nitric oxide in penile erection and yawning induced by 5-HT1c receptor agonists in male rats." Naunyn Schmiedebergs Arch Pharmacol 351(4): 439-45.
The effect of the intracerebroventricular (i.c.v.) administration of NG-nitro-L-arginine methyl ester and NG-monomethyl-L-arginine, two inhibitors of nitric oxide (NO) synthase, on penile erection and yawning induced by 1-(3-chlorophenyl)-piperazine (m-CPP)- and N-(3-trifluoromethylphenyl)-piperazine (TFMPP), two selective 5HT1c receptor agonists, was studied in male rats. Both NO synthase inhibitors

(50-500 micrograms i.c.v.) prevented dose-dependently the behavioural responses induced by m-CPP (0.5 mg/kg s.c.) or by TFMPP (1 mg/kg s.c.), but NG-nitro-L-arginine methyl ester was about 4-5 times more potent than NG-monomethyl-L-arginine. The D-isomer of NG-monomethyl-L-arginine, which does not inhibit nitric oxide synthase, was ineffective. The inhibitory effect of NG-nitro-L-arginine methyl ester on m-CPP- and TFMPP-induced responses was prevented by the administration of L-arginine (1 mg i.c.v.). In contrast, NG-nitro-L-arginine methyl ester (20 micrograms) was ineffective when injected in the paraventricular nucleus of the hypothalamus, a brain area that plays a key role in the expression of these behavioural responses. m-CPP- and TFMPP-induced penile erection and yawning was prevented also by the i.c.v. administration of LY 83583 (50-200 micrograms) or methylene blue (50-400 micrograms), two inhibitors of guanylate cyclase but not by reduced hemoglobin (50-400 micrograms), a NO scavenger. The results suggest that central nitric oxide is involved in the expression of penile erection and yawning induced by 5-HT1c receptor agonists.

Melis, M. R. and A. Argiolas (1995). "Nitric oxide donors induce penile erection and yawning when injected in the central nervous system of male rats." Eur J Pharmacol 294(1): 1-9.

In order to provide further support for a role of central nitric oxide as a mediator of penile erection and yawning, the nitric oxide donors sodium nitroprusside, hydroxylamine, isoamyl nitrite and S-nitroso-N-acetyl-penicillamine were injected into the lateral ventricles (i.c.v.) or into the paraventricular nucleus of the hypothalamus of male rats. Of the above compounds injected i.c.v., only isoamyl nitrite (10-100 micrograms) induced penile erection and yawning, while the others induced dramatic behavioral changes, such as motor hyperactivity and convulsions, that masked the above responses. Nevertheless, nitric oxide donors in doses ranging from 10 to 50 micrograms, for except S-nitroso-N-acetyl-penicillamine that was injected only at the dose of 10 micrograms and isoamyl nitrite that was not injected at all because of poor solubility, induced penile erection and yawning when injected in the paraventricular nucleus. Nitric oxide donor-induced responses were prevented by methylene blue and LY 83583, inhibitors of guanylate cyclase, the best known target of nitric oxide, given i.c.v. but not in the paraventricular nucleus. However, 8-bromo-guanosine 3':5'-cyclic monophosphate (8-Br-cGMP), a stable cGMP analog, and hemoglobin, a nitric oxide scavenger, were ineffective in inducing and preventing, respectively, penile erection and yawning when injected either i.c.v. or in the paraventricular nucleus. Nitric oxide donor-induced responses were also prevented by the nonapeptide oxytocin receptor antagonist d(CH2)5-Tyr(Me)-Orn8-vasotocin given i.c.v. but not in the paraventricular nucleus. The present results suggest that nitric oxide donors induce penile erection and yawning by activating central oxytocinergic transmission in the paraventricular nucleus of the hypothalamus via a cGMP-independent mechanism.

Lobo, L. L., R. de Medeiros, et al. (1995). "Atropine increases pilocarpine-induced yawning behavior in paradoxical sleep deprived rats." Pharmacol Biochem Behav 52(3): 485-8.

Paradoxical sleep (PS) deprivation has been suggested to induce supersensitivity of postsynaptic dopamine (DA) receptors and subsensitivity of acetylcholine (ACh) receptors. Yawning behavior is reduced after PS deprivation and is believed to result from an interaction between ACh and DA systems. Concomitant treatment of PS deprived animals with DA agonists reverses PS deprivation effects on stereotypy and aggressiveness. To examine this possibility on yawning behavior, rats were treated, during the deprivation period, with atropine, methamphetamine, haloperidol or distilled water. Following PS deprivation, rats were injected with apomorphine or pilocarpine and number of yawns was recorded. Atropine increased yawning of PS deprived rats induced by pilocarpine, but not by apomorphine. Treatment with methamphetamine and haloperidol did not change PS deprivation effect on pilocarpine- and apomorphine-induced yawning. The data suggest that reversal of PS deprivation-induced yawning inhibition is mediated distinctly by both acetylcholine and dopamine systems.

Kurashima, M., K. Yamada, et al. (1995). "Effects of putative dopamine D3 receptor agonists, 7-OH-DPAT, and quinpirole, on yawning, stereotypy, and body temperature in rats." Pharmacol Biochem Behav 52(3): 503-8.

7-OH-DPAT ((+/-)-2-(dipropylamino)-7-hydroxy-1,2,3,4-tetrahydronaphthalene) was recently identified as a dopamine receptor agonist having a > 100-, 1,000- and > 10,000-fold higher affinity for dopamine D3 than for D2, D4 and D1 receptors, respectively. Quinpirole (LY 171555) has also been reported to have a 113-fold greater affinity for dopamine D3 receptors than for D2 receptors. Therefore, we investigated the effects of these putative dopamine D3 receptor agonists on yawning, stereotypy and rectal temperature in rats (N = 424). 7-OH-DPAT and quinpirole administered subcutaneously (SC) at respective low doses of 10-250 micrograms/kg and 25-500 micrograms/kg elicited yawning behavior. The yawning induced by these agents was blocked by spiperone (0.5 mg/kg, SC) and scopolamine (0.5 mg/kg, SC) but was increased by intraperitoneal (IP) administration of pindolol (20 mg/kg). The yawning was also potentiated after treatment with reserpine. 7-OH-DPAT and quinpirole at respective high doses of 0.25 mg/kg (SC) and 0.5 mg/kg (SC) evoked slight stereotypy such as sniffing and licking, and this effect was enhanced by a selective dopamine D1 receptor agonist, SK&F 38393 (1-phenyl-2,3,4,5,-tetrahydro-(1H)-3-benzazepine-7,8-diol). 7-OH-DPAT (0.5 mg/kg, SC) and quinpirole (0.5 mg/kg, SC) decreased, but SK&F 38393 (10 mg/kg, SC) increased body temperature. However, the hyperthermia induced by SK&F 38393 was interestingly enhanced by 7-OH-DPAT and quinpirole.(ABSTRACT TRUNCATED AT 250 WORDS)

Koyuncuoglu, H. (1995). "The combination of tizanidine markedly improves the treatment with dextromethorphan of heroin addicted outpatients." Int J Clin Pharmacol Ther 33(1): 13-9.

According to the hypothesis implying that the main mechanism underlying opiate addiction is the blockade by opiates of NMDA receptor functions and subsequent upregulation and supersensitivity of the receptors, noncompetitive NMDA receptor blocker dextromethorphan (DM) has been successfully used in the heroin addict treatment. As the stimulation of NMDA receptors modulates the release of neurotransmitters and hormones such as NE, D, ACh, GH, LH, LSH, ACTH etc., all of which have been found responsible for the manifestation of abstinence syndrome signs including craving and neuronal death by excessive stimulation of NMDA receptors, the incomplete blockade of the NMDA receptors minimizes the intensity of the abstinence syndrome and provides the downregulation of the receptors. In the present study, tizanidine (TIZ), which inhibits the release of endogenous excitatory aminoacids by the agonistic activity on alpha 2-adrenoreceptors, was combined with DM to obtain further benefits. Forty-four male and three female heroin addicts were the subjects of the study. Their daily mean heroin intake was about 2.28 g street heroin. The main duration of heroin use was approximately 3.4 years. Two to three hours after abrupt withdrawal, the outpatients were given 15 mg DM every hour, 25 or 50 mg chlorpromazine (CPZ) + 4 mg TIZ every six hours and 10 mg diazepam + 10 mg hyoscine N-butyl Br + 250 mg dipyrone every six hours three hours following CPZ. The addicts were controlled twice a day. Yawning, rhinorrhea, perspiration, piloerection, restlessness, insomnia, emesis, diarrhea, craving, rejection of smoking and pupils were observed and/or questioned. Two of the 47 outpatients took heroin on the first days.(ABSTRACT TRUNCATED AT 250 WORDS)

Kostrzewa, R. M. (1995). "Dopamine receptor supersensitivity." Neurosci Biobehav Rev 19(1): 1-17.

Dopamine (DA) receptor supersensitivity refers to the phenomenon of an enhanced physiological, behavioral or biochemical response to a DA agonist. Literature related to ontogenetic aspects of this process was reviewed. Neonatal 6-hydroxydopamine (6-OHDA) destruction of rat brain DA neurons produces overt sensitization to D1 agonist-induced oral activity, overt sensitization of some D2 agonist-induced stereotyped behaviors and latent sensitization of D1 agonist-induced locomotor and some stereotyped behaviors. This last process is unmasked by repeated treatments with D1 (homologous "priming") or D2 (heterologous "priming") agonists. A serotonin (5-HT) neurotoxin (5,7-dihydroxytryptamine) and 5-HT2C receptor antagonist (mianserin) attenuate some enhanced behavioral effects of D1 agonists, indicating that 5-HT neurochemical systems influence D1 receptor sensitization. Unlike the relative absence of change in brain D1 receptor number, DA D2 receptor proliferation accompanies D2 sensitization in neonatal 6-OHDA-lesioned rats. Robust D2 receptor supersensitization can also be induced in intact rats by repeated treatments in ontogeny with the D2 agonist quinpirole. In these rats quinpirole treatments produce vertical jumping at 3-5 wk after birth and subsequent enhanced quinpirole-induced antinociception and yawning. The latter is thought to represent D3 receptor sensitization. Except for enhanced D1 agonist-induced expression of c-fos, there are no changes in the receptor or receptor-mediated processes which account for receptor sensitization. Adaptive mechanisms by multiple "in series" neurons with different neurotransmitters may account for the phenomenon known as receptor supersensitivity.

Kolasa, K., S. Consolo, et al. (1995). "Behavioral and biochemical changes after bilateral electrolytic lesions of the red nucleus of rat." Pharmacol Biochem Behav 51(1): 29-35.

Bilateral electrolytic lesions of the red nucleus (RN) of rat decreased apomorphine-induced stereotypy, increased haloperidol-induced catalepsy, reversed apomorphine-induced hypothermy, decreased spiroperidol-induced hypomotility, and BHT-920-induced yawning and penile erection episodes. Moreover, apomorphine antagonized haloperidol-induced catalepsy in the RN-lesioned group. The lesioned animals revealed depleted levels of dopamine and its metabolites in brain areas as well as serotonin and its metabolite. The brain areas analyzed were pyriform cortex, substantia nigra, striatum, enthorinal cortex, and cerebellum. Based on these results, it is very likely that the RN has a complex role in the behavior of rats as a consequence of dopaminergic-serotoninergic changes in the central nervous system.

Khroyan, T. V., D. A. Baker, et al. (1995). "Dose-dependent effects of the D3-preferring agonist 7-OH-DPAT on motor behaviors and place conditioning." Psychopharmacology (Berl) 122(4): 351-7.

Dose-dependent effects of 7-OH-DPAT on several behaviors, including place preference, were assessed. Three 2-day conditioning trials were conducted. On 1 day, animals received an injection of one of eight doses of 7-OH-DPAT (0-5 mg/kg) and were placed into a distinct compartment for 40 min. On the other day, animals received an injection of saline and were placed into a different compartment for 40 min. Locomotion, sniffing, and yawning were measured following the first and last injection of 7-OH-DPAT. Place conditioning was assessed on the day following the last trial. 7-OH-DPAT produced a U-shaped dose-dependent change in locomotion and sniffing, and an inverted U-shaped dose-dependent change in yawning. Additionally, repeated administration of 0.1 mg/kg sensitized yawning, whereas 5 mg/kg sensitized locomotion. None of the doses of 7-OH-DPAT produced conditioned place preference, however, there was a trend for conditioned place aversion at 0.03 mg/kg. By contrast, LiCl (127 mg/kg) produced conditioned place aversion and amphetamine (1 mg/kg) produced conditioned place preference using the same conditioning parameters. A subsequent experiment in which the number of animals and conditioning trials were increased demonstrated that the 0.03 mg/kg dose of 7-OH-DPAT produced conditioned place aversion. 7-OH-DPAT has a higher affinity for D3 receptors relative to D2 receptors. Therefore, it is suggested that intermediate doses (0.01-0.1 mg/kg) that increase yawning, and decrease locomotion and sniffing, may preferentially occupy D3 receptors. Furthermore, the results suggest that these putative D3-preferring doses have weak aversive effects.

Hipolide, D. C. and S. Tufik (1995). "Paradoxical sleep deprivation in female rats alters drug-induced behaviors." Physiol Behav 57(6): 1139-43.

Paradoxical sleep deprivation (PSD) induces changes in behaviors induced by dopaminergic and cholinergic agonists, including increased aggressive behavior and stereotypy, decreased number of yawns, and shedding of bloody tears in male rats. In female rats, however, very little is known about the relationship between PSD and the effect of these drugs. The present study sought to examine this issue. As in males, PSD in females resulted in increased apomorphine-induced stereotypy, decreased pilocarpine-induced chromodacryorrhea, and hyperthermia. Unlike males, however, no apomorphine-induced aggressiveness or apomorphine- and pilocarpine-induced yawning were observed in PSD females. These findings suggest that female sexual hormones may affect the expression of some behaviors and not the neurotransmission as a whole, because drug-induced behaviors in PSD females were partly similar to those observed in PSD males.

Hiltunen, A. J., P. Lafolie, et al. (1995). "Subjective and objective symptoms in relation to plasma methadone concentration in methadone patients." Psychopharmacology (Berl) 118(2): 122-6.

Two rating scales, which were originally developed for measurements of objective and subjective signs of opiate withdrawal, were used to evaluate potential estimates (correlates) of methadone effects in relation to plasma methadone concentrations. Patients participating in our regular methadone maintenance treatment project were studied during 24 h after the intake of the daily methadone dose. Methadone concentrations in plasma were compared to the subjective (estimated by the patients) and objective (estimated by the investigator) signs of the drug effects before, and 2.5, 5, 9 and 24 h after intake of methadone. Some new items possibly related to rising methadone concentrations were added to the subjective scale. Results indicated that, for subjective ratings, the majority of the items investigated corresponded well with the plasma methadone concentrations. The most significant associations were found for the following items: low psychomotor speed, alertness, running nose, yawning and anxiety. For objective ratings, only the items rhinorrhea, piloerection and signs of anxiety were significantly associated with the methadone concentrations. These rating scales may, together with plasma methadone determinations, be of considerable value when making dose adjustments for methadone maintenance patients. Further work is, however, needed to establish concentration-effect relationships.

Hegadoren, K. M., M. T. Martin-Iverson, et al. (1995). "Comparative behavioural and neurochemical studies with a psychomotor stimulant, an hallucinogen and 3,4-methylenedioxy analogues of amphetamine." Psychopharmacology (Berl) 118(3): 295-304.

Spontaneous behaviours were assessed in freely moving rats after treatment with equimolar doses of drugs that share a basic amphetamine structure. The drugs used included a psychomotor stimulant [(+)-amphetamine (AMPH)], an hallucinogen [para-methoxyamphetamine (PMA)] and the entactogens 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA) and 3,4-methylenedioxy-N-ethylamphetamine (MDE). A detailed analysis of the frequency and duration of 30 different behaviours and the temporal organization of the behaviours was conducted in addition to measuring motor activity with an automated device. Levels of the biogenic amines and their acid metabolites in discrete brain regions and brain drug levels were also obtained. The automated motor activity measures discriminated among entactogens, the stimulant and the hallucinogen, but failed to distinguish between the hallucinogen and vehicle. Principal components analysis and cluster analysis of the frequencies and durations of the behaviours did not improve the classification of the drugs over the automated motor activity measures. Only the cluster analysis of the transitions between individual behaviours succeeded in differentiating the drug classes from each other and from vehicle treatment. All the behavioural measures classified one entactogen (MDE) as an hallucinogen. Cortical 5-hydroxytryptamine (5-HT) measures grouped MDE with the other entactogens but did not distinguish AMPH from vehicle. However, striatal dopamine measures differentiated AMPH from vehicle treatment. Variations in the durations of behavioural effects across drugs were associated with large differences in drug levels 3 h after injection. Although the neurochemical data provided a classification system that most closely parallels human subjective effects of these drugs, both the neurochemical and the behavioural measures supported the existence of an entactogen class distinct from a psychomotor stimulant and an hallucinogen.

Gully, D., F. Jeanjean, et al. (1995). "Neuropharmacological profile of non-peptide neurotensin antagonists." Fundam Clin Pharmacol 9(6): 513-21.

Neurotensin, an endogenous peptide widely distributed throughout the brain, fulfils neurotransmitter criteria. When administered centrally, neurotensin induces various effects and modulates the activity of the mesolimbic dopamine system. It antagonizes the behavioural action of dopamine in a manner similar, but not identical, to antipsychotic drugs. Neurotensin is even considered to be an endogenous neuroleptic. In fact, microinjection of neurotensin elicits different effects depending on both the dose and the cerebral structures into which the injection is made. Our work on the development of orally-active neurotensin antagonists has led to the identification of SR 48692, the first non-peptide antagonist of the neurotensin receptor, and some analogues. This small molecule reveals a surprising neuropharmacological profile. It antagonizes turning behaviour induced in mice and rats (after striatal or ventral tegmental area administration of neurotensin, respectively), hypolocomotion induced by intracerebroventricular injection of neurotensin in rats, and reverses the inhibitory effect of neurotensin (nucleus accumbens injection) on amphetamine-induced hyperlocomotion in rats. However, SR 48692 cannot reverse either dopamine release in the nucleus accumbens evoked by neurotensin injection in ventral tegmental area, or hypothermia and analgesia induced by intracerebroventricular injection of neurotensin. As direct and indirect dopamine agonists have been reported to promote neurotensin release in the cortex, behavioural studies were performed using injection of apomorphine. In these experiments, SR 48692 inhibited only turning and yawning. It did not antagonize other apomorphine-dependent effects such as climbing, hypothermia, hypo- or hyperlocomotion, penile erection and stereotypies. All together, these data raise the question of the existence of neurotensin receptor subtypes and confirm that the nature of neurotensin and dopamine interactions depends on the brain structures considered.

Gilbert, D. B. and S. J. Cooper (1995). "7-OH-DPAT injected into the accumbens reduces locomotion and sucrose ingestion: D3 autoreceptor-mediated effects?" Pharmacol Biochem Behav 52(2): 275-80.

7-hydroxy-N,N-di-n-propyl-2-aminotetralin (7-OH-DPAT) injected bilaterally in the nucleus accumbens (NAC) resulted in profound, noncatatonic, dose-dependent (0.3-3 mg total dose) hypolocomotion but without inducing yawning. It also decreased intake of a highly preferred 3% sucrose solution (1 microgram total dose). Systemic injection of 7-OH-DPAT (0.1-3.0 mg/kg, i.p.) similarly induced hypolocomotion while failing to induce yawning. In none of these studies did rats show any signs of hyperlocomotion or any stereotyped responses normally associated with D2 or mixed D1/D2 receptor stimulation. These data suggest that hypolocomotion elicited by 7-OH-DPAT in the NAC may be mediated at the D3 receptor as distinct from the D2 dopamine receptor. We discuss the possibility that the behavioural effects we observed are mediated at D3 autoreceptors.

Gallo, L. M. and S. Palla (1995). "Activity recognition in long-term electromyograms." J Oral Rehabil 22(6): 455-62.

Long-term electromyography with portable recorders allows the study of muscle activity in the natural environment to investigate whether muscle overuse or oral habits may contribute to initiate or perpetuate a myoarthropathy of the masticatory system. At present, little is known about the behaviour of masticatory muscles over long time periods. The aim of this preliminary study was to define parameters which allow the automatic recognition of different types of oral activities from the electromyogram form. A programme with functional and parafunctional activities was performed by four volunteers (total of 333 functional and 82 parafunctional recordings). Electromyograms of the masseter and temporal muscles were recorded by means of a self-developed portable intelligent solid state recorder. Signal mean level (mw) and dynamics (dw) within a sliding window were determined. Temporal muscle recordings allowed better discrimination between function and simulated parafunction. The average of mw for clenching was 51.4 +/- 3.5% and for tooth grinding 21.2 +/- 2% of the peak electromyogram value at maximum voluntary clench. At 0.96 s sliding window duration, clenching, tooth grinding and chewing signals had maximum separation, using dw/mw as parameters (average: 0.16 +/- 0.01 for clenching, 0.39 +/- 0.01 for teeth grinding and 0.88 +/- 0.01 for chewing).

Fujikawa, M., K. Yamada, et al. (1995). "Involvement of beta-adrenoceptors in regulation of the yawning induced by neuropeptides, oxytocin and alpha-melanocyte-stimulating hormone, in rats." Pharmacol Biochem Behav 50(3): 339-43.

The present study was undertaken to investigate whether beta-adrenoceptors are involved in regulation of yawning responses to oxytocin and alpha-melanocyte-stimulating hormone (alpha-MSH) in rats. Oxytocin administered intracerebroventricularly (ICV) at doses of 50 and 100 ng/rat elicited yawning. alpha-MSH (20 micrograms/rat, ICV) elicited not only yawning but also stretching and body shaking. RS-86 (2-ethyl-8-methyl-2,8-diazaspiro-(4,5)-decan-1,3-dion hydrobromide), a putative muscarinic M1 receptor agonist, administered ICV at a lower dose of 100 micrograms/rat and subcutaneously (SC) at doses of 0.25-2.5 mg/kg also elicited yawning. The yawning responses produced by these agents were markedly increased by intraperitoneal (IP) pretreatment with a beta-adrenoceptor antagonist, pindolol (20 mg/kg), which per se did not elicit yawning. The yawning induced by oxytocin (50 ng/rat, ICV) plus pindolol, but not that by alpha-MSH (20 micrograms/rat, ICV) or RS-86 (0.5 mg/kg, SC) plus pindolol, was inhibited by [d(CH2)5,Tyr(Me)2,Orn8]-vasotocin (100 ng/rat, ICV), an oxytocin receptor antagonist. The yawning induced by oxytocin, alpha-MSH, or RS-86 administered in combination with pindolol was inhibited by scopolamine (0.5 mg/kg, SC), a mucarinic receptor antagonist, without being affected by spiperone (0.5 mg/kg, SC), a dopamine D2 receptor antagonist. The results suggest that the yawning produced by the neuropeptides oxytocin and alpha-MSH is modulated by beta-adrenoceptor activity in an inhibitory manner as that produced by muscarinic M1 receptor agonists, and that it involves cholinergic, but not dopaminergic, activation.

Ferraz, H. B., S. M. Azevedo-Silva, et al. (1995). "[Apomorphine: an alternative in the control of motor fluctuations in Parkinson's disease]." Arq Neuropsiquiatr 53(2): 245-51.

Levodopa-induced motor fluctuations (MF) is a disabling complication of Parkinson's disease (PD) and is usually refractory to conventional treatment. Apomorphine, a dopamine agonist with affinity for both D1 and D2 receptors, has been emerged as an useful alternative in the management of MF of PD. The frequency of nausea and vomiting prevented its use in the past, but the simultaneous administration of domperidone has proved to be able to control these side effects. Although apomorphine has been successfully used to control levodopa-induced MF in other countries, it has not been considered in the management of PD in Brazil. We report here our initial experience with subcutaneous injections of apomorphine combined to oral domperidone. We administered apomorphine in doses ranging from 1.5 to 3 mg in four PD patients with MF of our outpatient clinic. All the doses administered switched the "off" state to a motor response qualitatively similar to what is seen in the "on" phase induced by levodopa, including the occurrence of dyskinesia. The latency to turn "on" after apomorphine ranged from 7 to 30 minutes and the duration of the response ranged from 60 to 85 minutes. We observed yawning in all four patients, labial paresthesia in one patient and an inspecific unpleasant sensation in another patient. These side effects were not

significant in our four patients. Our data show that the use of apomorphine adds a reliable and effective strategy in the management of MF of PD patients.

Ferrari, F. and D. Giuliani (1995). "Behavioural effects of the dopamine D3 receptor agonist 7-OH-DPAT in rats." Pharmacol Res 32(1-2): 63-8.
The putative selective dopamine (DA) D3 receptor agonist, 7-OH-DPAT (25-4000 micrograms kg-1), enhanced stretching-yawning and penile erection in male rats, besides respectively increasing and decreasing sedation at low (25-200 micrograms kg-1) and high (1600 and 4000 micrograms kg-1) doses and inducing stereotypy from 800 micrograms kg-1 upwards. The DA D2 antagonist, (-) eticlopride (10 and 20 micrograms kg-1), antagonized stretching-yawning and penile erection induced by a low dose of 7-OH-DPAT (50 micrograms kg-1) but not those produced by high doses (1600 and 4000 micrograms kg-1), when stereotyped behaviour, on the other hand, was potently inhibited. Comparative experiments performed with the DA agonist SND 919 gave similar results.

Cremer, C., S. R. de Barioglio, et al. (1995). "alpha-MSH-induced behavior: changes after diazepam and baclofen administration related with cyclic AMP levels." Peptides 16(5): 821-5.
The present work was performed to evaluate the participation of the benzodiacepinic GABAA and GABAB components upon excessive grooming, locomotion, rearing, and stretching/yawning syndrome induced by the intracerebroventricularly alpha-MSH administration by using GABAA and GABAB agonists. It also aims at evaluating possible relation between changes in cAMP levels in caudate-putamen and accumbens nuclei and the behavioral responses. Injection of diazepam or baclofen reduced the total behavioral scores in a dose-related manner as well as the cAMP levels with respect to the control values (animals treated with artificial cerebrospinal fluid). When diazepam was tested in animals simultaneously injected with alpha-MSH, behavioral scores decreased with respect to those treated with the peptide alone. Cyclic AMP also decreased after combined treatment (MSH + diazepam).

Casas, M., J. Guardia, et al. (1995). "The apomorphine test in heroin addicts." Addiction 90(6): 831-5.
Chronic administration of opiates to laboratory animals induces supersensitivity of the dopamine receptors in the cerebral areas innervated by the mesotelencephalic dopamine pathways. In humans, the in vivo study of the sensitivity of the dopamine neurotransmitter system in Parkinson's patients can be done by means of the apomorphine test, which consists of measuring the number of yawns induced by the subcutaneous administration of low doses of apomorphine (0.005 mg/kg). If chronic opiate use in humans, as in experimental animals, results in supersensitivity of the dopamine systems, the apomorphine test could differentiate between heroin addicts and healthy volunteers, with the former showing greater number of yawns. In order to test this hypothesis we carried out the apomorphine test in two groups of subjects: a group of male heroin addicts attending our Addiction Treatment Centre for detoxification and the other group consisting of healthy volunteer male university students. Results showed that subcutaneous apomorphine administration induced a greater number of yawns ($p < 0.05$) in the group of heroin addicts as compared with the group of healthy volunteers, suggesting that heroin addicts present an enhanced sensitivity of the dopamine nuerotransmitter system.

Brus, R., W. Felinska, et al. (1995). "Prenatal ethanol diminishes reactivity of presumed dopamine D3 receptors in rats." Pol J Pharmacol 47 (2): 109-14.
Ethanol abuse in pregnancy is known to produce serious damage to the developing central nervous system of mammalian species. As with several other classes of nerves, the ontogenetic influence of ethanol on dopamine (DA) nerves is long-lived. To test whether reactivity of DA receptors might be altered by prenatal ethanol administration, rats were given 10% (v/v) ethanol in their drinking water, starting 10 days before mating and continuing to the end of pregnancy. Male offspring were tested at 3 months for behavioral effects known to be induced by DA agonists acting at specific subtypes of DA receptors. The oral activity dose-effect curve for SKF 38393, a DA D1 agonist, was not altered from control. However, quinpirole-induced yawning behavior, reputedly a DA D3-associated event, was markedly impaired in the male rats that had been exposed in utero to ethanol. These findings indicate that prenatal ethanol exposure may predominately produce diminished reactivity of the DA D3, but not DA D1 subtype of DA receptor.

Bourson, A., E. Borroni, et al. (1995). "Determination of the role of the 5-ht6 receptor in the rat brain: a study using antisense oligonucleotides." J Pharmacol Exp Ther 274(1): 173-80.
The purpose of the present study was to determine possible physiological functions of the 5-ht6 receptor using antisense oligonucleotides (AOs) in male rats. Repeated intracerebroventricular treatment with AOs but not with a scrambled form of the antisense sequence (SO) gave rise to a specific behavioral syndrome of yawning, stretching and chewing and caused a 30% reduction in the number of [3H]-lysergic acid diethylamide binding sites (measured in the presence of 300 nM spiperone). Neither sequence, however, had any effect on other parameters measured (e.g., locomotor activity, body weight, food intake, body temperature and nociception). The specific behavioral syndrome did not appear to be caused by modulation of dopaminergic neurotransmission since no changes in the tissue levels of either dopamine or its metabolites 3,4-dihydroxyphenylacetic acid and homovanillic acid were seen. Furthermore, haloperidol (0.03 mg/kg s.c.) did not reduce the number of yawns or stretches. An increase in cholinergic neurotransmission did appear to be involved since the behavioral syndrome was dose-dependently antagonized by atropine. The present study suggests that 5-ht6 receptors are functionally expressed in the rat brain, where one of their functions appears to be the control of cholinergic neurotransmission.

Allison, K., S. Ivanova, et al. (1995). "Behavioural response to SKF 38393 and quinpirole following chronic antidepressant treatment." Eur J Pharmacol 277(2-3): 139-44.
The effects of chronic administration of antidepressant drugs (21-22 days s.c. via osmotic mini-pumps) on the behavioural responses of male Sprague-Dawley rats to (-)-quinpirole hydrochloride (0.05 mg kg-1 s.c., 5 min) and (+/-)-SKF 38393 hydrochloride (10 mg kg-1 s.c., 5 min) were investigated. Desipramine hydrochloride (10 mg kg-1 per day), phenelzine sulphate (10 mg kg-1 per day) and clorgyline hydrochloride (1 mg kg-1 per day) attenuated the suppression of locomotor activity induced by quinpirole, a dopamine D2-like receptor agonist, while clomipramine hydrochloride (10 mg kg-1 per day) was without effect. Yawning elicited by quinpirole was absent in phenelzine- and clorgyline-treated rats, but unaffected in rats treated chronically with desipramine and clomipramine. SKF 38393, a dopamine D1-like receptor agonist, significantly increased locomotor activity and time spent grooming in control animals. There were no significant effects of antidepressants on the behavioural responses to SKF 38393.

Yamaguchi, Y. and H. Kobayashi (1994). "Effects of apomorphine, physostigmine and vasoactive intestinal peptide on penile erection and yawning in diabetic rats." Eur J Pharmacol 254(1-2): 91-6.
The present report describes for the first time the effects of systemic administration of apomorphine and of physostigmine, as well as the effects of central and systemic administration of vasoactive intestinal peptide (VIP), on penile erection and yawning in rats with streptozotocin-induced diabetes. Systemic administration of apomorphine induced both penile erection and yawning in non-diabetic rats but not in diabetic rats, while that of physostigmine induced only yawning in non-diabetic rats, and neither yawning nor penile erection in diabetic rats. Intracerebroventricular administration of VIP induced both penile erection and yawning in non-diabetic rats, but neither was induced in diabetic rats. Application of VIP as an ointment to the surface of the glans penis induced penile erection but not yawning in both non-diabetic and diabetic rats. Thus, penile erection and yawning are less easily induced in diabetic rats than in non-diabetic rats. Grooming occurred whenever penile erection was induced, but was not associated with yawning.

Van Sweden, B., L. Vanderhoven, et al. (1994). "Excessive yawning." Acta Neurol Belg 94(3): 150-1.

Stancampiano, R., M. R. Melis, et al. (1994). "Penile erection and yawning induced by 5-HT1C receptor agonists in male rats: relationship with dopaminergic and oxytocinergic transmission." Eur J Pharmacol 261(1-2): 149-55.
1-(3-Chlorophenyl)piperazine (m-CPP) (0.1-4 mg/kg s.c.) and N-(3-trifluoromethylphenyl)-piperazine (TFMPP) (0.5-4 mg/kg s.c.), 5-HT1C receptor agonists, but not 8-hydroxy-dipropylamino-tetralin (8-OH-DPAT) (0.1 and 0.2 mg/kg s.c.), a 5-HT1A receptor agonist, induced penile erection and yawning with a U-inverted dose-response curve in male rats. The maximal effect was found with 0.5 mg/kg s.c. of m-CPP and with 1 mg/kg s.c. of TFMPP. The m-CPP (0.5 mg/kg s.c.) and TFMPP (1 mg/kg s.c.) responses were prevented by mianserin (0.2 mg/kg s.c.) and by ritanserin (1 mg/kg s.c.) given 15 min before m-CPP and TFMPP. In contrast, m-CPP- or TFMPP-induced penile erection and yawning were not antagonized by haloperidol (0.1 mg/kg s.c.) or by [d(CH2)5Tyr(Me)2,Orn8]vasotocin (5 micrograms i.c.v.). Apomorphine- and oxytocin-induced penile erection, but not yawning, was also antagonized by mianserin and less effectively by ritanserin. The results suggest that 5-HT1C receptor agonist-induced penile erection and yawning are not mediated by increased dopaminergic and/or oxytocinergic transmission, and raise the possibility that a neuronal dopamine-oxytocin-5-HT link is involved in the control of penile erection and not necessarily of yawning in male rats.

Sachs, B. D., K. Akasofu, et al. (1994). "Effects of copulation on apomorphine-induced erection in rats." Pharmacol Biochem Behav 48(2): 423-8.
By testing the effects of antecedent copulation on subsequent apomorphine-induced penile erection we sought to test an implicit assumption in the research on drug-induced "spontaneous" erection--namely, that this research provides information relevant to the regulation of erection in copula. In experiment 1, male rats were observed after being injected SC with 0, 15, 30, 60, or 120 micrograms/kg apomorphine (APO); 60 micrograms/kg yielded the maximum probability of erection and yawning. In experiment 2, males were injected with 60 micrograms/kg APO after no exposure to females, after three intromissions, or after copulation to sexual satiety. There was no significant effect of three intromissions, but sexually sated males displayed no erections, the first evidence that copulation affects drug-induced erections. In experiment 3, males had one ejaculation, three intromissions, or no exposure to females immediately before injection with APO (60 micrograms/kg, SC) or ascorbic acid vehicle. APO induced both erection and yawning, but neither behavior was reliably affected by copulation in APO-treated males. Among vehicle-treated males, those having three intromissions or one ejaculation before the test had shorter erection latencies and more erections than males not exposed to females. Thus, a relatively small amount of copulation resulted in a level of erectile response similar to that of APO-treated males. Optimal doses of APO may be no more effective in promoting erection in male rats than are the natural neurochemical sequelae to copulation.

Rigon, A. R., M. Reis, et al. (1994). "Effects of carbaryl on some dopaminergic behaviors in rats." Gen Pharmacol 25(6): 1263-7.
1. The effects of acute oral administration of carbaryl (10-80 mg/kg), a carbamate insecticide, on some experimental models for detecting dopaminergic activity were examined in rats. Also, serum biochemical variables following carbaryl treatments were determined. 2. Carbaryl (20 and 40 mg/kg) significantly increased the number of apomorphine-induced yawns and at dose of 80 mg/kg it prolonged the duration time of haloperidol-induced catalepsy. Pretreatment with carbaryl failed to affect apomorphine-induced stereotypes. 3. Carbaryl significantly reduced blood cholinesterase activity and elevated blood glucose levels and SGOT and SGPT activities. 4. These results indicate that low oral doses of carbaryl can cause behavioral and toxicological effects in rats.

Poncelet, M., J. Souilhac, et al. (1994). "Effects of SR 48692, a selective non-peptide neurotensin receptor antagonist, on two dopamine-dependent behavioural responses in mice and rats." Psychopharmacology (Berl) 116(2): 237-41.
One major mechanism underlying the central action of neurotensin is an interaction with the function of dopamine (DA)-containing neurons. In addition, direct or indirect DA agonists have been reported to promote neurotensin release. We have found that SR 48692, a non-peptide neurotensin receptor antagonist (0.04-0.64 mg/kg orally), antagonizes (50-65%) yawning induced by apomorphine (0.07 mg/kg SC) or bromocriptine (2 mg/kg IP) in rats, and turning behaviour induced by intrastriatal injection of apomorphine (0.25 micrograms), (+) SKF 38393 (0.1 micrograms), bromocriptine (0.01 ng) or (+) amphetamine (10 micrograms) in mice. Other apomorphine-induced effects in mice and rats such as climbing, hypothermia, hypo- and hyper-locomotion, penile erections and stereotypies were not significantly modified by SR 48692. Taken together, these data suggest that neurotensin may play a permissive role in the expression of some but not all behavioural responses to DA receptor stimulation.

Poggioli, R., A. Benelli, et al. (1994). "Old rats are unresponsive to the behavioral effects of adrenocorticotropin." Eur J Pharmacol 271 (2-3): 253-7.
In 28 month-old male rats, the i.c.v. injection of adrenocorticotropin [ACTH-(1-24)] (4 micrograms/rat) did not induce the typical behavioral syndrome (excessive grooming, stretching, yawning, penile erections). This indicates that the behavioral effects of melanocortins are age-dependent, suggesting either an aging-linked impairment of the nervous circuitries involved or a reduction of the number (or affinity, or both) of the brain melanocortin receptors in the elderly.

Nunes Junior, G. P., S. Tufik, et al. (1994). "Decreased muscarinic receptor binding in rat brain after paradoxical sleep deprivation: an autoradiographic study." Brain Res 645(1-2): 247-52.
Previous work demonstrated that paradoxical sleep deprivation (PSD) leads to a decrease in yawning behavior elicited by cholinergic agonists, suggesting that a downregulation of cholinergic muscarinic receptors may occur after PSD. More recent work using intracerebral injections of muscarinic agonists has suggested a critical role for M2 receptors in paradoxical sleep. In this study [3H]AF-DX 384 was used to investigate the effects of PSD on M2-type cholinergic receptors throughout the brain using quantitative autoradiography. After 96 h of paradoxical sleep deprivation, [3H]AF-DX 384 binding was generally reduced throughout the brain, and significantly so in the olfactory tubercle (-20%), n. accumbens (-23%), frontal caudate-putamen (-16%), islands of Callejas (-20%), piriform cortex (-24%), lateral (-26%) and medial (-24%) septum, anteromedial (-19%), ventrolateral (-22%), and lateral geniculate (-15%) nuclei of thalamus, deep layers of the superior colliculus (-15%), entorhinal cortex (-12%) and subiculum (-23%). [3H]AF-DX 384 binding was reduced in pontine structures, but not to a higher degree than in other brain areas. The observed downregulation of M2-type muscarinic receptors after PSD may be causally related to the previously reported decrease in cholinergically induced behaviors after PSD.

Nigam, A. K., R. P. Srivastava, et al. (1994). "Naloxone-induced withdrawal in patients with buprenorphine dependence." Addiction 89(3): 317-20.
Naloxone-induced withdrawal was studied in seven patients currently dependent only on injecting buprenorphine, within 3 to 6 hours of their last dose. Withdrawal severity began to rise from 5 minutes and reached a peak at 60 minutes after 1.2 mg naloxone given intravenously. The mean withdrawal severity score was significantly higher at 30, 60 and 90 minutes compared to the baseline. The most frequent withdrawal signs and symptoms were mydriasis, systolic hypertension, tachypnoea, muscle pains, yawning, anxiety, restlessness and craving.

Melis, M. R., A. Mauri, et al. (1994). "Apomorphine-and oxytocin-induced penile erection and yawning in intact and castrated male rats: effect of sexual steroids." Neuroendocrinology 59(4): 349-54.
The effect of apomorphine (80 micrograms/kg s.c.) and oxytocin (30 ng i.c.v.) on penile erection and yawning was studied in intact and castrated male rats. In castrated rats both apomorphine and oxytocin responses were abolished. In these animals, testosterone (100 microgramS/kg s.c. once a day for 3 days), restored penile erection while estradiol benzoate (10 micrograms/kg s.c. once a day for 3 days) restored yawning induced by both compounds. 5-Dihydrotestosterone (DHT) or progesterone (each at a dose of 100 micrograms/kg s.c. once a day for 3 days) were ineffective. Given together, estradiol benzoate and DHT partially restored apomorphine- and oxytocin-induced yawning and penile erection, whereas estradiol benzoate and progesterone restored only yawning. Estradiol benzoate-induced recovery of yawning was prevented by the antiestrogen tamoxifen (1 mg/kg s.c. once a day for 3 days). In intact rats, progesterone increased and estradiol benzoate decreased apomorphine- and oxytocin-induced yawning without modifying penile erection, although oxytocin-induced yawning was prevented much less by estradiol benzoate than that induced by apomorphine. Testosterone or DHT were ineffective on both responses. Estradiol benzoate inhibition of apomorphine- and oxytocin-induced yawning was prevented by tamoxifen, which per se failed to modify apomorphine and oxytocin responses, as well as by testosterone or progesterone. The present results suggest that apomorphine- and oxytocin-induced penile erection and yawning are endocrine-dependent and differentially modulated by sexual steroids, suggesting that the mechanisms controlling the two behaviors are different even though they are often associated.

Melis, M. R., R. Stancampiano, et al. (1994). "Penile erection and yawning induced by paraventricular NMDA injection in male rats are mediated by oxytocin." Pharmacol Biochem Behav 48(1): 203-7.
The effect of N-methyl-D-aspartic acid (NMDA), (+-)-alpha-amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid (AMPA), or (+-)-trans-1-amino-1,3-cyclo-pentanedicarboxylic acid (ACPD) (5-60 ng in 0.3 microliter of saline) microinjected in the paraventricular nucleus of the hypothalamus on penile erection and yawning was studied in male rats. NMDA induced both penile erection and yawning in a dose-dependent manner. AMPA and ACPD also induced penile erection but less potently than NMDA, but were ineffective in causing yawning. NMDA effect on penile erection and yawning was prevented by (+)-MK-801 (0.05-0.1 mg/kg IP, 10 min before NMDA), by the oxytocin antagonist d(CH2)5Tyr(Me)-Orn8- vasotocin (50-100 ng ICV 10 min before NMDA), but not by haloperidol (0.1-0.5 mg/kg IP 10 min before NMDA). The results suggest that NMDA induces penile erection and yawning by increasing oxytocinergic transmission by acting in the paraventricular nucleus of the hypothalamus.

Melis, M. R., R. Stancampiano, et al. (1994). "Prevention by NG-nitro-L-arginine methyl ester of apomorphine- and oxytocin-induced penile erection and yawning: site of action in the brain." Pharmacol Biochem Behav 48(3): 799-804.
The effect of NG-nitro-L-arginine methyl ester (NAME), a potent inhibitor of nitric oxide (NO) synthase, injected into different brain areas on penile erection and yawning induced by apomorphine or oxytocin was studied in male rats. The compound was found to be able to prevent the above behavioral responses dose dependently when injected into the paraventricular nucleus of the hypothalamus (PVN), but not in the caudate nucleus, medial septum, preoptic area, and the CA1 field of the hippocampus. When injected in the PVN, 5 micrograms of NAME induced a 30% reduction of apomorphine and oxytocin responses, while 20 micrograms induced an almost complete reduction. The effect of NAME seems to be related to the inhibition of guanylate cyclase secondary to the prevention of NO formation, because a dose-dependent reduction of apomorphine and oxytocin responses was obtained also with the inhibitor of guanylate cyclase methylene blue injected intracerebroventricularly (100-400 micrograms ICV), but not into the PVN. The results provide further support for a neurotransmitter role of central NO in the control of penile erection and yawning.

Melis, M. R., R. Stancampiano, et al. (1994). "Nitric oxide synthase inhibitors prevent N-methyl-D-aspartic acid-induced penile erection and yawning in male rats." Neurosci Lett 179(1-2): 9-12.
The effect of NG-nitro-L-arginine methylester (NAME) and N-mono-methyl-L-arginine (NMMA), inhibitors of nitric oxide (NO) synthase on penile erection and yawning induced by N-methyl-D-aspartic acid (NMDA) injected in the paraventricular nucleus of the hypothalamus (PVN) was studied in male rats. NAME (75-150 micrograms) and NMMA (250-500 micrograms), but not N-monomethyl-D-arginine (D-NMMA)(250-500 micrograms) prevented both responses in a dose-dependent manner when given intracerebroventricularly (i.c.v.) 15 min before NMDA (50 ng). NMDA-induced penile erection and yawning was also prevented by the guanylate cyclase inhibitor methylene blue (200-400 micrograms i.c.v.), but not by the NO scavenger methemoglobin (50-100 micrograms i.c.v.). NAME (10-20 micrograms), but not Methylene blue or methemoglobin (10-20 micrograms), prevented NMDA-induced responses also when injected in the PVN 15 min before NMDA. The present results suggest that NMDA-induced penile erection and yawning is mediated by an increased NO synthesis in the PVN.

Maier, S. E., C. J. Hardy, et al. (1994). "Brain and cerebrospinal fluid motion: real-time quantification with M-mode MR imaging." Radiology 193(2): 477-83.
PURPOSE: To assess motion of brain parenchyma and cerebrospinal fluid (CSF) with magnetic resonance (MR) phase imaging in real time. MATERIALS AND METHODS: Repetitive excitation of a cylinder with two-dimensional selective excitation followed by one-dimensional imaging along the cylinder axis yielded profiles analogous to those of M-mode echography. Bipolar gradients provided velocity sensitivity in an arbitrary spatial direction. RESULTS: Brain and CSF of healthy volunteers exhibited periodic motion in the frequency range of normal heart rate. Both brain hemispheres showed periodic squeezing of the ventricles, with peak velocities up to 1 mm/sec followed by a slower recoil. Superimposed on the regular displacement of the brain stem was a slow, respiratory-related periodic shift of the neutral position. During the Valsalva maneuver, the brain stem showed initial caudal and subsequent cranial displacement of 2-3 mm. Coughing produced a short swing of CSF in the cephalic direction. CONCLUSION: Real-time MR phase imaging allows observation of non-periodic events in brain and CSF motion.

Lang, A., A. Soosaar, et al. (1994). "Pharmacological comparison of antipsychotic drugs and sigma-antagonists in rodents." Pharmacol Toxicol 75(3-4): 222-7.

We compared antipsychotic drugs (haloperidol, chlorpromazine and clozapine) and sigma antagonists (remoxipride, cinuperone, alpha-(4-fluorophenyl)-4-(-fluoro-2-pyrimidinyl)-1-piperazine butanol (BMY 14802) and rimcazole) in the radio-ligand binding and behavioural experiments in rodents. A good correlation was established between the affinity of compounds at dopamine2-receptors in the striatum and their ability to block apomorphine-, amphetamine- and quipazine-induced behavioural effects in rodents. By contrast, no correlation was found between the behavioural effects of these drugs and their affinity at dopamine1-5-HT2- and sigma receptors. The rank order of potency among the studied antipsychotic drugs in the behavioural tests and at dopamine2-receptors was following: haloperidol >> chlorpromazine > or = clozapine. The effectiveness of chlorpromazine and clozapine was nearly similar against apomorphine-induced aggressiveness and yawning, whereas at 5-HT2-receptors clozapine was more active than chlorpromazine. The weak activity of sigma antagonists at dopamine2 receptors could be a possible reason why these compounds were less effective in the behavioural studies compared to antipsychotic drugs. However, the antagonism of remoxipride against apomorphine-induced stereotypy and aggressiveness is not related to its activity at sigma receptors, because the other sigma antagonists did not block these effects of apomorphine. It is probable that remoxipride exerts its action through blocking of dopamine2 receptors. In conclusion, the present study revealed only weak activity of sigma antagonists in the behavioural models widely used to study the antipsychotic drugs. Therefore, the antipsychotic activity of sigma antagonists is doubtful.

Juszkiewicz, M., A. Chodkowska, et al. (1994). "The influence of antineoplaston A5 on the central dopaminergic structures." Drugs Exp Clin Res 20(4): 161-7.

Antineoplastons are naturally occurring cytodifferentiating agents. Chemically, antineoplastons are medium and small sized peptides, amino acid derivatives and organic acids which exist in blood, tissues and urine. In clinical trials in advanced cancer, in addition to the anticancer activity it was observed that patients suffering from both cancer and Parkinson's disease exhibited marked improvement in parkinsonian symtomatology when treated with antineoplaston A5. The present study was designed to analyse the influence of A5 on central dopaminergic structures. Mice and rats were given A5 intraperitoneally at three different dosage levels. Experiments conducted included spontaneous locomotor activity, amphetamine-induced yawning and erections, catalepsy, the effect on the level and utilization of noradrenaline and dopamine in the brain and the influence of prolonged and chronic treatment on the haloperidol-induced catalepsy. It has been demonstrated that A5 stimulates the central dopaminergic receptors. It diminishes the cataleptic response to haloperidol and enhances the incidence of apomorphine-induced yawning. Biochemical studies demonstrated increased concentration of dopamine and noradrenaline in the brain and diminished utilization of both catecholamines.

Jaw, S. P., M. Makimura, et al. (1994). "Involvement of kappa-opioid receptors in opioid dependence/withdrawal: studies using butorphanol." Eur J Pharmacol 257(1-2): 153-60.

The dependence liability of a class of opioid agonist/antagonist analgesics, e.g. pentazocine, butorphanol, and buprenorphine, is widely recognized. However, the relative involvement of mu-, delta-, and kappa-opioid receptors mediating physical dependence on these compounds is not completely known. In the present study, butorphanol dependence was produced by continuous intracerebroventricular (i.c.v.) infusion of butorphanol (26 nmol/h) for 3 days in male Sprague-Dawley rats. Nor-binaltorphimine, a long-acting kappa-opioid receptor antagonist, and naloxone, a nonspecific antagonist, were administered i.c.v. to precipitate withdrawal in butorphanol-dependent animals, so as to investigate the involvement of central kappa-opioid receptors in opioid dependence. ED50 ratios (naloxone/nor-binaltorphimine) for eliciting withdrawal signs were: teeth-chattering (1.25), yawning (2.13), and ejaculation (0.72). Our data indicate that nor-binaltorphimine precipitated withdrawal behaviors similar to those precipitated by naloxone. It appears that central kappa-opioid receptors may play a major role in the development of butorphanol dependence in rats.

Issa, F. G., S. Porostocky, et al. (1994). "Effect of sleep and sighing on upper airway resistance in mongrel dogs." J Appl Physiol 77(2): 856-61.

We investigated the effect of sleep and sighing on supratracheal resistance in unrestrained mongrel dogs breathing through the nose by comparing within-breath changes in upper airway pressure-flow relationship in control, sigh, and five postsigh breaths recorded during wakefulness and during non-rapid-eye-movement and rapid-eye-movement sleep. A sigh breath was characterized by a high tidal volume and was typically followed by an apnea of a variable duration. Sleep had little or no effect on supratracheal resistance, measured at peak flow rates, during quiet breathing (awake 7.3 +/- 0.4, non-rapid eye movement 8.3 +/- 0.4, and rapid eye movement 6.8 +/- 0.4 cmH2O.l-1.s). The resistance was identical in the early part of inspiration in control and sigh breaths but increased during the augmented phase of sigh breaths. Resistance at peak inspiratory flow was higher in sigh breaths than in control breaths in all sleep states. The flow-pressure profile of postsigh breaths was identical to that of control breaths in all sleep states. We conclude that upper airway resistance is essentially unaffected by sleep state in the mongrel dog and that sighing increases upper airway resistance regardless of sleep state.

Heaton, J. P. and S. J. Varrin (1994). "Effects of castration and exogenous testosterone supplementation in an animal model of penile erection." J Urol 151(3): 797-800.

The dependence of erectile behavior on androgen functioning is well established. Castration produces loss of both libido and potency in man and animals. The present study, using an animal model for potency, demonstrates the dependence of centrally induced erectile behavior on an intact androgen milieu. Castrated rats failed to produce an erection in response to apomorphine, an agent shown to produce erection in nearly all normal rats. Administration of exogenous testosterone propionate in dosages exceeding 60 micrograms./kg. produced a significant increase in erectile behavior. Yawning, an essentially parallel phenomenon to the stimulation of the erectile response, was also decreased following castration and responded similarly to increasing amounts of exogenous testosterone, demonstrating the influence of androgen functioning on the central nervous system. It was concluded that testosterone is a necessary prerequisite for the maintenance of a centrally induced erectile and yawning response. In an animal model of penile erection, testosterone increases the number of erections in a dose-dependent manner in castrated rats. The dependence of the erectile response on testosterone is, at least in part, centrally mediated.

Genedani, S., M. Bernardi, et al. (1994). "Influence of ifenprodil on the ACTH-induced behavioral syndrome in rats." Eur J Pharmacol 252(1): 77-80.

Ifenprodil--an antagonist at the modulatory site of the NMDA receptor complex sensitive to polyamines--intraperitoneally injected at doses of 3 or 10 mg/kg, dose dependently prevented the behavioral syndrome induced by intracerebroventricular administration of adrenocorticotropin (ACTH)-(1-24) in adult male rats (excessive grooming, stretching, yawning, penile erections). These data further support a role of the brain ornithine decarboxylase (ODC)-polyamine system in the ACTH-induced behavioral syndrome, and may suggest an involvement of excitatory amino acids.

Ge, Y., M. Li, et al. (1994). "[Clinical assessment of physical dependence potential of dihydroetorphine hydrochloride (DHE)]." Yao Xue Xue Bao 29(4): 256-60.

This paper reports the DHE substitution clinical trial in 38 heroin addicts. The CINA (Clinical Institute Narcotic Assessment) scale was used to assess physical dependence potential. The CINA scale contains 10 opioid withdrawal signs (nausea, vomiting, gooseflesh, sweating, restlessness, tremor, larcrimation, nasal congestion, yawning, changes in heart rate and systolic blood pressure) and 3 opiate withdrawal symptoms (abdominal pain, muscle pain and feeling hot or cold). For each subject admitted to the Drug Detoxification and Treatment Center his (her) status on each of the 13 items of CINA were immediately rated. Then, naloxone 0.4 mg was injected iv to precipitate withdrawal symptoms and at 5, 10, 15 min after the naloxone injection, the CINA score of each patient was rated again. The differences among the scores of pre- and post-naloxone injection is a measurement of the degree of withdrawal symptoms. Then, a single dose of DHE was administered sublingually to each patient, all withdrawal symptoms disappeared. These results show that DHE can compete with naloxone for opioid receptors. A good dose-response relationship was found between the 100% suppressive withdrawal sign doses of DHE and the degree of withdrawal sign in heroin addicts. The physical dependence potential of DHE given to heroin addicts sublingually was probably more than that of methadone given to heroin addicts orally by making reference to the report of Dr. Peachy.

Ferrari, F. and D. Giuliani (1994). "The selective D2 dopamine receptor antagonist eticlopride counteracts the ejaculatio praecox induced by the selective D2 dopamine agonist SND 919 in the rat." Life Sci 55(14): 1155-62.

The selective D2 antagonist eticlopride, at a dose (0.01 mg/kg, s.c.) that fails to modify the normal behavior of rats, significantly reversed all the behavioral effects exerted by the selective D2 agonist SND 919 (0.1 mg/kg, i.p.), namely, the stimulation of stretching-yawning, penile erection and sedation and the inhibition of grooming. In the copulatory test, eticlopride at the same dose did not affect animal sexual behavior but potently counteracted the reduction in mount and intromission frequency and latency to ejaculation induced by SND 919 at 0.1 mg/kg, a behavioral pattern which might possibly be proposed as an animal model for human ejaculatio praecox.

Feranchak, A. P., S. R. Orenstein, et al. (1994). "Behaviors associated with onset of gastroesophageal reflux episodes in infants. Prospective study using split-screen video and pH probe." Clin Pediatr (Phila) 33(11): 654-62.

To identify behaviors associated with the onset of gastroesophageal reflux episodes in infants both systematically and prospectively, each of 10 patients (aged 2 to 32 weeks) was studied during 2 hours of intraluminal esophageal pH probe monitoring, using a split-screen audiovisual recording technique. Videotape analysis of eight infants who had scoreable reflux events revealed six discrete behaviors closely associated temporally (P < .001 to < .05) with the onset of reflux events: "discomfort" (crying or frowning), "emission" (of liquid or gas, i.e., regurgitation, drooling, or burping), yawning, stridor, stretching, and mouthing. Three behaviors (hiccuping, sneezing, and thumb-sucking) were infrequent but were significantly associated with onset of reflux events in one or two patients each. A tenth behavior, coughing or gagging, was significantly associated with onset of reflux events in two patients, but not in the rest, despite relatively frequent occurrence. Exploration of temporal relations between reflux and each behavior suggested that discomfort, emission, mouthing, and cough-gag may have caused reflux episodes, and that all 10 of the behaviors may have been caused by reflux episodes. These findings and a "quiet period" immediately preceding episodes in six of the infants suggest interesting pathophysiologic mechanisms in infants which require further evaluation.

Doherty, P. C. and P. A. Wisler (1994). "Stimulatory effects of quinelorane on yawning and penile erection in the rat." Life Sci 54(7): 507-14.
Quinelorane, a highly selective D2 dopamine agonist, was assessed for its ability to induce the penile erection/stretch-yawn syndrome. Quinelorane (0.1-100 micrograms/kg s.c.) or saline vehicle was administered to adult male Sprague-Dawley rats just prior to a 30 min. observation period. Significant dose-related increases in erections were observed in the drug treated animals at 3-100 micrograms/kg. Yawning was also increased at 3-100 micrograms/kg, with highest levels occurring at 10 micrograms/kg. Defecation was stimulated between 10 and 100 micrograms/kg. The stimulatory effects of 30 micrograms/kg of quinelorane on erection, yawning and defecation were blocked by haloperidol (0.1-0.3 mg/kg) but not by domperidone (0.1-1.0 mg/kg). No significant effects of quinelorane on seminal emission were observed. These findings indicate that in addition to its stimulatory effects on sexual activity, quinelorane also acts on D2 receptors in the central nervous system to stimulate erection in the penile erection/stretch-yawn model.

Deputte, B. L., J. Johnson, et al. (1994). "Behavioral effects of an antiandrogen in adult male rhesus macaques (Macaca mulatta)." Horm Behav 28(2): 155-64.
This study was designed to determine how to suppress behavioral effects of androgens with a pure non-steroidal antiandrogen, Hydroxyflutamide (OHF). The major dependent variable was yawning behavior of castrated adult male rhesus macaques. Injections of testosterone propionate (TP) increased yawning frequency and cessation of TP injections produced a decrease in yawning frequency. A similar decrease was observed with simultaneous injections of TP and OHF. It has been found that the dose of OHF injected subcutaneously should be 80 times that of TP to block the effects of either physiological or supraphysiological doses of TP.

Del Bene, E., M. Poggioni, et al. (1994). "Video assessment of yawning induced by sublingual apomorphine in migraine." Headache 34(9): 536-8.
A double-blind, placebo-controlled study was carried out in 14 migraineous outpatients and 8 control subjects to assess yawning response to 0.25 mg of sublingual apomorphine, a dopamine receptor agonist, by means of an audiovisual technique. Apomorphine induced a significantly higher number of yawns than placebo in both groups of subjects, but the effect was significantly greater in migraine sufferers than in controls. The result seems to confirm the previous reported hyper-responsiveness to pharmacological dopaminergic stimulation in migraine sufferers. Moreover, the audiovisual technique seems to be an appropriate tool to study yawning response in man.

Blin, O., O. Rascol, et al. (1994). "A single report of hemiplegic arm stretching related to yawning: further investigation using apomorphine administration." J Neurol Sci 126(2): 225-7.
We observed a stroke patient with an infarct of the internal capsule interrupting the pyramidal tract who stretched his hemiplegic arm during spontaneous and apomorphine-induced yawning. The putative mechanism by which yawning can induce the paradoxical motor response of the plegic arm in the patient might be the functional efficiency of a pathway projecting directly from the stimulated basal ganglia to lower motor systems in the brainstem.

Bartholomew, R. E. (1994). "Disease, disorder, or deception? Latah as habit in a Malay extended family." J Nerv Ment Dis 182(6): 331-8; discussion 339-41.
Thirty-seven cases of latah are examined within the author's Malay extended family (N = 115). Based on ethnographic data collected and a literature review, cases are readily divisible into two broad categories: habitual (N = 33) and performance (N = 4). The first form represents an infrequent, culturally conditioned habit that is occasionally used as a learned coping strategy in the form of a cathartic stress response to sudden startle with limited secondary benefits (i.e., exhibiting brief verbal obscenity with impunity). In this sense, it is identical to Western swearing. Performers are engaged in conscious, ritualized social gain through the purported exploitation of a neurophysiological potential. The latter process is essentially irrelevant, akin to sneezing or yawning. It is concluded that latah is a social construction of Western-trained universalist scientists. The concept of malingering and fraud in anthropology is critically discussed.

Banks, R. J., L. Mozley, et al. (1994). "The angiotensin converting enzyme inhibitors captopril and enalapril inhibit apomorphine-induced oral stereotypy in the rat." Neuroscience 58(4): 799-805.
The possible functional interaction between angiotensin and dopamine mechanisms in the rat was investigated by examining the effects of the angiotensin converting enzyme inhibitors captopril and enalapril on apomorphine-induced stereotypy. Apomorphine-induced behaviour was observed, and recorded using a keypad linked to a microcomputer. In agreement with previous findings, low doses of apomorphine induced a syndrome of vacuous mouth movements, penile grooming, yawning and immobility whereas at higher doses the yawning syndrome disappeared to be replaced with sniffing, licking and gnawing. Two antagonism studies were carried out. In the first the effects of captopril on apomorphine-induced behaviour were compared with those of the classical neuroleptic haloperidol, and in the second dose-response curves for the effects of captopril and enalapril on apomorphine-induced behaviour were determined. Captopril had no effect on the apomorphine-induced yawning syndrome whereas this was blocked by haloperidol. In contrast, both captopril and haloperidol blocked oral stereotypy (licking and gnawing) induced by apomorphine but had no effect on sniffing induced by the dopamine agonist. Selective blockade of apomorphine-induced oral stereotypy by angiotensin converting enzyme inhibition was confirmed in the second study in which both captopril and enalapril were observed to antagonize apomorphine-induced gnawing. The inhibition of apomorphine-induced gnawing by enalapril correlated with inhibition of brain angiotensin converting enzyme, but not lung angiotensin converting enzyme, by the drug as assessed by ex vivo penetration studies. These data suggest that angiotensin converting enzyme inhibition modulates the expression of apomorphine-induced oral stereotypy, a response that is thought to be mediated by postsynaptic dopamine receptors.(ABSTRACT TRUNCATED AT 250 WORDS)

Aloe, F. (1994). "Yawning." Arq Neuropsiquiatr 52(2): 273-6.
The ubiquitousness of normal yawning and the existence of abnormal yawning warrant an understanding of this reflex. Its mechanisms and functional role are not entirely known. A review of the literature reveals that yawning is a brain stem arousal reflex with both peripheral and central loops subserving reversal of brain hypoxia or hypoxemia. Behaviorally, yawning is a semi-involuntary act that occurs also because of loss of interest in the surroundings and it is not necessarily associated with fatigue. Socio-environmental factors can influence the emergence of yawning. Dopaminergic, acetylcholinergic, ACTHergic and oxytocinergic systems are involved in the generation and modulation of yawning in animal experimentation.

Zharkovsky, A., J. Moisio, et al. (1993). "Role of dopamine receptors in the dual effect of naloxone on quinpirole-induced yawning in morphine pretreated rats." Naunyn Schmiedebergs Arch Pharmacol 347(5): 478-82.
The present study was undertaken to determine the state of sensitivity of dopamine D2/D3 receptors involved in the mediation of yawning behaviour at various times following acute morphine administration to rats. Morphine (3.0 mg/kg, s.c.) induced a biphasic effect on locomotor activity: an initial inhibitory phase lasting for about 30 min was after about an hour followed by a phase of locomotor activation lasting for about 60 min. Dopamine D2/D3 receptor agonist quinpirole (0.01-0.1 mg/kg, s.c.) induced yawning behaviour in rats. Morphine given at 15 or 60 min before (inhibitory phase) inhibited the yawning response to quinpirole (0.1 mg/kg) but not when given at 90 or 120 min before (stimulatory phase). Naloxone (1.0 mg/kg) given 10 min before quinpirole restored yawning inhibited by morphine pretreatment during the inhibitory phase (15-60 min after morphine). However, during the morphine-induced stimulatory phase naloxone strongly inhibited the yawning response to quinpirole. D1 receptor antagonist SCH 23390 [R-(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3- benzazepin-7-ol hemimaleate] at 0.01 mg/kg did not affect quinpirole-induced yawning or its inhibition by morphine. However, in rats which received morphine 90 min prior to testing yawning, SCH 23390 enhanced quinpirole-induced yawning behaviour as compared with morphine- or saline-pretreated animals. The data obtained in the present study indicate that morphine pretreatment initially induces a lack of responsiveness of the D2/D3 receptors mediating yawning behaviour and subsequently increases their sensitivity.(ABSTRACT TRUNCATED AT 250 WORDS)

Zharkovsky, A., A. M. Totterman, et al. (1993). "Concurrent nimodipine attenuates the withdrawal signs and the increase of cerebral dihydropyridine binding after chronic morphine treatment in rats." Naunyn Schmiedebergs Arch Pharmacol 347(5): 483-6.
The effect of chronic administration of dihydropyridine calcium channel antagonist nimodipine (1 mg/kg/day) given concurrently with morphine on the signs of morphine withdrawal and on the [3H]nitrendipine binding in the rat brain has been investigated. Chronic morphine administration in increasing daily doses from 20 mg/kg to 70 mg/kg for 24 days and consequent withdrawal for 24 h induced loss of body weight, wet dog shakes, episodes of writhing and yawning behaviour. The density of [3H]nitrendipine binding was elevated in the cortex and limbic structures but not in the striatum after chronic morphine treatment. Chronic concurrent administration of nimodipine prevented the loss of body weight and reduced the scores of wet dog shakes and writhing, but did not affect yawning behaviour at 24 h after morphine withdrawal. The concurrent nimodipine treatment also prevented the rise in the density of central dihydropyridine binding sites which occurred upon chronic morphine treatment. These results suggest that chronic nimodipine treatment attenuates the development of the withdrawal signs which occur upon the termination of chronic morphine treatment by preventing the up-regulation of the central dihydropyridine-sensitive binding sites.

Wong, V., G. C. Ho, et al. (1993). "Alternating hemiplegia syndrome: electroencephalogram, brain mapping, and brain perfusion SPECT scan study in a Chinese girl." J Child Neurol 8(3): 221-6.
A 3-year-old Chinese girl with alternating hemiplegia syndrome failed to respond to anticonvulsants, antimigrainous drugs, and calcium channel blockers. She made a complete remission with a 4-week course of steroid, and relapsed after steroid withdrawal. Electroencephalogram and brain mapping during the hemiplegic attack showed unilateral high-voltage sharp slow-wave discharges in the temporo-occipital region contralateral to the hemiplegic side and diffuse high-voltage slowing during attacks of quadriplegia or other clinical manifestation such as dullness, lethargy, or yawning. Brain perfusion single photon emission computed tomographic (SPECT) scan study during the attack showed decreased uptake in the temporoparietal region contralateral to the hemiplegic side and in the ipsilateral basal ganglia, whereas the perfusion was normal between attacks. Electroencephalogram background activity was improved while the child was in clinical remission with steroid treatment. Computed tomographic and magnetic resonance imaging scans of the brain were normal. Carotid angiogram failed to show any structural or dynamic changes of the carotid arteries. The possible mechanism underlying alternating hemiplegia

syndrome might be transient and reversible cerebral ischemia with high-voltage slow-wave discharges shown in the electroencephalogram and decreased perfusion in SPECT scan.

Van den Buuse, M. (1993). "Effects of 7-hydroxy-N,N-di-n-propylaminotetralin on behaviour and blood pressure of spontaneously hypertensive rats." Eur J Pharmacol 243(2): 169-77.
The in vivo effects of administration of the putative dopamine D3 receptor agonist 7-hydroxy-N,N-di-n-propylaminotetralin (7-OH-DPAT) were investigated in spontaneously hypertensive rats (SHR) and normotensive wistar-Kyoto controls (WKY). The i.p. injection of 7-OH-DPAT induced hyperactivity in WKY at 10 mg/kg, but only an inhibition of exploratory locomotor activity was observed in SHR at 1 mg/kg. In WKY and SHR with unilateral lesions of the nigrostriatal system, s.c. injection of 0.01-1 mg/kg of 7-OH-DPAT induced dose-dependent contralateral turning behaviour. This response was more pronounced in SHR than in WKY. The s.c. injection of 0.03, but not of 0.01 or 0.1 mg/kg, of 7-OH-DPAT induced yawning in WKY and SHR. The i.v. injection of 0.1 or 1 mg/kg of 7-OH-DPAT induced an immediate rise in blood pressure in both WKY and SHR. Pretreatment with the dopamine receptor antagonist haloperidol partially prevented this pressor response and, in addition, unmasked a late fall in blood pressure in SHR. The s.c. injection of 1 mg/kg of 7-OH-DPAT induced a decrease in body temperature, which was more pronounced in SHR than in WKY. This effect could be inhibited by pretreatment with haloperidol, but a residual hypothermia remained in SHR. These results suggest that 7-OH-DPAT induces a variety of effects in vivo, many of which may be mediated by dopamine D2 receptors or non-dopaminergic receptors. Thus, more selective dopamine D3 receptor agonists or -antagonists are needed to further explore the role of dopamine D3 receptors in vivo.(ABSTRACT TRUNCATED AT 250 WORDS)

Urba-Holmgren, R., A. Santos, et al. (1993). "Two inbred rat sublines that differ in spontaneous yawning behavior also differ in their responses to cholinergic and dopaminergic drugs." Behav Brain Res 56(2): 155-9.
This work compares the sensitivities of high-yawning (HY) and low-yawning (LY) sublines of Sprague-Dawley rats to dopaminergic and cholinergic yawning-inducing drugs. HY animals are significantly more sensitive to apomorphine and (-)3PPP than LY animals. Physostigmine is a less effective yawning-inducer in HY than in LY rats. With pilocarpine no differences were detected between both sublines in regard to its yawning-inducing activity. Since yawning behavior is subject to dopaminergic (inhibitory) and cholinergic (excitatory) influences, it is suggested that the genetic differences between these sublines affect the dopaminergic pathways that normally regulate yawning frequency.

Skorzewska, A., Y. Tesfaye, et al. (1993). "Effect of scopolamine on spontaneous yawning in men." Neuropsychobiology 27(1): 17-20.
The effect of scopolamine hydrobromide (0.4 mg s.c.) on spontaneous yawning was studied in 16 male volunteers in a double-blind study. Scopolamine (or placebo) was given 60 min before (-60 min) placebo (physiological saline s.c.) (time 0 min) and yawning monitored from -15 to +60 min by recording displacement of the lower jaw and storing the traces on diskettes. After placebo, the number of yawns was 5.3 +/- 1.4 (means +/- SE) and after scopolamine pretreatment 4.3 +/- 1.6 (p = NS). Drowsiness was assessed with the Stanford Sleepiness Scale and the Analog Sleepiness Scale at -15, 0, +20, +40, +60 min. There was no significant correlation between total sleepiness scores (area under the curve, 0 min to +60 min), peak sleepiness score or peak increment in sleepiness score and number of yawns on either scale. These data suggest that (a) spontaneous yawning in man is not mediated by a central muscarinic cholinergic link, and (b) the assumed relationship between drowsiness and yawning remains to be verified experimentally.

Pomerantz, S. M., B. C. Hepner, et al. (1993). "5-HT1A and 5-HT1C/1D receptor agonists produce reciprocal effects on male sexual behavior of rhesus monkeys." Eur J Pharmacol 243(3): 227-34.
Research has indicated that serotonin (5-HT) is involved in regulating male sexual behavior in rodent, as well as primate species. The present study was designed to further characterize 5-HT influences on male sexual behavior of rhesus monkeys. Experiment 1 examined the effects of 5-HT1A and 5-HT1C/1D receptor stimulation on penile erections and yawning behavior. Administration of the 5-HT1C/1D receptor agonist, m-chlorophenylpiperazine (m-CPP, 0.8 and 3.0 mg/kg), facilitated the occurrence of penile erection, and at doses greater than 0.2 mg/kg stimulated yawning. By contrast, the 5-HT1A receptor agonist, 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT, 0.01-0.2 mg/kg) did not significantly influence penile erections or yawning behavior. Experiment 2 evaluated the effects of m-CPP and 8-OH-DPAT on the behavior of male monkeys in the presence of a sexually receptive female monkey which the males could see, hear and smell, but not physically contact. Administration of m-CPP along with presentation of a receptive female stimulated penile erections to a greater extent than they were stimulated by either one of these manipulations alone. Administration of 8-OH-DPAT (0.1 and 0.2 mg/kg) produced a decrease in the percent of monkeys exhibiting penile erections in the presence of the female. In this experiment, yawning was affected in opposite directions, with m-CPP stimulating and 8-OH-DPAT decreasing the frequency of yawning. Experiment 3 assessed the effects of m-CPP on male copulatory behavior of rhesus monkeys. Administration of m-CPP (0.8-3.0 mg/kg) produced a dose-dependent decline in the percent of males initiating copulation and achieving ejaculation.(ABSTRACT TRUNCATED AT 250 WORDS)

Melis, M. R. and A. Argiolas (1993). "Nitric oxide synthase inhibitors prevent apomorphine- and oxytocin-induced penile erection and yawning in male rats." Brain Res Bull 32(1): 71-4.
The effect of NG-nitro-L-arginine methyl ester and NG-monomethyl-L-arginine, two inhibitors of nitric oxide synthase, on apomorphine- and oxytocin-induced penile erection and yawning, was studied in male rats after intravenous and intracerebroventricular administration. Both compounds prevented dose-dependently apomorphine and oxytocin responses, when given systemically (5-50 mg/kg) or centrally (30-500 micrograms per rat), but NG-nitro-L-arginine methyl ester was about 5 times more potent than NG-monomethyl-L-arginine. The D-isomer of NG-monomethyl-L-arginine, which does not inhibit nitric oxide synthase, was ineffective. The results suggest that central nitric oxide is involved in the expression of penile erection and yawning induced by apomorphine and oxytocin.

Kostrzewa, R. M., R. Brus, et al. (1993). "Low-dose quinpirole ontogenically sensitizes to quinpirole-induced yawning in rats." Pharmacol Biochem Behav 44(2): 487-9.
It is known that dopamine (DA) receptors can be sensitized by repeated treatments with quinpirole during postnatal development. This study was undertaken to determine whether low-dose quinpirole treatments might sensitize receptors to quinpirole-induced yawning behavior. Rats were treated with quinpirole HCl (50 micrograms/kg per day) or saline at four different periods of ontogeny: a) the 10th day of gestation to day of birth; b) 1st-11th days after birth; c) 12th-22nd days from birth; or d) 23rd-33rd days from birth. The numbers of yawns occurring in 1 h after a challenge dose of quinpirole HCl (50 micrograms/kg, IP) was determined at 6 weeks. Rats exposed prenatally to quinpirole demonstrated increased numbers of yawns following the third dose of quinpirole (2-day interval between doses). In rats exposed postnatally to quinpirole, there was a 70-300% increase in the yawning response, with the greatest response occurring in the group treated with quinpirole from birth to 11 days from birth. The findings demonstrate that quinpirole receptors are sensitized by a low dose of quinpirole, 60-fold lower than previously shown. It is suggested that sensitized receptors are of the DA D3 subclass.

Kostrzewa, R. M., J. Guo, et al. (1993). "Ontogenetic quinpirole treatment induces vertical jumping activity in rats." Eur J Pharmacol 239 (1-3): 183-7.
Repeated ontogenetic treatment with quinpirole produces enhanced quinpirole-induced yawning and antinociceptive actions in adult rats. We now report the occurrence of a bizarre jumping behavior in rats so treated. Rats were treated daily from birth with quinpirole HCl (3.0 mg/kg per day x 28 days i.p., salt form) or saline vehicle. After each daily injection, the rats were observed for at least 1 h. Starting on the 18th day after birth, quinpirole treatment was associated with the appearance of jumping behavior. On the 20th day after birth a dose-effect relationship was found for quinpirole HCl (0.10-3.0 mg/kg), with maximal jumping activity occurring between 30 and 150 min after the 3.0 mg/kg dose. On the 26th day after birth, both spiperone HCl (0.30 mg/kg i.p.) and SCH 23390 HCl (0.30 mg/kg i.p.) attenuated the quinpirole effect. At 34 days the jumping response was virtually absent. The age-related jumping behavior appears to be another manifestation of the abnormal responses mediated by supersensitized dopamine receptors in quinpirole-primed rats. Based on the ability of dopamine D1 and D2 receptor antagonists to attenuate this effect, quinpirole-induced jumping behavior may be a reflection of cooperativity of dopamine D1 and D2 receptor types.

Klein, D. F. (1993). "False suffocation alarms, spontaneous panics, and related conditions. An integrative hypothesis." Arch Gen Psychiatry 50(4): 306-17.
A carbon dioxide hypersensitivity theory of panic has been posited. We hypothesize more broadly that a physiologic misinterpretation by a suffocation monitor misfires an evolved suffocation alarm system. This produces sudden respiratory distress followed swiftly by a brief hyperventilation, panic, and the urge to flee. Carbon dioxide hypersensitivity is seen as due to the deranged suffocation alarm monitor. If other indicators of potential suffocation provoke panic this theoretical extension is supported. We broadly pursue this theory by examining Ondine's curse as the physiologic and pharmacologic converse of panic disorder, splitting panic in terms of symptomatology and challenge studies, reevaluating the role of hyperventilation, and reinterpreting the contagiousness of sighing and yawning, as well as mass hysteria. Further, the phenomena of panic during relaxation and sleep, late luteal phase dysphoric disorder, pregnancy, childbirth, pulmonary disease, separation anxiety, and treatment are used to test and illuminate the suffocation false alarm theory.

Jolicoeur, F. B., M. A. Gagne, et al. (1993). "Atypical neuroleptic-like behavioral effects of neurotensin." Brain Res Bull 32(5): 487-91.
To better characterize the neuroleptic-like properties of neurotensin, the dose-related effects of the peptide on the following behavioral phenomena were examined: a) the yawning-penile erection syndrome induced by small doses of the dopamine agonists apomorphine and N-propylnorapomorphine (NPA); b) yawning produced by the anticholinesterase physostigmine, and c) stereotyped climbing and sniffing produced by a larger dose of apomorphine. Several doses of the peptide were injected intraventricularly 30 min prior to drug administration. Results indicate that neurotensin markedly decreased yawning and penile erections produced by both apomorphine and NPA. These effects were seen with relatively small doses (0.9-3.75 micrograms). Neurotensin also potently decreased physostigmine-induced yawning with the initial inhibitory effect seen with 50 ng of the peptide. Apomorphine-induced climbing was significantly attenuated with 30.0 and 60.0 micrograms neurotensin, whereas stereotyped sniffing was unaffected, even by doses as large as 120.0 micrograms. These findings suggest that neurotensin might antagonize dopamine autoreceptors and indicate that the peptide possess central anticholinergic activity. Furthermore, these results lend support to the hypothesis that neurotensin's profile of central actions resemble that of atypical neuroleptics.

Jaw, S. P., B. Hoskins, et al. (1993). "Opioid antagonists and butorphanol dependence." Pharmacol Biochem Behav 44(3): 497-500.
Butorphanol has been known to act on mu-, delta-, and kappa-opioid receptors, mu- and possibly delta-receptors are thought to mediate morphine dependence. Relative to morphine, butorphanol has a higher affinity for mu- and delta-receptors. In the present study, beta-funaltrexamine (beta-FNA) and naltrindole (NTI) (nonequilibrium mu- and delta-antagonist, respectively) were used to precipitate withdrawal in butorphanol-dependent rats. It was found that beta-FNA (12, 24, 48, and 100 nM) did not elicit significant withdrawal behaviors, while NTI caused teeth-chattering (100 nM), wet shakes (100 nM), forepaw tremors (24 nM), yawning (48 and 100 nM), ejaculation (24 nM), and urination (100 nM). The present results indicate that delta-opioid receptors may be involved in mediating butorphanol dependence, while the involvement of mu-opioid receptors needs to be further investigated.

Jaw, S. P., M. Makimura, et al. (1993). "Effects of nor-binaltorphimine on butorphanol dependence." Eur J Pharmacol 239(1-3): 133-40.
Butorphanol has been shown to act on mu-, delta-, and kappa-opioid receptors. However, the relative involvement of different opioid receptor subtypes in butorphanol dependence is not known. In the present study, nor-binaltorphimine, a long-acting non-peptide kappa-opioid receptor antagonist, was employed to mask central kappa-opioid receptors before and during the induction of butorphanol dependence in rats, so that the involvement of kappa-opioid receptors could be elucidated. The results revealed that treatment with nor-binaltorphimine markedly blocked naloxone-precipitated withdrawal signs of escape behavior, teeth-chattering, wet shakes, ptosis, body weight loss, and hypothermia at all doses tested, and attenuated the withdrawal symptoms of forepaw tremors (24 nmol: $P < 0.001$) and diarrhea (12 nmol: $P < 0.05$; 24 nmol: $P < 0.01$). In contrast, nor-binaltorphimine had no effect on yawning, ejaculation, nor urination in butorphanol-infused rats undergoing withdrawal. Three days of butorphanol infusion significantly increased KD values (in the cortex and striatum), decreased Bmax (in the cortex only) of [3H]U-69,593 binding, and shifted Ki of nor-binaltorphimine against [3H]U-69,593 (4.5 nM) binding in the cortex by more than 10-fold. Treatment with nor-binaltorphimine blocked the effects of butorphanol on kappa-opioid receptors. It is therefore concluded that kappa-opioid receptors are involved in mediating escape behavior, teeth-chattering, wet shakes, forepaw tremors, ptosis, diarrhea, weight loss, and hypothermia in butorphanol-dependent rats undergoing withdrawal. Furthermore, kappa-opioid receptors become desensitized to agonists (in the cortex and striatum), down-regulated (in the cortex), and supersensitive to antagonists in butorphanol-dependent rats.

Jaw, S. P., B. Hoskins, et al. (1993). "Involvement of delta-opioid receptors in physical dependence on butorphanol." Eur J Pharmacol 240 (1): 67-72.
Butorphanol, a synthetic agonist/antagonist, has been shown to act on mu-, delta- and kappa-opioid receptors. However, the relative involvement of opioid receptor subtypes in mediating butorphanol dependence is not known. In the present study, naltrindole, a delta-selective non-peptide antagonist, was administered intracerebroventricularly (i.c.v.) to mask supraspinal delta-opioid receptors before and during the induction of butorphanol dependence. Treatment with naltrindole (0.1, 1, or 10 nmol/5 microliters per rat) significantly blocked naloxone-, a nonspecific antagonist, precipitated butorphanol withdrawal behaviors (escape behavior, teeth-chattering, wet shakes, forepaw tremors, ptosis, diarrhea, body weight loss, and hypothermia) at all doses tested, and decreased ejaculation at 0.1 nmol in butorphanol-infused rats. In contrast, naltrindole treatment had no effect on yawning, nor urination. These results indicate that central delta-opioid receptors are involved in mediating butorphanol dependence in rats.

Ikoma, Y., T. Akai, et al. (1993). "[Effects of terguride, an ergot alkaloid derivative, on the central nervous system: biochemical and behavioral studies]." Nippon Yakurigaku Zasshi 102(2): 113-29.
Effects of terguride, a 9,10-dihydrogenated derivative of lisuride, on the central nervous system were investigated in rodents in comparison with those of lisuride. In vitro binding studies in rat brains showed that terguride, similar to lisuride, had a high affinity for D2-, 5-HT1A-, 5-HT2-, alpha 1- and alpha 2-receptors. Terguride, as does lisuride, induced hypomotility and yawning at low doses in rats, suggesting its presynaptic D2-agonist action. Terguride, unlike the postsynaptic D2-agonist lisuride, induced neither hypermotility nor stereotypy in rats and guinea pigs, but suppressed the hypermotility and stereotypy induced by apomorphine. Terguride suppressed haloperidol-induced catalepsy in rats and induced contralateral rotations in unilaterally 6-OHDA-lesioned rats, as does lisuride. These effects may be due to the postsynaptic D2 partial agonist action. Terguride, unlike lisuride, neither induced the serotonin syndrome nor generalized to the discriminative stimuli of the 5-HT1A- agonist 8-OH-DPAT in rats. Terguride did not induce head twitch in mice. Terguride blocked noradrenaline-induced lethality and clonidine-induced hypothermia at high doses in mice. Repeated administration of terguride did not affect the behavioral actions in rats. Thus, the effects of terguride on the central nervous system seems to be produced by mediation of the agonist and partial agonist actions at presynaptic and postsynaptic D2- receptors, respectively.

Heaton, J. P. and S. J. Varrin (1993). "Effects of streptozotocin-induced diabetes on dopaminergic functioning in the rat: analysis of yawning behavior." Pharmacol Biochem Behav 44(3): 601-4.
Apomorphine, a dopamine receptor agonist, causes yawning in rats. It has been suggested that the analysis of yawning behavior provides an index of dopamine autoreceptor function. Dopamine turnover in the substantia nigra of diabetic rats has been shown to be decreased following administration of amphetamine or apomorphine (17,21). Yawning behavior after 4 weeks of streptozotocin (STZ)-induced diabetes in Wistar rats was significantly lowered when compared with their age-matched normal controls. Yawning behavior was not further diminished after an 8-week duration of diabetes mellitus; however, a significant recovery in yawning was seen by 20 weeks of diabetes. Yawning in rats after 20 weeks of STZ-induced diabetes mellitus is not significantly different from that seen in normal control rats. The results suggest that in STZ-induced diabetes of only 4 weeks duration a measurable change in the substrate for yawning has occurred.

Ferrari, F., F. Pelloni, et al. (1993). "Behavioural evidence that different neurochemical mechanisms underly stretching-yawning and penile erection induced in male rats by SND 919, a new selective D2 dopamine receptor agonist." Psychopharmacology (Berl) 113(2): 172-6.
The behavioural effects induced in male Wistar rats by SND 919, a new drug reputed to have selective agonistic activity at D2 dopamine (DA) receptors, were studied. The following aspects of behaviour were considered: motor activity, stretching-yawning (SY), penile erection (PE) and stereotyped behaviour (SB). Intraperitoneal injection (IP) of the drug (0.01-20 mg/kg) induced an SY syndrome in the form of a bell-shaped dose-response curve, the effect being maximal at the dose of 0.1 mg/kg and disappearing completely at 10 mg/kg. SND 919 also potently elicited PE; this latter effect, however, was not coincident with SY induction, being maximal at 1 mg/kg and persisting at 10 and 20 mg/kg. SND 919-induced SY was potently antagonized by pretreatment not only with the D2 antagonist, L-sulpiride (20 mg/kg), but also with the alpha 2 antagonist, yohimbine (1, 3 mg/kg), and the more selective alpha 2 antagonist, idazoxan (1, 2 and 5 mg/kg). While sulpiride also decreased SND 919-induced PE, idazoxan at all doses and yohimbine at 1 mg/kg did not affect this behaviour. Inhibition of motor activity was induced by the D2 agonist at low doses (0.05, 0.1 mg/kg), while at high doses (1, 10 and 20 mg/kg), it was actually replaced by a form of SB characterized by downward sniffing and licking. When, for comparison, the D2 agonist, RU 24213 (0.1-20 mg/kg IP), was tested for PE, SY, motor activity and SB, it displayed a behavioural pattern very similar to that obtained with SND 919. Idazoxan (2 mg/kg), administered before RU 24213 (10 mg/kg), significantly antagonized the drug-induced SY, but not PE.(ABSTRACT TRUNCATED AT 250 WORDS)

Ferrari, F., F. Pelloni, et al. (1993). "Behavioural profile in the chicken of CQ 32-084 and CQP 201-403, two dopamine agonists." Pharmacol Biochem Behav 45(1): 117-22.
CQ 32-084 and CQP 201-403, two ergot derivatives that previous behavioural studies in rats had suggested to be differently active on dopamine (DA) receptors, were IP injected into male chickens. Both compounds strongly modified the animals' behaviour. CQ 32-084 led to sedation, increased yawning, and decreased preening, while CQP 201-403 exerted a biphasic activity: At a low dose, it elicited sedation and yawning; at high doses, however, it induced a state of excitation manifested by diminished sedation and yawning, enhanced preening, and pecking. The sedation, increased yawning, and decreased preening induced by the two DA agonists were reversed by the D2-selective antagonist, sulpiride. The present studies indicate that, from a behavioural point of view, chickens respond similarly to rats to the DA agonists CQ 32-084 and CQP 201-403, which differ in their selectivity of action on the various DA receptor subtypes.

Ferrari, F. and D. Giuliani (1993). "Behavioural effects induced in rats and chicks by D2 dopamine agonists." Physiol Behav 54(4): 695-700.
In a first series of experiments, different selective dopamine D2 receptor agonists (B-HT 920, B-HT 958, SND 919, CQ 32-084, CQP 201-403, and lisuride) and the D1/D2 agonist apomorphine were IP injected into adult male rats. At low doses, they elicited repeated episodes of penile erection and stretching-yawning: at all doses tested, B-HT 920, B-HT 958, and CQ 32-084 also induced hypomotility, a sign that, in the case of high doses of SND 919, CQP 201-403, lisuride, and apomorphine, was replaced by stereotyped behaviour. In a second series of experiments, the same D2 agonists and the mixed D1/D2 agonist apomorphine were IP injected at the same doses into chicks. The following behavioural signs were observed: hypomotility, sleep-like state, and stereotyped pecking. The results show that: 1. there are similarities between the behavioural effects induced by the DA agonists in rats and chicks; and 2. in both species some behavioural signs elicited by the DA ergic compounds are useful pointers to their specific neurochemical activity.

Ferrari, F. and D. Giuliani (1993). "Influence of idazoxan on the dopamine D2 receptor agonist-induced behavioural effects in rats." Eur J Pharmacol 250(1): 51-7.
The behavioural effects in rats of the dopamine D2 receptor agonists, lisuride, B-HT 920 and SND 919, were variously influenced by pre-treatment with the selective alpha 2-adrenoceptor antagonist, idazoxan (2 mg/kg), depending on the nature of the effect in question and the doses of agonist employed. The influence of idazoxan on drug-induced stretching-yawning, penile erection, sedation, stereotyped behaviour, aggressiveness and mounting is described and tentatively interpreted in neurochemical terms, account being taken of the activity of respective alpha 2-adrenoceptor antagonist and dopamine receptor agonists used, at alpha 2-adrenoceptors and at different dopamine D2 receptor subtypes, pre- and postsynaptically located.

de Wied, D. (1993). "Melanotropins as neuropeptides." Ann N Y Acad Sci 680: 20-8.

Damsma, G., T. Bottema, et al. (1993). "Pharmacological aspects of R-(+)-7-OH-DPAT, a putative dopamine D3 receptor ligand." Eur J Pharmacol 249(3): R9-10.
The R-(+)-isomer of 7-hydroxy-2-(N,N-di-n-propylamino)tetralin (7-OH-DPAT) bound with a more than 200-fold higher affinity to cloned human dopamine D3 receptors (Ki = 0.57 nM) than to dopamine D2 receptors; the corresponding S-(-)-enantiomer had considerably less affinity

for both dopamine receptor subtypes, indicating that the known enantiomer selectivity of 7-OH-DPAT for the 'classical' dopamine D2 receptor subtype extends to the recently discovered dopamine D3 receptor subtype. In rats R-(+)-7-OH-DPAT dose dependently (10-1000 nmol/kg) decreased dopamine release and induced yawning, while sniffing behaviour occurred at the highest dose tested (1000 nmol/kg). The possibility that the inhibition of dopamine release and the elicitation of yawning are mediated by dopamine D3 receptors is considered.

Daly, S. A. and J. L. Waddington (1993). "Behavioural effects of the putative D-3 dopamine receptor agonist 7-OH-DPAT in relation to other "D-2-like" agonists." Neuropharmacology 32(5): 509-10.
The putative D-3 dopamine receptor agonist 7-OH-DPAT (10 micrograms/kg, s.c.) reduced spontaneous activity in rats, without inducing yawning; higher doses (0.1-10.0 mg/kg, s.c.) stimulated non-stereotyped sniffing, locomotion and chewing, which were attenuated by the selective D-1 antagonist BW 737C (5.0 mg/kg, s.c.) without release of any atypical behaviours. Low doses of 7-OH-DPAT may act on inhibitory D-3 receptors, while higher doses may act at stimulatory D-3 or other "D-2-like" receptors that participate in cooperative but not oppositional interactions with D-1 receptors.

Crowley, T. J., E. A. Williams, et al. (1993). "Buprenorphine and cocaine effects on social behavior of monkeys." Drug Alcohol Depend 31(3): 235-45.
We administered for 2 weeks intramuscular buprenorphine 0.3 mg/kg per day (and in a separate series, its vehicle) to each of 7 male, group-living Macaca fuscata (Japanese Snow Monkeys). Animals received one injection of cocaine 0.75 mg/kg and one of saline (about Days 9 and 14) in each series; after each of these doses ethologic observers recorded for 3 h the frequency of occurrence of 64 separate social, self-care, position and other behaviors. Cocaine alone changed the frequency of many behaviors. Buprenorphine alone only reduced the frequency of eating, yawning and ejaculation. The drugs had no interactive effects on behavior. In a dose reported to suppress monkeys' heroin and cocaine self-administration, buprenorphine showed remarkably few disruptions of normal group behavior. But it neither reversed nor enhanced cocaine's behavioral effects.

Conceicao, I. M. and R. Frussa-Filho (1993). "Effects of a single administration of buspirone on catalepsy, yawning and stereotypy in rats." Braz J Med Biol Res 26(1): 71-4.
In the present study, the effects of a single administration of buspirone (0.1, 0.3, 1.0, and 3.0 mg/kg sc-30 min before testing) on three dopamine-related behaviors were evaluated in 4-month old male Wistar rats (7-10 animals per group). Buspirone decreased haloperidol (2.0 mg/kg ip)-induced catalepsy in a dose-dependent manner (from 7.30 to 5.09 1n of s compared to the untreated control group). Apomorphine (0.06 mg/kg sc)-induced yawning was also dose-dependently reduced (from 26.7 to 0.9 yawns in 30 min) and so was apomorphine (1.0 mg/kg sc)-induced stereotypy (from 32.9 to 5.9, sum of scores). The present results indicate that buspirone presents unique pharmacological effects related to dopaminergic transmission not only in biochemical but also in behavioral terms.

Collins, P., C. L. Broekkamp, et al. (1993). "Electromyographical differentiation of the components of perioral movements induced by SKF 38393 and physostigmine in the rat." Psychopharmacology (Berl) 112(4): 428-36.
Facial electromyography (EMG) coupled with visual observation was used to investigate spontaneous and drug induced perioral movements in freely moving rats. Four separate perioral behaviours were identified; facial tremor, purposeless chewing, gaping and yawning. Facial tremor, yawning and gaping but not purposeless chewing produced characteristic EMG signals. Normal rats displayed a low level of purposeless chewing, occasional bursts of facial tremor but not gaping or yawning. Each burst of facial tremor was accompanied by a transient increase in purposeless chewing. Administration of the D1 agonist SKF 38393 induced a dose related increase in bursts of facial tremors and consequently an increase in the total number of purposeless chews. Gaping and yawning were not induced by SKF 38393 administration. Administration of the cholinesterase inhibitor physostigmine (0.1-0.4 mg/kg) induced a dose related increase in the total number of purposeless chews, but primarily these were not associated with facial tremor. Administration of physostigmine also increased gaping and yawning. Administration of the D1 antagonist SCH 23390 almost abolished facial tremor in normal treated rats but only partially reduced that induced by SKF 38393 and physostigmine. SCH 23390 reduced purposeless chewing in SKF 38393 treated rats but not in normal or physostigmine treated animals. Administration of the cholinergic antagonist atropine almost abolished facial tremor in normal and physostigmine treated rats, but only reduced by 46% that induced by SKF 38393. Atropine reduced purposeless chewing in normal, physostigmine and SKF 38393 treated animals. Physostigmine induced gaping and yawning were abolished by atropine administration.(ABSTRACT TRUNCATED AT 250 WORDS)

Collins, P., C. L. Broekkamp, et al. (1993). "Effect of chronic trifluoperazine administration and subsequent withdrawal on the production and persistence of perioral behaviours in two rat strains." Psychopharmacology (Berl) 112(4): 437-44.
The effect of chronic administration of trifluoperazine on the perioral movement profile of Wistar and Sprague-Dawley rats was examined. Perioral movements were characterised by visual observations, coupled with electromyographic recording from the masseter muscle. In drug-naive animals from both strains the spectrum of perioral behaviours was essentially identical, primarily consisting of purposeless chewing, accompanied by occasional bursts of facial tremor and teeth chattering, with occasional yawning. Each burst of facial tremor was accompanied by a transient increase in the rate of purposeless chewing. Wistar rats exhibited a higher level of spontaneous purposeless chewing compared to Sprague-Dawley rats. In both strains, chronic administration of trifluoperazine (5 mg/kg per day, PO) for 5 months induced an increase in perioral behaviour, which primarily consisted of enhanced purposeless chewing. In Wistar rats the drug-induced increase in purposeless chewing was accompanied by an increase in the incidence of yawning, with no change in the incidence of either facial tremor or teeth chattering. In contrast, Sprague-Dawley rats displayed a drug-induced increase in purposeless chewing, accompanied by an increase in the incidence of facial tremor and teeth chattering, but not yawning. In Wistar rats withdrawal of trifluoperazine diminished but did not reverse the drug-induced increase in purposeless chewing. Drug withdrawal also precipitated a transient increase in the incidence of facial tremor and teeth chattering, but had no effect on yawning. In Wistar rats, the level of purposeless chewing and the incidence of yawning remained elevated above control levels for at least 13 weeks after drug withdrawal.(ABSTRACT TRUNCATED AT 250 WORDS)

Boone, D. R. and S. C. McFarlane (1993). "A critical view of the yawn-sigh as a voice therapy technique." J Voice 7(1): 75-80.
The purpose of this study was to take a critical look at a voice therapy technique known as the yawn-sigh. The voiced sigh as an approach in voice therapy has had increased use in recent years, particularly with problems of vocal hyperfunction. In this study, the physiology of the yawn-sigh was studied with video nasoendoscopy in eight normal subjects; their taped voices were also studied acoustically for possible fundamental frequency and format changes in producing selected vowels under normal and sigh conditions. Although each subject was given a model by the examiner of a yawn-sigh, one of the eight subjects could not produce a true yawn-sigh. Endoscopic findings for seven of the eight subjects performing the yawn-sigh demonstrated retracted elevation of the tongue, a lower positioning of the larynx, and a widened pharynx. Acoustic analyses for the seven subjects producing the sigh found a marked lowering of the second and third formants. Implications for using the yawn-sigh in voice therapy are given, such as using a modified "silent" yawn-sigh, as an easy method for producing greater vocal tract relaxation.

Berzin, F. and C. R. Fortinguerra (1993). "EMG study of the anterior, superior and posterior auricular muscles in man." Anat Anz 175(2): 195-7.
Anterior, superior and posterior auricular muscles were studied electromyographically by means of wire electrodes. During ear movement the three muscles acted as a group and the movement was always directed upwards and backwards. The highest electrical activities were observed during natural smiling and yawning. Mouth opening without the drawing backwards of the comissura labiorum and the displacement of galea aponeurotica also produced electrical activity by the auricular muscles, with however, less intensity and in only 50% of the cases studied.

Barthalmus, G. T., L. K. Hardin, et al. (1993). "MAO-A and -B inhibitors selectively alter Xenopus mucus-induced behaviors of snakes." Pharmacol Biochem Behav 44(2): 321-7.
Skin mucus of the frog Xenopus laevis, contacted orally by snakes, induces dyskinetic oral movements and climbing behavior that promote escape. The mucus contains peptides and indoleamines known to produce drug-induced movement disorders in other species. We hypothesized that inhibition of monoamine oxidase-A (MAO-A) by N-methyl-N-propargyl-3-(2,4-dichlorophenoxy)-propylamine [clorgyline (CLG)] and MAO-B by R(-)-N, alpha-Dimethyl-N-2-propynyl-benzene-ethanamine [L-deprenyl (LDL)] would selectively modify mucus-induced behaviors by elevating norepinephrine and serotonin (with CLG), phenylethylamine (with LDL), or dopamine (with both drugs). In Experiment 1 (EXP1), adult snakes received mucus and/or 20 micrograms/g (IP) of both drugs. In EXP2, juveniles received mucus and/or 5, 10, and 20 micrograms CLG or LDL. CLG given alone had no effect on tongue flicking, activity, and climbing (EXP1,2). LDL alone decreased tongue flicking in EXP2 and increased climbing (EXP1,2). Given with mucus, both drugs further lowered the tongue flicking rates attenuated by mucus (EXP1,2); only LDL potentiated mucus-induced climbing. Yawning was the only mucus-induced dyskinesia attenuated (20 micrograms CLG, adults; 20 micrograms LDL, juveniles). We suggest that dopamine and/or phenylethylamine, the substrates for MAO-B, may promote mucus-induced climbing and tongue flicking but may have some protective role against mucus-induced yawning in water snakes.

Aurich, C., J. E. Aurich, et al. (1993). "Naloxone affects gastrointestinal functions and behaviour in horses." Dtsch Tierarztl Wochenschr 100(8): 314-5.
Clinical effects of the opioid antagonist naloxone were investigated in healthy horses. Naloxone caused a transient increase in the frequency of defecations, a softening of the faeces and alterations in the intensity of abdominal borborygmi. Total serum protein concentrations decreased. Behavioural changes like frequent yawning and flehmen occurred, heart rate decreased and respiratory rate tended to increase but no clinical signs of distress or pain were observed. It can be concluded that in healthy animals naloxone had only minor side-effects and could be used to investigate the physiological functions of endogenous opioids in horses.

Zarrindast, M. R. and A. Jamshidzadeh (1992). "Inhibitory effect of morphine on yawning induced by cholinoceptor and dopamine D2 receptor activation in rats." Br J Pharmacol 105(3): 675-8.
1. Bromocriptine (2, 4 and 8 mg kg-1, i.p.), physostigmine (0.05, 0.1 and 0.2 mg kg-1, i.p.) and pilocarpine (1, 3 and 5 mg kg-1,

i.p.) induced dose-dependent yawning in rats. 2. These responses were reduced in a dose-dependent manner by pretreatment with morphine. 3. The inhibitory effect of morphine was reversed by naloxone. 4. Naloxone alone induced slight but significant yawning. 5. The present results suggest that morphine inhibits yawning in rats at an opiate receptor downstream from the sites at which cholinoceptor and dopamine D2 activation induce yawning. The anatomical location of these sites remains to be established.

Varrin, S. and J. P. Heaton (1992). "Age-related changes in apomorphine-induced erections." Neurobiol Aging 13(1): 175-7.
Advancing age produces a noticeable and well-documented decline in erectile function in humans. The effects of aging on the ability of apomorphine to stimulate erection and yawning behavior in rats was studied in our bioassay for potency. At the age of seven months, rats failed to respond to the same dose of apomorphine which, just one month earlier, produced erections. Erectile function was then tested in thirty-two seven-month-old rats naive to apomorphine injections, and these rats also failed to respond. Experimentally naive rats of six months of age were then tested and apomorphine produced reliable erections. It is felt that an alteration in dopamine autoreceptor function may be occurring in the central nervous system of rats at approximately seven months of age rendering them incapable of responding to apomorphine with penile erections.

Ushijima, I., Y. Mizuki, et al. (1992). "Behavioral effects of dilazep on cholinergic, dopaminergic, and purinergic systems in the rat." Pharmacol Biochem Behav 43(3): 673-6.
This study examined the effects of 1,4-bis[3-(3,4,5-trimethoxy benzoyloxy)-propyl] perhydro-1,4-diazepine (dilazep; Comelian) on central dopaminergic, cholinergic, and purinergic neuronal systems in rats. Intraperitoneal injections of dilazep (1-5 mg/kg) produced yawning responses, the most effective dose being 2 mg/kg. Dilazep potentiated physostigmine-induced yawning but not pilocarpine- and bromocriptine-induced yawning. Dilazep-induced yawning was not affected by low doses of haloperidol or sulpiride, but was completely inhibited by atropine, a muscarinic M1 receptor antagonist. Dilazep-induced yawning, as well as physostigmine-induced yawning, were markedly inhibited by pretreatment with SK & F 38393, a dopamine D1 receptor agonist, and were potentiated by SCH23390, a dopamine D1 receptor antagonist that alone does not elicit yawning. Caffeine, an adenosine receptor antagonist, inhibited dilazep- and physostigmine-induced yawning responses but N6-cyclohexyl adenosine (CHA) and N6-(L-phenylisopropyl, adenosine (L-PIA), adenosine A1 receptor agonists, were inactive. These results suggest that because the effects of dilazep on central cholinergic neurons are similar to those of physostigmine dilazep may potentiate indirectly the action of endogenous acetylcholine. Cholinergic neurons activated by dilazep may be modulated by postsynaptic dopamine D1 receptor activity but may not be affected by dopamine D2 receptor activity. Furthermore, the stimulatory effects of dilazep on cholinergic neuron may not be due to an inhibition of dopamine D1 receptors via purinergic (adenosine A1 receptor) stimulation by dilazep.

Urba-Holmgren, R., B. Holmgren, et al. (1992). "Age-dependent changes in serotonergic modulation of yawning in the rat." Pharmacol Biochem Behav 43(2): 483-6.
Serotonin (5-HT) effects on physostigmine (PHY)-induced yawning were studied in LY Sprague-Dawley rats by injecting Lu 10 171 (citalopram), a specific 5-HT uptake blocker, and two antagonists--methiothepine and ritanserin--which differ slightly in the selectivity of their actions on different 5-HT receptor subtypes. Infant and young rats show significant increases in PHY-induced yawning when preinjected with citalopram (5-10 mg/kg). Two-month-old animals show this effect only with 10 mg/kg. With adult animals (3-5 months old), the effect is the opposite: Yawning decreases. The facilitory effect in infant and young rats was counteracted by methiothepine but not by ritanserin, suggesting that it is mediated through 5-HT1A or 5-HT1B receptor subtypes. The inhibitory effect of citalopram in adult rats was unmodified by the two antagonists used, leaving open the possibility that it is mediated by 5-HT3 receptors.

Stancampiano, R., M. R. Melis, et al. (1992). "Apomorphine- and oxytocin-induced penile erection and yawning in male rats: effect of pertussis toxin." Brain Res Bull 28(2): 315-8.
The effect of the intracerebroventricular (ICV) administration of pertussis toxin on penile erection and yawning induced by apomorphine and oxytocin was studied in male rats. Pertussis toxin (2 micrograms ICV) prevented the above behavioral responses to apomorphine (80 micrograms/kg SC) and oxytocin (30 ng ICV) on day 3 and 4, but not on day 0 and 1 after treatment. Oxytocin and apomorphine responses were restored on day 6. Similar results were obtained by microinjecting pertussis toxin (0.5 microgram) in the paraventricular nucleus of the hypothalamus, the most sensitive brain area for the induction of penile erection and yawning by oxytocin and apomorphine. The results suggest that G proteins are involved in the expression of above responses to apomorphine and oxytocin.

Stahle, L. (1992). "Do autoreceptors mediate dopamine agonist--induced yawning and suppression of exploration? A critical review." Psychopharmacology (Berl) 106(1): 1-13.
The hypothesis that stimulation of dopamine autoreceptors is the mechanism by which dopamine agonists induce yawning and suppression of exploration is critically examined. It is shown that the relation between reduced extracellular dopamine levels, assessed by microdialysis, and behavioural effects of dopamine agonists, a dopamine synthesis inhibitor and a granule storage blocker is highly inconsistent. The time-course and duration of the behavioural effects of dopamine agonists differ from the reduction of extracellular dopamine. Amphetamine cotreatment is shown to increase dopamine levels, while yawning and suppression of exploration can still be induced. The data strongly indicate that autoreceptors are not the mediators of these behavioural effects. It is proposed that postsynaptic receptors mediate dopamine agonist induced yawning and suppression of exploration. Evidence is also presented showing that yawning and suppression of exploration are not functionally equivalent.

Simon, P., B. Guardiola, et al. (1992). "5-HT1A receptor agonists prevent in rats the yawning and penile erections induced by direct dopamine agonists." Psychopharmacology (Berl) 108(1-2): 47-50.
The new compound (+) S-20499, an amino chromane derivative (8[-4[N-(5-methoxychromane-3yl)N-propyl]aminobutyl] azaspiro[4-5] decane-7,9 dione), is a high affinity full 5-HT1A agonist. We have investigated its effects on dopaminergic transmission. (+) S-20499 displayed a 10(-8) M affinity for D2 dopamine (DA) receptors, 100 fold lower than for 5-HT1A receptors. The hypothermic effect of the drug was reversed by haloperidol in mice, suggesting that it behaves as a direct dopamine agonist. However, increasing doses of (+) S-20499 induced neither yawning nor penile erections, which constitute characteristic responses of direct DA agonists administered at low doses. In addition, (+) S-20499 prevented the apomorphine (100 micrograms/kg SC) induced yawning and penile erections. This inhibition appears to result from the stimulation of 5-HT1A receptors since it is an effect shared by both buspirone (from 5 mg/kg) and 8-OH-DPAT (from 0.10 mg/kg). In addition, when rats are treated with the 5-HT1A receptor antagonist tertatolol (2-5 mg/kg; SC), increasing doses of (+) S-20499 elicit the expected yawns and penile erections. It is concluded that the 5-HT1A agonist property opposes to that of D2 dopamine receptor stimulation with regard to yawning and penile erections.

Schroth, G. and U. Klose (1992). "Cerebrospinal fluid flow. II. Physiology of respiration-related pulsations." Neuroradiology 35(1): 10-5.
Cerebrospinal fluid (CSF) flow in the cerebral aqueduct and spinal canal was analysed using real-time magnetic resonance imaging measurement techniques. Respiration-induced rhythmic modulation of the cardiac-related oscillating CSF pulsation in the cerebral aqueduct and spinal canal was found. Deep inspiration was immediately followed by a marked increase in downward CSF flow in the cervical spinal canal, whereas a delay of about two heart beats was seen before downward flow from the third to the fourth ventricle increased. This pattern was also detected during yawning and was followed by a marked increase of blood flow in the internal jugular vein.

Schnur, P., M. Espinoza, et al. (1992). "Blocking naloxone-precipitated withdrawal in rats and hamsters." Pharmacol Biochem Behav 43(4): 1093-8.
Three experiments studied the effects of putative antagonists of opiate withdrawal in hamsters and rats. In Experiment 1, the calcium channel antagonists verapamil (20 mg/kg) and nifedipine (20 mg/kg) failed to antagonize naloxone (1 mg/kg)-precipitated withdrawal in hamsters implanted with two 75-mg morphine pellets, whereas clonidine (0.4 mg/kg), the alpha 2-adrenergic agonist, blocked most withdrawal signs. In Experiment 2, clonidine (0.4 mg/kg) and verapamil (20 mg/kg) were tested against naloxone-precipitated withdrawal in hamsters made acutely dependent by a single injection of morphine (15 mg/kg). As in Experiment 1, clonidine but not verapamil was effective. In Experiment 3, the effects of verapamil on naloxone-precipitated withdrawal were studied in morphine-pelleted rats and hamsters. In rats implanted with two morphine pellets, verapamil (20 mg/kg) reversed naloxone-precipitated withdrawal. By contrast, in hamsters implanted with either one or two morphine pellets neither of two doses of verapamil (20 and 30 mg/kg) was effective. These results are discussed in terms of species' differences in sensitivity to calcium channel blockers.

Ruthrich, H. L., G. Grecksch, et al. (1992). "Influence of modified casomorphins on yawning behavior of rats." Peptides 13(1): 69-72.
Apomorphine-induced yawning was completely suppressed in animals treated with 5 nmol [D-Pro4]casomorphin (CM) (ICV), 10 nmol [D-Phe3]CM (ICV) or 10 nmol [D-Pip4]CM (ICV). The apomorphine-induced yawning was also decreased, by des-Tyr analogs, but only by about 50%. Physostigmine (0.15 mg/kg, IP) induced yawning. The physostigmine-induced yawning was suppressed by 5 nmol [D-Pro4]CM and 10 nmol [D-Phe3]CM. Both [des-Tyr-D-Phe3]CM and [des-Tyr-D-Pip4]CM were without effect, whereas [des-Tyr-D-Pro4]CM increased significantly the physostigmine-induced yawning. The results suggest that dopaminergic transmission can be modulated by beta-casomorphin derivatives, thus resulting in a decrease in yawning. In the case of the des-tyrosine derivatives, we can assume a dopaminergic modulation, too. An increase in serotonergic activity might be supposed for [des-Tyr-D-Pro4]CM.

Qian, X. B., O. J. Andy, et al. (1992). "Cocaine-induced brainstem seizures and behavior." Integr Physiol Behav Sci 27(2): 117-29.
A variety of abnormal sensory/motor behaviors associated with electrical discharges recorded from the bilateral brainstem were induced in adult WKY rats by mechanical (electrode implants) and DC electrical current stimulations and by acute and chronic administration of cocaine. The electrode implant implicated one side or the other of the reticular system of the brainstem but subjects were not incapacitated by the stimulations. Cocaine (40 mg/kg) was injected subcutaneously for an acute experiment and subsequent 20 mg/kg doses twice daily for 3 days in a chronic study. Cocaine generated more abnormal behaviors in the brainstem perturbation group, especially the electrically perturbated subjects. The abnormal behaviors were yawning, retrocollis, hyperactivity, hypersensitivity, "beating drum" behavior, squealing, head bobbing, circling, sniffing, abnormal posturing, and facial twitching. Shifts in the power frequency spectra of

the discharge patterns were noted between quiet and pacing behavioral states. Hypersensitivity to various auditory, tactile, and visual stimulation was present and shifts in the brainstem ambient power spectral frequency occurred in response to tactile stimulation. These findings suggest that the brainstem generates and propagates pathological discharges that can be elicited by mechanical and DC electrical perturbation. Cocaine was found to activate the discharge system and thus induce abnormal behaviors that are generated at the discharge site and at distant sites to which the discharge propagates. Cognitive functions may also be involved since dopaminergic and serotonergic cellular elements at the brainstem level are also implicated.

Melis, M. R., R. Stancampiano, et al. (1992). "Prevention by morphine of apomorphine- and oxytocin-induced penile erection and yawning: site of action in the brain." Neuropsychopharmacology 6(1): 17-21.

The effect of morphine administered systemically or into the paraventricular nucleus of the hypothalamus (PVN) on penile erection and yawning induced either by oxytocin or by the dopaminergic agonist apomorphine was studied in male rats. Systemic morphine (0.5 to 5 mg/kg intraperitoneally [IP]) prevented in a dose-dependent manner penile erection and yawning induced by the intracerebroventricular injection (ICV) of oxytocin (30 ng) or by the subcutaneous (SC) administration of apomorphine (80 micrograms/kg). Morphine (0.1 to 5 micrograms), but not U-69,593 (5 micrograms), injected into the PVN 10 minutes before oxytocin or apomorphine, was found to be able to prevent penile erection and yawning induced by the unilateral PVN microinjection of oxytocin (10 ng) or apomorphine (50 ng). The morphine-induced prevention of these behavioral responses was abolished by pretreatment with naloxone (3 mg/kg IP) 15 minutes before morphine. The present results suggest that morphine prevents apomorphine- and oxytocin-induced penile erection and yawning by inhibiting the activity of oxytocinergic neurons through mu-type receptors in this hypothalamic nucleus.

Melis, M. R., R. Stancampiano, et al. (1992). "Hippocampal oxytocin mediates apomorphine-induced penile erection and yawning." Pharmacol Biochem Behav 42(1): 61-6.

Repeated episodes of penile erection and yawning can be induced in male rats either by low doses of the dopaminergic agonist apomorphine or by oxytocin given systematically or into a lateral ventricle (ICV), respectively, or after microinjection of the two substances directly in the paraventricular nucleus (PVN) of the hypothalamus. These behavioral responses are prevented in a dose-dependent manner by the ICV administration of the potent oxytocin antagonist d(CH2)5Tyr(Me)-Orn8-vasotocin. In contrast, the PVN injection of d(CH2)5Tyr(Me)-Orn8-vasotocin (1-30 ng), while effective in preventing oxytocin effect, was unable to prevent apomorphine response. On the other hand, apomorphine-, but not oxytocin-induced penile erection and yawning was prevented by electrolytic lesion of the medial septum (MS). Such a lesion decreased oxytocin content by about 45% in the hippocampus. The above results suggest that the hypothalamic-hippocampal oxytocinergic pathway mediates apomorphine-induced penile erection and yawning and that oxytocin is involved at different levels in the CNS for the control of these behavioral responses.

Melis, M. R., R. Stancampiano, et al. (1992). "Effect of excitatory amino acid receptor antagonists on apomorphine-, oxytocin- and ACTH-induced penile erection and yawning in male rats." Eur J Pharmacol 220(1): 43-8.

The effect of excitatory amino acid receptor antagonists, (5R,10S)-(+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclo-hepten-5, 10-imine hydrogen maleate ((+)-MK-801), (+/-)-3-(2-carboxy-piperazin-4-yl)-propyl-1-phosphonic acid (CPP), 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) and (+/-)-2-amino-4-phosphonobutanoic acid (AP-4), on penile erection and yawning induced by subcutaneous apomorphine (80 micrograms/kg), intracerebroventricular (i.c.v.) oxytocin (30 ng) and adrenocorticotropin (ACTH)-(1-24) (10 micrograms) was studied in male rats. Intraperitoneal (0.1-0.4 mg/kg) and i.c.v. (10-50 micrograms) (+)-MK-801 prevented dose dependently the penile erection and yawning induced by the three drugs. The (+)-MK-801 effect coincided with the appearance of head weaving, body rolling, hyperlocomotion and ataxia. Haloperidol (0.5 mg/kg i.p.) antagonized the prevention by (+)-MK-801 of oxytocin responses. Penile erection but not yawning was also prevented by high, but not low doses of CPP and CNQX, which impaired motor performance, AP-4 was ineffective at all doses tested. The above compounds were ineffective when injected into the paraventricular nucleus of the hypothalamus, the brain area where apomorphine and oxytocin act to induce penile erection and yawning. The results suggest that excitatory amino acid transmission is not involved in the expression of penile erection and yawning induced by the above compounds.

Kropf, W., J. Krieglstein, et al. (1992). "Effects of stimulation of putative dopamine autoreceptors on electroencephalographic power spectrum in comparison with effects produced by blockade of postsynaptic dopamine receptors in rats." Eur Neuropsychopharmacol 2(4): 467-74.

Alterations in cortical EEG activity in male rats produced by putative agonists at dopamine (DA) autoreceptors and by antagonists at postsynaptic DA receptors were compared in order to study, whether an impairment in dopaminergic neurotransmission via two different mechanisms might result in similar or different effects. Simultaneously to the EEG recordings, gross behaviour was observed. Putative agonists at DA autoreceptors (apomorphine 0.05 mg/kg, quinpirole 0.05 mg/kg, or talipexole 0.02 mg/kg s.c.) produced increases in the power in all of the frequency bands, except beta-2, with the most pronounced increase in the delta band. These EEG alterations were accompanied by hypokinesia, ptosis and yawning. In contrast, antagonists at DA receptors (haloperidol 0.1 mg/kg i.p., D2 blocker) or SCH 23390 (0.2 mg/kg i.p., D1 blocker) led to little increases in the delta band, but more pronounced increases in the alpha-2 band. Behavioural signs were hypokinesia, but little ptosis and yawning. The combination of both blockers produced, in addition, strong increases in the delta band and behavioural signs of ptosis and yawning. These results suggest that activation of putative dopamine autoreceptors produces EEG patterns and behavioural patterns different from those produced by blockade of either D1 or D2 postsynaptic dopamine receptors. In contrast, the effects following a stimulation of putative DA autoreceptors, which are expected to decrease the release of the agonist and its action at postsynaptic D1 and D2 receptors, were very similar to those found after a combined blockade of both types of postsynaptic dopamine receptors.

Kimura, H., K. Yamada, et al. (1992). "Role of adrenergic neuronal activity in the yawning induced by tacrine and NIK-247 in rats." Pharmacol Biochem Behav 43(4): 985-91.

The present experiments were performed to investigate the potential role of central adrenergic neurons in regulating occurrence of yawning in rats. Intraperitoneal injection of tacrine (THA) or 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta(b)-quinoline monohydrate HCl (NIK-247), cholinesterase inhibitors, induced yawning, which was markedly increased by pretreatment with the beta-adrenoceptor antagonist, pindolol. The yawning evoked by tacrine or NIK-247 given alone or in combination with pindolol was inhibited by pretreatment with scopolamine but not by mecamylamine or spiperone. Treatment with tacrine or NIK-247 increased acetylcholine content of the striatum, but this effect was not enhanced by pindolol, which per se did not affect basal acetylcholine content. Moreover, pretreatment with the central adrenaline synthesis inhibitors, (+-)-2,3-dichloro-alpha-methylbenzylamine HCl (LY-78335) and 2-cyclooctyl-2-hydroxyethylamine HCl (UK-1187A), increased tacrine-induced yawning. Subcutaneous injection of talipexole (B-HT 920), a dopamine D2 receptor agonist, evoked yawning, which was also increased by pindolol, LY-78335, and UK-1187A. These receptors antagonists and synthesis inhibitors per se did not cause yawning responses. The results suggest that the beta-adrenoceptor blockade and the inhibition of adrenaline synthesis facilitate the occurrence of yawning induced by cholinergic and dopaminergic agonists, and thus the central adrenergic neuronal systems may be implicated in the regulation of yawning responses.

Ferrari, F., F. Pelloni, et al. (1992). "Effect of the D2-autoreceptor agonist B-HT 958 on both spontaneous and ACTH-induced stretching, yawning and grooming in the rat." Life Sci 50(14): 1013-9.

The D2 autoreceptor agonist B-HT 958, intraperitoneally injected into Wistar male rats in a novel environment, significantly increased stretching and yawning (SY) while inhibiting grooming. Pretreatment with the D2 antagonist sulpiride reversed these effects, antagonizing SY and restoring grooming. Similarly, when B-HT 958 was administered to rats in their home cages, it elicited SY and abolished grooming; moreover, when administered before the i.c.v. injection of adrenocorticotropin hormone, dose-dependently enhanced SY and strongly antagonized the typical syndrome of intensified grooming induced by the peptide. The possible relationship between SY and grooming and the involvement of D2 autoreceptors are discussed.

Ferrari, F., F. Pelloni, et al. (1992). "Suppressive effect of the dopamine D2 receptor agonist B-HT 920 on rat grooming." Eur J Pharmacol 216(3): 345-50.

The effect of the D2 agonist B-HT 920 was examined on three behavioural models of induced grooming in the rat. B-HT 920 potently inhibited the grooming elicited by a novel environment, whereas it stimulated the stretching-yawning syndrome. Pretreatment with the selective dopamine D2 receptor antagonist, sulpiride, reversed the phenomenon. When B-HT 920 was administered to rats before water immersion, it similarly antagonized total grooming; wet-dog shakes, detected in these same animals, were potently inhibited. Finally, B-HT 920 displayed inhibitory activity towards adrenocorticotropin hormone-induced excessive grooming. On the basis of these effects, the role of D2 receptor subtypes in the modulation of grooming is discussed.

Ferrari, F., F. Pelloni, et al. (1992). "B-HT 920-induced effects on rat feeding behaviour." Pharmacol Res 26(3): 285-92.

Wistar rats, deprived of food for 15 h, were injected with B-HT 920 and 20 min later presented with their normal diet in their individual home cages. The parameters considered were latency to feeding and food intake which was determined 0.5, 1, 2, 3, 6 and 24 h later. B-HT 920 significantly reduced latency to feeding at 0.1, 0.5 and 1 mg/kg; food intake was increased by doses of 0.05 and 0.1 mg/kg 3 and 6 h after treatment and decreased by a dose of 1 mg/kg at 3 h. The amount of food eaten over a 24 h period by the various groups did not differ. At this time rats received a second injection of the drug at the same dosages, and preweighed food was presented again 20 min later. We confirmed that latency to feeding is lowered by B-HT 920 at 0.1, 0.5 and 1 mg/kg, doses which also induced feeding in sated rats within the first half-hour and even after 1 h in the case of the highest dose. Since penile erection and stretching and yawning, signs typically induced by all DA D2 agonists, were observed after B-HT 920 at 0.05, 0.1 and 0.5 mg/kg, discussion centres on the possible mechanisms involved in the B-HT 920-induced effects.

Dey, S. and R. H. Singh (1992). "Modification of apomorphine-induced behaviour following chronic swim exercise in rats." Neuroreport 3(6): 497-500.

Four week swim exercise schedule (45 min day-1, 6 days each week) in rats led to a significant adaptive change in functional responsiveness of dopamine receptors (auto-receptors) in the nigrostriatal and mesolimbic system that was evident from the modification of

behavioural responses elicited by a low dose of apomorphine, a direct acting dopamine receptor agonist. Thus, a remarkable increase in yawning response, development of full blown stereotypy, as well as profound attenuation of locomotory and hypothermic response was observed in exercise-trained rats as compared with the non-exercise group (control), following intraperitoneal administration of 0.3 mg kg-1 of apomorphine.

Cohen, A. J. (1992). "Fluoxetine-induced yawning and anorgasmia reversed by cyproheptadine treatment." J Clin Psychiatry 53(5): 174.

Cameron, J. L., S. M. Pomerantz, et al. (1992). "Dopaminergic stimulation of oxytocin concentrations in the plasma of male and female monkeys by apomorphine and a D2 receptor agonist." J Clin Endocrinol Metab 75(3): 855-60.
Administration of the dopamine receptor agonist apomorphine causes a dose-dependent increase in plasma oxytocin concentrations and dose-specific behavioral changes in rodents. To investigate whether dopamine receptor agonists will elicit similar neuroendocrine and behavioral effects in primates, we administered graded doses of apomorphine and the respective dopamine D1 and D2 receptor agonists, CY 208-243 and LY 163502, to monkeys and monitored plasma concentrations of oxytocin and behavior. Five female rhesus, two male rhesus, and two male cynomolgus monkeys had chronic indwelling venous catheters implanted and were maintained on standard jacket/tether/swivel systems to allow remote blood sample collection. During experiments, blood samples were collected 10 and 5 min before drug injection and at 2- to 120-min intervals after each injection. Apomorphine (50-400 micrograms/kg) and LY 163502 (10-100 micrograms/kg) elicited dose-dependent stimulations of oxytocin secretion. CY 208-243 (100-400 micrograms/kg) did not significantly affect oxytocin secretion. Low doses of apomorphine (50-100 micrograms/kg) and LY 163502 (10-25 micrograms/kg) elicited yawning, and high doses of apomorphine (200-400 micrograms/kg) and LY 163502 (50-100 micrograms/kg) elicited stereotypic behaviors. No behavioral effects of CY 208-243 (100-400 micrograms/kg) were observed. The magnitude of the oxytocin secretory responses varied among animals, but was similar in male and female monkeys. In summary, apomorphine and LY 163502 both elicited dose-related stimulation of oxytocin secretion coupled with dose-specific behavioral changes in male and female monkeys, while no effects of CY 208-243 on these parameters were observed. We conclude that dopamine receptor agonists, and in particular D2 agonists, may be useful tools for studies exploring the physiological and behavioral actions of oxytocin in primates.

Antoniou, K. and E. Kafetzopoulos (1992). "Behavioral effects of amphetamine and apomorphine after striatal lesions in the rat." Pharmacol Biochem Behav 43(3): 705-22.
It is well established that denervation of the dorsal striatum by its dopaminergic afferents attenuates the stereotyped response to d-amphetamine, which can be considered as an extreme form of motor activation. However, it is difficult to sustain the view that this structure serves primary motor control function because the role of dopamine in the striatum remains difficult to understand. In this study, we compared the effects of two dopaminergic agonists, d-amphetamine and apomorphine, after dorsal striatal lesions with ibotenic acid using a computerized scoring of the behavior. Although d-amphetamine- and apomorphine-induced locomotor activity was no different between lesioned and nonlesioned rats in photobeam activity cages, the structure of their behavioral pattern was quite different. Freezing, a usual response after d-amphetamine, was blocked by the lesion. Lesioned rats exhibited less standing than nonlesioned after d-amphetamine, apomorphine, or saline treatment. Moving was increased in lesioned rats after a low dose of d-amphetamine (0.5 mg/kg) or apomorphine (0.5 mg/kg), while d-amphetamine induced in the same rats an increase of rearing. Stereotyped behavior after both drugs at high doses was not affected by striatal lesion. These results indicate that the dorsal striatum is not involved only in the control of stereotypy, as has been suggested using 6-hydroxydopamine lesions, but also plays a major role in the mediation of behavioral activation in response to stimulant drugs.

Yamada, K. and T. Furukawa (1991). "[Behavioral effects of a new antidepressant, setiptiline]." Nippon Yakurigaku Zasshi 97(1): 31-9.
Behavioral effects of setiptiline, a new tetracyclic compound (1,2,3,4-tetrahydro-2-methyl-9H-dibenzo [3,4:6,7] cyclohepta [1,2-C] pyridine maleate), were investigated to determine its pharmacological characteristics as an antidepressant in rats and mice, as compared with amitriptyline, a tricyclic antidepressant, and promethazine, a neuroleptic possessing an antihistaminic profile. Setiptiline exerted a weak stimulatory action on ambulation, spontaneous motor-activity, observed by the open field method in rats and potentiated the stimulatory effects of methamphetamine. Setiptiline also shortened the duration of immobility in rats forced to swim and inhibited catalepsy induced by haloperidol, yawning by physostigmine, body shaking as well as head twitch by 5-hydroxytryptophan in combination with Ro4-4602 and body shaking by morphine-withdrawal in rats. On the other hand, the drug did not exhibit an antagonistic effect on the hypothermia produced by reserpine in mice. From the results, it is suggested that setiptiline seems to have antidepressive activities that are pharmacologically dissimilar to those of tricyclic antidepressants.

Xu, J. H., Y. Ikeda, et al. (1991). "Bio-feedback and the yawning breath pattern in voice therapy: a clinical trial." Auris Nasus Larynx 18 (1): 67-77.
A breathing technique, or effective breath method is important for both singers and speakers for effective vocalization, and also useful for helping people with a voice problem. Here a diaphragm support breath pattern was used in voice therapy for patients with vocal nodules, recurrent laryngeal nerve paralysis, and incomplete glottal closure. Singing teachers use a technique, called the diaphragm breath support. This is called the yawning breath pattern (YBP) in our voice clinic and is used in teaching the patients with some kinds of voice disorder. In order to correct patients' breath pattern, an equipment system was designed to check their breath patterns conveniently in voice therapy practice. A respiratory kinematic sensor which connected to a TV monitor was attached to the patients' rib cage near the diaphragm, and by bio-feedback, patients could observe and adjust their breath pattern to the desired pattern during vocalization. In each of the 10 outpatient sessions, the patients performed for 20 to 30 min, and were instructed to practice at home for 3 or more times daily. The YBP method was applied to 91 patients, 17 males and 74 females, with ages ranging from 17 to 79 years. Of the 91 patients 41 had vocal nodules, 20 had recurrent laryngeal nerve paralysis and 30 had incomplete glottal closure associated with chronic laryngitis and sulcus vocalis. Most of the patients could master the YBP technique successfully. The higher the patients' ability to master the YBP was the better the results of both voice tests and subjective evaluation. The scientific background of the YBP method and its clinical effects in voice therapy was reviewed.

Van Erp, A. M., M. R. Kruk, et al. (1991). "Grooming induced by intrahypothalamic injection of ACTH in the rat: comparison with grooming induced by intrahypothalamic electrical stimulation and i.c.v. injection of ACTH." Brain Res 538(2): 203-10.
Intracerebroventricular (i.c.v.) injection of adrenocorticotropic hormone (ACTH) elicits grooming in the rat, but the neural organization of this response is still obscure. Electrical stimulation (EHS) in an area around the hypothalamic paraventricular nucleus (PVH) also elicits grooming. This hypothalamic area contains many ACTH-immunoreactive fibres. Injection of ACTH1-24 (0.3 microgram/0.3 microliters) in the same area elicits intense grooming responses in the rat. Latency, intensity and precise patterning of the grooming response are dependent upon the exact site of injection. Comparison of grooming responses elicited by EHS, ACTH injected i.c.v. and ACTH injected in the PVH reveals that these are slightly dissimilar. This may provide clues as to the brain mechanisms involved in the organization of the different components of grooming. EHS does not elicits scratching and even reduces 'spontaneous' scratching. Also, EHS-elicited grooming is characterized by short pauses. The time-course of appearance of yawning differs between ACTH-PVH and ACTH-i.c.v. injections. Excited locomotion elicited only by ACTH-i.c.v. is apparently caused by ACTH-sensitive systems outside the PVH. The results suggest that the ACTH-containing part of the hypothalamus around the PVH is crucially involved in the organization of grooming behaviour. We believe that at this level in the brain, the subroutines of grooming, scratching and yawning are integrated into one skin maintenance behaviour.

Tesfaye, Y., A. Skorzewska, et al. (1991). "Hazard of yawning." Cmaj 145(12): 1560.

Taylor, J. R., J. D. Elsworth, et al. (1991). "Grafting of fetal substantia nigra to striatum reverses behavioral deficits induced by MPTP in primates: a comparison with other types of grafts as controls." Exp Brain Res 85(2): 335-48.
Fetal substantia nigra (SN) cells were transplanted into the caudate nucleus (CN) of four vervet monkeys (Cercopithecus aethiops sabaeus) that had been treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). MPTP treatment appears to produce a syndrome similar to that observed in patients with idiopathic Parkinson's disease. Normal and parkinsonian behaviors were quantitated by trained observers 5 days/week. Twenty-eight behaviors based on previous factor analyses were individually scored and rated. Parkinsonian signs included freezing, head and limb tremor, difficulty in eating, delayed initiation of movement, poverty of movement, tremor that stopped with intention, decreased response to threats, and lying immobile in the cage. These signs were combined to give an overall rating of parkinsonism. A summary measure of 'normal' healthy behavior was also examined, including such behaviors as yawning, scratching, self-grooming, shifting, and eating. Overall ratings of parkinsonism increased and those of healthy behavior decreased after MPTP. In the 4 monkeys grafted with fetal SN cells into the CN, behavior returned to pre-treatment levels by the time of sacrifice (2, 5, or 7.5 months after grafting). Three control subjects were transplanted with either SN cells into an inappropriate brain site (cortex) or inappropriate, non-dopaminergic, cells (cerebellar) into the CN. Subjects were also compared with three control animals that did not receive MPTP but received cryopreserved or fresh SN and other cells into the CN. Only MPTP-treated subjects that received SN cells into the CN showed evidence of a reversal of the MPTP syndrome after transplantation. In addition, grafting in animals that were not MPTP-treated did not appear to affect behavior. This paper reports the specific behavioral effects of severe MPTP toxicity that were or were not reversed after transplantation and suggests that only fetal SN cells grafted into the CN may be able to reverse behavioral deficits in MPTP-treated monkeys.

Stoessl, A. J., E. Szczutkowski, et al. (1991). "Behavioural effects of selective tachykinin agonists in midbrain dopamine regions." Brain Res 565(2): 254-62.
The effects of selective NK-1, NK-2 and NK-3 tachykinin agonists in midbrain dopamine cell containing regions were investigated in the rat. The NK-3 agonist senktide induced locomotion, rearing and sniffing following infusion into the substantia nigra pars compacta, and to a lesser extent in the ventral tegmental area. These behavioural responses were not seen following infusion of the selective NK-1 agonist [Sar9,Met (O2)11]SP or the NK-2 agonist [N1e10]NKA4-10. In contrast, grooming was induced only by the NK-1 agonist administered into the substantia nigra. Yawning, chewing mouth movements and wet dog shakes were all seen following infusion of senktide into the ventral tegmental area. These findings suggest that (i) dopamine-mediated behavioural responses seen following tachykinin administration into the

midbrain are dependent upon stimulation of NK-3 tachykinin receptors, (ii) tachykinin-induced grooming is mediated by stimulation of NK-1 receptors and (iii) some of the previously described 5-HT mediated behaviours seen following administration of NK-3 tachykinin agonists are probably generated by stimulation of 5-HT cell bodies in the ventral tegmental area.

Sherer, D. M., S. A. Smith, et al. (1991). "Fetal yawning in utero at 20 weeks gestation." J Ultrasound Med 10(2): 68.

Roeling, T. A., A. M. van Erp, et al. (1991). "Behavioural effects of NMDA injected into the hypothalamic paraventricular nucleus of the rat." Brain Res 550(2): 220-4.
Electrical stimulation of the hypothalamic paraventricular nucleus (PVH) and of the adjacent dorsal hypothalamic area (DHA) evokes grooming behaviour. Microinjections of low doses of kainic acid, an agonist of the kainate type of glutamate receptors, into the same area evokes the same behaviour. To test whether other glutamate receptors are involved, microinjections with N-methyl-D-aspartic acid (NMDA) were made into the PVH/DHA area and the behaviour was observed. From the total observation time (30 min) up to 73% was spent on grooming, accompanied by yawning. Pronounced feeding behaviour was also noticed at 3 injection sites but not until 23 min after injection. Conclusions are that neurones within the PVH/DHA area are involved in grooming behaviour, possibly via glutamatergic innervation. The interaction between grooming and feeding behaviour at the level of the PVH is discussed.

Pomerantz, S. M. (1991). "Quinelorane (LY163502), a D2 dopamine receptor agonist, acts centrally to facilitate penile erections of male rhesus monkeys." Pharmacol Biochem Behav 39(1): 123-8.
The present study examined the effects of a specific D2 dopamine receptor agonist, quinelorane (LY163502), on male sexual responding of rhesus monkeys. The effects of quinelorane were assessed by observing the behavioral responses of male rhesus monkeys to a sexually receptive female monkey that they could see, hear, and smell, but not physically contact. Quinelorane (IM) treatment produced dose-dependent effects on male sexual responding. Penile erections and masturbation were markedly facilitated following treatment with either 2.5 or 5 micrograms/kg quinelorane. Higher doses of quinelorane (10 and 25 micrograms/kg) generally did not further augment sexual responding, but rather resulted in a return in sexual responding to control vehicle levels. Quinelorane had a biphasic effect on yawning behavior of the monkeys with low doses (2.5 and 5 micrograms/kg) facilitating yawning and high doses (25 micrograms/kg) inhibiting yawning. Quinelorane in the dose-range (1-25 micrograms/kg) being evaluated did not reliably influence stereotypic behavior. In order to determine whether quinelorane acts centrally or peripherally to stimulate male sexual behavior, the ability of the peripherally active dopamine antagonist, domperidone, and the centrally active dopamine antagonist, haloperidol, to block the facilitation of sexual behavior produced by quinelorane treatment was examined. Administration of domperidone (50-200 micrograms/kg) failed to block quinelorane's effects on sexual behavior, whereas treatment with haloperidol (5-20 micrograms/kg) prevented quinelorane from stimulating male sexual responding. These experiments provide further evidence that dopaminergic mechanisms may play a role in the regulation of male sexual behavior of rhesus monkeys and, in particular, demonstrate the sexual stimulant properties of agents that provide central stimulation to D2 dopamine receptor sites.

Paulus, M. P. and M. A. Geyer (1991). "A scaling approach to find order parameters quantifying the effects of dopaminergic agents on unconditioned motor activity in rats." Prog Neuropsychopharmacol Biol Psychiatry 15(6): 903-19.
1. Three experiments were conducted in the Behavioral Pattern Monitor (BPM) to assess the effects of the D1 agonist SKF-38393, the D2 agonist quinpirole, and the interaction of the D2 antagonists haloperidol with amphetamine or cocaine on the amount, the structure, and the unpredictability of micro-events of rat exploratory behavior. 2. SKF-38393 (0.3, 1.0, 3.0, and 10.0 mg/kg) did not change the amount of motor behavior indicated by the temporal scaling exponent alpha, a descriptor of the local degree of acting, during a 60 min exposure in the BPM. However, SKF-38393 (3.0, and 10.0 mg/kg) significantly increased the spatial scaling exponent d, indicating an increased component of local circumscribed movements. 3. Quinpirole (0.03, 0.1, 0.3, and 1.0 mg/kg) produced a biphasic dose response with respect to the amount of motor behavior. Low doses (0.03, 0.1) significantly decreased the local degree of acting, whereas alpha returned to control group levels for higher doses (0.3, 1.0 mg/kg). The change in activity was accompanied by a significant increase of local movements, i.e. d was increased for the lower doses. 4. Haloperidol (15.0 micrograms/kg) reduced a slightly increased d measure for amphetamine (1.0 mg/kg) treated animals and increased a significantly reduced d for cocaine (20.0 mg/kg) treated animals, without affecting the increases of motor activity induced by both treatments. 5. It is concluded that the structure of motor activity provides an important measure of unconditioned motor behavior, which can be affected independently of the typically measured amount of motor activity.

Nouel, D. and J. Costentin (1991). "Inhibition of apomorphine-induced yawning and penile erection by neurotensin." Peptides 12(4): 755-9.
The yawns and penile erection elicited in rats by apomorphine (100 micrograms/kg SC) are dose-dependently suppressed by the enkephalinase-resistant analog of NT, [D-Trp11]NT, intracerebroventricularly (ICV) injected (10-120 ng per rat). This antagonistic effect was shared by NT (0.75-3 micrograms per rat) administered ICV. The yawns induced by pilocarpine (2 mg/kg IP) were similarly antagonized by [D-Trp11]NT (30-120 ng per rat). The enkephalinase inhibitor acetorphan (5 mg/kg IV) reduced in a naloxone (2 mg/kg, SC)-resistant manner the apomorphine-induced penile erection or yawning.

Mukai, S., C. Mukai, et al. (1991). "Ankyloglossia with deviation of the epiglottis and larynx." Ann Otol Rhinol Laryngol Suppl 153: 3-20.
We observed ankyloglossia to be usually accompanied by displacement of the epiglottis and larynx. Infants with this disease developed dyspnea and skin and hair abnormalities. In addition, they had other symptoms, such as a dark forehead, a frowning expression, a dark color around the lips, scanty eyebrows, swelling around the palpebrae, harsh respiratory sounds, hard crying, snoring, and frequent yawning. In spite of these abnormalities, they had been considered to be healthy by their pediatricians. Arterial oxygen percent saturation (SaO2) was measured while the infants were asleep, suckling, and awake. The results revealed that their SaO2 was unstable and slightly low. The symptoms and signs of this disease were very similar to those observed in victims of sudden infant death syndrome before their death. Correction of the ankyloglossia and deviation of the epiglottis and larynx resulted in great improvement of these signs as well as a stabilization and increase of SaO2.

Lynch, M. R. (1991). "Dissociation of autoreceptor activation and behavioral consequences of low-dose apomorphine treatment." Prog Neuropsychopharmacol Biol Psychiatry 15(5): 689-98.
1. Low dose dopaminergic agonist effects have been used as a behavioral screen for identifying compounds with selective autoreceptor activity. 2. However, results from several recent investigations suggest that these behaviors may not be generated from an autoreceptor substrate but rather from a subpopulation of postsynaptic dopamine receptors with a high affinity for the agonist. 3. In support of this hypothesis, the present investigation reports that both hypomotility and yawning, induced in the rat with 0.07 mg/kg apomorphine, were not paralleled by autoreceptor-induced reductions in transmitter metabolism from either mesolimbic or neostriatal dopamine regions.

Kostrzewa, R. M. and R. Brus (1991). "Is dopamine-agonist induced yawning behavior a D3 mediated event?" Life Sci 48(26): PL129.

Kostrzewa, R. M. and R. Brus (1991). "Ontogenic homologous supersensitization of quinpirole-induced yawning in rats." Pharmacol Biochem Behav 39(2): 517-9.
Yawning in male rats is a behavior that may be induced by a group of dopamine receptors when low doses of dopamine-receptor agonists are administered. To determine whether agonist treatments during postnatal development could produce a long-lived supersensitization of these dopamine receptors, rats were treated daily for the first 28 days from birth with quinpirole HCl (3.0 mg/kg/day, IP), an agonist that acts at D2 and D3 receptors. At 8 to 10 weeks from birth the dose-effect curve for quinpirole-induced yawning demonstrated that a supersensitization of dopamine receptors for yawning behavior had occurred. Yawning at the optimal dose of quinpirole HCl (100 microgram/kg, IP) was increased 2-fold. The Bmax and Kd for D2 receptor binding in rat striatum were unaltered in this group of rats. These findings indicate that dopamine receptors can be ontogenically "primed" or supersensitized, and that the phenomenon apparently is not related to changes in striatal D2 receptor binding characteristics.

Holmgren, B., R. Budelli, et al. (1991). "Food anticipatory yawning rhythm in the rat." Acta Neurobiol Exp (Wars) 51(3-4): 97-105.
The effect of feeding schedules on the daily rhythm in spontaneous yawning activity was studied in high yawning (HY) Sprague-Dawley rats. If the animals are fed ad libitum and changed from a standard 12-12 light-dark (LD) illumination regime to constant light (LL), the normal predark circadian peak in yawning disappears, to be replaced, after 3 weeks, by two or more ultradian smaller peaks in yawning frequency. Restriction of food availability to 2-2:30 regular hours of the day, in rats under LL conditions, leads to the appearance of a significant preprandial (food anticipatory) peak in yawning. A similar eating-fasting daily cycle of 2-22 h in rats under LD conditions determines the disappearance of the pre-dark peak in yawning activity, and a significant shift in higher yawning frequency towards the couple of hours preceding food availability. This result suggests that restricted feeding is more potent than the LD transition in the entrainment of the daily rhythm in yawning activity.

Hietala, J., J. Lappalainen, et al. (1991). "Chronic D1-receptor blockade: effects on D2-receptor agonist-induced yawning in rats." J Pharm Pharmacol 43(4): 278-9.
The effects of chronic treatment with the selective D1 dopamine receptor antagonist SCH 23390 (0.25 mg kg-1 s.c. twice daily for 18 days, 4 days withdrawal on yawning induced by the D2-receptor agonist quinpirole has been investigated. Low doses of quinpirole (20 and 50 micrograms kg-1 s.c.) induced dose-related yawning behaviour in rats. The yawning response to quinpirole was not significantly different in the presence or absence of SCH 23390 pretreatment. However, chronic treatment with SCH 23390 alone significantly suppressed yawning behaviour. The results suggest that chronic D1-receptor blockade with SCH 23390 does not alter the function of the D2-receptor population mediating yawning behaviour. However, after withdrawal it may result in behavioural activation as seen by suppression of yawning behaviour in the present study.

Hecht, K., W. F. Vogt, et al. (1991). "[Relationship between insomnia and arterial hypotension]." Pneumologie 45 Suppl 1: 196-9.
The relations between insomnia and blood pressure were investigated in 151 patients (56 men and 95 women). It was found that 37.1% of the patients were normotensive, whereas 31.8% suffered from arterial hypertension and 31.1% from arterial hypotension. There was

practically no difference between normotensives and hypertensives in respect of disturbed behavioral patterns of sleep, but an entirely different picture was presented by the arterial hypotensives. Characteristic features of hypotonic insomnias were (mostly in women) prolonged time before falling asleep, frequent awakening at night associated with tachycardia and long-lasting increased excitability, starting difficulties in the morning, depressive conditions, compulsive yawning and falling asleep during daytime, tiredness, lack of "drive" and reduced physical and mental efficiency. This pattern of signs and symptoms was enhanced by hypnotics and tranquilisers. During sleep blood pressures down to 50/35 Torr were measured. It is assumed that the low blood pressure results in hypoxic and hypoglycaemic conditions in the brain. Spontaneous awakening is considered to be an emergency reaction triggered by the deficient cerebral blood flow.

Heaton, J. P. and S. Varrin (1991). "The impact of alcohol ingestion on erections in rats as measured by a novel bio-assay." J Urol 145(1): 192-4.

In rats, a syndrome of yawning and penile erection results from the administration of low doses of apomorphine, a dopamine receptor agonist shown to stimulate dopamine autoreceptors. Ethanol has been shown to influence dopamine metabolism. Low doses of ethyl alcohol (0.25 mg./kg.) failed significantly to alter apomorphine-induced yawning or penile erection, while 0.5 mg./kg. decreased erectile behavior but did not significantly alter the number of yawns. A reduction in both yawning and penile erection in response to apomorphine challenge was seen after the acute intraperitoneal injection of relatively high doses (1.0-3.0 mg./kg.) of ethanol. Two possible mechanisms of action may explain these phenomena. Alcohol may interfere with dopaminergic receptor mechanisms, or conversely, alcohol, through its actions on central dopamine metabolism may alter a second neurotransmitter/neuropeptide more directly responsible for the production of apomorphine-induced yawning and penile erection, possibly oxytocin.

Heaton, J. P. and S. J. Varrin (1991). "Metoclopramide decreases apomorphine-induced yawning and penile erection." Pharmacol Biochem Behav 38(4): 917-20.

Acute administration of metoclopramide, a dopamine (D2) antagonist, reduced both apomorphine-induced yawning and penile erections. Metoclopramide, prominent in clinical use as an effective antiemetic, has been shown to be associated with decreased erectile function in humans. Experimentally naive rats were given a standardized dose of apomorphine and one of a range of doses of metoclopramide. The study shows that metoclopramide decreases the erectile response to apomorphine and suggests that the erectile difficulties experienced in humans after metoclopramide treatment may be a result of interference with a central dopaminergic mechanism(s).

Heaton, J. P., S. J. Varrin, et al. (1991). "The characterization of a bio-assay of erectile function in a rat model." J Urol 145(5): 1099-102.

The investigation of biological phenomena in impotence using an animal system requires a determination of the erectile capabilities of the animal. Rats respond reliably to apomorphine by the exhibition of a phenomenon of erections and yawns. This property has been used to form the basis of a bio-assay of erectile integrity in the rat. We compared rats treated with placebo alone, sham operated rats, rats rendered surgically impotent and castrated rats with and without testosterone. Rats did not respond to placebo. The sham operated rats remained normal in all measured respects (2.66 erections/rat/30 minutes). Surgically impotent rats yawned normally but had no erections. Castrated rats did not have erections and had diminished yawning (3.21 yawns/rat/30 minutes vs. 7.7 for controls p less than .001) but responded normally after testosterone administration. The bio-assay is useful as a standard test of erectile function in the rat.

Greco, M. and R. Baenninger (1991). "Effects of yawning and related activities on skin conductance and heart rate." Physiol Behav 50(5): 1067-9.

Accompanying physiological changes may clarify the functions of yawning, an act that is ubiquitous in the animal kingdom. The skin conductance, muscle tension, and heart rate of 30 young adult humans were recorded before, during, and after their yawns. These measures were also taken in 20 control subjects who merely opened their mouths or took deep breaths. Yawning, mouth opening and deep breathing each increased arousal initially, as measured by skin conductance. Some cumulative effects of successive yawns were found.

Ferrari, F. and F. Claudi (1991). "Behavioural evidence for central D-2 dopamine receptor agonistic effect by some 2-(fluorohydroxyphenyl) ethylamines." Pharmacol Biochem Behav 38(1): 131-4.

The IP injection of 2-(4-fluoro-3-hydroxyphenyl)ethylamines. (FDA 24), N-n-propyl-N-(2-phenylethyl)-2-(3-fluoro-4-hydroxyphenyl) ethylamine (FDA 27F) and N-n-propyl-N-(2-phenylethyl)-2-(4-fluoro-3-hydroxyphenyl) ethylamine (FDA 40) into adult male rats induced the stretching and yawning (SY) syndrome, FDA 24 being the least active. Moreover, FDA 27F and FDA 40 potentiated penile erection (PE) with respect to controls. For both signs (PE and SY), FDA 40 was the most potent of the three compounds. These effects, which are considered typical signs of central D-2-dopamine (DA) receptor stimulation, were dose-related and significantly inhibited by pretreatment with the selective D-2 DA antagonist, sulpiride, but not by domperidone, which does not cross the hematoencephalic barrier. In previous binding studies, FDA 27F and FDA 40 showed high affinity and selectivity for D-2 DA receptors, while FDA 24 had a low affinity for both D-1 and D-2 DA receptors. The present data show that FDA 27F and FDA 40 cross the blood-brain barrier and exert an agonistic effect on the central D-2 DA receptors. These results also provide evidence of the value of PE and SY tests as sensitive tools for the study of DA-neurochemical mechanisms.

Ferrari, F., F. Pelloni, et al. (1991). "Hyperphagic effect of B-HT 920 in a modified X-maze test." Arch Int Pharmacodyn Ther 311: 20-31.

The influence on rat-feeding behavior of B-HT 920 (a selective agonist of D2DA receptors at low doses, but also a potent stimulant of alpha 2-adrenoceptors at high doses) was examined using a new experimental model. The apparatus adopted was an X-maze with alternate open and covered arms, each baited with two food-pellets. Individual rats were placed in the apparatus and observed for 5 min. Two essential aspects of rat behavior in the presence of food were considered: tasting and feeding. A number of parameters were recorded: latency to tasting and feeding; interval between tasting and feeding; total feeding time. We also took into account the type of arm in which the rats indulged in their first bout of tasting and feeding. In the first series of experiments, B-HT 920 was injected intraperitoneally (0.1, 1, 2 and 3 mg/kg) into fed and fasted rats; in the second series, the drug was injected intracerebroventricularly (10, 20 and 80 micrograms/rat) into fasted rats. In both experimental conditions, the drug significantly modified the animals' feeding behavior and affected their natural preference for the closed arms as places of choice in which to feed. Comparison of the results with those obtained using norepinephrine (20 micrograms/rat, intracerebroventricularly), a well-known hyperphagic agent, shows that B-HT 920 strongly stimulates feeding. Also, the results of the intracerebroventricular experiments confirm that the effect on feeding appears at doses that are active both on alpha 2-adrenoceptors and on D2DA receptors, as can be deduced from penile erection and stretching and yawning elicited in rats by the same D2DA stimulant doses. The involvement of the latter receptors in feeding has been investigated by means of a new series of experiments with rats treated with the D2DA antagonist sulpiride, before B-HT 920 at 100 micrograms/kg. The possible mechanisms underlying B-HT 920-hyperphagic effects and the value of the X-maze feeding test as a simple procedure indicative of changes in rat feeding and emotionality are discussed in the light of these latest findings.

Donat, J. F. and F. S. Wright (1991). "Unusual variants of infantile spasms." J Child Neurol 6(4): 313-8.

During evaluation of video-electroencephalograms (EEGs) performed in our laboratory, we identified 11 patients who had unusual repetitive movements that appeared to be variants of infantile spasms. Movements included yawning, facial grimacing, eye movements, and transient focal motor activity. These symptoms coincided with generalized attenuation, slow-wave transients, or other EEG ictal changes characteristic of infantile spasms. The background EEGs showed true or modified hypsarrhythmia. This series of patients shows that infantile spasms may be extremely subtle and clinically atypical. Patients who have these variants may or may not also have typical infantile spasms. In some patients, the seizures appear to be time-related or medication-induced modifications of more typical infantile spasms.

Czyrak, A., E. Mogilnicka, et al. (1991). "Some central pharmacological effects of the calcium channel antagonist flunarizine." J Neural Transm Gen Sect 83(3): 179-88.

Our earlier studies showed that dihydropyridine calcium channel antagonists have some central pharmacological effects. Flunarizine is considered to be a calcium channel antagonist; therefore this study was aimed at investigating the effect of flunarizine (given in single doses of 5, 10 and 20 mg/kg p.o.) in behavioural models in which calcium channel antagonists of the dihydropyridine type were previously studied. Flunarizine inhibited the apomorphine-induced stereotypy and yawning behaviour in rats. It decreased the hypothermia induced by a low dose of apomorphine in mice, but not that one induced by high dose of it. The quinpirole-induced hypothermia was also reduced. In the tests used for evaluation of the effect on the serotonergic system, flunarizine decreased the 5-HTP-induced head twitches and partly antagonized the fenfluramine- and quipazine-induced hyperthermias (at a high ambient temperature). In the forced swimming test flunarizine was inactive in mice and rats. The obtained results indicate that flunarizine exerts central antagonistic effects on the dopaminergic and serotonergic systems and has no antidepressant activity. Flunarizine differs from calcium channel antagonists of the dihydropyridine type, which have no dopamine-antagonistic activity and show anti-depressant-like properties.

Code, R. A. and A. H. Tang (1991). "Yawning produced by dopamine agonists in rhesus monkeys." Eur J Pharmacol 201(2-3): 235-8.

Yawning was recorded from five rhesus monkeys restrained in a chair after i.m. injection of dopaminergic compounds: apomorphine (0.03 mg/kg), quinpirole (0.01 mg/kg), and (-)-3-(3-hydroxyphenyl)-N-(1-propyl)piperidine (1 mg/kg). SKF 38393 or physostigmine produced no yawning. Yawning from apomorphine was blocked by chlorpromazine or SCH 23390 (0.03 mg/kg). Sulpiride (10 mg/kg) was ineffective. The difference between rats and monkeys in their yawning response to dopaminergic compounds is discussed.

Buonamici, M., S. Mantegani, et al. (1991). "FCE 23884, substrate-dependent interaction with the dopaminergic system. I. Preclinical behavioral studies." J Pharmacol Exp Ther 259(1): 345-55.

FCE 23884, a newly synthetized ergoline derivative, shows dopamine (DA) agonist or antagonist properties depending on the functional state of the biological substrate. The compound behaves as a full DA antagonist in normal animals, but shows full agonist properties in denervated models in the same dose range. In normal animals, FCE 23884 impairs Sidmans avoidance in rats, reduces spontaneous locomotion in mice and monkeys and antagonizes apomorphine-induced climbing behavior in mice, yawning in rats, emesis in dogs and amphetamine-induced toxicity in grouped mice. After experimental procedures resulting in severe DA depletion, FCE 23884 behaves as a powerful DA-agonist mainly

at D-1 receptors. FCE 23884 induces contralateral turning behavior in 6-hydroxydopamine-lesioned rats and reverses 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced akinesia in monkeys and reserpine-induced hypokinesia in mice. These results indicate that the antagonist or agonist activity of FCE 23884 is substrate-dependent and mostly related to the presence or absence of DA. This leads to the apparently paradoxical suggestion that the compound could be useful both in psychotic states and extrapyramidal diseases, i.e., in clinical conditions characterized by either excessive or impaired DAergic neurotransmission.

Bonuccelli, U., P. Piccini, et al. (1991). "Naloxone partly counteracts apomorphine side effects." Clin Neuropharmacol 14(5): 442-9.
The effects of naloxone on side effects provoked by apomorphine (APO) administration in patients with parkinsonian syndrome have been studied. The group under study included eight patients with Parkinson's disease and four with parkinsonism who received 100 micrograms/kg s.c. APO acutely to test dopaminergic responsiveness. All patients were treated with 20 mg domperidone tablets t.i.d. and then for 2 consecutive days (in double blind fashion) were given a 2-hour i.v. saline infusion alone or with naloxone (8 mg) starting 30 min before APO administration. In both groups, naloxone delayed the appearance of sleepiness, and reduced the intensity of yawning, sleepiness, nausea, and vomiting as compared with saline. These findings indicate a potential usefulness of naloxone and other opioid antagonists in preventing acute APO side effects.

Blin, O., J. P. Azulay, et al. (1991). "[Yawning. Physiopathology and neuropharmacology]." Therapie 46(1): 37-43.
Yawning is a common physiological phenomenon, induced by hunger, sleepiness or impersonation. Its behavioral aim seems to be an effort to vigilance. There are numerous pathological reasons explaining yawning, as for example global (infectious, metabolic and toxical) or focal neurological diseases. The modification of yawning in pathology where a dopaminergic dysfunction is to be found, as well as some data of animal experimentation, support when it takes place the dopaminergic system's implication. The pre-synaptical receptor's role had been suggested for a long time but actually yawning seems to be linked with a D1-D2 cooperation. The cholinergic system probably control a final effective pathway. We also imply the peptidergic, serotoninergic, androgine and opiace systems. If the localization of a putative center of yawning is impossible, the nigrostriatal dopaminergic pathway, the paraventricular nucleus of hypothalamus and the pituitary gland play a major role. Yawning can be used as a functioning index of the dopaminergic system in vivo in the human being.

Blin, O., J. P. Azulay, et al. (1991). "Apomorphine-induced yawning in migraine patients: enhanced responsiveness." Clin Neuropharmacol 14(1): 91-5.
Migraine patients usually exhibit hypersensitivity to dopaminergic agonists, but the tests used (such as the so called "piribedil test") preferentially assess the sensitivity of the peripheral dopaminergic receptors. Apomorphine-induced yawning may be useful in the evaluation of central dopaminergic receptor sensitivity. Nine migraine patients were included in an age- and sex-matched control study. They had been without treatment for 1 month and free of a migraine attack for at least 7 days. Apomorphine hydrochloride (5 micrograms/kg) was administered subcutaneously, and yawning was recorded by two observers. The cumulative number of yawns as a function of time was studied. The comparison of the regression graphs showed a significant difference between migraine patients and controls. Migraine patients exhibited enhanced responsiveness to apomorphine challenge. This finding supports the hypothesis of a constant central dopaminergic hypersensitivity.

Blau, J. N. (1991). "Migraine postdromes: symptoms after attacks." Cephalalgia 11(5): 229-31.
To determine the nature and duration of symptoms after the headache phase of migraine, 40 migraineurs (11 with and 29 without an aura) were given a questionnaire to complete on the day after a migraine attack. The most common symptoms that remained were physical and mental tiredness, subdued or depressed mood, impaired concentration, reduced physical activities and yawning; weak or clumsy limbs, head tenderness, neck ache or stiffness, impaired sight and altered fluid balance were less frequent. The number of symptoms ranged from 2 to 11 (average 6) per patient lasting for a mean of 18 h, usually the whole of the next day. Symptoms after the main migraine attack can help to diagnose migraine particularly when there is no aura before the onset of headache. Eliciting postdromes aids patient-doctor rapport and confidence. The range of symptoms lends support to the notion that the whole of the brain is involved in the aftermath of migraine attacks.

Bertschy, G., S. Vandel, et al. (1991). "[Yawning and sexual excitation under clomipramine. Role of serotoninergic mechanisms. Apropos of 2 cases]." Encephale 17(6): 515-7.
We report two cases of a singular side effect induced by clomipramine, one in a man, the other in a woman (both patients were beninese). This consisted of the occurring of the association of very frequent yawning and sexual excitation (sexual excitation with vaginal lubrification for the woman and hypogastric feeling of sexual pleasure for the man). It appeared after a few days of ambulatory treatment of a depression with clomipramine 75 mg/day. Clomipramine and demethylclomipramine blood levels were respectively 85 and 95 ng/ml and 70 and 80 ng/ml for the two patients. Three similar cases had been reported in the literature with this same tricyclic antidepressant. Recently a first case has been reported with fluoxetin. On this basis, it could be suggested that serotoninergic mechanisms are involved in the development of such clinical manifestations. But it seems reasonable to consider that serotoninergic mechanism could interact with a dopaminergic one. In favour of this hypothesis is the implication of dopaminergic mechanisms in yawning in man or in the association yawning--penile erections in the rat. Some others clinical arguments are discussed.

Beninger, R. J., E. J. Mazurski, et al. (1991). "Receptor subtype-specific dopaminergic agents and unconditioned behavior." Pol J Pharmacol Pharm 43(6): 507-28.
When all of the data concerning the role of D1 and D2 receptors in the control of unconditioned behaviors are taken together a fairly consistent picture begins to emerge. Considering first the normosensitive animals, it appears that D1 and D2 receptors are interdependent in their involvement in the control of locomotor activity. Stimulation of either receptor subtype leads to increases in activity although D2 agonists generally have a larger effect on activity than D1 agonists. Subeffective doses of D1 and D2 agonists (or D1 and D2 antagonists) have a synergistic action when co-administered. Injections of antagonists specific for either receptor subtype leads to a decrease in unstimulated locomotor activity or a diminution in the effects of agonists stimulating either receptor subtype. Besides locomotor activity, stimulation of D2 receptors produces yawning but a consistent effect on grooming has not been seen; D2 receptor stimulation also produces stereotyped behaviors. Again, there seems to be an interdependence between the two receptor subtypes; yawning or stereotypy produced by D2 receptor stimulation is blocked by either D2 or D1 antagonists. Stimulation of D1 receptors produces grooming and small perioral movements but not stereotyped behaviors like those typically seen following large doses of D2 agonists or DA agonists not specific a receptor subtype. Unlike D1 receptor-stimulated locomotor activity which is antagonized by D2 receptor blockers, grooming and perioral movements are not (but see Ref. 81). Thus, D1 receptor-mediated grooming and perioral movements seem to be exceptions to the otherwise general finding that co-stimulation of the two receptor subtypes needed for the expression of D1 or D2 agonist effects in normosensitive rats and mice. The apparent need to stimulate both D1 and D2 receptors to produce locomotor and some other unconditioned behaviors in normosensitive animals is lost in chronically denervated animals that are supersensitive to the effects of DA or DA agonists. However, there appear to be important species differences. Generally, in rodents undergoing unilateral or bilateral 6-OHDA-induced destruction of the nigrostriatal DA system, the locomotor effects of D1 agonists are not blocked by D2 antagonists and those of D2 agonists are not blocked by D1 antagonists. Similar results have been reported following chronic treatments with catecholamine depleting drugs. Thus, stimulation of either D1 or D2 receptors alone in DA supersensitive rodents appears to be sufficient to produce locomotor activity. In primates made DA supersensitive either with MPTP or as a result of Parkinson's disease, on the other hand, D2 but not D1 agonists are effective in reversing locomotor deficits.(ABSTRACT TRUNCATED AT 400 WORDS)

Argiolas, A. and G. L. Gessa (1991). "Central functions of oxytocin." Neurosci Biobehav Rev 15(2): 217-31.
Oxytocin, the peptide well-known for its hormonal role in parturition and lactation, is present in several extrahypothalamic brain areas besides the neurohypophyseal system. The peptide is found in neurons which send their projections to brain areas containing specific oxytocin-binding sites. Oxytocin is also released from its synapses in a calcium-dependent fashion and may be the precursor of potent behaviorally active neuropeptides. These findings suggest that this ancient neuropeptide acts as a neurotransmitter in the central nervous system. We have attempted to review the most recent behavioral, morphological, electrophysiological and neurochemical studies providing evidence that oxytocin plays an important role in the expression of central functions, such as maternal behavior, sexual behavior (penile erection, lordosis and copulatory behavior), yawning, memory and learning, tolerance and dependence mechanisms, feeding, grooming, cardiovascular regulation and thermoregulation.

Antoniou, K. and E. Kafetzopoulos (1991). "A comparative study of the behavioral effects of d-amphetamine and apomorphine in the rat." Pharmacol Biochem Behav 39(1): 61-70.
A wide range of doses of d-amphetamine and apomorphine were injected into rats, in order to better characterize and compare dopaminergic agonist-induced behavioral effects. The study was carried out using a computerized technique for the quantification and analysis of various behavioral elements. Although both drugs increased motor activity and provided dose-dependent stereotyped responses, the whole pattern of behavior in the open field showed a different structure. d-Amphetamine in doses that did not produce stereotyped responses induced a wide range of varied behavioral elements with increased frequency but decreased mean duration, while apomorphine induced a more restricted behavioral profile. Furthermore, a higher frequency of freezing reaction was observed after d-amphetamine treatment in low doses but not after apomorphine treatment. Both drugs in high doses elicited a similar stereotyped syndrome characterized by repetitive movements of great duration, but at low doses the behavioral pattern was completely different. The apomorphine-induced syndrome was characterized mainly by moving and sniffing, interrupted by rearing, while the amphetamine-induced syndrome by sniffing and moving, interrupted by standing and freezing.

Yamada, K., S. Matsumoto, et al. (1990). "Potentiation of yawning responses to the dopamine receptor agonists B-HT 920 and SND 919 by pindolol in the rat." J Neural Transm Gen Sect 79(1-2): 19-24.
Subcutaneous injection of B-HT 920, a dopamine D2-receptor agonist, in doses ranging from 5 to 100 micrograms/kg, induced yawning behavior in rats. Yawning was also elicited by low doses (25-500 micrograms/kg sc) of SND 919, a newly synthesized dopamine receptor agonist. The yawning evoked by B-HT 920 or SND 919 was increased by the beta-adrenoceptor antagonist pindolol (20 mg/kg ip) which alone did not induce yawning. Stereotyped behavior did not appear after B-HT 920 or SND 919 given alone or in combination with pindolol. The results

suggest that SND 919 as well as B-HT 920 has stimulatory activity at dopamine D2-receptors, and that pindolol may exert its enhancement of the yawning response to dopamine receptor agonists via blockade of beta-adrenoceptors.

Yamada, K., M. Nagashima, et al. (1990). "Possible involvement of differing classes of dopamine D-2 receptors in yawning and stereotypy in rats." Psychopharmacology (Berl) 100(2): 141-4.
The present experiments were performed to investigate differences in the properties of the dopamine D-2 receptors related to yawning and stereotypy. Subcutaneous injection of talipexole (B-HT 920) (10-250 micrograms/kg) or SND 919 ((S)-2-amino-4,5,6,7-tetrahydro-6-propylamino-benzothiazole) (25-500 micrograms/kg) evoked yawning behavior with bell-shaped responses. However, SK&F 38393 (1-phenyl-2,3,4,5-tetrahydro-(1H)-3-benzazepine-7,8-diol) (0.5-10 mg/kg SC) did not elicit yawning and decreased yawning responses to low doses of talipexole (25 micrograms/kg SC) or SND 919 (100 micrograms/kg SC). These low but effective doses for inducing yawning of talipexole or SND 919 in combination with SK&F 38393 (0.5-10 mg/kg SC) did not elicit stereotypy. In contrast, yawning behavior was not produced after very high doses of talipexole (500 micrograms/kg SC) or SND 919 (1000 micrograms/kg SC) given alone or in combination with SK&F 38393 (0.5-10 mg/kg SC). These extremely high doses of talipexole or SND 919 evoked slight stereotypy, which was enhanced by the combined treatment with SK&F 38393. The present results suggest that the dopamine D-2 receptors related to yawning are more sensitive to dopamine receptor agonists than those related to stereotypy, and that concurrent stimulation of postsynaptic dopamine D-1 receptors with D-2 receptors reduces the incidence of yawning but enhances that of stereotypy.

Weinberg, W. A. and R. A. Brumback (1990). "Primary disorder of vigilance: a novel explanation of inattentiveness, daydreaming, boredom, restlessness, and sleepiness." J Pediatr 116(5): 720-5.
We present a novel condition, designated as a primary disorder of vigilance, that has symptoms which overlap those of attention deficit-hyperactivity disorder. Vigilance is the state of being watchful, awake, and alert. When vigilance is lost, the individual has difficulty sustaining attention. The most obvious evidence of lowered vigilance is motor restlessness (fidgeting and moving about, yawning and stretching, talkativeness, or a combination of these) to improve alertness when sitting or standing still or when involved in tasks requiring continuous mental performance. When prevented from being active to stay awake, persons with lowered vigilance will stare off, daydream, show minor hyperactivity, and finally may fall asleep. They will also have decreasing attention to current activities and usually avoid or lose interest in structured or repetitive activities (complaining of boredom and monotony). The primary disorder of vigilance (for which criteria have been established) is a dominantly inherited condition with onset in early childhood and worsening symptoms with age. Persons with the primary disorder of vigilance have a remarkably kind and caring temperament. When untreated this disorder can cause chronic failure at school and work, but when properly recognized it responds well to treatment with stimulant medication and schedules that avoid sameness and repetition.

Urba-Holmgren, R., N. Trucios, et al. (1990). "Genotypic dependency of spontaneous yawning frequency in the rat." Behav Brain Res 40(1): 29-35.
By inbreeding we have obtained two sublines of Sprague-Dawley rats which differ significantly in spontaneous mean yawning frequency (MYF). In generation F21 of the high-yawning (HY) subline MYF was 21.5 yawns/h (y/h) in males and 1.95 y/h in females, at the age of 2 months. In the low-yawning (LY) subline, in generation F16 the MYF was 0.9 y/h in males and only 0.5 y/h in females. During the first 15 days there are no differences in yawning frequency between HY and LY rats. Thereafter yawning increases with age, more steeply in the HY subline. The results of reciprocal crosses between both sublines indicate that the LY character is partially dominant over the HY one.

Tesfaye, Y. and S. Lal (1990). "Hazard of yawning." Cmaj 142(1): 15.

Stoessl, A. J., C. T. Dourish, et al. (1990). "Pharmacological characterization of the behavioural syndrome induced by the NK-3 tachykinin agonist senktide in rodents: evidence for mediation by endogenous 5-HT." Brain Res 517(1-2): 111-6.
The effects of various manipulations of brain 5-HT mechanisms on the behavioural responses induced by the selective NK-3 tachykinin agonist senktide in rodents were assessed. Senktide elicited wet dog shakes in the rat which were attenuated by the 5-HT1C/2 antagonist mianserin and the selective 5-HT2 antagonist altanserin. Senktide-induced forepaw treading was stereospecifically attenuated by the 5-HT1A + B antagonist (-)-alprenolol. Senktide also elicited chewing mouth movements and yawning, which were unaffected by mianserin, altanserin, (+)- or (-)-alprenolol, or the selective 5-HT3 antagonist ICS 205-930, but attenuated by the muscarinic antagonist scopolamine. Penile grooming elicited by senktide was attenuated by mianserin, but was unaffected by the other antagonists. Senktide-induced wet dog shakes were enhanced by the 5-HT reuptake inhibitors citalopram and fluoxetine, suppressed by the monoamine oxidase (MAO)-B inhibitor pargyline, but unaffected by the MAO-A inhibitor clorgyline. Forepaw treading was potentiated by citalopram and clorgyline, but not significantly altered by fluoxetine or pargyline. Depletion of 5-HT by p-chlorophenylalanine (PCPA) in the rat attenuated senktide-induced wet dog shakes and forepaw treading. Neither PCPA nor 5,7-dihydroxytryptamine affected senktide-induced behaviours in the mouse, but the degree of brain 5-HT depletion caused by these treatments in mice was relatively small. These findings indicate that stimulation of NK-3 tachykinin receptors by senktide results in a complex behavioural syndrome which is mediated by multiple 5-HT receptors, and dependent upon intact stores of endogenous 5-HT. Independent stimulation of brain cholinergic mechanisms by senktide is also confirmed.

Stahle, L. and U. Ungerstedt (1990). "Yawning and suppression of exploration induced by dopamine agonists: no relation to extracellular striatal levels of dopamine." Pharmacol Biochem Behav 35(1): 201-9.
The present study was aimed at testing the hypothesis that yawning and suppression of exploration induced by low doses of dopamine agonists in the rat are caused by a reduction of synaptic dopamine levels. The decrease in extracellular levels of dopamine in the corpus striatum induced by alpha-methyl-p-tyrosine (alpha MPT, 50-200 mg/kg IP), reserpine (2-5 mg/kg SC) and apomorphine (APO, 0.05 mg/kg SC) was measured in microdialysis experiments. Reserpine and alpha MPT reduced the dopamine levels to the same extent as APO. Exploratory behaviour was suppressed by APO, but not by alpha MPT (50 and 100 mg/kg) when tested in a separate experiment. Reserpine (2 mg/kg) suppressed exploration after 4 hr, but not after 3 hr. Changes in extracellular levels of dopamine were tested simultaneously with changes in yawning in another group of rats implanted with guide cannulae for microdialysis probes. There was a discrepancy in the time-course for the induction of yawning as compared to the changes in extracellular dopamine levels after APO (0.05 mg/kg) as well as after pergolide (0.02 mg/kg SC). Yawning appeared before and lasted shorter than the decrease in dopamine. The time-courses for APO-induced suppression of exploration and yawning were similar. The dose-response curve for APO-induced yawning was not changed by alpha MPT (200 mg/kg), while the suppression of exploration induced by APO, but not by pergolide, was enhanced by pretreatment with alpha MPT. The results show that yawning and suppression of exploration induced by dopamine agonists are not related to changes in extracellular levels of dopamine. It is proposed that these behaviours may be mediated by postsynaptic receptors.

Pomerantz, S. M. (1990). "Apomorphine facilitates male sexual behavior of rhesus monkeys." Pharmacol Biochem Behav 35(3): 659-64.
In the present study, a novel sexual behavior paradigm was used to study the effects of the dopamine agonist, apomorphine, on male sexual behavior of rhesus monkeys. In Experiment 1, the effects of apomorphine treatment were assessed by observing the behavioral responses of male rhesus to a sexually receptive female monkey that they could see, hear, and smell, but could not physically contact. Apomorphine treatment produced a spectrum of behavioral effects that differed depending on the dose of drug administered. Low doses of apomorphine (25-100 micrograms/kg) stimulated yawning, moderate doses (50-200 micrograms/kg) facilitated male sexual responses associated with the genitals including penile erection and masturbation, and high doses (greater than 200 micrograms/kg) elicited stereotypic behavior. Experiment 2 examined whether the behavioral responses of male monkeys to apomorphine treatment were influenced by the stimulus female. Apomorphine treatment facilitated penile erections in tests in which a stimulus female was present, but did not facilitate erections in tests in which she was absent. In sum, these experiments provide preliminary evidence that dopaminergic mechanisms may play a role in the regulation of male sexual behavior of rhesus monkeys.

Pentecost, R. A., 3rd (1990). "A do-it-yourself guide to assembling skilled nursing facilities." Healthtexas 46(7): 10-1.
No one in Texas hospital doubts the need for more skilled nursing care facilities. patients are leaving sooner and sicker, creating discharge-planning logjams. Few nursing facilities offer the subacute care these patients need--and in the current climate their operators can be increasingly selective about whom they choose to admit. These factors, coupled with lowered rates of hospital occupancy and yawning Medicare reimbursement gaps, are all reasons that furnishing skilled nursing care is an increasingly attractive option for Texas hospital administrators. For hospitals considering furnishing various long-term subacute care options, A. Ray Pentecost III, DrPH, offers a nuts-and-bolts guide. Pentecost, who is both a licensed architect and nursing home administrator, is director of the Health Environments Institute in The College of Architecture at the University of Houston, and is also president of Gerontological Health Consultants Inc. of Katy, Texas.

Panksepp, J. and L. Normansell (1990). "Effects of ACTH(1-24) and ACTH/MSH(4-10) on isolation-induced distress vocalization in domestic chicks." Peptides 11(5): 915-9.
The effects of centrally administered ACTH(1-24) and ACTH(4-10) on isolation-induced distress vocalizations (DVs) were assessed in the presence or absence of social cues (mirrored and plain environments). A dose-response analysis indicated that ACTH(1-24) at doses of 0.5 nM and above increased DVs relative to controls when the animals were tested in mirrored or social environments which reduce baseline levels of calling. This effect, however, was short-lived (approx. 15 min). When tested again 1 hr after injection, the treated animals did not differ from controls. ACTH/MSH(4-10) had no effect on vocalization when the animals were tested immediately after injection, but marginally increased calling when animals were tested an hour later. In addition to vocalization changes, ACTH(1-24) induced squatting when animals were isolated in the test boxes, and yawning, head shaking, wing flapping and preening when animals were reunited after testing. ACTH(1-24)-treated chicks also exhibited longer latencies to close their eyes when they were held in the cupped hands of the experimenter. Taken together, the results suggest that ACTH(1-24) induces a central state of arousal in chicks that resembles fear/anxiety.

Neumann, B. G., L. R. Troncone, et al. (1990). "Modifications on dopaminergic and cholinergic systems induced by the water tank technique: analysis through yawning behavior." Arch Int Pharmacodyn Ther 308: 32-8.
Animals deprived of REM sleep by the water tank technique show an important decrease in frequency of yawning, induced by

dopaminergic (apomorphine in low doses) and cholinergic (physostigmine and pilocarpine) agonists, if they are tested immediately after the 96 hr of deprivation. In order to understand the mechanisms underlying the effects of REM sleep deprivation on dopaminergic and cholinergic systems, we decided to test the animals after a recovery period of 24 hr. It was observed that apomorphine-induced yawning was still significantly reduced, whereas pilocarpine-induced yawning had returned to normal. The findings suggest that REM sleep deprivation alters dopaminergic and cholinergic systems in different ways: it seems that the interference on the dopaminergic system is prior and stronger than on the cholinergic system, thus its recovery demands more time.

Mizukami, K. and M. Ishibashi (1990). "Very young infants yawn or cry after watching animated programs." J Dev Behav Pediatr 11(3): 163.

Lynch, M. R. (1990). "Behavioral evidence for dopamine receptor subsensitivity following chronic haloperidol." Neuropsychobiology 24(2): 102-8.

When treated chronically with haloperidol, rats show progressively enhanced behavioral suppression, mimicking the delay of onset seen clinically with neuroleptics. To investigate potential neurochemical mechanisms underlying this delay, low-dose apomorphine treatment was administered after withdrawal from 21 days of 0.1 mg/kg haloperidol, to probe for depolarization inactivation or autoreceptor supersensitivity. This haloperidol treatment was subthreshold for inducing either dopamine autoreceptor supersensitivity or postsynaptic supersensitivity as evidenced by equivalent metabolic reductions in chronically treated neuroleptic versus vehicle groups, and an absence of stereotypical responding in either condition. However, haloperidol treated rats appeared subsensitive to yawning induced by 0.07 mg/kg apomorphine. This latter response appears to be generated from an as yet unidentified postsynaptic dopaminergic substrate. The present observation suggests that, within a therapeutically relevant dose range, repeated neuroleptic administration induces a complex set of neuroadaptive processes (both up- and down-regulation of pre- and postsynaptic sites) in the underlying substrate for these drugs' behavioral and biochemical effects.

Lobo, L. L., B. G. Neumann, et al. (1990). "Effects of REM sleep deprivation of ACTH-induced yawning." Pharmacology 40(3): 174-8.

Central administration of ACTH in rats induces yawning and stretching. In order to study the effects of REM sleep deprivation on ACTH-induced yawning, the peptide was injected immediately after the REM sleep deprivation period or 24 h later. REM sleep deprivation impaired ACTH-induced yawning, but after a 24-hour recovery period, rats displayed a number of yawns similar to those in control animals. Implications for an involvement of dopaminergic and mainly cholinergic systems are discussed.

Laping, N. J. and V. D. Ramirez (1990). "Yawning behavior in male rats is associated with decreases in in vivo DOPAC efflux from the caudate nucleus." Behav Brain Res 36(1-2): 65-72.

Young adult male rats were implanted with a push-pull cannula aimed at the dorsal and rostral areas of the caudate nucleus. Perfusate samples were collected at two-minute intervals for approximately one hour and assayed for DOPAC concentrations. Simultaneously, yawning, penile erections and grooming behavior were recorded. Yawns were induced by systemic prolactin or apomorphine injections. While mean DOPAC efflux was elevated following prolactin (PRL) and apomorphine decreased mean DOPAC efflux as expected, yawns and penile erections induced by both compounds were associated with rapid momentary decreases in DOPAC efflux in these living animals. Although yawning was associated with significant decreases in DOPAC output, not every momentary DOPAC decrease was associated with a yawn, suggesting that the 'yawning generator' most likely requires additional inputs for the expression of a yawn.

Koyuncuoglu, H. and B. Saydam (1990). "The treatment of heroin addicts with dextromethorphan: a double-blind comparison of dextromethorphan with chlorpromazine." Int J Clin Pharmacol Ther Toxicol 28(4): 147-52.

According to the hypothesis that the development of physical dependence on and tolerance to opiates depends on the inhibition by opiates of L-asparaginase and L-glutaminase activities in the brain, and the blockade by opiates of the aspartatergic/glutamatergic receptors especially NMDA, four female and fourty-four male heroin addicts were included in a double-blind clinical trial. Four mg chlorpromazine (CPZ) was administered every hour and 10 mg diazepam (DIA) every 6 hours to a group consisting of two female and nineteen male inpatients. The remaining subjects received 15 mg non-opioid antitussive dextromethorphan (DM) instead of CPZ. The withdrawn addicts were controlled twice a day and yawning, lacrimation, rhinorrhoea, perspiration, goose flesh, muscle tremor, dilated pupils, anorexia, joint and muscle aches, restlessness, insomnia, emesis, diarrhea, craving and rejection of smoking as abstinence syndrome signs were observed and rated on a scale of 1, 2 and 3 points according to their intensity. All signs, except perspiration and emesis, were significantly less intense in the group given DM + DIA than CPZ + DIA. The other plus points included the immediate stop of craving and the early onset of smoking in DM + DIA group. The results are considered to be supporting evidence for the hypothesis emphasizing the blockade of NMDA receptors by opiates in opiate addiction. Furthermore, the decrease caused by non-opioid NMDA antagonists in the responsiveness of NMDA receptors appears very promising for the treatment of opiate addicts.

Kleinrok, Z., J. Szponar, et al. (1990). "Studies on the participation of the dopaminergic system in the central effects of chelidonine." Pol J Pharmacol Pharm 42(5): 417-24.

Chelidonine administered to rats in doses of 25, 50, 100 and 200 mg/kg ip exerted an inhibitory effect on the dopaminergic structures in the rat. It was shown that chelidonine decreased amphetamine- and apomorphine-induced hyperactivity and inhibited amphetamine and apomorphine sterotype. Besides, chelidonine significantly inhibited the yawning and penile erection produced by apomorphine. However, chelidonine potentiated also catalepsy caused by haloperidol. In doses of 100 and 200 mg/kg ip chelidonine depressed the whole brain dopamine (DA) concentrations and enhanced DA utilization.

Kirstein, C. L., J. Traber, et al. (1990). "ACTH-induced behaviors and their modulation by serotonergic agonists differ in neonatal and weanling rat pups." Psychopharmacology (Berl) 100(2): 151-8.

Four-day-old (P4) and 21-22-day-old (P21-22) rat pups received an intracisternal injection of either ACTH1-16NH2 or saline followed by a subcutaneous (SC) injection of saline, the serotonergic (5HT)1A agonists 8-OH-DPAT or ipsapirone, the 5HT1B agonist TFMPP or the 5HT2 agonist DOI. The ontogeny of ACTH-induced behaviors including grooming, yawn and stretch as well as various serotonin-related behaviors were recorded via time-sampling at 20 s intervals for a test duration of 50 min. ACTH induced slight but significant increases in grooming at P4, along with a significant increase in yawning. At this age the 5HT1B agonist TFMPP induced substantial increases in grooming, with no effect of the other agonists on this behavior. All of the serotonergic agonists, however, decreased ACTH-induced yawning at P4. At P21-22 ACTH induced more robust grooming than that observed at P4, although different in nature from adult-typical ACTH-induced grooming. This ACTH-induced grooming at P21-22 was attenuated by all of the serotonergic agonists. ACTH-induced yawning at P21-22 was not affected by the serotonergic agonists while ACTH-induced stretching was increased by the 5HT1B agonist TFMPP at this age. These data provide additional evidence of differential mediation of various ACTH-induced behaviors, and support other reports of ontogenetic alterations in the response to serotonergic manipulations during the neonatal to weanling age period.

Kamerling, S. G., J. G. Hamra, et al. (1990). "Naloxone-induced abdominal distress in the horse." Equine Vet J 22(4): 241-3.

Endogenous opioid peptides have been implicated in the regulation of pain perception, behaviour, gastrointestinal activity and other physiological responses. However, the functional role of these peptides in the horse has yet to be elucidated. The opioid antagonist, naloxone, is often administered to infer endogenous opioid effects. In the present study, naloxone (0.75 mg/kg bodyweight) was administered to eight Thoroughbred racehorses and a number of behavioural and autonomic responses were measured. Naloxone produced rapid onset diarrhoea, restlessness, abdominal checking, tachycardia, tachypnoea, paradoxical yawning and diaphoresis. These responses described an acute abdominal distress syndrome similar to spasmodic colic. Results from this study suggest that, in the horse, endogenous opioids: 1) influence behaviour, 2) modify intestinal activity and sensation, and 3) if perturbed, may be involved in pathophysiology of colic.

Delini-Stula, A. and C. Hunn (1990). "Effects of single and repeated treatment with antidepressants on apomorphine-induced yawning in the rat: the implication of alpha-1 adrenergic mechanisms in the D-2 receptor function." Psychopharmacology (Berl) 101(1): 62-6.

Acute (10 or 20 mg/kg IP) and subchronic (2 x 5 or 10 mg/kg IP daily for 7 days) effects of desipramine, imipramine, maprotiline, (+)- and (-)-oxaprotiline enantiomers as well as selective 5-HT-uptake inhibitors citalopram and ifoxetine on yawning, induced by low doses of apomorphine, were investigated in the rat. In addition, the effects of alpha-1 receptor agonist adrafinil and antagonist prazosin were also tested. After acute treatment, desipramine, the stereoselective NA-uptake inhibiting (+)-enantiomer of oxaprotiline, and the alpha-1 agonist adrafinil, markedly and significantly suppressed yawning. Prazosin, in contrast, clearly potentiated it. This potentiating effect was abolished by the pretreatment with (+)-oxaprotiline and adrafinil. Other drugs were inactive. After subchronic administration, yawning was antagonized by NA-uptake-inhibiting antidepressants, including imipramine and maprotiline. By comparison to the acute treatment, the inhibitory effects of desipramine and (+)-oxaprotiline were considerably enhanced. Neither selective 5-HT-uptake inhibitors nor (-)-oxaprotiline (levoprotiline) were active. Antidepressants therefore modulate the functional activity of D-2 receptors, activated by low doses of apomorphine, predominantly by the virtue of their noradrenergic enhancing properties. This modulatory effect appears to be mediated by alpha-1 adrenergic receptors.

de Wied, D. (1990). "Neurotrophic effects of ACTH/MSH neuropeptides." Acta Neurobiol Exp (Wars) 50(4-5): 353-66.

Numerous experiments with peptides related to ACTH/MSH, and involving tests such as avoidance, approach, discrimination and rewarded behavior indicate that these peptides possess neuroactive effects on learning, motivation, attention, and concentration. In addition, ACTH/MSH neuropeptides affect social behavior, interact with opiate binding sites, and possess antiepileptic properties. Other CNS effects which can be demonstrated after intracranial administration only are grooming behavior, stretching, yawning and sexual behavior. The effects reside mainly in the N-terminal part of ACTH (ACTH-(4-10); ACTH-(7-16) and are dissociated from the peripheral corticotrophic effect. Several substitutions in the sequence ACTH-(4-9) led to a highly selective, potent and orally active neuropeptide with a marked loss of endocrine effects. Thus H-Met(O2)-Glu-His-Phe-D-Lys-Phe-OH (Org 2766) appeared to be 1,000 times more active on avoidance behavior than ACTH-(4-10) but to contain 1,000 times less melanotrophic activity. It also had a markedly reduced steroidogenic, fat mobilizing and opiate-like activity. ACTH/MSH peptides also possess neurotrophic activities as derived from studies on regeneration of damaged nerve cells. Animal studies show beneficial effects of semichronic treatment of the ACTH-(4-9) analogue Org 2766 on nerve crush regeneration in animals. The

activity for this effect resides in the sequence ACTH-(6-10). The neurotrophic influence is evident both at the sensory and the motor function level. The protective effect of Org 2766 is also found in other neuropathies as a result of diabetes mellitus and chemotherapy. (ABSTRACT TRUNCATED AT 250 WORDS)

Cowan, A. and C. W. Murray (1990). "Effect of nor-binaltorphimine on the behavior of mice and rats receiving multiple injections of U-50,488." Prog Clin Biol Res 328: 303-6.

Chouard, C. H. and D. Bigot-Massoni (1990). "[Mechanisms and physiologic role of yawning]." Ann Otolaryngol Chir Cervicofac 107(3): 145-53.
As well as being present in all mammals, yawning occurs, at least in its mandibular component, in all vertebrates. The existence of pathological and pharmacologically induced yawning justifies study of this everyday ENT reflex. Its mechanism remains uncertain. The most likely hypothesis would seem to be stimulation of the reticular system of the brain-stem by signals originating in masseteric neuromuscular spindles sensitive to stretching. Serotoninergic inhibition from the dorsal raphe, a fall in hypothalamic dopaminergic inhibitory tone, followed by ocytocinergic hippocampal activation and then more diffuse cholinergic activation of cranial nerve motor nuclei seems likely. Various hormonal or socio-environmental influences can modify the activity of these different systems. The physiological consequences and the communicative value of yawning become more diversified with the phylogenetic evolution of the subject. Yawning appears to correspond to an alertness reflex which has acquired a paralinguistic value with evolution and may have a role in protection or social cohesion.

Bourson, A. and P. C. Moser (1990). "Yawning induced by apomorphine, physostigmine or pilocarpine is potentiated by dihydropyridine calcium channel blockers." Psychopharmacology (Berl) 100(2): 168-72.
Previous studies have shown that dihydropyridine (DHP) calcium channel blockers can potentiate yawning induced by apomorphine in rats. The present study was undertaken to examine whether or not this interaction was seen with other compounds that induce yawning or if it represented a specific interaction with dopaminergic mechanisms. Yawning induced by apomorphine (40 micrograms/kg SC), physostigmine (50 micrograms/kg SC) or pilocarpine (1 mg/kg SC) was dose-dependently potentiated by the DHP calcium channel blocker nifedipine (1.25-10 mg/kg IP). Nimodipine (1.25-5 mg/kg IP) and nitrendipine (1.25-5 mg/kg IP) also significantly increased the yawning response. The DHP calcium channel blockers alone induced only a low incidence of yawning. The effects of nifedipine on physostigmine-induced yawning were reversed by the DHP calcium channel activator BAY K 8644 which also inhibited yawning induced by physostigmine (100 micrograms/kg SC) and pilocarpine (2 mg/kg SC). In contrast to the DHP compounds, diltiazem (2.5-10 mg/kg IP) and verapamil (2.5-10 mg/kg IP) failed to potentiate yawning. Sulpiride (10 mg/kg SC) antagonised the nifedipine potentiation of apomorphine-induced yawning but not that of physostigmine-induced yawning; atropine (2.5 mg/kg SC) antagonised both effects. These results support the hypothesis that this effect of dihydropyridine compounds is not dependent on, nor mediated through, dopaminergic mechanisms.

Blin, O., M. Durup, et al. (1990). "Akathisia, motility, and locomotion in healthy volunteers." Clin Neuropharmacol 13(5): 426-35.
Apomorphine (10 micrograms/kg subcutaneously with oral domperidone 10 mg), oral sultopride (50 mg), and placebos were given to nine normal volunteers, using a Latin-square design and double-blind procedures. A battery of tests was applied before the dose, and after the dose after time lapses of 15, 45, 90, 105, 120, and 180 min. Spatiotemporal and dynamic gait parameters, gait stability, and modulations remained unchanged with all three treatments. Apomorphine induced repeated yawning in all subjects. Akathisia was observed in four of nine subjects with sultopride. Sultopride was associated with drowsiness and sleepiness on visual analog scales. Akathisia may be related to decreased dopaminergic activity in the prefrontal cortex and mesocortical dopamine system blockade. The imbalance between mesocortical and nigrostriatal dopaminergic systems might explain the fact that sultopride in our experiment modified spontaneous behavior but not volitional behavior. Thus, it is possible to discriminate between two types of increased motor activity, and motility must be distinguished from locomotor activity.

Blin, O., G. Masson, et al. (1990). "Apomorphine-induced blinking and yawning in healthy volunteers." Br J Clin Pharmacol 30(5): 769-73.
Yawning and spontaneous blink rate (SBR) are two physiological reflexes which have been incompletely examined but one neurobiological step of these two behaviours seems, at least in part, dopamine-dependent. The reference dopaminergic agonist, apomorphine hydrochloride (0.5, 1, and 2 micrograms kg-1 s.c.), was compared with a placebo in a double-blind latin-square design, and was shown to induce yawning and increase SBR in a population of eight healthy volunteers. These two behavioral effects were not dose-related. The individual SBR differences were correlated with the individual number of yawns for all the four treatments at the 10-30 min interval. Thus, parallel yawning and SBR behaviour suggests a similar pharmacological mechanism. Apomorphine-induced yawning and blinking may be therefore of use in the evaluation of central dopaminergic pathways in man.

Barthalmus, G. T. and K. B. Meadows (1990). "SCH 23390: D-1 modulation of oral dyskinesias induced in snakes by Xenopus skin mucus." Pharmacol Biochem Behav 36(4): 843-6.
The granular gland skin secretion of Xenopus laevis induces seven involuntary oral dyskinesias and climbing behavior in the water snake Nerodia sipedon. In a previous study the D-2 receptor antagonist, haloperidol (HAL), selectively potentiated mucus-induced yawning and chewing but attenuated fixed gaping; other oral behaviors were unaffected; HAL alone induced no dyskinesias and failed to modify mucus-induced decreases in tongue flicking, cage climbing and activity. As skin compounds have neuroleptic properties known to induce human and animal dyskinesias, we hypothesized that D-1 receptor antagonism may modulate the four of seven mucus-induced dyskinesias and the climbing not altered by HAL. We found that, like HAL, SCH 23390 (SCH) potentiated mucus-induced yawning, attenuated fixed gaping and had no effect on climbing. Unlike HAL's potentiation of chewing, SCH attenuated chewing and potentiated writhing tongue movements. SCH alone, like skin mucus, attenuated tongue flicking and activity but, given with mucus, SCH increased tongue flicking and activity to control levels. Compared to the HAL study, results suggest that mucus-induced yawning and fixed gaping are similarly modulated by both HAL and SCH, while these drugs have opposite effects on writhing tongue and chewing. SCH given alone or with frog mucus had unique effects on activity and normal tongue flicking.

Argiolas, A., M. R. Melis, et al. (1990). "Oxytocin-induced penile erection and yawning: role of calcium and prostaglandins." Pharmacol Biochem Behav 35(3): 601-5.
The effect of verapamil, flunarizine, nimodipine, nicardipine, and nifedipine, calcium channel inhibitors, and of indomethacin and aspirin, inhibitors of prostaglandin synthesis, on penile erection and yawning induced by oxytocin was studied in male rats. All calcium channel inhibitors given intraperitoneally (IP) 60 min before the intracerebroventricular (ICV) injection of oxytocin (30 ng) prevented in a dose-dependent manner oxytocin effect. Nimodipine and nicardipine were the most effective being active at doses between 5 and 20 mg/kg, while the others were active at doses higher than 15 mg/kg. Prevention of oxytocin effect was also seen after ICV injection of the above compounds. Unlike calcium channel inhibitors, indomethacin given either IP (10 and 50 mg/kg) or ICV (50 micrograms), or aspirin (100 mg/kg IP) were ineffective. Microinjection of calcium, but not of prostaglandin E2 and prostaglandin F2 alpha in the paraventricular nucleus of the hypothalamus, the brain area most sensitive for the induction of the above behavioral responses by oxytocin, induced a symptomatology similar to that induced by oxytocin. The present results suggest that calcium might be the second messenger which mediates the expression of penile erection and yawning induced by oxytocin.

Argiolas, A., M. R. Melis, et al. (1990). "Role of calcium in the expression of ACTH-induced stretching, yawning and penile erection." Brain Res Bull 24(6): 853-6.
The effect of omega-conotoxin GVIA, a potent and selective inhibitor of N-type calcium channels and of the organic calcium channel inhibitors nimodipine, verapamil and flunarizine, on stretching, yawning and penile erection induced by ACTH 1-24 was studied in male rats. omega-Conotoxin (1-10 ng ICV 15 min before ACTH, 10 micrograms ICV), but not carboxymethylated omega-conotoxin, induced a dose-dependent prevention of all ACTH effects. In contrast, organic calcium channel inhibitors (20 mg/kg IP 30-60 min before ACTH) failed to modify ACTH-induced stretching and yawning but induced a 25% decrease in the number of penile erection episodes induced by the peptide, and prevented, like ICV omega-conotoxin, oxytocin- and apomorphine-induced yawning and penile erection. When injected in the paraventricular nucleus of the hypothalamus, omega-conotoxin prevented the above behavioral responses induced by apomorphine and oxytocin but not by ACTH 1-24. The present results suggest that ACTH induces stretching, yawning and penile erection by mobilizing calcium through central omega-conotoxin-sensitive calcium channels in brain sites different from those sensitive to oxytocin and apomorphine.

Argiolas, A., M. R. Melis, et al. (1990). "Omega-conotoxin prevents apomorphine- and oxytocin-induced penile erection and yawning in male rats." Pharmacol Biochem Behav 37(2): 253-7.
The effect of the intracerebroventricular (ICV) administration of omega-conotoxin GVIA on penile erection and yawning induced by oxytocin or by the dopaminergic agonist apomorphine was studied in male rats. The peptide toxin, 1-10 ng given ICV 5 min before oxytocin (30 ng ICV) or apomorphine (80 micrograms/kg SC), but not its carboxymethylated (CM) derivative, prevented the above behavioral responses in a dose-dependent manner. Similarly, omega-conotoxin (5 ng) unilaterally injected in the paraventricular nucleus of the hypothalamus (PVN) prevented penile erection and yawning induced by the microinjection of oxytocin (10 ng) or apomorphine (50 ng) in the PVN. omega-Conotoxin injected in the PVN, but not in the preoptic area, prevented also penile erection and yawning induced by systemic apomorphine (80 micrograms/kg SC). ICV omega-conotoxin was unable to prevent stereotypy induced by apomorphine (500 micrograms/kg SC). The present results provide further evidence that calcium plays a major role in the expression of penile erection and yawning and that apomorphine and oxytocin induce these behavioral responses by mobilizing calcium through omega-conotoxin-sensitive (N-type) calcium channels.

(1990). "Hazard of yawning." Cmaj 142(6): 533.

Zarrindast, M. R. and M. Poursoltan (1989). "Interactions of drugs acting on central dopamine receptors and cholinoceptors on yawning responses in the rat induced by apomorphine, bromocriptine or physostigmine." Br J Pharmacol 96(4): 843-8.
1. Yawning was induced by subcutaneous (s.c.) injection of low doses of apomorphine to rats. This effect decreased with increasing doses of the drug. 2. Intraperitoneal (i.p.) pretreatment of animals with sulpiride (D2-receptor blocker) reduced the frequency of the yawns induced by apomorphine, while SCH 23390 (D1-receptor blocker, s.c.) pretreatment increased the small number of yawns which was induced by

higher doses of apomorphine. Administration of SCH 23390 alone to rats also produced a low degree of yawning. 3. Apomorphine-induced yawning was decreased in animals treated with SK&F 38393 (D1-agonist, i.p.), atropine (i.p.) or theophylline (i.p.). 4. Intraperitoneal injection of bromocriptine (D2-agonist) in rats also induced dose-dependent yawning. The effect was decreased in animals pretreated with sulpiride, while SCH 23390 pretreatment did not change bromocriptine-induced yawning significantly. Pretreatment of animals with SK&F 38393, atropine or theophylline reduced the number of yawns induced by bromocriptine. 5. Physostigmine (i.p.) but not neostigmine (i.p.) also induced yawning. The effect was antagonized by atropine or theophylline but not by sulpiride. Administration of SK&F 38393 decreased yawning induced by physostigmine. This inhibitory influence of SK&F 38393 was reduced by SCH 23390 in pretreated animals. Treatment of animals with SCH 23390 or bromocriptine increased the frequency of yawns induced by physostigmine. 6. It is concluded that D2-receptor activation elicits yawning through influence on cholinergic mechanisms, whereas D1-receptor stimulation decreases yawning behaviour by a negative influence on the cholinergic system.

Zarkovsky, A. M. and K. S. Cereska (1989). "Effect of the D1 receptor agonist SKF 38393 on some behavioural effects of apomorphine in rats." Naunyn Schmiedebergs Arch Pharmacol 339(4): 383-6.

The dopamine receptor agonist apomorphine in experiments on rats in low doses (0.025-0.2 mg/kg, s.c.) induced yawning which reflected a selective activation of presynaptic dopamine receptors. In high doses (0.25-1.0 mg/kg) apomorphine induced stereotyped sniffing and yawning in consequence of postsynaptic D2 receptor activation. Dopamine D1 receptor agonist SKF 38393 inhibited yawning induced by low doses of apomorphine. The inhibitory effect of SKF 38393 on apomorphine-induced yawning was attenuated by pretreatment with specific D1 receptor antagonist SCH 23390 [2-(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine-7-ol). On the other hand however, SKF 38393 potentiated sniffing induced by the high doses of apomorphine without affecting gnawing. These data indicate that D1 receptor activation modulates both pre- and postsynaptic effects of apomorphine in opposite directions.

Yamada, K., N. Matsuo, et al. (1989). "Dopamine receptor blocking action of a dibenzothiepin derivative isofloxythepin in rats." Clin Exp Pharmacol Physiol 16(2): 109-16.

1. Subcutaneous injection of isofloxythepin or haloperidol inhibited exploratory behaviour, methamphetamine (3 mg/kg)-induced hyperactivity and bromocriptine (15 mg/kg)-induced yawning, and also elicited catalepsy. 2. Isofloxythepin and haloperidol increased concentrations of dihydroxyphenylacetic acid in the striatum and elevated serum prolactin levels. 3. The results suggest that isofloxythepin, as well as haloperidol, blocks the action of the dopamine D2-receptors in the striatum, nucleus accumbens and pituitary.

Yamada, K., S. Matsumoto, et al. (1989). "Involvement of central beta-adrenoceptors in the regulation of yawning responses." Naunyn Schmiedebergs Arch Pharmacol 340(1): 26-30.

A behavioral study was performed in an attempt to understand the role of central beta-adrenoceptors in yawning in rats. Yawning was evoked by apomorphine and piribedil, mixed dopamine D1/D2-receptor agonists, but not by SK&F 38393 [1-phenyl-2,3,4,5-tetrahydro-(1H)-3-benzazepine-7,8-diol], a dopamine D1-receptor agonist. The apomorphine-induced yawning was increased by pindolol, propranolol, indenolol, alprenolol and bukumolol which block the central beta-adrenoceptors, but not by the peripheral beta-adrenoceptor antagonists, carteolol and atenolol. These beta-adrenoceptor antagonists given alone did not elicit yawning. Conversely, the yawning was inhibited by salbutamol, a beta-adrenoceptor agonist, without being affected by prazosin, an alpha-adrenoceptor antagonist. The combined administration of SK&F 38393 and the beta-adrenoceptor antagonists did not induce yawning. The yawning elicited by either apomorphine or piribedil in combination with pindolol was suppressed by spiperone and YM-09151-2 [cis-N-(1-benzyl-2-methyl-pyrrolidin-3-yl)-5- chloro-2-methoxy-4-methylamino-benzamide], dopamine D2-receptor antagonists, and scopolamine, a muscarinic receptor antagonist, but not by SCH 23390 [R(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3- benzazepine-7-ol], a dopamine D1-receptor antagonist. Physostigmine or pilocarpine induced yawning, which was also enhanced by pindolol and propranolol. This enhanced yawning was inhibited by scopolamine, but not by spiperone, YM-09151-2 and SCH 23390.(ABSTRACT TRUNCATED AT 250 WORDS)

Whyte, S. and P. Darveniza (1989). "A review of 20 cases of spastic dysphonia." Clin Exp Neurol 26: 177-81.

Twenty patients with the distinct nosological entity of adductor spastic dysphonia (SD) were seen at St Vincent's Hospital, Sydney over a 6-year period. Nine of these patients also experienced a tremulous voice associated with evidence of an essential tremor (ET) elsewhere, including head, trunk and limbs. The mean age of onset in patients with SD was 45 years and in those with SD with ET was 52 years. In 10 patients the onset was gradual, with the remaining 10 experiencing an abrupt onset, in 3 related to an upper respiratory tract infection and in 7 to psychosocial stress. Factors which frequently resulted in a worsening of speech included stress, public speaking, tiredness, strong emotions, upper respiratory tract infections and prolonged use of the voice. In patients with SD alone temporary relieving factors included spontaneous statements, use of a quiet voice, slow speech, high and low pitch, yawning, chewing, swallowing, laughing and on first waking in the morning. The response to therapy was variable. Two patients underwent recurrent laryngeal nerve sectioning.

Vergoni, A. V., R. Poggioli, et al. (1989). "Tolerance develops to the behavioural effects of ACTH-(1-24) during continuous i.c.v. infusion in rats, and is associated with increased hypothalamic levels of beta-endorphin." Neuropeptides 14(2): 93-8.

In rats, the continuous infusion of ACTH-(1-24) into a brain lateral ventricle (0.5 micrograms/h in the volume of 1.11 microliters, for 7 days) caused a significant inhibition of the subsequent behavioural response to the acute intracerebroventricular injection of the same peptide. Tolerance developed to all the most typical signs of the ACTH-induced behavioural syndrome (grooming, stretching, yawning, penile erection, inhibition of food intake), and was associated with a significant increase in the hypothalamic levels of beta-endorphin immunoreactivity.

Torre, E. and M. E. Celis (1989). "alpha-Melanotropin induced excessive grooming involves brain acetylcholine possible interaction in the ventral tegmental area." Acta Physiol Pharmacol Latinoam 39(1): 49-56.

Alpha-melanotropin (alpha-MSH) injected into the ventral tegmental area (VTA) or intraventricularly (icv) elicits excessive grooming. The icv infusion of the peptide also induces the stretching-yawning syndrome (SYS). The present study demonstrates that intra-peritoneal, icv or VTA administration of atropine, suppresses alpha-MSH-induced behavior elicited by i cv or VTA injections of the peptide. Experimental evidence is presented suggesting that alpha-MSH may act specifically on a cholinergic afferent to the VTA. The results appear to indicate that a neural target distinct from the dopamine system may be formerly activated by the peptide to elicit behavioral changes such as excessive grooming.

Timmerman, W., I. N. Rusk, et al. (1989). "The effects of the enantiomers of the dopamine agonist N-0437 on food consumption and yawning behaviour in rats." Eur J Pharmacol 174(1): 107-14.

The enantiomers of the potent and selective dopamine (DA) D-2 receptor agonist 2-(N-propyl-N-thienylethyl-amino)-5-hydroxytetralin, N-0437, were tested for their effects on palatable food consumption and yawning behaviour in rats. (-)-N-0437 (1.0 and 5.0 mumols/kg). This confirms the agonistic action of (-)-N-0437 on postsynaptic receptors as food consumption is considered to be related to stimulation of postsynaptic DA receptors. Yawning behaviour was stimulated by (-)-N-0437 (0.5 mumol/kg) and could be antagonized by the autoreceptor-selective antagonist (+)-UH 232 (25 mumols/kg), which suggests an agonistic action on DA autorecptors. (+)-N-0437 (5.0 and 10.0 mumols/kg) also reduced food consumption and the effect could be antagonized by YM 09151-2 (0.03 mumol/kg). The weaker effect of (+)-N-0437 on food intake in comparison to that induced by (-)-N-0437 can be explained if it assumed that (+)-N-0437 is a partial agonist. (+)-N-0437 did not induce yawning behaviour in rats, suggesting that autoreceptors mediating the release of DA may be involved in stimulating yawning by DA agonists.

Stoessl, A. J., M. T. Martin-Iverson, et al. (1989). "Effects of ageing on the behavioural responses to dopamine agonists: decreased yawning and locomotion, but increased stereotypy." Brain Res 495(1): 20-30.

Sensorimotor function and the behavioural responses to a range of doses of subcutaneous apomorphine were assessed in mature (6-8 months) and old (23-26 months) Sprague-Dawley rats of comparable weight. In addition, the locomotor activity response of 12-month-old and 24-month-old rats to continuous infusions (14 days by osmotic minipump) of a selective dopamine D2 agonist. (+)-4-propyl-9-hydroxynaphthoxazine (PHNO, 10 micrograms/h) was investigated. Measures of spontaneous locomotor activity and motor coordination revealed impairments in the aged animals. Low doses of apomorphine (10-50 micrograms/kg), which preferentially activate dopamine autoreceptors, induced yawning, chewing mouth movements and penile grooming. The frequency of yawning and duration of penile grooming were significantly decreased in the old animals. In contrast, 200 micrograms/kg of apomorphine induced stereotyped sniffing and licking or gnawing, and these responses were significantly increased in the aged animals. There was a 25% decrease in striatal dopamine levels in the aged animals in this experiment. PHNO increased the amplitude of the circadian rhythms in locomotor activity exhibited by mature rats, and daytime tolerance to the stimulant effects of PHNO was reversed by stress in these animals. Both of these effects were attenuated in the aged rats. These findings suggest that (1) the dopamine receptors mediating yawning and stereotypy have different anatomical locations (2) ageing is associated with decreased responsiveness to stimulation of dopamine autoreceptors, consequent upon the loss of dopaminergic nerve terminals, and (3) while the functional response to selective stimulation of postsynaptic D2 receptors decreases with age, the postsynaptic response to a mixed D1/D2 agonist increases.

Starec, M., D. Waitzova, et al. (1989). "Effect of RG-tannin on yawning behaviour induced by apomorphine or physostigmine in rats." Act Nerv Super (Praha) 31(1): 71-2.

Stahle, L. and U. Ungerstedt (1989). "Discrepancy in the time course of EMD 23448 induced yawning and reduction of extracellular dopamine." Psychopharmacology (Berl) 97(2): 275-6.

Stahle, L. and U. Ungerstedt (1989). "Yawning and suppression of exploration in amphetamine-treated rats, incompatibility with the autoreceptor hypothesis." Psychopharmacology (Berl) 97(4): 553-60.

The hypothesis that yawning and suppression of exploration, induced by low doses of dopamine agonists, are mediated by stimulation of dopamine autoreceptors was tested by studying the influence of amphetamine on these behavioural models and on extracellular levels of

dopamine sampled by microdialysis. Behaviour was measured in a holeboard apparatus. A low dose of amphetamine (0.2 mg/kg) caused slight activation of habituated rats. The same dose of amphetamine completely counteracted the decrease in extracellular dopamine levels caused by pergolide (0.02 mg/kg) and, instead, elevated the dopamine levels to 300% above baseline. The same or higher doses of amphetamine (0.5-1.0 mg/kg) did not completely antagonise suppression of exploration or yawning induced by apomorphine (0.05 mg/kg) or pergolide (0.02 mg/kg). The results suggest that both yawning and suppression of exploration induced by low doses of dopamine agonists are not mediated by dopamine autoreceptors, since these behaviours could be elicited when the extracellular levels of dopamine were elevated above baseline. The alternative hypothesis that these behaviours are mediated by sensitive post-synaptic receptors is suggested. It was also found that combined treatment with SCH 23390 (0.05 mg/kg) and amphetamine (2 mg/kg) induced yawning, which further supports the new hypothesis.

Spina, L., R. Longoni, et al. (1989). "SKF 38393 potentiates yawning induced by LY 171555: further evidence against the autoreceptor hypothesis of yawning." Psychopharmacology (Berl) 98(4): 567-8.

The effect of concurrent D-1 receptor stimulation by SKF 38393 on the expression of yawning elicited by D-2 receptor stimulation with LY 171555 was studied in the rat. A low dose of SKF 38393 (2.5 mg/kg SC), while failed to elicit yawning, potentiated the effectiveness of LY 171555 in eliciting yawning at all the doses tested (12.5, 25 and 50 micrograms/kg SC) and this effect was abolished by SCH 23390 (0.012 mg/kg SC). The results indicate that in analogy with typical post-synaptic dopaminergic effects (hypermotility-stereotypy), yawning elicited by a D-2 agonist is facilitated by concurrent stimulation of D-1 receptors and therefore is consistent with previous evidence that yawning in response to a D-2 agonist is not mediated by autoreceptors.

Oman, R. E., S. J. Sullivan, et al. (1989). "Yawning: a possible confounding variable in EMG biofeedback studies." Biofeedback Self Regul 14 (4): 339-46.

An elderly hemiplegic patient participating in an EMG biofeedback training program was observed to produce a synergistic flexion movement of the plegic (determined by functional evaluations) upper limb while yawning. In the course of the training sessions the electrical activity of the anterior deltoid (the target muscle) was recorded during yawning. These peak EMG values were greatly facilitated in comparison with the session mean peak values obtained during an attempted maximum voluntary isometric contraction (shoulder flexion) of the same limb (e.g., Trial 1: 85.00 vs. 4.33 microV). The possibility of yawning as a confounding variable in EMG biofeedback studies is presented and discussed.

Modell, J. G. (1989). "Repeated observations of yawning, clitoral engorgement, and orgasm associated with fluoxetine administration." J Clin Psychopharmacol 9(1): 63-5.

Melis, M. R., A. Argiolas, et al. (1989). "Evidence that apomorphine induces penile erection and yawning by releasing oxytocin in the central nervous system." Eur J Pharmacol 164(3): 565-70.

Oxytocin (10 and 30 ng) injected into a lateral ventricle (i.c.v.) or the dopamine agonist apomorphine (40 and 80 micrograms/kg) injected subcutaneously induced repeated episodes of penile erection and yawning in male rats. The concomitant administration of the two substances did not produce any further increase in the number of penile erection and yawning episodes. Penile erection and yawning induced by either oxytocin or apomorphine were antagonized in a dose-dependent manner by i.c.v. pretreatment with the oxytocin antagonists [d(CH2) 5Tyr(Me)-Orn8]vasotocin, [Pen1,Phe(Me)2,Thr4,Orn8]oxytocin and [d(CH2)5Tyr(Me)-Arg8]vasopressin, with a rank order of potency that follows their antioxytocic activity. (i.e. [d(CH2)5Tyr(Me)-Orn8]vasotocin congruent to [Pen1,Phe(Me)2,Thr4,Orn8]-oxytocin greater than [d(CH2)5Tyr (Me)-Arg8]vasopressin). The results suggest that apomorphine induces penile erection and yawning by releasing oxytocin in the central nervous system.

Melis, M. R., A. Argiolas, et al. (1989). "Oxytocin-induced motor disturbances: relationship with penile erection and yawning." Pharmacol Biochem Behav 34(3): 673-5.

The intracerebroventricular (ICV) injection of oxytocin at doses between 5 and 100 ng induced repeated episodes of penile erection and yawning, while at doses between 100 ng and 10 micrograms it induced motor disturbances often culminating in barrel rotation in rats. The intensity of motor disturbances was inversely correlated to the number of yawning and penile erection episodes. Pretreatment with the dopaminergic agonist apomorphine (80 and 240 micrograms/kg SC) failed to modify the incidence of motor disturbance induced by high doses of oxytocin, but markedly reduced the intensity of the symptomatology in a dose-dependent manner. The present results suggest that high doses of oxytocin induce motor disturbances which mask penile erection and yawning, and that brain dopaminergic systems have a protective role against this symptomatology.

Matsumoto, S., K. Yamada, et al. (1989). "Potentiation by serotonergic inhibition of yawning induced by dopamine receptor agonists in rats." Pharmacol Biochem Behav 32(3): 815-8.

Low doses of the dopamine D2-receptor agonist, B-HT 920 (25 micrograms/kg, SC), and the dopamine D1/D2-receptor agonists, apomorphine (50 micrograms/kg, SC) and piribedil (1 mg/kg, SC), evoked yawning. However, the dopamine D1-receptor agonist, SK&F 38393 (2 mg/kg, SC), failed to induce yawning. The yawning responses induced by B-HT 920, apomorphine or piribedil were markedly increased without eliciting stereotypy by pretreatment with reserpine (5 mg/kg, IP, 24 hr). These yawning responses were also enhanced by p-chlorophenylalanine (PCPA) (300 mg/kg, IP, 72 hr), but not by alpha-methyl-p-tyrosine (300 mg/kg, IP, 6 hr). The yawning induced by B-HT 920 given alone and in combination with reserpine or PCPA was inhibited by spiperone (0.5 mg/kg, IP) or scopolamine (0.5 mg/kg, IP), but not by SCH 23390 (0.5 mg/kg, IP). The present results suggest that yawning is evoked by stimulation of dopamine D2-receptors having a high affinity and consequent muscarinic activation, and that the yawning induced by dopamine receptor agonists is potentiated by decreases in serotonergic neuron activity.

Matsumoto, S., K. Yamada, et al. (1989). "Occurrence of yawning and decrease of prolactin levels via stimulation of dopamine D2-receptors after administration of SND 919 in rats." Naunyn Schmiedebergs Arch Pharmacol 340(1): 21-5.

SND 919 [S)-2-amino-4,5,6,7-tetrahydro-6-propylamino-benzothiazole) is expected to have a potent and selective dopamine D2-receptor agonistic activity. From this information, the present study was performed to investigate effects of SND 919 on yawning behavior and prolactin secretion in rats. Subcutaneous injections of SND 919 (25-500 micrograms/kg, s.c.) elicited yawning responses. Its dose-response curve was bell-shaped with maximal effects at a dose of 100 micrograms/kg. Yawning behavior was also evoked by the putative dopamine autoreceptor agonists, talipexole (6-allyl-2-amino-5,6,7,8-tetrahydro-4H-thiazolo [4,5-d]azepine) (B-HT 920) (5-100 micrograms/kg, s.c.) and (+)-3-PPP ((+)-3-(3-hydroxyphenyl)-N-n-propylpiperidine) (5-15 mg/kg, s.c.). The yawning induced by SND 919 (100 micrograms/kg, s.c.) as well as talipexole (25 micrograms/kg, s.c.) was inhibited by pretreatment with dopamine D2-receptor antagonists such as spiperone (0.5 mg/kg, i.p.) and YM-09151-2 (cis-N-(1-benzyl-2-methylpyrrolidin-3-yl)-5-chloro-2-methoxy-4-met hylamino- benzamide) (0.1 mg/kg, i.p.), or the muscarinic receptor antagonist, scopolamine (0.5 mg/kg, i.p.). However, the yawning was not affected by the dopamine D1-receptor antagonist, SCH 23390 (R(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine-7-o l) (0.5 mg/kg, i.p.). Stereotypy such as licking and biting was not observed following the administration of SND 919, talipexole and (+)-3-PPP. Administration of SND 919, talipexole or (+)-3-PPP in respective yawn-inducing doses caused a reduction in both the basal prolactin levels and the alpha-methyl-p-tyrosine-induced hyperprolactinemia.(ABSTRACT TRUNCATED AT 250 WORDS)

Ljungberg, T., L. Stahle, et al. (1989). "Effects of repeated administration of low doses of apomorphine in three behavioural models in the rat." J Neural Transm Park Dis Dement Sect 1(3): 165-75.

A low dose of the dopamine (DA) receptor agonist apomorphine (APO 0.05 mg/kg) was given repetitively and the effects were tested in three different behavioural models: reduction of spontaneous locomotion, induction of yawning and decrease in water intake in water-deprived animals. The APO-induced suppression of exploration and decrease in water intake were not affected by a previous injection of APO given 1 or 3 hours before the test dose of APO. There was a small, but significant, decrease in the induction of yawning by a previous dose of APO given 1 hour or 30 min before the test dose. However, pretreatment with APO 3 hours before the test dose did not diminish the yawning response. It is suggested that the dopaminergic mechanisms mediating APO induced yawning are different from those mediating decrease in water intake and suppression of exploration. The results are also discussed in relation to the proposed efficiency of low doses of DA agonists in the treatment of various neurological and psychiatric disorders.

Ljungberg, T. and L. Stahle (1989). "The reduction of water intake in rats caused by a low dose of apomorphine is unaltered by alpha-methyl-p-tyrosine: are autoreceptors not involved?" J Neural Transm Gen Sect 78(3): 265-9.

Low doses of the dopamine (DA) agonist apomorphine (APO) induces a behavioural syndrome characterized by reduced spontaneous activity, reduced food and water intake and induction of yawning and penile erections. Traditionally these effects of APO have been considered to be caused by a preferential stimulation of DA autoreceptors, causing a decreased amount of transmitter at the postsynaptic receptors. If this is so, it could be hypothesized that 1) the same behavioural effects should be obtained if DA transmission is decreased by some other means, for example by synthesis inhibition, and that 2) the response to APO should be altered if DA transmission is already lowered. It was found that high doses of alpha-methyl-p-tyrosine (alpha-MPT; 50-200 mg/kg) did not reduce water intake in thirsty rats, which low doses of APO do. It was further found that pretreatment with alpha-MPT did not alter the response to APO. These results are difficult to reconcile with the DA autoreceptor hypothesis claiming that behavioural effects of low doses of APO are caused by a decreased release of DA. An alternative interpretation is that low doses of APO stimulates a certain population of sensitive postsynaptic D-2 receptors.

Lal, S., Y. Tesfaye, et al. (1989). "Apomorphine: clinical studies on erectile impotence and yawning." Prog Neuropsychopharmacol Biol Psychiatry 13(3-4): 329-39.

1. The erectile response to the short-acting dopamine (DA) receptor agonist, apomorphine (Apo) HCl (0.25, 0.5, 0.75 and 1.0 mg sc), and placebo was evaluated in 28 impotent patients and penile circumference monitored using a mercury strain gauge and strip chart recording. 2. A full erection (increment in penile circumference greater than 2 cm and lasting at least one minute) occurred in 17 patients with Apo; no erection developed after placebo. An erection occurred in 6/8 patients with impaired glucose tolerance, 2/6 patients with diabetes

mellitus and in both patients on lithium. 3. Nine patients who responded to Apo were treated in an open trial with bromocriptine; 6 reported improvement in potency. 4. Impairment in DA function may play a role in idiopathic impotence and in impotence associated with impaired glucose tolerance and diabetes mellitus. 5. An erectile response to Apo may predict therapeutic response to bromocriptine or other long acting dopaminergic agents. 6. Lithium, which inhibits DA-sensitive adenylate cyclase, does not prevent Apo-induced erections. This provides further support indicating that Apo induces erections by an effect on D2 receptors. 7. The yawning response to placebo and four doses of Apo HC1 (3.5, 5.0, 7.0, and 10.5 ug/kg sc) was evaluated in five normal men using a polygraphic technique. The yawning response was also assessed in normal young (less than 30 yrs; N = 16) and elderly (greater than 60 yrs; N = 12) volunteers. 8. Under experimental conditions of study, placebo induced spontaneous yawning. This was antagonized by 3.5 and 5.0 ug/kg Apo HC1 but increased by 7.0 ug/kg Apo HC1. These observations are compatible with the view that Apo HC1 in doses of 3.5-5.0 ug/kg stimulates presynaptic DA receptors whereas 7.0 ug/kg stimulates postsynaptic DA receptors. 9. Spontaneous and Apo-induced yawning were significantly decreased in the elderly which suggests that D2 receptor function declines with normal aging.

Koyama, S. (1989). "[Partial oxygen tension of middle ear cavity in a normobaric environment]." Nippon Jibiinkoka Gakkai Kaiho 92(1): 68-77.
The present theory of eustachian tube function and middle ear ventilation posits that oxygen absorbed by the middle ear mucosa causes negative middle ear pressure which is relieved by periodic opening of the eustachian tube during swallowing and yawning. Measured by a PO2 sensor (Clark type) inserted into the middle ear cavity of normal adults through the eustachian tube, the partial oxygen pressure of the tympanic cavity was found 53.7 +/- 6.5 Torr (N:22). It was about one-third of ambient pressure (about 150 Torr), and showed no change when the eustachian tube was opened by swallowing. Our second study measured the effect of alterations in the systemic arterial blood oxygenation on middle ear gas exchange in 23 guinea pigs ventilated using 21% (room air), 50%, 70% and 100% oxygen at constant carbon dioxide blood gas tension. Partial oxygen tension (PO2) of middle ear cavity was measured by inserting a PO2 sensor into the tympanic bulla through a bore hole. The following results were obtained: (1) PO2 of the middle ear cavity was 39.3 +/- 2.2 Torr at room air, 42.2 +/- 0.84 Torr at 50%, 46.6 +/- 1.1 Torr at 70% and 54.5 +/- 3.7 Torr at 100% oxygen breathing. (2) There was a significant correlation between PO2 of the middle ear cavity and systemic arterial hyperoxygenation noted. Y = 30.79 + 0.056.X (r = 0.9440) (3) The rate of oxygen diffusion in the middle ear cavity was 2.665 x 10(-5) ml/min/cm2 and the rate of oxygen absorption in the middle ear space was 2.874 x 10(-5) ml/min/cm2. No significant difference between the rate of diffusion and that of absorption of oxygen in the middle ear cavity was noted. In our third study, electron microscopy shows that the submucosal capillaries of the human mastoid cells are structures which facilitate the intra- and extravascular transport of substances. It is known from these results that tympanic cavity pressure is kept equal to ambient pressure, or slightly higher to atmospheric pressure, by the respiratory function of the middle ear and mastoid cells so that outflow of air from the tympanic cavity to the pharyngeal orifice occurs during the ventilation of the eustachian tube at ambient pressure and inflow of air from the pharynx to the tympanic cavity is prevented in the absence of environmental pressure changes. The middle ear cavity has respiratory function, and in particular, such function of the mastoid cavity, which is larger in volume than the tympanic cavity, plays a significant role.(ABSTRACT TRUNCATED AT 400 WORDS)

Klein, D. F. (1989). "Repeated observations of yawning, clitoral engorgement, and orgasm associated with fluoxetine administration." J Clin Psychopharmacol 9(5): 384.

Dourish, C. T., E. N. Herbert, et al. (1989). "Blockade of apomorphine-induced yawning in rats by the dopamine autoreceptor antagonist (+)-AJ 76." Neuropharmacology 28(12): 1423-5.
The effects of the putative, selective dopamine autoreceptor antagonist (+)-AJ 76 on yawning, penile grooming and mouth movements induced by small doses of apomorphine in male rats were examined. Yawning induced by 0.05mg/kg apomorphine was dose dependently blocked by (+)-AJ-76, significant decreases being observed at 0.86 and 3.5mg/kg of the drug. A dose of 0.86mg/kg (+)-AJ 76 caused a two fold shift to the right of the apomorphine dose response curve for yawning. In contrast, (+)-AJ 76 had no effect on penile grooming and vacuous mouth movements induced by small doses of apomorphine. This pattern of results is similar to that observed after bilateral 6-hydroxydopamine-induced lesions of the substantia nigra which also blocked apomorphine-induced yawning but spared penile grooming and mouth movements. Previous studies have suggested that (+)-AJ 76 is a selective dopamine autoreceptor antagonist that has little or no effect on behaviour mediated by post-synaptic dopamine receptors. Therefore, these data provide further support for the hypothesis that apomorphine-induced yawning is mediated by dopamine autoreceptors.

Doger, E., R. Urba-Holmgren, et al. (1989). "GABAergic modulation of yawning behavior." Pharmacol Biochem Behav 34(2): 237-40.
The hypothetical modulation by GABAergic neurons of yawning behavior in the rat was explored with GABA-active drugs. Gamma-acetylenic-GABA, a specific inhibitor of GABA-T, increases yawning frequency when injected at a dose of 7 mg/kg. Baclofen, a GABAB agonist (3 mg/kg), inhibits yawning completely; GABA antagonists, bicuculline and picrotoxin, at subconvulsant doses, also decrease yawning. All drugs were injected intraperitoneally with the exception of apomorphine, which was injected subcutaneously. It is suggested that GABAB receptors play a role in yawning behavior by modulating ACh release, and that GABAA receptors may modify yawning frequency by modulating inhibitory influences on ACh neurons.

Crosby, L. and L. C. Parsons (1989). "Clinical neurologic assessment tool: development and testing of an instrument to index neurologic status." Heart Lung 18(2): 121-9.
The clinical neurologic assessment tool (CNA) is a 21-item instrument assessing response to verbal and tactile stimulation, ability to follow commands, muscle tone, body position, movement, chewing, and yawning in the patient with head trauma. The CNA was developed to detect subtle changes in the patients' neurologic status that may indicate transitions in the comatose state. The CNA has been extensively pilot tested. Reliability determined by using Cronbach's alpha revealed an internal consistency of 0.96. Concurrent validity testing with the Glasgow Coma Scale indicated a strong positive correlation, r = 0.94. Construct validity was assessed with factor analysis using 0.50 for a loading criterion. Three factors were demonstrated: general level of consciousness, muscle tone and resistance, and chewing or yawning. Discriminant function analysis revealed that the CNA scores correctly classified 95.1% of the patient observations into their respective Glasgow Coma Scale categories. The CNA is reliable, valid, convenient, and easily scored and captures the subtle changes in the patient with head trauma.

Cooper, S. J., I. N. Rusk, et al. (1989). "Yawning induced by the selective dopamine D2 agonist N-0437 is blocked by the selective dopamine autoreceptor antagonist (+)-UH 232." Physiol Behav 45(6): 1263-6.
Yawning and stretching responses were elicited in rats by a small dose (0.3 mg/kg) of the highly selective dopamine D2 agonist, N-0437. The responses were blocked by the highly selective dopamine autoreceptor antagonist, (+)-UH 232 (3.0 mg/kg), but not by raclopride at a dose which selectively blocks postsynaptic D2 receptors. The results strongly confirm the view that yawning and stretching are behavioral responses elicited by stimulation of presynaptic D2 receptors.

Bourson, A., A. J. Gower, et al. (1989). "The effects of dihydropyridine compounds in behavioural tests of dopaminergic activity." Br J Pharmacol 98(4): 1312-8.
1. The effects of the dihydropyridine calcium channel blocker nifedipine and the activator Bay K 8644 were investigated in different behavioural tests involving dopaminergic systems. These were the discriminative stimulus induced by amphetamine, rotational behaviour in rats with unilateral 6-hydroxydopamine (6-OHDA) lesions and apomorphine-induced yawning in rats. 2. The yawning induced by apomorphine (40 micrograms kg-1 s.c.) was significantly potentiated by nifedipine (5-10 mgkg-1 i.p.). Bay K 8644 (0.05-0.5 mgkg-1 i.p.) dose-dependently inhibited yawning induced by apomorphine (80 micrograms kg-1 s.c.) and, at 0.4 mgkg-1, inhibited the nifedipine potentiation of apomorphine-induced yawning. In contrast to their effects on apomorphine-induced yawning, nifedipine and Bay K 8644 had no effect on apomorphine-induced penile erection. 3. Bay K 8644 (0.06-0.5 mgkg-1 i.p.) and nifedipine (5-20 mgkg-1 i.p.) had no dose-related effect on the discrimination performance of rats trained to discriminate amphetamine from saline. However, nifedipine dose-dependently reduced the response rate of amphetamine-treated rats. Bay K 8644 had no effect on this measure except at high doses that also caused disruption. 4. Neither nifedipine (5-10 mgkg-1 i.p.) nor Bay K 8644 (0.06-0.5 mgkg-1 i.p.) affected the turning behaviour induced by amphetamine (1 mgkg-1 i.p.) in rats with unilateral 6-OHDA lesion of the medial forebrain bundle, and did not induce turning themselves. 5. As the dihydropyridine compounds affected apomorphine-induced yawning but not penile erection, and did not affect amphetamine-induced rotation or drug discrimination, it seems unlikely that they are affecting dopamine release in vivo.

Bourson, A. and P. C. Moser (1989). "The effect of pre- and postoperative procedures on physostigmine- and apomorphine-induced yawning in rats." Pharmacol Biochem Behav 34(4): 915-7.
Previous experiments have shown that the potentiation of physostigmine-induced yawning by nifedipine is abolished by sham-lesioning procedures in rats, whereas the nifedipine potentiation of apomorphine-induced yawning is unaffected. The present results demonstrate that either the presurgical drug treatment (desmethylimipramine and pentobarbital) or 7 days isolation was alone sufficient to reduce the yawning response to physostigmine and abolish its potentiation by nifedipine. The sham-lesioned rats responded normally to a combination of apomorphine and nifedipine. These results suggest that the stress associated with standard operative procedures can differentially affect drug interactions with yawning induced by either apomorphine or physostigmine and that caution should be exercised when interpreting results from animals that have been similarly stressed.

Berzin, F. (1989). "Occipitofrontalis muscle: functional analysis revealed by electromyography." Electromyogr Clin Neurophysiol 29(6): 355-8.
The occipital and frontal bellies of the right occipitofrontalis muscle were studied electromyographically in thirty volunteers in various movements, using a special steel electrode (80 microns diameter). The occipital and frontal bellies have independent actions despite the galea aponeurotica. The frontal belly initially raises the homolateral eyebrow, followed by a displacement of the galea aponeurotica, drawing the scalp forward; therefore it is active in the formation of the transversal wrinkling in the forehead. The occipital belly eventually can be active during raising of the eyebrown, nevertheless it does not interfere with the action of the frontal belly. The occipital belly alone is responsible for drawing back the galea aponeurotica. The occipital belly is also active during smiling and yawning,

and can be active during the movements of the auricula.

Barthalmus, G. T. (1989). "Neuroleptic modulation of oral dyskinesias induced in snakes by Xenopus skin mucus." Pharmacol Biochem Behav 34 (1): 95-9.
The skin mucus of the African clawed frog Xenopus laevis promotes escape from the American water snake Nerodia sipedon by inducing oral dyskinesias. As Xenopus mucus contains peptides and indoleamines with known neuroleptic properties, and because neuroleptics are the chief cause of drug-induced orofacial dyskinesias in humans, the hypothesis was tested that the neuroleptic haloperidol (HAL) would induce oral dyskinesias when given alone and would potentiate dyskinesias in Nerodia if injected prior to oral application of Xenopus mucus. Mucus alone induced yawning, gaping, fixed yawning, fixed gaping, writhing tongue movements, gular and chewing movements, and climbing behavior, but attenuated locomotor activity. HAL given IP alone at 0.05 and 0.5 microgram/g was ineffective. However, HAL greatly potentiated mucus-induced yawning but attenuated the fixed gaping seen when only mucus was applied. Data support the hypothesis that Xenopus skin mucus has neuroleptic properties and that Xenopus' antipredatory defense is in part related to chemical induction of orofacial and climbing behavior in snake predators.

Barros, H. M., S. Braz, et al. (1989). "Behavioural manifestations elicited by apomorphine, influence of the route of administration." Pharmacology 38(5): 335-40.
In order to investigate the influence of the route of administration on behavioural effects induced by apomorphine (APO), 6 increasing doses were administered by intraperitoneal and by subcutaneous route to male Wistar rats. Dose-response curves for stereotypy, rearing, sedation, grooming, yawning and penile erection were calculated. The occurrence of stereotypy precluded other behavioural manifestations. APO was more potent when administered subcutaneously, with potency ratios between the routes of 10.4 for stereotypy, 4.6 for sedation, 6.8 for grooming, 11.8 for yawning and 7.5 for penile erection.

Askenasy, J. J. (1989). "Is yawning an arousal defense reflex?" J Psychol 123(6): 609-21.
Despite the fact that yawning is a reality of everyday life, its study is not included in the curriculum of medical schools, and most medical textbooks barely mention its existence. Two factors may help to explain this puzzling situation: (a) yawning's borderline position between psychology and neurology, and (b) researchers' lack of understanding as to why people yawn. After review of the literature and personal observation, it is concluded that yawning is a complex arousal defense reflex located in the reticular brainstem with a peripheral and central arche, whose aim is to reverse brain hypoxia. Yawning occurs with loss of interest (boredom) and may or may not be associated with fatigue. By reversing drowsiness, yawning avoids a decreased concentration capacity resulting from borderline hypoxia. It is hoped that this article will stimulate further research on the phenomenon.

Argiolas, A., M. R. Melis, et al. (1989). "Oxytocin-induced penile erection and yawning in male rats: effect of neonatal monosodium glutamate and hypophysectomy." Psychopharmacology (Berl) 97(3): 383-7.
Penile erection and yawning induced by the intracerebroventricular (ICV) injection of oxytocin (10-1000 ng) was studied in hypophysectomized rats and in rats neonatally treated with monosodium glutamate (MSG), a treatment that depletes hypothalamic opiomelanocorticotropin-derived peptides without altering their pituitary and circulating concentration. Oxytocin effect was strongly reduced by hypophysectomy, but not by neonatal MSG. Testosterone replacement (50 micrograms/kg/day for 23 days) partially reversed the effect of hypophysectomy on penile erection, but not on yawning. The present results suggest that oxytocin does not induce penile erection and yawning by releasing an ACTH-derived peptide from hypothalamic opiomelanotropinergic neurons, and that the pituitary gland exerts a permissive role on the expression of the above behavioural responses induced by oxytocin.

Argiolas, A., M. R. Melis, et al. (1989). "Penile erection and yawning induced by oxytocin and related peptides: structure-activity relationship." Peptides 10(3): 559-63.
The potency of several oxytocin-related peptides in inducing penile erection and yawning after injection into a lateral ventricle of male rats was compared. Substitution of two amino acids in the oxytocin molecule or deletion of the C-terminal glycinamide as in des-GlyNH2-oxytocin [oxytocin(1-8)] reduced oxytocin potency in inducing both effects, the rank order being: oxytocin greater than [Thr4,Gly7]-oxytocin congruent to isotocin [(Ser4,Ile8]-oxytocin) greater than vasopressin [(Phe3,Arg8]-oxytocin) greater than des-GlyNH2-oxytocin. Oxytocin's ability to induce penile erection and yawning was abolished by permanent opening of the disulfide bridge by reduction and carboxymethylation. Oxytocin(1-6) and oxytocin(7-9) were also inactive. Penile erection and yawning induced by oxytocin-related peptides were antagonized in a dose-dependent manner by nonapeptide antagonists with a rank order of potency that follows their antioxytocic activity (d[(CH2)5Tyr(Me)Orn8]-vasotocin congruent to [Pen1,Phe(Me)2,Thr4,Orn8]-oxytocin greater than d[(CH2)5Tyr(Me)Arg8]-vasopression). Carboxymethylated oxytocin, oxytocin(1-6), and oxytocin(7-9) were devoid of antagonistic activity. The present results suggest that central oxytocin receptors mediating the expression of penile erection and yawning are structurally related to those present in the uterus and in the mammary gland.

Argiolas, A., M. R. Melis, et al. (1989). "Calcium channel inhibitors prevent apomorphine- and oxytocin-induced penile erection and yawning in male rats." Eur J Pharmacol 166(3): 515-8.
The effect of i.p. injection of the calcium channel inhibitors, verapamil, flunarizine, nifedipine, nimodipine and nicardipine, on penile erection and yawning induced by the dopamine agonist, apomorphine, or by oxytocin was studied in male rats. The five compounds antagonized in a dose-dependent manner the behavioral responses induced either by apomorphine or oxytocin. Nimodipine and nicardipine were found to be the most potent, being active in doses between 5 and 20 mg/kg, while nifedipine, verapamil and flunarizine were active in doses higher than 15 mg/kg. The results suggest that calcium is involved in the expression of the above-mentioned behavioural responses.

Wimalaratna, H. S. and R. Capildeo (1988). "Is yawning a brainstem phenomenon?" Lancet 1(8580): 300.

Wilson, R. F., M. L. Marcus, et al. (1988). "Pulmonary inflation reflex: its lack of physiological significance in coronary circulation of humans." Am J Physiol 255(4 Pt 2): H866-71.
In awake dogs, voluntary deep inspiration results in a marked, reflex-mediated increase in coronary blood flow. To study this reflex in humans, we subselectively measured coronary blood flow velocity (CBFV) with a 3-F coronary Doppler catheter in 12 subjects with angiographically normal coronary arteries. In each subject, intracoronary papaverine increased CBFV to 4.8 +/- 0.2 X resting CBFV and reduced coronary resistance to 0.20 +/- 0.01 X resting coronary resistance, demonstrating normal vasodilator reserve in the vessel under study. Valsalva maneuver reduced CBFV to 0.67 +/- 0.09 X resting CBFV and increased coronary resistance to 1.37 +/- 0.20 X resting coronary resistance (P less than 0.05 vs. control). Maximum voluntary inspiration, however, did not significantly change CBFV (peak response 1.03 +/- 0.05 X resting CBFV) or coronary resistance (0.96 +/- 0.04 X resting). To determine whether augmentation of resting alpha-adrenergic tone would potentiate the reflex, eight patients performed a sustained 33% maximal handgrip for 2 min. Maximal deep inspiration during handgrip failed to result in any significant change in CBFV or coronary resistance. These studies demonstrate that the canine pulmonary inflation reflex has little or no physiological significance in the coronary circulation of conscious humans. Additionally, these data suggest that the magnitude of reflex control of the coronary circulation may vary considerably between dogs and humans.

Weller, M. P. (1988). "Yawning." Lancet 1(8591): 950.

Ushijima, I., Y. Mizuki, et al. (1988). "The mode of action of bromocriptine following pretreatment with reserpine and alpha-methyl-p-tyrosine in rats." Psychopharmacology (Berl) 95(1): 29-33.
The ability of bromocriptine (BRC), a selective dopamine D-2 receptor agonist, to induce yawning responses was studied in rats pretreated with reserpine and alpha-methyl-p-tyrosine (alpha-MPT). BRC (1 20 mg/kg IP) evoked yawning responses, which were pronounced at 2.5 mg/kg and characterized by the head moving downward. Higher doses of BRC (5 20 mg/kg) dose-dependently delayed the onset and peak time of yawning. A low dose of the selective D-1 dopamine receptor agonist SK&F38393 did not induce yawning but enhanced the BRC-induced response. Pretreatment with reserpine (1 and 5 mg/kg SC), alpha-MPT (100 and 300 mg/kg IP) and reserpine (1 mg/kg) plus alpha-MPT (100 mg/kg) was able to significantly reduce BRC-induced yawning. The inhibitory effects were prevented by a low dose of SK&F38393 (0.5 mg/kg IP). In particular, combined treatment with reserpine (5 mg/kg) and BRC (10 and 20 mg/kg) elicited upright fighting and jumping behaviors which were inhibited by haloperidol (1 mg/kg IP), a non-selective D-1 and D-2 receptor antagonist, SCH23390 (0.05 mg/kg SC). a selective D-1 receptor antagonist, or sulpiride (20 mg/kg IP), a potent D-2 receptor antagonist, and were potentiated by SK&F38393 (0.5 mg/kg). SCH23390 (0.05 mg/kg) decreased BRC-induced yawning and the apomorphine (low doses)-induced potentiation of BRC yawning, and prevented the apomorphine (high doses)-induced reduction of BRC yawning. SCH23390 also inhibited apomorphine-induced stereotypy and BRC-induced potentiation of apomorphine stereotypy.(ABSTRACT TRUNCATED AT 250 WORDS)

Ushijima, I., Y. Mizuki, et al. (1988). "Multifocal sites of action involved in dopaminergic-cholinergic neuronal interactions in yawning." Psychopharmacology (Berl) 95(1): 34-7.
Bromocriptine (BRC), a dopamine D-2 receptor agonist, physostigmine, an anticholinesterase agent and pilocarpine, a muscarinic cholinergic receptor agonist, produced yawning in rats, with the most effective doses being 2.5 mg/kg, 0.2 mg/kg and 4 mg/kg, respectively. BRC-induced yawning was inhibited by high doses of SK&F38393 (5 and 10 mg/kg), a selective D-1 receptor agonist. BRC or SK&F38393 alone did not induced stereotyped behaviors. However, when BRC was administered after SK&F38393 (5.0 and 10 mg/kg), stereotyped behaviors occurred; i.e., mainly sniffing at 2.5 and 5.0 mg/kg BRC, and mainly licking and biting 10 and 20 mg/kg BRC. A high dose of apomorphine (4 mg/kg IP) completely inhibited physostigmine-induced yawning (physostigmine yawning) but did not affect pilocarpine-induced yawning (pilocarpine yawning). BRC (2.5 20 mg/kg) increased physostigmine yawning in an additive fashion. Pilocarpine yawning was completely blocked by either low or high doses of BRC. The inhibitory effect of BRC on pilocarpine yawning was reversed by sulpiride (20 mg/kg). alpha-Methyl-p-tyrosine (alpha-MPT; 100 and 200 mg/kg) did not affect physostigmine yawning but diminished pilocarpine yawning. Furthermore, physostigmine (0.2 mg/kg) inhibited apomorphine (4.0 mg/kg)-induced hyperlocomotion and sniffing but not licking and biting, whereas pilocarpine (4.0 mg/kg) had the opposite effect.(ABSTRACT TRUNCATED AT 250 WORDS)

Ushijima, I., C. Tsutsumi, et al. (1988). "[Effects of bifemelane on central dopaminergic and cholinergic systems in rats]." Yakubutsu Seishin Kodo 8(4): 463-70.
The study served to examine the effects of bifemelane on central dopaminergic-cholinergic neuronal mechanisms in rats. Bifemelane (5-20 mg/kg) evoked yawning responses, the frequency being low. Bifemelane (10 mg/kg) as well as bromocriptine (2.5 mg/kg) potentiated physostigmine (0.2 mg/kg)-, bromocriptine (2.5 mg/kg)- or apomorphine (0.1 and 0.5 mg/kg)-induced yawning but completely inhibited pilocarpine-induced yawning. Pretreatment with sulpiride (20 mg/kg) and a low dose of haloperidol (0.02 mg/kg) reversed the stimulatory effect of bifemelane on physostigmine-induced yawning and the inhibitory effect of the drug on pilocarpine-induced yawning, whereas atropine (5 mg/kg) diminished these yawning responses. SK&38393 (2.0 mg/kg), a dopamine D-1 receptor agonist, markedly potentiated bifemelane- and bromocriptine-induced yawning but inhibited physostigmine-induced yawning, and did not affect pilocarpine-induced yawning. The increased yawning responses were blocked by atropine and a low dose of haloperidol. Bifemelane (10 mg/kg) and bromocriptine (2.5 mg/kg) tended to increase apomorphine (5 mg/kg)-induced oral stereotypy, such as licking and biting, but the increase was not significant. These results suggest that the effects of bifemelane on central dopaminergic and cholinergic neurons may be similar to those of bromocriptine.

Szechtman, H., J. M. Cleghorn, et al. (1988). "Sensitization and tolerance to apomorphine in men: yawning, growth hormone, nausea, and hyperthermia." Psychiatry Res 23(3): 245-55.
This study investigated whether the indices of dopaminergic function, yawning and growth hormone release induced by apomorphine, as well as the drug-induced nausea and hyperthermia, show sensitization or tolerance to repeated injections. Five normal volunteers received 12 injections of apomorphine hydrochloride (0.75 mg/70 kg) every 2 weeks. Yawning, as measured by the latency of onset and the time of peak activity, showed sensitization. The growth hormone response showed no change. Feelings of nausea and hyperthermia showed tolerance to repeated injections. These findings suggest that yawning may be a suitable index of dopaminergic function in studies of schizophrenia.

Stoessl, A. J., C. T. Dourish, et al. (1988). "The NK-3 tachykinin agonist senktide elicits yawning and chewing mouth movements following subcutaneous administration in the rat. Evidence for cholinergic mediation." Psychopharmacology (Berl) 95(4): 502-6.
The selective NK-3 tachykinin receptor agonist senktide elicited yawning, chewing mouth movements and sexual arousal following subcutaneous administration (0.1-1.0 mg/kg) in the rat. These responses were not significantly affected by the dopamine antagonist haloperidol (0.03 mg/kg) or by 6-hydroxydopamine lesions of the nigrostriatal projection. In contrast, the behaviours were markedly attenuated by the peripheral and central muscarinic antagonist scopolamine (1 mg/kg), but not by the peripheral muscarinic antagonist N-methylscopolamine (1 mg/kg). These findings suggest that stimulation of NK-3 receptors produces yawning, chewing and sexual arousal by directly activating central cholinergic neurons.

Stelzig, S. and W. Hoffmann (1988). "[The yawning behavior of rats following application of dopaminergic agonists--dose and time effect relationship]." Pharmazie 43(2): 140-1.

Stelzig, S. and W. Hoffmann (1988). "[The effect of reserpine pretreatment on yawning behavior in rats]." Pharmazie 43(9): 656.

Patra, P., T. K. Gunness, et al. (1988). "Physiologic variations of the internal jugular vein surface, role of the omohyoid muscle, a preliminary echographic study." Surg Radiol Anat 10(2): 107-12.
The action of the omohyoid muscle on the hemodynamics of the internal jugular vein is controversial. For some authors, contraction of this muscle, by tightening the cervical fascia, promotes jugular venous return. For others, contraction of this muscle compresses the jugular vein in its cervical path. With this latter point in mind, the hemodynamics of the internal jugular vein have been studied in its cervical path by echography in 10 healthy volunteers. One hundred twenty measurements of the venous surface were made at rest, with the mouth open and during deep inspiration. In the last 2 situations, evidence of a significant increase in the venous surface was found above the omohyoid muscle. These data confirm the role of compression of the vein by the omohyoid muscle, leading to modifications in intracerebral venous hemodynamics, which can be affected in yawning.

Opp, M. R., F. Obal, Jr., et al. (1988). "Effects of alpha-MSH on sleep, behavior, and brain temperature: interactions with IL 1." Am J Physiol 255(6 Pt 2): R914-22.
Changes in rabbit sleep-wake activity, brain temperature (Tbr), and behavior were studied after intracerebroventricular injections of a putative endogenous antipyretic, alpha-melanocyte-stimulating hormone (alpha-MSH), and of an endogenous pyrogen, interleukin 1 (IL 1-beta). alpha-MSH (0.1-50.0 micrograms) dose dependently increased wakefulness (W) and decreased Tbr, non-rapid-eye-movement sleep (NREMS), and rapid-eye-movement sleep (REMS). NREMS was more sensitive than REMS to the suppressive effects of low alpha-MSH doses. EEG slow-wave activity in NREMS decreased after alpha-MSH treatment. alpha-MSH elicited stretching, yawning, and signs of sexual excitation. IL 1 (20 and 40 ng) induced fever and excess NREMS. alpha-MSH administered 30 min after IL 1 (40 or 20 ng IL 1 + 0.1, 0.5, or 5.0 micrograms alpha-MSH) significantly attenuated IL 1-induced fever and excess NREMS. IL 1 failed to alter the behavioral effects of alpha-MSH. Despite alpha-MSHs effect on rabbit behavior, total motor activity time did not increase, indicating that increased W after alpha-MSH cannot be attributed to behavioral activation. These results suggest that, besides acting as an endogenous antipyretic, alpha-MSH might be involved in regulation of IL 1-induced sleep.

Murray, C. and A. Cowan (1988). "Neuroadaptation of rats to kappa agonists U-50,488 and tifluadom." NIDA Res Monogr 81: 136-42.
1. When U50 was given to rats over 5 d by twice-daily s.c. injection (but not when delivered by osmotic minipump), buprenorphine and naloxone each precipitated strong, qualitatively distinct, behavioral syndromes. 2. The same dose of buprenorphine provoked similar behaviors in rats given chronic U50 and chronic TIF (analogous s.c. injection protocols), suggestive of neuroadaptation to kappa agonists as a class. This adaptation clearly contrasts with that to chronic mu agonists. 3. The buprenorphine-induced syndrome was characterized by oral stereotypies which had an onset of about 5 min and a duration greater than 4 hr. The intensity was dependent on the dose of agonist injected. 4. The naloxone-induced syndrome was characterized by repetitive yawning and writhing. 5. If oral stereotypy, yawning and writhing are considered to represent an abstinence syndrome, then it will be necessary to use multiple or more selective kappa antagonists to fully unveil kappa dependence in the rat. 6. The present data indicate a strong trend toward the parallel development of tolerance in rats given a similar course of chronic U50 injections as those tested for physical dependence.

Mora, S. and G. Diaz-Veliz (1988). "LHRH antagonizes yawning and genital grooming induced by apomorphine in rats." Pharmacol Biochem Behav 31(3): 717-20.
The effects of the pretreatment with LHRH on the behavioral effects induced by low doses of apomorphine were studied in male rats. Three doses of apomorphine (31.25, 62.50 and 125 micrograms/kg) were subcutaneously administered two hours after LHRH 100 micrograms/kg or solvent SC treatment. Apomorphine induced repeated episodes of yawning and genital grooming. Pretreatment with LHRH abolished or reduced yawning and genital grooming induced by the three doses of apomorphine, suggesting that the peptide could induce subsensitivity of DA receptors responsible for yawning and genital grooming.

Melis, M. R., A. Argiolas, et al. (1988). "Oxytocin-induced penile erection and yawning: structure-activity relationship studies." Pharmacol Res Commun 20(12): 1117-8.

Laping, N. J. and V. D. Ramirez (1988). "Prolactin-induced yawning behavior requires an intact nigro-striatal dopamine system." Pharmacol Biochem Behav 29(1): 59-62.
Herein, we evaluate the importance of the nigro-striatal dopamine system in prolactin-, apomorphine-, and physostigmine-induced yawning behavior. Bilateral 6-OH-dopamine lesions of the substantia nigra were performed on male rats (2-4 months old). The lesioned as well as control rats were injected with either physiological saline, physostigmine (200 micrograms/kg), apomorphine (50 micrograms/kg), or ovine prolactin (0.25 micrograms/kg) 72 hours after the surgical procedure. The results show that bilateral lesions of the substantia nigra did not affect physostigmine-induced yawning whereas both apomorphine- and prolactin-induced yawning were reduced by the lesion. Following the observation period the caudate nuclei were removed and analyzed for dopamine (DA) and dihydroxyphenylacetic acid (DOPAC) content. The lesions reduced DA and DOPAC content in all treatment groups compared to the respective intact groups. Also, both DA and DOPAC concentrations were lower in the intact apomorphine and prolactin treated groups compared to intact saline controls, at times that were temporally related to the display of yawning behavior suggesting a decrease in dopamine activity following apomorphine and prolactin treatment. Interestingly, DA and DOPAC concentrations were higher in the lesioned apomorphine group compared to lesioned saline controls; however, in the lesioned prolactin group only the DA concentrations were higher when compared to lesioned saline controls. These results indicate that prolactin- and apomorphine-induced yawning require an intact nigro-striatal dopamine system and that these substances induce yawning by different mechanisms.

Lal, S. (1988). "Apomorphine in the evaluation of dopaminergic function in man." Prog Neuropsychopharmacol Biol Psychiatry 12(2-3): 117-64.
1. Apomorphine (Apo), a short acting dopamine (DA) receptor agonist, stimulates growth hormone (GH) secretion, decreases prolactin secretion, induces yawning, penile erections and other physiological effects in man. An effect on behavior, movement disorders and alcoholism has also been described. 2. Apo-mediated responses are used to evaluate DA function in psychiatric and neurological disorders. Many of the studies in schizophrenia using the GH response to Apo as an index of central DA function are difficult to interpret because of failure to control for key variables. 3. The GH response to Apo is a useful system to evaluate the effects of various drugs including peptides which may not cross the blood brain barrier on DA function in man. 4. Apo is a potent sedative. Specific antimanic, antischizophrenic, and anticraving effects in alcoholics have not been convincingly demonstrated. Side effects of Apo and failure to use active placebo make double-blind studies difficult. 5. Apo improves parkinsonian symptoms and certain forms of reflex epilepsy but beneficial effects in other involuntary movement disorders requires further documentation. 6. Apo may be a useful agent to evaluate DA function in impotent patients and predict a therapeutic response to long-acting dopaminergic agents. 7. Impairment of DA function may play a role in diabetic impotence. 8. The development of a simple polygraphic method to monitor the yawning response to Apo may facilitate clinical

studies on the basic physiology of yawning in man and the use of the yawning response as a measure of central DA function in schizophrenia and other clinical disorders. 9. The use of Apo with 18F-fluorodeoxyglucose positron emission tomography to examine regional DA function in man opens up a promising area of research. 10. Though long-acting orally active aporphine DA agonists and antagonists have been developed the problem of tolerance may limit their therapeutic potential.

Kishimoto, O. (1988). "[Age-related modification of dopaminergic-cholinergic neuronal interaction in rats]." Yakubutsu Seishin Kodo 8(4): 443-51.

A behavioral study was performed in an attempt to understand the effect of age (rats aged 2, 6, 12, 18, or 24 months) on the dopaminergic-cholinergic neuronal mechanism involved in yawning and stereotyped behaviors induced by dopaminergic and cholinergic drugs. Intraperitoneal (ip) injection of a low dose of apomorphine (0.1 mg/kg), which preferentially activates presynaptic dopamine autoreceptors, produced a lower frequency of yawning responses in 12- and 24-month-old rats than in 2-month-old rats. A high dose of apomorphine (0.5 mg/kg) which stimulates both pre- and post-synaptic dopamine receptors produced the most pronounced stereotyped behavior in 12-month-old rats. The peak times for apomorphine-induced stereotypy shifted to the right between 2- and 12- and 24-month-old rats, and the duration of the stereotypy also increased in 12- and 24-month-old rats as compared with 2-month-old rats. It is suggested that decreased function of the presynaptic dopamine receptors might contribute to the increased stereotypy induced by apomorphine with increasing age in the rat. Yawning responses induced by pilocarpine (4 mg/kg) were reduced in 6- to 24-month-old rats whereas those by physostigmine (0.2 mg/kg) were not affected in rats of any age. These results suggest that differential pathways are involved in dopaminergic-cholinergic neuronal interaction, and that with increasing age, cholinergic neurons activated by cholinesterase inhibition (endogenous acetylcholine) were not affected but those by a direct acetylcholine agonist (muscarinic M-1 receptor agonist) were diminished.

Kennett, G. A. and G. Curzon (1988). "Evidence that mCPP may have behavioural effects mediated by central 5-HT1C receptors." Br J Pharmacol 94(1): 137-47.

1. The effects of 1-(3-chlorophenyl)piperazine (mCPP) and 1-[3-(trifluoromethyl)phenyl] piperazine (TFMPP) on activity of rats in a novel cage, and on the rotorod and elevated bar co-ordination tests was examined. 2. Peripherally administered mCPP and TFMPP dose-dependently reduced locomotion, rearing, and feeding scores but not grooming of freely fed rats placed in a novel observation cage. Yawning behaviour was increased. Similar effects were also observed after injection of mCPP into the 3rd ventricle. 3. Co-ordination on a rotating drum of both untrained and trained rats was impaired following mCPP but co-ordination on an elevated bar was not. 4. The hypoactivity induced by mCPP was opposed by three antagonists with high affinity for the 5-hydroxytryptamine (5-HT1C) site; metergoline, mianserin, cyproheptadine and possibly also by a fourth antagonist mesulergine. Metergoline, mianserin and cyproheptadine also opposed the reduction in feeding scores. However, neither effect of mCPP was antagonized by the 5-HT2-receptor antagonists ketanserin or ritanserin, the 5-HT3-receptor antagonist ICS 205-930, the 5-HT1A and 5-HT1B-receptor antagonists (-)-pindolol, (-)-propranolol and (+/-)-cyanopindolol or the 5-HT1A-, 5-HT2- and dopamine receptor antagonist spiperone. The specific alpha 2-adrenoceptor antagonist idazoxan was also without effect. 5. Hypoactivity induced by TFMPP was similarly antagonized by mianserin but unaffected by (+/-)-cyanopindolol. 6. These results suggest that the hypoactivity is mediated by central 5-HT1C-receptors and that mCPP and possibly TFMPP may be 5-HT1C-receptor agonists. 7. As mianserin, cyproheptadine and mesulergine in the absence of mCPP did not increase locomotion but increased the number of feeding scores, the activation of 5-HT1C-receptors may be of physiological importance in the control of appetite. The possible relevance of these results to the therapeutic and side-effects of clinically used antidepressants (particularly trazodone and mianserin) and anorexigenic drugs is discussed.

Izquierdo, I. (1988). "Now you'll start yawning and you won't know why." Trends Pharmacol Sci 9(4): 119.

Heishman, S. and M. Stitzer (1988). "Acute opioid physical dependence in humans: naloxone dose response effects." NIDA Res Monogr 81: 195-201.

Green, P. G. and N. M. Lee (1988). "Dynorphin A-(1-13) attenuates withdrawal in morphine-dependent rats: effect of route of administration." Eur J Pharmacol 145(3): 267-72.

Rats were made tolerant to morphine by subcutaneous implantation of morphine alkaloid pellets. Three days after pellet implantation, withdrawal was induced by pellet removal and was assessed 6 h later. Immediately prior to withdrawal assessment, rats were injected with dynorphin A-(1-13) either i.th. (via a catheter), i.c.v. (via a cannula) or i.v. (via the tail vein). When administered i.th. in the dose range 1.25-5 nmol/rat, dynorphin A-(1-13) attenuated withdrawal over the 40 min observation period. Similarly, dynorphin A-(1-13) administered i.v. (37.5-150 nmol/kg) attenuated withdrawal, though only over the first 20 min following administration. Dynorphin A-(1-13) up to 10 nmol/rat had no effect on withdrawal scores. These data indicate that dynorphin acts at spinal sites to suppress withdrawal in morphine-dependent rats and may play a role in tolerance and dependence mechanisms.

Ferrari, F. and V. Mangiafico (1988). "Effect of isolation on dopaminergic agonist-induced penile erections and stretching and yawning in male rats." Behav Brain Res 28(3): 309-13.

Adult male rats reared in social isolation for 28 +/- 2 days were compared with animals housed in groups and pairs for frequency of penile erection (PE) and stretching and yawning (SY) elicited by dopaminergic (DA) autoreceptorial doses of B-HT 920 and n-N-propylnorapomorphine (NPA). PE and SY were consistently lower in the isolated group with respect to the other two groups, which did not differ significantly. The present experiments show the importance of housing conditions in modulating behavioural responses to DA agonists, a result that was confirmed when adult male rats, isolated or paired immediately after weaning until the day of tests (56 +/- 2 days), were treated with B-HT 920. In this case, however, not only isolated but also paired rats differed from grouped rats of the same age in their response to B-HT 920.

Ferrari, F., V. Mangiafico, et al. (1988). "Imidazole and yohimbine antagonize hypomotility, penile erection, stretching and yawning induced in rats by BHT 920, a selective dopamine autoreceptor agonist." Pharmacol Res Commun 20(9): 827-37.

When the azepine derivative BHT 920, a putative agonist at dopamine autoreceptors, was injected i.p. into adult male rats at 100 micrograms/kg, it induced numerous penile erections, stretching and yawning and sedation, all considered typical signs of central DA autoreceptor stimulation, but did not elicit stereotyped behaviour. Imidazole (37.5-150 mg/kg i.p.) and the alpha 2 antagonist yohimbine (0.5-1 mg/kg i.p.) both antagonized the behavioural effects of BHT 920. In the light of the proposed selective action of the drugs used, the possible involvement of specific receptors for the modulation of these forms of behaviour, as well the possible relevance of the data presented, are briefly discussed.

D'Mello, D. A., F. M. Vincent, et al. (1988). "Yawning as a complication of electroconvulsive therapy and concurrent neuroleptic withdrawal." J Nerv Ment Dis 176(3): 188-9.

Among the various reported neuropsychological effects of electroconvulsive therapy are amnesia, delirium, peripheral neuropathy, headaches, and seizures. A case history is presented that describes a previously unreported neurological sequela: the development of intractable yawning during a course of electroconvulsive therapy. Neuropathophysiological mechanisms possibly relating to this phenomenon are discussed.

Cronin, T. G., Jr. (1988). "Yawning: an early manifestation of vasovagal reflex." AJR Am J Roentgenol 150(1): 209.

Bickel, W. K., M. L. Stitzer, et al. (1988). "Acute physical dependence in man: effects of naloxone after brief morphine exposure." J Pharmacol Exp Ther 244(1): 126-32.

This study assessed the effects of i.m. naloxone (10 mg) 6 hr after acute i.m. injections of morphine (0, 1, 3, 5.6, 10 and 17 mg). Naloxone reversed residual morphine-produced respiratory depression, miosis and subjective reports of drug "high." In addition, naloxone precipitated signs and symptoms characteristic of opioid withdrawal. Subjective report measures of "bad" drug effects and specific opioid withdrawal symptoms increased as a function of morphine pretreatment dose, as did observer-rated signs of withdrawal. Yawning was the most prominent observed sign, whereas yawning and irritability were the most consistently reported subjective symptoms. Peak withdrawal effects were seen within 15 min post-naloxone. The results of this study confirm previous reports of acute physical dependence in man and extend those findings by demonstrating a morphine dose-response function.

Bertolini, A., R. Poggioli, et al. (1988). "Cross-species comparison of the ACTH-induced behavioral syndrome." Ann N Y Acad Sci 525: 114-29.

Barthalmus, G. T. and W. J. Zielinski (1988). "Xenopus skin mucus induces oral dyskinesias that promote escape from snakes." Pharmacol Biochem Behav 30(4): 957-9.

African clawed frogs fed to American water snakes induced yawning and gaping which slowed ingestion and facilitated the frogs' escape without inducing flavor aversion. The peptide and/or indolealkylamine contents of the frog's poison glands caused the effect because frogs with purged glands did not induce these behaviors and rarely escaped. Poison gland mucus, applied orally, elicited similar oral movements. The frog's clear lubricating mucus was inactive. As several compounds in the poison glands have known neuroleptic properties, the oral behaviors may be induced by neural mechanisms reported to govern neuroleptic-induced orofacial dyskinesia in schizophrenics.

Argiolas, A., M. R. Melis, et al. (1988). "Yawning and penile erection: central dopamine-oxytocin-adrenocorticotropin connection." Ann N Y Acad Sci 525: 330-7.

Argiolas, A., M. R. Melis, et al. (1988). "Central dopamine-oxytocin-adrenocorticotropin link in the expression of yawning and penile erection." Ann Ist Super Sanita 24(3): 377-82.

(1988). "Is yawning a brainstem phenomenon?" Lancet 1(8585): 596.

Ushijima, I., Y. Mizuki, et al. (1987). "Effects of age on behavioral responses to dopamine agonists in the rat." Eur J Pharmacol 138(1): 101-6.

This study served to examine the differential effects of age (rats aged 2 or 12 months) on behavioral responses induced by bromocriptine and apomorphine. Intraperitoneal (i.p.) injection of bromocriptine or apomorphine produced a lower frequency of yawning responses, in 12-month-old rats than in 2-month-old rats. Apomorphine produced a more pronounced stereotyped behavior in 12-month-old rats than in 2-month-old rats. Apomorphine, at 0.1 mg/kg administered after bromocriptine (1.0-20 mg/kg) potentiated yawning behavior. The frequency of yawning in 2-month-old rats was pronounced at 2.5 mg/kg of bromocriptine but only at 5 mg/kg 12-month-old rats. Apomorphine (0.1 mg/kg) did not produce perioral behavior in 2-month-old rats but did in 12-month-old rats. The apomorphine (1.0 mg/kg)-induced stereotypy was stimulated dose dependently by bromocriptine in 2-month-old-rats but not in 12-month-old rats. Bromocriptine did not produce this behavior when administered alone. Pretreatment of 2-month-old rats with reserpine, a catecholamine depletor, plus alpha-methyl-p-tyrosine, a tyrosine hydroxylase inhibitor, inhibited the yawning induced by bromocriptine but potentiated that induced by apomorphine. Such treatment did not significantly alter either bromocriptine or apomorphine-induced yawning responses in 12-month-old rats. The apomorphine-induced stereotypy in 2-month-old rats was markedly potentiated by catecholamine depletion but was not affected in 12-month-old rats. These results suggest that the increasing effect on stereotypy and decreasing effects on yawning in the 12-month-old rats seem to result in an alteration of potency and of the ratio of D-2 versus D-1 receptor activity.

Urba-Holmgren, R. and B. Holmgren (1987). "Effects of metoclopramide on spontaneous and pharmacologically-induced yawning in the rat." Bol Estud Med Biol 35(3-4): 203-6.

Tufik, S., L. R. Troncone, et al. (1987). "Does REM sleep deprivation induce subsensitivity of presynaptic dopamine or postsynaptic acetylcholine receptors in the rat brain?" Eur J Pharmacol 140(2): 215-9.

Yawning behavior was used to evaluate the sensitivity of presynaptic dopamine receptors and postsynaptic acetylcholine receptors of normal and REM sleep-deprived (REMSD) rats. The results show a lowering of the dose-response curve obtained with apomorphine and pilocarpine, as well as a shift to the right in the curve obtained with physostigmine. These results suggest that REMSD induces subsensitization of presynaptic dopamine receptors and/or postsynaptic acetylcholine receptors with different characteristics related to the mechanism of action of the cholinomimetic agent employed.

Stoessl, A. J., C. T. Dourish, et al. (1987). "Apomorphine-induced yawning in rats is abolished by bilateral 6-hydroxydopamine lesions of the substantia nigra." Psychopharmacology (Berl) 93(3): 336-42.

Apomorphine-induced yawning was studied in male rats with bilateral 6-hydroxydopamine lesions of the substantia nigra. Apomorphine 10, 20 and 50 micrograms/kg SC induced dose-dependent yawning in unoperated controls and animals with sham lesions. In the lesioned animals (in which the mean striatal dopamine depletion was 67%), the maximum yawning response rate was greatly attenuated with no evidence that the dose response curve was shifted in either direction. Furthermore, blockade of yawning in the lesioned animals was not simply due to suppression by other stereotyped behaviours, since there was no evidence of increased sniffing or chewing in these animals. These data provide further support for the hypothesis that apomorphine-induced yawning is mediated by dopamine autoreceptors and requires intact nigrostriatal projections.

Serra, G., M. Collu, et al. (1987). "Yawning is elicited by D2 dopamine agonists but is blocked by the D1 antagonist, SCH 23390." Psychopharmacology (Berl) 91(3): 330-3.

The subtype of dopamine (DA) receptors mediating the yawning response to DA agonists was determined in rats. Yawning was elicited both by the mixed D1-D2 agonist apomorphine and by the specific D2 agonist LY 171555, but not by the selective D1 agonist SKF 38393. Both apomorphine- and LY 171555-induced yawning were antagonized not only by the selective D2 antagonist sulpiride but, unexpectedly, also by the selective D1 antagonist SCH 23390. The results suggest that DA receptors mediating the yawning response are of the D2 type, and that these receptors are connected with D1 receptors in such a way that the blockade of the latter results in the functional inactivation of the former.

Serra, G., W. Fratta, et al. (1987). "Hypophysectomy prevents ACTH-induced yawning and penile erection in rats." Pharmacol Biochem Behav 26 (2): 277-9.

The intracerebroventricular administration of ACTH1-24 (3-5 micrograms/rat) produced a behavioural syndrome characterized by recurrent episodes of penile erection and yawning in rats. Hypophysectomy prevented ACTH1-24-induced yawning and penile erection. These results suggest that pituitary has a "trophic" action not only on peripheral target organs but also on structures in brain controlling specific behavioural responses.

Sandyk, R. (1987). "Excessive yawning and progressive supranuclear palsy." Int J Neurosci 34(1-2): 123-4.

Provine, R. R., B. C. Tate, et al. (1987). "Yawning: no effect of 3-5% CO2, 100% O2, and exercise." Behav Neural Biol 48(3): 382-93.

Using human college-age subjects, the present study tested the commonly cited but previously untested hypothesis that yawning is facilitated by higher than normal levels of CO2 or lower than normal levels of O2 in the blood by comparing the effect on yawning of breathing 100% O2 and gas mixtures with higher than normal levels of CO2 (3 or 5%) with compressed air, the control condition. If yawning is a response to heightened blood CO2, the CO2 mixtures should increase yawning rate and/or duration. If low blood O2 produced yawning, breathing 100% O2 should inhibit yawning. The CO2/O2 hypothesis was rejected because breathing neither pure O2 nor gases high in CO2 had a significant effect on yawning although both increased breathing rate. A second study found that exercise sufficient to double breathing rate had no effect on yawning. The two studies suggest that yawning does not serve a primary respiratory function and that yawning and breathing are triggered by different internal states and are controlled by separate mechanisms.

Okuyama, S., H. Shimamura, et al. (1987). "Relation between yawning behavior and central serotonergic neuronal system in rats." Naunyn Schmiedebergs Arch Pharmacol 335(6): 667-72.

Subcutaneously (s.c.) administered apomorphine (0.0125-0.4 mg/kg) or physostigmine (0.025-0.4 mg/kg) to rats elicited yawning. The dose-response curves were bell-shaped. The peak effects of apomorphine and physostigmine were observed with a dose of 0.1 mg/kg of each drug. Yawning elicited by apomorphine (0.1 mg/kg) or physostigmine (0.1 mg/kg) was reduced by intraperitoneally (i.p.) administered 5-hydroxytryptophan (5-HTP, 50-200 mg/kg, given 30 min before). Yawning elicited by apomorphine but not by physostigmine was enhanced by p-chlorophenylalanine (p-CPA, 25-400 mg/kg i.p., given 24 h before). Apomorphine elicited but not physostigmine-elicited yawning was enhanced by pretreatment with 5,7-dihydroxytryptamine (5,7-DHT, 8 micrograms/rat, given 14 days before into the dorsal raphe). This treatment led to a 35% depletion of serotonin (5-HT) in the striatum. 5-HTP, p-CPA or 5,7-DHT given alone did not elicit yawning. Bilateral, intrastriatal microinjection of apomorphine (1.5-50 micrograms/site) but not physostigmine (5-50 micrograms/site) elicited yawning. The dose-response curve was also bell-shaped. These results indicate that central serotonergic pathways play an important role in modulating drug-elicited yawning in rats.

Nowak, K. and K. Kuschinsky (1987). "Conditioning of behavioural effects produced by an intermediate dose of apomorphine: hypokinesia, ptosis and stereotypies." Naunyn Schmiedebergs Arch Pharmacol 336(3): 262-6.

Apomorphine, in an intermediate dose (0.18 mg/kg s.c.) decreased dopamine turnover and produced signs generally attributed to a decrease in dopaminergic neurotransmission, e.g. ptosis and yawning, as well as signs of an increased stimulation of dopamine receptors in dopaminoceptive target neurones, e.g. stereotyped sniffing. In contrast, the former signs were exclusively observed after smaller doses and the latter after larger doses of apomorphine. Since it had been shown in previous studies that these signs, except yawning, could be conditioned in association with discriminative stimuli in the environment, the present study using conditioning experiments with this intermediate dose aimed at determining, 1. the time course of each conditioned response, 2. the interaction of conditioned and unconditioned responses, and 3. the conditions under which hypokinesia occurred. In each series, conditioned animals were compared with pseudoconditioned controls. Rats were conditioned for 8 days with apomorphine, and on day 9, treated with saline in presence of the conditional stimuli (a test cage in combination with acoustic and olfactory stimuli). In contrast to pseudoconditioned controls, ptosis and stereotyped behaviour were observed in conditioned rats, sometimes occurring alternatingly. These signs closely resembled the direct, unconditioned pharmacological effects. In addition, akinesia occurred after conditioning, although it was never manifest as a pure drug response, nor during the conditioning period. In contrast, yawning was observed in pseudoconditioned as well as in conditioned rats, although slightly more frequently in the former animals. Subsequently, the rats were again conditioned (or pseudoconditioned) on days 10-14 with apomorphine and both groups tested with the same dose (0.18 mg/kg) of apomorphine in the presence of the conditioned stimuli.(ABSTRACT TRUNCATED AT 250 WORDS)

Moller, H. G., K. Nowak, et al. (1987). "Conditioning of pre- and post-synaptic behavioural responses to the dopamine receptor agonist apomorphine in rats." Psychopharmacology (Berl) 91(1): 50-5.

We investigated whether pharmacological effects of the dopamine agonist apomorphine can be conditioned by establishing an association of apomorphine administration with exteroceptive cues. Apomorphine was repeatedly administered and subsequently, the rat was put into a test cage and exposed to an acoustic and an olfactory stimulus ("conditioned rats"). Control animals ("pseudoconditioned" rats) were treated with the same pharmacological schedule of apomorphine not temporally associated with the stimuli. On the test day, both groups were injected with saline and exposed to the stimuli described. The stereotyped behaviour produced by large doses of apomorphine (0.5 or 2.0 mg/kg SC), namely sniffing, licking and gnawing, could be conditioned in a pronounced way. During the conditioning period, a change in the stereotypies was observed with regard to the time-course (earlier occurrence) and to the character of the stereotypies (from sniffing to licking and gnawing), when 0.5 mg/kg apomorphine was used, but not with the dose of 2.0 mg/kg. The conditioned responses showed a relatively uniform distribution during the observation period with some increase towards the end of the observation period. Some signs produced by a low dose of apomorphine (0.07 mg/kg SC), namely hypomotility and ptosis, but not yawning, could also be conditioned, although in a less pronounced way. An intermediate dose of apomorphine (0.18 mg/kg SC) produced both signs observed after large doses and those observed after

a small dose, occurring alternatingly. Both types of signs could be conditioned using this dosage. Conditioning did not alter striatal or mesolimbic dopamine turnover.(ABSTRACT TRUNCATED AT 250 WORDS)

Moller, H. G., K. Nowak, et al. (1987). "Studies on interactions between conditioned and unconditioned behavioural responses to apomorphine in rats." Naunyn Schmiedebergs Arch Pharmacol 335(6): 673-9.

Interactions between the direct (unconditioned) behavioural effects apomorphine and its conditioned effects after pairing with previously neutral stimuli were studied. Rats were injected once daily for 3-12 times, with apomorphine (2.0 mg/kg or 0.5 mg/kg or 0.07 mg/kg s.c. the dose kept constant in each series), in the presence of defined environmental stimuli (a wire cage in association with an acoustic and an olfactory stimulus) as conditional stimuli. The two larger doses produced stereotyped sniffing, licking, and gnawing, the smallest dose akinesia, ptosis, yawning and penile erections. During the conditioning phase, the drug produced most of the effects with increasing intensity and in the case of the stereotypies, there also was a shift to higher scores of stereotypy, with a reduced latency in onset of the signs. On the test day, 1 day after the last administration of apomorphine, the conditioned rats as well as "pseudoconditioned" controls were treated with a test dose of apomorphine in the presence of the conditional stimuli. Pseudoconditioned rats had been treated with the same pharmacological schedule of apomorphine and had the same familiarity with the stimuli, but both were kept separate. A test dose of 0.5 mg/kg of apomorphine produced stereotypies with a significantly higher score and shorter latency in onset in conditioned than in pseudoconditioned rats. Rats conditioned with the lowest dose showed a significantly longer total duration and a shorter latency in onset of akinesia and ptosis.(ABSTRACT TRUNCATED AT 250 WORDS)

Melis, M. R., A. Argiolas, et al. (1987). "Apomorphine-induced penile erection and yawning: site of action in brain." Brain Res 415(1): 98-104.

Microinjection of the dopamine (DA) agonist apomorphine into the paraventricular nucleus of the hypothalamus (PVN) induced penile erection and yawning in rats. A significant effect was elicited by a dose of apomorphine as low as 5 ng. The symptomatology usually began within 5 min after the microinjection, lasted for 30-50 min, and was identical to that induced by the systemic administration of the drug. Stereotypy and hypermotility were never observed after apomorphine microinjection into the PVN, even at the highest dose tested (1 microgram). Microinjections of the same doses of apomorphine into the hypothalamic ventromedial and dorsomedial nucleus, preoptic area, caudate nucleus, nucleus accumbens and substantia nigra, were ineffective. LY 171555, a specific D2 Da receptor agonist, and (+)-3-PPP, but not (-)-3-PPP nor the specific D1 DA receptor agonist SKF 38393, were as effective as apomorphine when injected into the PVN. Apomorphine-induced penile erection and yawning were antagonized by pretreatment with neuroleptic drugs, such as haloperidol, (-)-sulpiride, a specific D2 DA antagonist, and SCH 23390, a specific D1 DA antagonist. The present results suggest that the PVN is the brain area where D2 DA agonists act to induce penile erection and yawning. Moreover, since the PVN contains the cell bodies of a group of incerto-hypothalamic DA neurons, the above results suggest for the first time a possible involvement of the incerto-hypothalamic DA system in the expression of penile erection and yawning.

Longoni, R., L. Spina, et al. (1987). "Permissive role of D-1 receptor stimulation by endogenous dopamine for the expression of postsynaptic D-2-mediated behavioural responses. Yawning in rats." Eur J Pharmacol 134(2): 163-73.

Low doses of BHT 920, LY 171555 and (+)3PPP, three dopamine agonists selective for D-2 receptors, induced yawning in rats. This effect was reduced by the selective D-1 antagonist SCH 23390 but the antagonism did not exceed a 50% reduction from the control values. In contrast, the selective D-2 antagonist (-)sulpiride completely abolished agonist-induced yawning. A 6 h reserpine pretreatment (5 mg/kg i.p.), which depletes brain dopamine (DA) by about 95%, reduced agonist-induced yawning by an extent similar to SCH 23390; in the reserpinized rats, SCH 23390 completely lost the property of blocking agonist-induced yawning while (-)sulpiride retained it. Two 5HT receptor antagonist, ketanserin and metergoline failed to influence agonist-induced yawning. The reportedly selective D-1 agonist, SKF 38393, failed to induce yawning in normal rats as well as in rats pretreated with reserpine 6 or 16 h earlier. If one excludes that SCH 23390 and the D-2 agonists interact with the same DA-receptors, the data are consistent with the possibility that stimulation of D-1 receptors by endogenous DA plays a permissive-facilitatory role for the behavioural expression of D-2 receptor activation.

Longoni, R., L. Spina, et al. (1987). "Permissive role of D-1 receptor stimulation for the expression of D-2 mediated behavioral responses: a quantitative phenomenological study in rats." Life Sci 41(18): 2135-45.

The syndrome of behavioral stimulation induced in male Sprague-Dawley rats by two dopaminergic agents was studied by distinguishing specific behavioral items and quantifying them in terms of their incidence. The specific D-2 agonist LY 171555 elicited yawning, genital grooming, exploratory behavior, downward sniffing and licking but failed to induce gnawing even at high doses. On the other hand, the D-1/D-2 agonist apomorphine elicited the full stereotyped syndrome including gnawing. Depletion of endogenous dopamine (DA) by alpha-methyltyrosine (alpha-MT) prevented the ability of LY 171555 to elicit all the items of behavioral stimulation including the stereotyped ones (sniffing and licking). In contrast, the ability of apomorphine to induce stereotypies was not reduced by depletion of endogenous DA by alpha-MT pretreatment. Blockade of D-1 receptors with SCH 23390 abolished the capacity of both LY 171555 and apomorphine to elicit all the items of behavioral stimulation. In alpha-MT pretreated rats, administration of low doses of the D-1 agonist SKF 38393 (2.5 mg/kg s.c.) reinstated the ability of LY 171555 to elicit behavioral stimulation and eventually conferred the ability of inducing gnawing. The results support the hypothesis that stimulation of D-1 receptors exerts a permissive role for the expression of behavioral stimulation following D-2 receptor stimulation. Endogenous DA appears to provide sufficient D-1 input to permit full expression of yawning, genital grooming, exploratory behavior, downward sniffing and licking following D-2 stimulation; pharmacological stimulation of D-1 in addition to D-2 receptors seems however necessary for full expression of the highest rank stereotypy item, gnawing.

Lal, S., A. Grassino, et al. (1987). "A simple method for the study of yawning in man induced by the dopamine receptor agonist, apomorphine." Prog Neuropsychopharmacol Biol Psychiatry 11(2-3): 223-8.

Apomorphine (Apo), a dopamine (DA) receptor agonist, induces yawning by stimulating central DA autoreceptors. Few data are available on Apo-induced yawning in man. A simple method for recording and measuring Apo-induced yawning by measuring the displacement of the lower jaw using a pair of linearlized magnetometers with one sensor attached to the forehead just below the hairline and the other under the chin is described. The output of the magnetometers is fed into a DC amplifier and displayed on a strip chart recorder. Complete concordance between evaluators reading the tracings and between observed yawning and recorded yawns was found. Measuring Apo-induced yawning may provide a simple approach to evaluating DA autoreceptor function in normal subjects and in patients with psychiatric and neurological disorders. Preliminary data show that Apo-induced yawning is more marked in women than in men. This is in contrast to spontaneous and drug-induced yawning in animals which is predominantly a male phenomenon. Sleep appears to inhibit Apo-induced yawning.

Koch, P., H. Montagner, et al. (1987). "Variation of behavioral and physiological variables in children attending kindergarten and primary school." Chronobiol Int 4(4): 525-35.

Twenty-one children aged 5-6 years (mean age: 71.2 months; S.D. = 2.7) were videotaped in 4 different kindergartens throughout the school day for a period of one week. Eighteen of these children were then followed up after the summer holidays and videotaped for one week while attending the first year of primary school. The behaviors measured for each child were yawning and general motor activity. It was found that: (1) The frequency of yawning appears to be 5 times higher in the first year of primary school than in the last year of kindergarten; (2) Throughout the school-day the percentage of yawning children is higher in the first year of primary school, with the exception of the 1400-1430 period; (3) In the first year of primary school, the percentage of yawning children and the frequency of yawning peak between 900 and 930 and 1430 and 1500; (4) In this school institution the percentage of children who get up from their chair and spontaneously move above increases from the beginning to the end of each school-day. Three cardio-vascular variables were investigated in 17 children of the sample population: heart rate, systolic and diastolic blood pressure. We found that: (1) The lowest values for heart rate in the first year of primary school are in agreement with the classical data of child development, as the children are 5-6 months older than in the last year of kindergarten. However, this is not the case at 1400 when the heart rate peaks at a higher level in the first year of primary school; (2) If the evolution in time of the blood pressure agrees in both institutions with the classical data of human chronobiology, i.e. the maximum values at 1400, the differences in mean level at all times during the school day between both institutions do not agree with what is commonly accepted, i.e. an increase in blood pressure with age; (3) The amplitude of the variations of the heart rate and blood pressure from one 30-min period to another throughout the school day is significantly higher in primary school. The comparison of the data obtained in both school institutions suggests that the observed differences are related to sharp modifications in school rhythms and constraints when the children go from the last year of kindergarten to the first year of primary school.

Gower, A. J. (1987). "Effects of acetylcholine agonists and antagonists on yawning and analgesia in the rat." Eur J Pharmacol 139(1): 79-89.

The ability of acetylcholine muscarinic agonists, injected subcutaneously (s.c.) to elicit yawning and analgesia (tail-flick response) in rats was examined. Yawning was elicited by physostigmine, RS86 and pilocarpine with an inverted 'U'-shaped dose-response relationship; maximal effects occurred at 0.1, 0.5 and 2.0 mg/kg respectively. Neostigmine (0.05-0.2 mg/kg); arecoline (0.5-2.0 mg/kg); bethanecol (0.1-10 mg/kg) and McN-A-343 (5-20 mg/kg) had marginal or no activity. In contrast, dose-related analgesia was obtained following oxotremorine (0.01-0.3 mg/kg) and arecoline (0.5-4.0 mg/kg) and physostigmine (0.1-0.4 mg/kg), RS86 (0.25-2.5 mg/kg) and pilocarpine (0.5-8.0 mg/kg). The effects of acetylcholine antagonists on physostigmine-induced yawning and physostigmine-induced analgesia were also investigated. Following their s.c. injection, trihexyphenidyl, atropine, dicyclomine, secoverine and methylatropine but not pirenzepine, inhibited both yawning and analgesia; there were clear differences in their potencies on the two responses. Pirenzepine, intracerebroventricularly (i.c.v.), inhibited yawning (ED50 value 5.7 micrograms/rat) but not analgesia (3-100 micrograms/rat). The results are discussed in terms of a possible functional differentiation of central muscarinic receptors.

Beck, T., H. G. Moller, et al. (1987). "Alterations in regional energy metabolism in rat brain produced by small and by large doses of apomorphine: possible relations to autoreceptors." Eur J Pharmacol 139(2): 139-46.

Dose-dependent changes in behavioural patterns and in local cerebral glucose utilization (LCGU) following subcutaneous application of apomorphine were measured in conscious, unrestrained rats by means of a scoring system and of the autoradiographic [C14]2-deoxyglucose technique, respectively. The behavioural patterns of akinesia, ptosis, yawning and penile erections were scored. Akinesia and ptosis were

most prominent after 0.02 and 0.07 mg/kg apomorphine but not after 0.18 mg/kg. Maximal scores for yawning and penile erections were obtained after 0.07 mg/kg. LCGU was not significantly changed after 0.07 mg/kg except for decreases in the cingulate cortex and hypothalamus. Apomorphine 0.5 mg/kg decreased LCGU in the cingulate, parietal and occipital cortex, anteromedial and lateral thalamus and lateral habenula but increased it in laminae IV and VI of the sensorimotor cortex, in the parafascicular nucleus of the thalamus, and in some parts of the basal ganglia and related nuclei. Similar changes in LCGU occurred after 2.0 mg/kg apomorphine, which also increased LCGU in the ventral tegmental area. The lower dose did not produce changes in LCGU opposite to those occurring after larger doses. The data obtained with LCGU do not support the idea that behavioural effects after low doses of apomorphine are elicited by activation of dopamine autoreceptors.

Argiolas, A., M. R. Melis, et al. (1987). "Yawning: neurochemistry, physiology and pathology." Cephalalgia 7 Suppl 6: 131-7.

Argiolas, A. and G. L. Gessa (1987). "Oxytocin: a powerful stimulant of penile erection and yawning in male rats." Adv Biochem Psychopharmacol 43: 153-63.

Argiolas, A., M. R. Melis, et al. (1987). "d(CH2)5Tyr(Me)-[Orn8]vasotocin, a potent oxytocin antagonist, antagonizes penile erection and yawning induced by oxytocin and apomorphine, but not by ACTH-(1-24)." Eur J Pharmacol 134(2): 221-4.
Intraventricular (i.c.v.) injection of d(CH2)5-Tyr(Me)-[Orn8]vasotocin, a potent oxytocin antagonist, antagonized in a dose-dependent manner (10-100 ng) penile erection and yawning induced by the systemic injection of apomorphine (80 micrograms/kg s.c.) or by the i.c.v. injection of oxytocin (30 ng). In contrast, the oxytocin antagonist, even at the dose of 10 micrograms, did not modify penile erection and yawning induced by the i.c.v. injection of ACTH-(1-24). These results suggest that apomorphine, but not ACTH-(1-24), induce penile erection and yawning by releasing oxytocin in some brain area.

Argiolas, A., M. R. Melis, et al. (1987). "Monosodium glutamate does not alter ACTH- or apomorphine-induced penile erection and yawning." Pharmacol Biochem Behav 26(3): 503-7.
The effect of the intracerebroventricular (ICV) injection of ACTH 1-24 (1, 5 and 10 micrograms) or the subcutaneous administration of apomorphine (20 and 80 micrograms/kg SC) on spontaneous penile erection and yawning was studied in rats treated with monosodium glutamate (MSG), a treatment that depletes hypothalamic ACTH, alpha-MSH and endorphin-like peptides. Neonatal MSG treatment failed to antagonize either apomorphine- or ACTH-induced yawning in male and female rats, or to alter the number of penile erection episodes induced by the two substances in male rats. In contrast, hypophysectomy, that does not alter the concentration of hypothalamic ACTH and alpha-MSH, caused a marked prevention of apomorphine- and ACTH-induced responses, in agreement with previous studies. The results suggest that the integrity of opiomelanotropinergic neurons in the hypothalamus is not necessary for the induction of yawning and penile erection by ACTH-derived peptides, and that apomorphine and other dopamine agonists apparently do not induce penile erection and yawning by releasing an ACTH-derived peptide in brain.

Argiolas, A., M. R. Melis, et al. (1987). "Paraventricular nucleus lesion prevents yawning and penile erection induced by apomorphine and oxytocin but not by ACTH in rats." Brain Res 421(1-2): 349-52.
The effect of electrolytic lesion of the paraventricular nucleus of the hypothalamus (PVN) on yawning and penile erection induced by apomorphine, oxytocin and adrenocorticotropic hormone (ACTH1-24) was studied in male rats. In sham-operated rats, apomorphine (50 micrograms/kg s.c.), oxytocin (30 ng i.c.v.), and ACTH1-24 (10 micrograms i.c.v.) significantly increased the number of yawning and penile erection episodes. In PVN-lesioned rats, apomorphine- and oxytocin-, but not ACTH-induced responses were strongly reduced. These results confirm our previous observations showing that the PVN has a crucial role in the expression of yawning and penile erection induced by dopamino-mimetic drugs and oxytocin, and suggest that ACTH-derived peptides induce the above responses by a mechanism not involving PVN hypothalamic dopamine or oxytocin.

Yamada, K., M. Tanaka, et al. (1986). "Involvement of septal and striatal dopamine D-2 receptors in yawning behavior in rats." Psychopharmacology (Berl) 90(1): 9-13.
A behavioral study was performed in an attempt to understand the neuronal mechanisms involved in yawning behavior in rats. Subcutaneous injections of low doses of apomorphine (0.05-0.25 mg/kg) or piribedil (0.2-1.0 mg/kg), which preferentially activate presynaptic dopamine autoreceptors at those doses, evoked yawning. Marked yawning responses were also elicited by both 3-PPP (5-20 mg/kg, SC) and TL-99 (1-2 mg/kg, SC). SK & F 38393, a dopamine D-1 receptor agonist, at doses ranging from 0.1 to 8.0 mg/kg (SC) induced neither yawning nor stereotypy. However, bromocriptine (0.5-32.0 mg/kg, SC), a dopamine D-2 receptor agonist, induced yawning for which the dose-response curves showed a bell-shaped form. After a higher dose of 32 mg/kg (SC) bromocriptine, some rats occasionally showed sniffing and sawdust chewing. Yawning responses induced by systemic injection of apomorphine, piribedil, 3-PPP or bromocriptine were wholly suppressed after treatment with sulpiride (10 mg/kg SC), a dopamine D-2 receptor antagonist. Bilateral injections of apomorphine (20 micrograms/side X 2), piribedil (100 micrograms/side X 2) or 3-PPP (50, 100 micrograms/side X 2) into the striatum or septum also elicited marked yawning. The results indicate that low doses of apomorphine, piribedil, 3-PPP, TL-99 or bromocriptine elicit yawning by stimulating dopamine D-2 receptors and striatal and septal dopaminergic systems may be related to the occurrence of yawning behavior.

Tonnaer, J. A., M. Van Vugt, et al. (1986). "In vitro interaction of ACTH with rat brain muscarinic receptors." Peptides 7(3): 425-9.
ACTH-(1-24) inhibits the in vitro binding of the muscarinic antagonist [3H]QNB to membranes from rat brain. The magnitude of inhibition is dependent on the concentration of ACTH-(1-24). Kinetic analysis indicates a pure competitive inhibition which is suggestive of a reversible interaction of ACTH with muscarinic receptors. A mechanism involving an interaction of ACTH-(1-24) with the phospholipid core of the receptors is suggested. Structure activity studies point to a relation with reported effects of intracerebroventricularly administered ACTH on the turnover rate of acetylcholine and the ACTH-induced stretching and yawning syndrome.

Takeda, Y., Y. Kamiya, et al. (1986). "Effect of injection of CCK-8 into the nucleus caudatus on the behavior of rats." Jpn J Pharmacol 40 (4): 569-75.
This report deals with the effect of cholecystokinin octapeptide (CCK-8) on the regulation of the behavior stimulated by dopaminergic drugs. Bilateral injection of CCK-8 (1 microgram per side) into the nucleus caudatus significantly reduced the locomotor hyperactivity induced by methamphetamine. Stereotyped sniffing and yawning occurred after intrastriatal administration of apomorphine (20 micrograms per side). Injections of CCK-8 into the nucleus caudatus completely inhibited the sniffing, but did not affect the yawning induced by apomorphine. It also had no effect on the basal dopamine (DA) level or the methamphetamine-induced DA level in the striatum. These results suggest that the injection of CCK-8 into the nucleus caudatus selectively inhibited the function of the dopaminergic system in the striatum, and blocked post-synaptic DA receptors.

Szechtman, H. (1986). "Effects of pretreatment with naloxone on behaviours induced by a small dose of apomorphine." Pharmacol Biochem Behav 24(6): 1779-83.
The opiate antagonist, naloxone, was used to determine whether endogenous opioids modulate behavioural effects induced by a low dose of apomorphine. Before administering apomorphine (0.075 mg/kg) or saline, rats were pretreated with naloxone (1 mg/kg) or saline. Each subject received all 4 possible treatments (saline-saline, saline-apomorphine, naloxone-saline, and naloxone-apomorphine) in random order. Naloxone reduced the frequency and altered the timing of apomorphine-induced yawning, reduced the frequency of apomorphine-induced stretching, potentiated the effect of apomorphine on delaying grooming of the body, and did not affect the hypoactivity induced by apomorphine. Moreover, like apomorphine, naloxone itself reduced activity. Furthermore, naloxone and apomorphine injected together increased the latency to groom the face. These results suggest that in some circuits, endogenous opioids interact with dopaminergic autoregulatory mechanisms.

Serra, G., M. Collu, et al. (1986). "Dopamine receptors mediating yawning: are they autoreceptors?" Eur J Pharmacol 120(2): 187-92.
Yawning was induced in rats by the (+) enantiomer of 3PPP, while (-)-3PPP was inactive. Yawning was present 24, but not 1, 6 and 12 h after reserpine treatment. The (+)-3PPP-induced yawning was antagonized by haloperidol and sulpiride but not by domperidone. Reserpine-induced yawning was antagonized by sulpiride and by alpha-methyltyrosine suggesting that this behavior may be induced by endogenously released dopamine. Reserpine-pretreatment potentiated (+)-3PPP-induced yawning. The results argue against the view that yawning is the behavioural correlate of autoreceptor-mediated inhibition of DA transmission, and suggest that this behaviour is due to the stimulation of a special population of central postsynaptic DA receptors.

Salamone, J. D., M. D. Lalies, et al. (1986). "Behavioural and pharmacological characterization of the mouth movements induced by muscarinic agonists in the rat." Psychopharmacology (Berl) 88(4): 467-71.
Pilocarpine administered in doses of 1.25-10.0 mg/kg (IP) produced a variety of mouth movements in the rat. The most frequent of these movements was a chewing behaviour, which increased up to a mean frequency of over 40 per min at the highest doses. Tongue protrusion and gaping also showed dose-dependent increases. Yawning tended to increase in some doses, though these increases were not significant, and yawning was relatively infrequent. Pre-treatment with scopolamine reduced these responses, while pre-treatment with methyl scopolamine did not. Injections of oxotremorine or arecoline, but not carbachol, produced dose-related increases in mouth movements similar to those produced by pilocarpine. These results suggest that mouth movements in the rat are caused by stimulation of central muscarinic receptors. This may prove to be an important behavioural sign of central cholinomimetic activity.

Phoenix, C. H. and K. C. Chambers (1986). "Threshold for behavioral response to testosterone in old castrated male rhesus macaques." Biol Reprod 35(4): 918-26.
The sexual behaviors of old, intact (N = 5) and old, castrated (N = 6) rhesus macaque males were compared in six series of pair tests with receptive females. The castrated monkeys were tested when untreated and when given five doses of testosterone propionate (TP; 0.004, 0.016, 0.064, 0.256, and 1.024 mg/kg of body weight) in consecutive months. The serum testosterone (T) level was determined for each male before and after each series of tests. When untreated, none of the castrated males ejaculated, and yawning was significantly less in

these monkeys than in intact males-no other behavioral measures differed significantly. Within 2 weeks of daily injections of 0.004 mg of TP/kg, two males ejaculated, and all differences in measures of ejaculation were eliminated. A third male ejaculated after 1 week of treatment with 0.016 mg of TP/kg. Yawning values did not differ during and after treatment with 0.064 mg of TP/kg. Although final mean serum T levels were six times higher in castrated (24.3 ng/ml) than in intact males (4.2 ng/ml), sexual performance levels did not exceed those of intact males.

Okuyama, S., H. Shimamura, et al. (1986). "Electrophysiological and behavioral assessments of dopamine autoreceptor activation to apomorphine in rats." Arch Int Pharmacodyn Ther 284(2): 246-54.

Single neuronal activity was recorded extracellularly in the substantia nigra pars compacta (SNC) in rats anesthetized with chloral hydrate. Haloperidol in a dose of 10 micrograms/kg had no significant effects on the SNC neurons. R(-)apomorphine (cumulative i.v. dose of 40 micrograms/kg, given as: 5, 5, 10 and 20 micrograms/kg) inhibited the firing rate of dopaminergic neurons, in a dose-dependent manner. Haloperidol (cumulative i.v. dose of 10 micrograms/kg, as: 2.5, 2.5 and 5 micrograms/kg) reversed the effect of apomorphine. Complete reversal of the firing rate to haloperidol was observed with a dose of 10 micrograms/kg. In rats pretreated with 10 micrograms/kg of haloperidol, there was a dramatic shift to the right of the apomorphine dose-response curve (cumulative i.v. dose of 800 micrograms/kg, as: 50, 50, 100, 200 and 400 micrograms/kg), and this inhibition was reversed by haloperidol (cumulative i.v. dose of 400 micrograms/kg, as: 50, 50, 100 and 200 micrograms/kg). Apomorphine in doses of 40 micrograms/kg and 800 micrograms/kg elicited yawning behavior and stereotypy, respectively. Apomorphine in a dose of 800 micrograms/kg elicited stereotypy in rats treated 3 min before with 10 micrograms/kg of haloperidol. Therefore, electrophysiological determinations of events in the SNC dopaminergic neurons are given support by the behavior observed in these rats.

Nemeth-Coslett, R. and R. R. Griffiths (1986). "Naloxone does not affect cigarette smoking." Psychopharmacology (Berl) 89(3): 261-4.

In order to provide information about the hypothesis that endogenous opioids mediate the reinforcing properties of cigarette smoking, the present study examined the effects of naloxone, an opioid antagonist, on cigarette smoking in seven normal volunteers. The study used experimental procedures that had previously been shown sensitive for detecting the effects of other drugs, (including a nicotine antagonist) on smoking. Isolated subjects smoked their regular brand of cigarettes freely in a naturalistic laboratory environment while watching television or reading. Sixty minutes before each 2 h smoking session subjects received an IM injection of naloxone HCl (0.0625, 0.25, 1.0, or 4.0 mg/kg) or placebo. Each subject received each treatment three times in a mixed order across days. Naloxone did not significantly affect any measure of cigarette smoking including number of cigarettes, number of puffs, or expired air carbon monoxide level. Naloxone did, however, produce significant dose-related increases in subject ratings of yawning, stretching, and relaxation. The results of the present study provide no support for the endogenous opioid theory of smoking reinforcement.

Morelli, M., R. Longoni, et al. (1986). "Antagonism of apomorphine-induced yawning by SCH 23390: evidence against the autoreceptor hypothesis." Psychopharmacology (Berl) 89(2): 259-60.

The ability of apomorphine to induce yawning (YWG) in normal and reserpinized rats and its interaction with SCH 23390, a potent and specific D-1 receptor antagonist, was studied. Apomorphine was more potent in inducing YWG in reserpine-pretreated as compared to control rats. SCH 23390, in low doses (0.05 mg/kg SC), was able to significantly reduce the YWG evoked by apomorphine both in control and in reserpine-pretreated rats. The results indicate that D-1 receptors contribute to YWG elicited by apomorphine and contradict the idea that this effect is mediated by DA autoreceptors.

Morato, G. S. and R. N. Takahashi (1986). "Lack of the effect of ketamine on some dopaminergic behaviors in rats." Braz J Med Biol Res 19 (3): 403-9.

The effects of ketamine on some experimental models for detecting dopaminergic activity were studied in rats. Small doses of ketamine (0.3 and 0.5 mg/kg, ip) induced yawning behavior while higher doses (15 and 30 mg/kg, ip) inhibited both apomorphine- and amphetamine-induced stereotyped behaviors. Ketamine (up to 60 mg/kg, ip) per se failed to elicit typical stereotype or catalepsy similar to that induced by dopamine agonists or antagonists, respectively. Ketamine may have acted as an agonist on dopaminergic autoreceptors. These results do not support the view that the behavioral effects of ketamine are mediated by purely dopaminergic mechanisms.

Mogilnicka, E., K. Wedzony, et al. (1986). "Desipramine induces yawning behaviour in rats." Neuropharmacology 25(7): 783-6.

Yawning behaviour in rats injected subcutaneously with antidepressant drugs was studied by direct observation. Desipramine (0.1-30 mg/kg) elicited yawning that began 15-20 min after injection and lasted for 60 min, and the dose-response curve showed a bell-shaped form. Desipramine (10 mg/kg) elicited the maximal effect (mean number of yawns 13.6). Haloperidol (0.02 mg/kg), spiperone (0.2 mg/kg), pimozide (4 mg/kg), reserpine (7.5 mg/kg), alpha-methyl-p-tyrosine (250 mg/kg) and scopolamine (0.5 mg/kg) markedly reduced yawning induced by desipramine, whereas prazosin (1 mg/kg) and phenoxybenzamine (5 mg/kg) were without effect. These findings indicate that desipramine induces yawning by a dopaminergic mechanism, and that endogenous dopamine (DA) is necessary for its occurrence. Yawning was observed also after administration of imipramine, clomipramine, trazodone, its metabolite m-chlorophenylpiperazine and (+/-)sulpiride. These drugs given in a similar dose-range to desipramine produced a weaker effect than desipramine. Selective and potent inhibitors of the uptake of noradrenaline (NA) or 5-hydroxytryptamine (5-HT), (+)oxaprotiline and citalopram, did not elicit yawning. A possibility is considered that certain antidepressant drugs induced yawning through an influence on dopaminergic system.

Melis, M. R., A. Argiolas, et al. (1986). "Oxytocin-induced penile erection and yawning: site of action in the brain." Brain Res 398(2): 259-65.

Microinjection of oxytocin into the paraventricular nucleus of the hypothalamus or into the CA1 field of the hippocampus induced a dose-dependent increase in the number of penile erection and yawning episodes in male rats. The minimal effective dose of oxytocin injected into the paraventricular nucleus was 3 ng. This dose induced the above-mentioned behaviors in 60% of the treated rats. Doses of 9 ng or higher induced the symptomatology in more than 85% of the animals. On the other hand, when the peptide was injected into the CA1 field of the hippocampus, 9 ng bilaterally were necessary to elicit penile erection and yawning in 62% of the rats. Arg8-vasopressin, which only differs from oxytocin in two amino acids, induced penile erection and yawning when injected either into the paraventricular nucleus or into the hippocampus, but was 5-10 times less potent than oxytocin. Oxytocin injection into the lateral septum, caudate nucleus, subiculum, preoptic area, ventromedial nucleus and supraoptic nucleus, was ineffective. The powerful effect of oxytocin on the induction of yawning and penile erection, suggests a physiological role of hypothalamic and hippocampal oxytocin in the regulation of such responses.

Laping, N. J. and V. D. Ramirez (1986). "Prolactin induces yawning and the stretch-yawning syndrome in young adult male rats." Horm Behav 20 (1): 49-59.

Herein we report that subcutaneous injection of low doses of ovine prolactin (oPRL) induce yawning in young adult male rats. The most effective dose of oPRL in evoking yawning was 0.25 microgram/kg body weight (5.2 yawns/60 min at 1000 hr vs 0.3 in control animals). Doses of 0.025, 0.05, 2.5, 25, and 250 micrograms/kg were less effective. Interestingly, yawning in response to oPRL changes over the course of one circadian cycle with highest frequency at 1600 hr (11 yawns/80 min vs 2 yawns/80 min in animals injected with boiled oPRL). The onset of yawning in most oPRL-treated rats began approximately 40 min after oPRL injection, whereas with apomorphine the latency to the response was about 10 min. These results indicate that oPRL in addition to other hypophysial peptides such as ACTH and MSH can stimulate yawning. It is proposed that PRL after initial activation of the nigrostriatal dopamine system secondarily induces yawning by inhibition of this system via an autoreceptor-mediated negative feedback mechanism. This may explain the long latency to the response.

Jackson, A. and S. J. Cooper (1986). "An observational analysis of the effect of the selective kappa opioid agonist, U-50,488H, on feeding and related behaviours in the rat." Psychopharmacology (Berl) 90(2): 217-21.

The behaviour of partially pre-satiated rats consuming a sweet palatable food and treated with either vehicle or the specific kappa receptor agonist U-50,488H (0.1-3 mg/kg) was recorded on videotape. Analysis revealed that the hyperphagia induced by the kappa agonist (0.3-3 mg/kg) resulted from an increase in the duration of feeding and not from an increase in the local rate of eating. The increase in duration was due, in turn, to a greater frequency of bouts of feeding. The kappa agonist also increased the latency to the final feeding bout. The effect of U-50,488H was consistent with de-satiation, so that the increase in feeding duration was in evidence from the start of the test period, while the temporal pattern of later satiation was preserved but lagged behind that of control animals. At the largest dose, other recorded activities (rearing, locomotor activity, grooming) were suppressed, with a marked increased in inactivity. At the lowest dose (0.1 mg/kg) there was a significant increase in grooming behaviour. The results are discussed with reference to an hypothesis of opioid function in the control of food intake.

Hirsch, M. D. and T. L. O'Donohue (1986). "Structural modifications of pro-opiomelanocortin-derived peptides alter their behavioral effects markedly." J Pharmacol Exp Ther 237(2): 378-85.

Previous findings showed that pro-opiomelanocortin-containing neurons and endocrine cells synthesize multiple forms of beta-endorphin (beta E) and alpha-melanocyte-stimulating hormone (alpha-MSH), and that tissue specific post-translational processing of pro-opiomelanocortin can change ratios of the forms of secreted peptides. We therefore investigated the structure-activity requirements for behavioral interactions between beta E1-31 and alpha-MSH. Adult, male Sprague-Dawley rats received i.c.v. administrations of various dose combinations of alpha-MSH and beta E peptides, and behavioral activities were quantitated over a 55-min period. The results showed that both alpha-MSH and beta E1-31 produced dose-related increases in grooming behaviors. alpha-MSH also induced a stretching and yawning syndrome (SYS). beta E1-31 had no effect on SYS but did produce catatonia. BE1-31 inhibited both the grooming and SYS produced by alpha-MSH in a dose-related manner, and alpha-MSH potentiated beta E1-31-induced catatonia. Both N-terminal acetylation and C-terminal modification reduced the effects of beta E1-31 and reduced the inhibition by beta E1-31 of alpha-MSH-induced effects. Although the C-terminal fragments beta E28-31, beta E30-31 and beta E6-31 were devoid of behavioral effects when administered alone, all three peptides inhibited the effects of alpha-MSH on grooming and SYS markedly. Both beta E28-31 and beta E30-31 also inhibited the effects of beta E1-31 and beta E1-27. These results indicate that many of the behavioral actions of beta E1-31 reside in the N-terminus, and modulatory effects on alpha-MSH actions reside in the C-terminus.(ABSTRACT TRUNCATED AT 250 WORDS)

Gower, A. J., H. H. Berendsen, et al. (1986). "Antagonism of drug-induced yawning and penile erections in rats." Eur J Pharmacol 122(2): 239-44.

A number of centrally active drugs were tested for antagonism of physostigmine- or apomorphine-induced yawning and for apomorphine-induced penile erections. The alpha 2-adrenoceptor antagonists piperoxan and idazoxan inhibited the yawning response without affecting the penile erections. The 5HT agonist quipazine and the histamine antagonist dexchlorpheniramine inhibited the yawning response more effectively than the penile erections. Dexchlorpheniramine even enhanced the apomorphine-induced penile erections and induced penile erections in physostigmine-treated rats. The 5HT antagonists metergoline and methysergide blocked the apomorphine-induced penile erections without affecting the yawning response. The alpha 2-adrenoceptor agonist clonidine, the dopamine antagonist sulpiride, the antihistaminic mepyramine and the benzodiazepine chlordiazepoxide inhibited both yawning and penile erections at the same dose level. The alpha 1-adrenoceptor antagonists prazosin and phenoxybenzamine were inactive. It is concluded that yawning and penile erections can be differentially affected by drug treatments. Also, while concomitant yawning and penile erections can be selectively induced by a class of dopamine receptor agonists, the same selectivity does not apply to antagonism of these induced behaviours.

Gmerek, D. E. and J. H. Woods (1986). "Kappa receptor mediated opioid dependence in rhesus monkeys." Life Sci 39(11): 987-92.

The kappa receptor-selective agonist U-50, 488 was administered chronically to rhesus monkeys. Tolerance developed to the overt behavioral effects of U-50,488 without cross-tolerance to morphine. Withdrawal behaviors produced by deprivation, naloxone or quadazocine administration in U-50, 488-dependent monkeys consisted of hyperactivity, excessive grooming, and yawning. The syndrome was suppressed in a dose-related manner by a kappa agonist, ethylketazocine, but not by doses of morphine that suppressed its own withdrawal. The mu-selective antagonist, beta-funaltrexamine, at doses which are active in morphine-dependent monkeys, did not precipitate withdrawal in U50, 488-dependent monkeys. Dependence, which is the result of activity at the kappa receptor, was distinct from morphine dependence.

Ferrari, F., R. Martinelli, et al. (1986). "Imidazole has similar behavioural effects to yohimbine." Psychopharmacology (Berl) 88(1): 58-62.

A number of animal behavioural models were used to study the activity of imidazole (IMID) on the central nervous system. IMID antagonized in a dose-related fashion penile erections (PE) as well as stretching and yawning (SY) elicited in male rats by B-HT 920, an alpha 2 and dopamine (DA) autoreceptor agonist. Inhibition of B-HT 920-induced PE and SY was also exhibited by haloperidol, a DA receptor blocker, and yohimbine, but not by prazosin, alpha 2 and alpha 1 receptor antagonists respectively. Moreover IMID behaved similarly to yohimbine in: 1) counteracting clonidine-induced hypothermia in mice; 2) antagonizing sedation and sleep induced by clonidine and B-HT 920 in chicks, while haloperidol was ineffective. When administered to sexually active rats before the copulatory test, IMID at low doses, significantly altered some aspects of mating, a result which is interpretable in terms of enhanced sexual arousal and resembling the aphrodisiac effect reported for yohimbine. The neurochemical mechanisms involved in these effects are discussed.

Berendsen, H. H. and A. J. Gower (1986). "Opiate-androgen interactions in drug-induced yawning and penile erections in the rat." Neuroendocrinology 42(3): 185-90.

The effects of pretreatment with drugs on drug-induced yawning and penile erection in intact and chronically castrated rats were investigated. Naloxone partially blocked yawning in intact rats and in castrated rats pretreated with dihydro-testosterone propionate (DHTP) but not in control castrates. In contrast, naloxone potentiated apomorphine-induced penile erections in intact rats. Morphine, haloperidol and atropine blocked yawning and penile erections. Methyl naloxone, methyl atropine and domperidone at doses which are selectively peripheral-acting had no effect on drug-induced yawning or penile erection indicating that both effects are mediated centrally. Pretreatment with morphine did not change the naloxone effects in intact rats. The results indicate a naloxone-androgen interaction in drug-induced yawning but the results with morphine are not consistent with a role of opiates in this interaction. The penile erection data support a direct opiate-dopamine receptor interaction in this response. The haloperidol and atropine effects support a cholinergic-dopaminergic interaction in both yawning and penile erections.

Beck, C. H., H. L. Chow, et al. (1986). "Dose-related response of male rats to apomorphine: snout contact in the open-field." Physiol Behav 37(5): 819-25.

Apomorphine (0.01 to 5 mg/kg, SC) was administered to male rats observed singly in the open-field. The behavior of each rat was coded using a microprocessor during 3 preinjection and 9 postinjection trials of 6 min duration over a 2 hr session. The behavior categories included grooming, yawning, turning, nodding and gnawing, as well as snout contact and nonsnout contact variants of locomoting, rearing and sitting. Dose-dependent increases in the time spent in snout contact with the field surface were noted throughout the complete dose range. Both the peak and duration of the snout contact epoch increased with the dose of apomorphine. The integrated time spent in all types of snout contact proved to be the best behavioral measure for discriminating between doses of apomorphine even though the topography of snout contact response changed as a function of the dose.

Argiolas, A., M. R. Melis, et al. (1986). "Oxytocin: an extremely potent inducer of penile erection and yawning in male rats." Eur J Pharmacol 130(3): 265-72.

The intracerebroventricular (i.c.v.) injection of oxytocin, in doses ranging from 5 to 90 ng (5-90 pmol) induced penile erection and yawning in male rats. Such response was not induced by doses of the peptide higher than 100 ng, nor by equimolar doses of i.c.v. [Arg8] vasopressin, ACTH-(1-24), alpha-MSH, rat corticotropin-releasing factor (rCRF), delta sleep-inducing peptide, neurotensin or substance P. Oxytocin-induced penile erection and yawning were prevented by atropine and morphine, but not by methylatropine or the opiate antagonist naloxone. Haloperidol, a dopamine receptor antagonist, was ineffective at low doses; it partially prevented penile erection but not yawning at high doses. Since oxytocin is present not only in the neurohypophysis but also in other brain areas, our results suggest that oxytocin is implicated in the regulation of penile erection and yawning, and provide further evidence that oxytocin acts as a neuropeptide in the central nervous system.

Arai, K., K. Kita, et al. (1986). "[Progressive dysautonomia in hemangioblastoma in the region of the fourth ventricle]." No To Shinkei 38 (2): 195-200.

Tumors of the posterior fossa presenting orthostatic hypotension are rare and only nine cases have been reported so far. The locations of almost all these tumors were near the fourth ventricle and three of them were hemangioblastoma. A case of a tumor of the fourth ventricle showing autonomic disturbances mainly composed of orthostatic hypotension is reported. A 42-year-old male was admitted to the Department of Neurology of Chiba University Hospital on June 25th, 1981 because of three years' history of autonomic disturbances including orthostatic syncope, impotence, urinary disturbance and bowel dysfunction such as vomiting, diarrhea and constipation. He also complained of weight loss and staggering of gait to the left side. On admission, the patient was emaciated being 50 kg in weight and 172 cm in height. Neurological examination revealed hippus of bilateral pupils in light reflex, saccadic eye movement, slightly hypoactive deep tendon reflexes, mild terminal oscillations in bilateral finger-to-nose test, oscillation in the left heel-to-knee test, staggering tendency of gait to the left, slightly impaired tactile and thermal sensations in distal parts of the legs. Autonomic disturbances were showed by orthostatic hypotension (BP 104-50 in supine and 70-40 in sitting position), impotence, weight loss, anorexia, decrease of sweating, spontaneous yawning and loss of sensation of bladder fullness. About 5 weeks after admission, he began to complain of temporal headache and showed impairment of memory, drowsiness, paroxysmal apnea and papilledema.(ABSTRACT TRUNCATED AT 250 WORDS)

Ushijima, I., Y. Mizuki, et al. (1985). "Characteristics of yawning behavior induced by apomorphine, physostigmine and pilocarpine." Arch Int Pharmacodyn Ther 273(2): 196-201.

Apomorphine, a dopamine receptor agonist, physostigmine, an anticholinesterase agent and pilocarpine, a cholinergic receptor agonist, produced yawning in rats, with the most effective doses being 0.25 mg/kg, 0.2 mg/kg and 4 mg/kg, respectively. The yawning induced by these drugs is characterized by differences in direction of head moving, tongue protruding and duration of the yawn. The apomorphine-induced yawn was characterized by a slow and wide opening of the mouth with the head moving mainly downward and with a marked protrusion of the tongue. The apomorphine-induced yawn was 3.6 sec in duration. Physostigmine elicited a similar yawn to that seen with apomorphine, except for moving of the head in the upward direction. The pilocarpine-induced yawn was characterized by the head moving forward with a high frequency but without tongue protrusion and lasted 1.8 sec. The frequency of physiological yawning was low, but the behavioral posture was almost similar to that of physostigmine-induced yawning. The characteristics of yawns induced by these agents were unchanged at all doses of the drugs. Different doses altered the frequency of yawning. After pretreatment with mecamylamine, the apomorphine- and physostigmine-induced tongue protruding was inhibited and the duration of the yawning induced by the both drugs was shortened. The results suggest that the behavioral features of yawning induced by apomorphine, physostigmine and pilocarpine differ from one another, and that physiological yawning as well as physostigmine-induced yawning may be mediated by endogenous acetylcholine which stimulates both muscarinic and nicotinic receptors.

Protais, P., C. Hermier, et al. (1985). "The discriminant dopamine antagonist property of benzamides is observed at various times after their systemic or intracerebroventricular administration." Neuropharmacology 24(9): 861-7.

The cataleptogenic effect or the antagonism of apormorphine-induced behaviour (climbing, sniffing, licking and yawning) shown by haloperidol, (+/-)sulpiride and (+/-)amisulpride were determined at different times after their intraperitoneal or intraventricular administration. After intraperitoneal injection, the ED50 or ID50 of haloperidol was similar for all the behavioural responses. On the other hand, sulpiride and amisulpride were effective on climbing and yawning in smaller doses than on sniffing, licking and catalepsy. The property of amisulpride to antagonize climbing at smaller doses than sniffing was still found whether this benzamide derivative was injected 30, 90, 150 or 240 min before testing. After the intraventricular administration of neuroleptics, a dissociated antagonist efficacy appeared for haloperidol, but that of sulpiride and amisulpride became much more marked than after their intraperitoneal injection. Amisulpride antagonized climbing in smaller doses than sniffing, whether administered intraventricularly 15, 30 or 120 min before testing. These results indicate that the dissociated dopamine antagonist efficacy of benzamides is long lasting and is observed even when the passage across the blood-brain barrier is avoided (i.c.v. route).

Poggioli, R., A. V. Vergoni, et al. (1985). "Influence of yohimbine on the ACTH-induced behavioural syndrome, in rats." Pharmacol Res Commun 17(7): 671-8.
In adult male rats, yohimbine at low doses (0.1, 0.5 and 1 mg/kg i.p.) potentiated, and at high doses (30.0 mg/Kg) antagonized, the behavioural syndrome induced by the intracerebroventricular injection of ACTH 1-24 (3 micrograms/rat) (stretching-yawning syndrome and penile erections). These results support the hypothesis that brain catecholaminergic systems play a positive role in the ACTH-induced behavioural syndrome.

Miyazaki, M., Y. Tanaka, et al. (1985). "[Attack of yawning, case report]." Rinsho Shinkeigaku 25(9): 1007-9.

McCorkell, S. J. (1985). "Fractures of the styloid process and stylohyoid ligament: an uncommon injury." J Trauma 25(10): 1010-2.
Fracture of an elongated styloid process or ossified stylohyoid ligament is uncommon. Neck or throat pain, decreased mobility, hoarseness, and mass in the neck are signs and symptoms of fracture. The inciting trauma may be as mild as yawning but more often blunt trauma of a serious nature, such as motor vehicle accident, is the cause. The diagnosis may be missed because of difficulty imaging the stylohyoid apparatus. Two cases are presented that demonstrate the variability of symptoms and trauma. Previous reports of similar injuries and selection of radiographic examinations, including computed tomography, are discussed.

Holmgren, B., R. Urba-Holmgren, et al. (1985). "Association of spontaneous and dopaminergic-induced yawning and penile erections in the rat." Pharmacol Biochem Behav 22(1): 31-5.
In a Sprague-Dawley-derived line of rats, selectively bred to establish a high incidence of spontaneous yawning behavior, the simultaneous and systematic monitoring of yawning and penile erections, during observation periods of one hour, demonstrates a linear correlation between these two behavioral patterns. Dose-effect curves of yawning and penile erections elicited by apomorphine and bromocriptine, and their inhibition by metoclopramide are quite similar. These results strongly suggest that yawning and penile erection are subject to some common regulating and modulating mechanisms, one of which seems to involve dopaminergic pathways.

Francesca, F. and G. Baggio (1985). "Influence of imidazole on behavioral effects induced by dopaminergic agonists in rats." Life Sci 36 (14): 1397-405.
Imidazole (IMI) (from 18.7 to 300 mg/Kg) i.p. injected in adult rats induced shaking, which was antagonized by both morphine (MOR) and haloperidol (HALO) but not by methysergide (MET). I.p. IMI pretreatment inhibited the penile erections (PE) and stretching and yawning (SY) typically elicited by N-n-propylnorapomorphine (NPA), a well-known CNS dopamine (DA) receptor stimulant, injected either i.p. or i.c.v., whereas it enhanced stereotyped behavior (SB). IMI had similar effects on the same parameters considered when injected before lisuride, an ergot derivative also active as a central DA receptor agonist. In this case not only SB but also and above all aggressiveness were markedly potentiated, both the signs appearing at doses of lisuride which were "per se" ineffective. Aggressiveness, like SB, was not sex linked and was antagonized by HALO and MOR, but not by MET. IMI alone potentiated the fighting induced by electrical shock, an effect which was abolished by HALO pretreatment. Considering the results obtained as a whole it is submitted that IMI antagonizes PE and SY through a selective blockade of a class of DA receptors, presumably DA presynaptic autoinhibitors, thus potentiating SB and aggressiveness, which involve stimulation of DA postsynaptic receptors.

Ferrari, F. and G. Baggio (1985). "Influence of cimetidine, ranitidine and imidazole on the behavioral effects of (+/-) N-n-propylnorapomorphine in male rats." Psychopharmacology (Berl) 85(2): 197-200.
Cimetidine injected IP 15 min before (+/-) N-n-propylnorapomorphine (NPA) antagonized in dose-dependent fashion the penile erections (PE) and stretching and yawning (SY) induced by this typical dopaminergic agonist in male rats. Ranitidine, which acts on H2 histamine receptors in much the same way as cimetidine despite its lack of an imidazole ring, failed to produce the same effect. On the other hand, imidazole itself was similar to cimetidine in antagonizing PE and SY induced by (+/-) NPA, whether injected IP or ICV. Neither imidazole nor cimetidine antagonized the stereotyped behaviour (SB) induced by (+/-) NPA. Indeed, imidazole reduced the latency of this response. A mechanism which may underly these effects is discussed, as well as the possible preclinical use of this test in animals.

Ferrari, F. (1985). "Sexual excitement and stretching and yawning induced by B-HT 920." Pharmacol Res Commun 17(6): 557-64.
The azepine derivative B-HT 920, a putative agonist at dopamine (DA) autoreceptors, injected IP in adult male rats, induced numerous penile erections (PE) and stretching and yawning (SY), considered typical signs of central DA receptor stimulation, without eliciting stereotyped behaviour (SB). Both signs induced by B-HT 920 were dose related and significantly enhanced with respect to controls from 10 to 1,000/micrograms/kg. Pretreatment with the neuroleptics haloperidol (0.025, 0.5 and 1 mg/Kg IP), sulpiride (20 and 40 mg/Kg) and alpha 2-antagonist yohimbine (1 and 3 mg/Kg IP) antagonized the behavioural effect of B-HT 920 whereas the alpha 1-antagonist prazosin (1 mg/Kg IP) had no effect on the response. The impressive activity of B-HT 920 in producing SY and PE, along with its inability to evoke SB, supports the role of DA autoreceptors in the regulation of SY and sexual behaviour.

Ferrari, F. (1985). "Behavioural pharmacology of imidazole, a potential antidepressant agent." Arch Int Pharmacodyn Ther 277(2): 303-12.
Imidazole (IMID) inhibited (+/-) N-n-propylnorapomorphine (NPA) and BHT-920 induced penile erections (PE) and stretching and yawning (SY) in rats as well as apomorphine (APO) induced hypothermia in mice, enhanced shock-elicited aggressiveness in rats and antagonized sleep induced by clonidine in chicks. IMID moreover displayed activity in behavioural tests used in specific screening for antidepressants, potentiating yohimbine toxicity in mice and antagonizing immobility time in the despair test, with a potency in some cases equal to imipramine. IMID per se, depressed motor activity in both mice and rats. The possible mechanism of action and receptors involved are briefly discussed as well as IMID's profile as an antidepressant drug.

Dourish, C. T., S. J. Cooper, et al. (1985). "Yawning elicited by systemic and intrastriatal injection of piribedil and apomorphine in the rat." Psychopharmacology (Berl) 86(1-2): 175-81.
The behavioural effects of systemic and intrastriatal injections of the dopamine agonists piribedil and apomorphine in male rats were examined. Bilateral application of piribedil (50 and 100 micrograms) or apomorphine (5, 10 and 20 micrograms) to the striatum produced yawning and chewing mouth movements accompanied by intermittent stretching and sexual arousal. Low doses of piribedil (1.25 and 2.5 mg/kg) and apomorphine (0.1 and 0.2 mg/kg) injected SC produced an identical yawning syndrome. Previous work has suggested that yawning elicited by systemic dopamine agonist treatment is a consequence of dopamine autoreceptor stimulation. Similarly, the most likely explanation of the present data is that yawning elicited by systemic and central dopamine agonist treatment was due to activation of dopamine autoreceptors. Systemic injection of haloperidol and scopolamine abolished yawning induced by intrastriatal piribedil and these data provide tentative support for the proposal that a dopamine-acetylcholine link may be involved in the expression of yawning.

Dourish, C. T. and P. H. Hutson (1985). "Bilateral lesions of the striatum induced with 6-hydroxydopamine abolish apomorphine-induced yawning in rats." Neuropharmacology 24(11): 1051-5.
The subcutaneous injection of 0.1 mg/kg apomorphine induced a syndrome consisting of yawning, chewing and sexual arousal in male rats. Bilateral lesions of the striatum induced with 6-hydroxydopamine abolished the drug-induced yawning, chewing and sexual arousal and produced a 58% depletion of the concentrations of dopamine in the striatum. These data suggest that apomorphine-induced yawning is mediated by presynaptic dopamine receptors (which may be autoreceptors). Furthermore, it appears that dopaminergic innervation of the striatum may play an important role in the production of yawning elicited by small doses of dopamine agonists.

Delbende, C., S. Jegou, et al. (1985). "[Role of alpha-MSH and related peptides in the central nervous system]." Rev Neurol (Paris) 141 (6-7): 429-39.
Alpha-melanocyte stimulating hormone (alpha-MSH) is a tridecapeptide secreted by intermediate lobe cells and synthesized in the brain as well. As a hormonal peptide, the physiological function of alpha-MSH consists mainly in the control of pigment movements within dermal melanophores. At the pituitary level, alpha-MSH secretion is under multifactorial control: it is inhibited by dopamine and GABA and stimulated by corticoliberin (CRF), thyroliberin (TRH), beta-adrenergic agonists and (or) serotonin. Identification of alpha-MSH containing neurons in the hypothalamus and other brain regions (septum, thalamus, mid-brain, striatum, hippocampus, cerebral cortex and spinal cord) has been carried out by means of immunological and biochemical techniques combined with bioassays. In the central nervous system (CNS) as in the hypophysis, alpha-MSH is synthesized from a high molecular weight precursor, pro-opiomelanocortin (POMC). Maturation of this protein yield similar end products in the hypothalamus and the intermediate lobe. Several peptides chemically related to alpha-MSH are generated including the desacetyl and monoacetyl (authentic alpha-MSH) forms; the latter has the greatest behavioral activity. The demonstration that alpha-MSH has numerous central nervous system effects has raised the possibility that this neuropeptide acts as a neuromodulator or a neurotransmitter. In the rat, intra-cerebroventricular administration of ACTH/MSH peptides induces the stretching-yawning syndrome (SYS) which is frequently preceded by excessive grooming. This excessive grooming is blocked by neuroleptics indicating that the central dopaminergic neurons are implicated in this behavioral effect of the peptide. alpha-MSH is involved in memory, arousal and attention; in hypophysectomized animals, the learning ability is restored after administration of MSH or related peptides. Injection of alpha-MSH delays also extinction of passive avoidance behavior and affects performances motivated by hunger as well as aggressive behavior. Recent studies concerning the role of alpha-MSH have been undertaken in human beings. The effects of MSH-related peptides favour a role of these peptides in arousal: they maintain a high level of vigilance and improve visual discrimination. These behavioral changes were accompanied by marked changes in CNS electrophysiology. Current studies, which aim at establishing a neurotransmitter function for alpha-MSH, concern the distribution and characterization of alpha-MSH receptors in the central nervous system and the mechanism controlling the release of neuronal alpha-MSH.

Buckingham, R. A., D. R. Stuart, et al. (1985). "Experimental evidence against middle ear oxygen absorption." Laryngoscope 95(4): 437-42.
The present theory of eustachian tube (ET) function and middle ear (ME) ventilation posits that oxygen absorbed by the ME mucosa causes negative ME pressure which is relieved by periodic opening of the ET during swallowing and yawning. After developing a method to cannulate the ET of mongrel dogs we connected the cannulas hermetically to manometers. This system excluded ET function and tested the

oxygen absorption capacity of the ME. When we controlled respiration and maintained blood gas PO2 and PCO2 at normal levels, we were unable to find any manometric evidence of negative pressure of gas absorption in the dog ME. Lowering the PCO2 and raising the PO2 of the blood by hyperventilation caused negative ME pressure which could be measured manometrically. We confirmed these findings with the tympanometer. Raising the PCO2 and lowering the PO2 by hypoventilation caused positive pressure in the ME. There is no evidence in these experiments that O2 absorption occurs or causes negative ME pressure in the dog. To the contrary there is evidence that elevated blood levels of the more diffusible CO2 cause an increase in the ME pressure and lowered CO2 level causes a negative ME pressure.

Braszko, J. J., K. Majewski, et al. (1985). "Effect of angiotensin II on some behavioral and neurochemical measures of the central serotonine system." Biomed Biochim Acta 44(9): 1359-68.

The effects of angiotensin II (AII) given intracerebroventricularly (icv.) on behaviors controlled by central serotonine (5-HT) and on some neurochemical measures of central 5-HT function have been investigated in rats. AII (0.1 and 0.5 micrograms) increased the 5-HT (20 micrograms, icv.) and L-tryptophan (200 mg/kg, ip.) induced hyposensitivity to painful electric stimuli delivered to the animals feet. Also AII (0.5 micrograms) intensified yawning, a 5-HT dependent behavior. This effect was decreased or abolished, respectively, by mianserin (3 mg/kg, i.p.) or cyproheptadine (1 mg/kg, i.p.), the 5-HT receptors blockers. AII, however, influenced neither the slight hyposensitivity of rats to electric current caused by 5-hydroxytryptophane (5-HTP, 12.5 and 25 mg/kg, ip.) nor the number of 'Wet-Dog' shakes evoked by 5-HTP (100 mg/kg, i.p.). Also, the peptide did change the rate of 5-HTP accumulation in brain measured after pretreatment of the animals with L-tryptophan (200 and 500 mg/kg, i.p.) preceded by the inhibition of central aromatic amino acid decarboxylase. In vitro AII (10(-5) - 10(-9) mol/l) did not affect release and only slightly increased uptake of 3H-5-HT by blood platelets. The data indicate that AII stimulates central 5-HT neurotransmission and that this action does not result from the peptide interference with the synthesis, release and uptake of 5-HT.

Bielert, C. (1985). "Testosterone propionate treatment of an XY gonadal dysgenetic chacma baboon." Horm Behav 19(4): 372-85.

Behavioral studies of an XY gonadal dysgenetic chacma baboon prior to and during testosterone propionate treatment were carried out. The orchidectomized dysgenetic individual, two intact males, a castrate male, and two ovariectomized females were pair-tested with a group of eight ovariectomized stimulus females prior to and during their treatment with estradiol benzoate. Three test series were carried out. One series occurred prior to any treatment of the agonadal focal subject animals. During this series it was only the intact males who showed behavior change during their testing with the estrogen treated females. A second test series occurred after a month of daily testosterone propionate injections (1 mg/kg/day) had been given to the four agonadal subjects. During this test series the castrate male ejaculated once with one of the estrogen-treated females. All of the treated subjects showed increases in their frequency of yawning. Upon completion of this test series the androgen dosage was increased (2 mg/kg/day) and 2 weeks later a third test series was carried out. During this series the castrate male ejaculated with five of his eight estrogen-treated partners. The yawning of all the treated subjects continued. As had been the case in the second series the XY gonadal dysgenetic individual continued to behave as did the ovariectomized females. None of these animals showed any increase in any measure of male sexual behavior. This study establishes the fact that a genetic male primate deprived of in utero exposure to testicular hormones will go on to develop as a normal genetic female and will fail to exhibit increased levels of male sexual behavior during androgen treatment.

Argiolas, A., M. R. Melis, et al. (1985). "Intraventricular oxytocin induces yawning and penile erection in rats." Eur J Pharmacol 117(3): 395-6.

Ushijima, I., K. Yamada, et al. (1984). "Muscarinic and nicotinic effects on yawning and tongue protruding in the rat." Pharmacol Biochem Behav 21(2): 297-300.

Physostigmine, an anticholinesterase agent, elicited yawning with a marked protrusion of the tongue and teeth chattering. Yawning and chattering were also observed after pilocarpine, a cholinergic agonist predominantly acting upon muscarinic receptors. Apomorphine at low doses (0.1-0.5 mg/kg), which preferentially activates presynaptic dopamine autoreceptors, elicited yawning, whereas at high doses (1-2 mg/kg) it produced stereotypy. Yawning induced by both cholinergic agonists and apomorphine was inhibited by scopolamine, a muscarinic receptor blocking agent, but not by methylscopolamine, a peripheral anticholinergic agent and mecamylamine, a nicotinic receptor blocking agent. Low dose (0.02 mg/kg) of haloperidol, which has been reported to block presynaptic dopamine autoreceptors, inhibited apomorphine-induced yawning but did not affect cholinergic agonist-induced yawning. Physostigmine-elicited tongue protruding was inhibited by mecamylamine. The results imply that yawning behavior is essentially associated with the stimulation of central muscarinic receptors, and that physostigmine also induces tongue protruding by activating the central nicotinic receptors.

Ushijima, I., Y. Noda, et al. (1984). "Modification of apomorphine-, physostigmine- and pilocarpine-induced yawning after long-term treatment with neuroleptic or cholinergic agents." Arch Int Pharmacodyn Ther 271(2): 180-8.

Chronic treatment with haloperidol, physostigmine and scopolamine exerted different effects on the frequency of yawning induced by apomorphine (0.25 mg/kg, i.p.), physostigmine (0.2 mg/kg, i.p.) and pilocarpine (4 mg/kg, i.p.) as compared with chronic treatment with saline. Haloperidol decreased the apomorphine- and physostigmine-induced yawning but not the pilocarpine-induced yawning. Physostigmine reduced only the pilocarpine-induced yawning without affecting the apomorphine- and physostigmine-induced yawning. However, physostigmine showed the most rapid onset- and peak-time of yawning induced by a high dose of physostigmine (0.75 mg/kg, i.p.) as well as that of pilocarpine (8 mg/kg, i.p.), and potentiated apomorphine (1 mg/kg, i.p.)-induced stereotypy, as compared with that observed in the saline group. Scopolamine potentiated the physostigmine- and pilocarpine-induced yawning but not the apomorphine-induced yawning. A single pretreatment with scopolamine (0.5 mg/kg, i.p.), however, depressed these yawning responses. The results suggest that yawning induced by physostigmine, but not by pilocarpine, may be modified by long-term treatment with haloperidol. The stereotypy mediated by the postsynaptic dopaminergic system, but not the yawning mediated by the presynaptic system, may be altered by chronic treatment with physostigmine, while long-term treatment with scopolamine seems to produce a supersensitivity to cholinergic receptors.

Szechtman, H. (1984). "Timing of yawns induced by a small dose of apomorphine and its alteration by naloxone." Prog Neuropsychopharmacol Biol Psychiatry 8(4-6): 743-6.

The report examines the temporal sequence of yawns induced by apomorphine and whether the opiate antagonist, naloxone, affects it. Before administering apomorphine (0.075 mg/kg) or saline, rats (n = 8) were pretreated with naloxone (1 mg/kg) or saline. Each subject received all 4 possible treatments (saline-saline, saline-apomorphine, naloxone-saline, and naloxone-apomorphine) in random order. Results indicate that yawning induced by apomorphine seems to come in fits; that is, there is a series of yawns spaced closely together and followed by a period of quiescence before the start of another cluster of yawns. Naloxone reduced the number of apomorphine-induced yawns, and the occurrence of very short inter-yawn intervals. It is suggested that the timing of yawns may provide useful information regarding some pathologies and that opiates may potentiate the action of dopaminergic systems.

Stahle, L. and U. Ungerstedt (1984). "Assessment of dopamine autoreceptor agonist properties of apomorphine, (+)-3-PPP and (-)-3-PPP by recording of yawning behaviour in rats." Eur J Pharmacol 98(2): 307-10.

Yawning behaviour in rats was studied by direct observation. Apomorphine dose dependently induced yawning: 0.05 mg/kg was most effective, 0.2 mg/kg induced locomotor and sniffing behaviour but less yawning. Sulpinide (2 and 10 mg/kg) dose dependently blocked the apomorphine (0.05 mg/kg)-induced yawning. (+)-3-PPP (1-10 mg/kg) induced yawning in a manner similar to that of apomorphine but (-)-3-PPP (1-10 mg/kg) did so only weakly. Yawning induced by (+)-3-PPP was blocked by sulpiride 10 mg/kg. It is concluded that (+)-3-PPP but not (-)-3-PPP is at least as effective as apomorphine to induce yawning in rats, indicating that (+)-3-PPP, but not (-)-3-PPP, is a pure agonist on dopamine autoreceptors.

Serra, G., M. Collu, et al. (1984). "Estrogens antagonize apomorphine-induced yawning in rats." Eur J Pharmacol 104(3-4): 383-6.

The administration of a small dose of apomorphine (50 micrograms/kg s.c.) induced repeated episodes of yawning in male rats. Short-term (3 days) treatment with 17 beta-estradiol antagonized apomorphine-induced yawning in male rats. Moreover, apomorphine induced yawning much less effectively in female than in male rats. These results suggest that both endogenous or exogenously administered estrogens induce subsensitivity of the DA receptors mediating yawning in rats.

Potterton, D. (1984). "From hospital to home, three. The yawning gap." Nurs Times 80(32): 34-5.

Poggioli, R., A. V. Vergoni, et al. (1984). "Influence of clonidine on the ACTH-induced behavioral syndrome." Eur J Pharmacol 101(3-4): 299-301.

In male rats, clonidine in a dose range of 1-3000 micrograms/kg i.p. antagonized the stretching-yawning syndrome induced by the intraventricular injection of ACTH-(1-24) (3 micrograms/rat) dose-dependently. On the other hand, the effect of clonidine on ACTH-induced penile erections was potentiation at low doses (5 and 10 micrograms/kg) and inhibition at the highest doses (1000 and 3000 micrograms/kg), the intermediate doses (50 and 100 micrograms/kg) being without effect. There was no relationship between these behavioral effects and the effect on arterial blood pressure.

Paroli, E., P. Nencini, et al. (1984). "Clinical and experimental evidence of an opiate-like activity of lefetamine." Pharmacol Res Commun 16(9): 915-22.

A case of lefetamine abuse (0.9-1.8 g/day in 15-30 i.m. divided doses) is reported. In this patient, the administration of naloxone precipitated a mild opiate-like withdrawal syndrome, characterized by mydriasis, piloerection, yawning and a slight increase of blood pressure. The complete withdrawal of lefetamine, substituted by a placebo regimen, aggravated these symptoms. Furthermore, experimental results showed that lefetamine induced a naloxone-reversible inhibition of the guinea-pig ileum contractile response to electric field stimulation, and that naloxone pretreatment of mice prevented lefetamine antinociceptive activity in the hot-plate test. The clinical and experimental findings suggest that lefetamine has an opiate-like activity.

Oitzl, M. S. and J. P. Huston (1984). "Electroencephalographic spreading depression and concomitant behavioral changes induced by intrahippocampal injections of ACTH1-24 and D-Ala2-Met-enkephalinamide in the rat." Brain Res 308(1): 33-42.
ACTH1-24 (0.5 or 10 micrograms = 0.17 or 3.45 nmol) and D-Ala2-Met-enkephalinamide (DAME; 10 micrograms = 17.05 nmol) were injected unilaterally into the hippocampus of freely moving rats to examine their effects on EEG activity, DC potentials and behavior. In 85% of the rats DAME elicited spreading depression (SD) with epileptiform discharges preceding and following the wave of SD. The following behavioral changes were recorded. DAME- and KCl-induced SD were accompanied by an increase in locomotor activity and wet-dog shaking behavior, which occurred only during the period of SD. After a wave of SD induced by DAME a biphasic pattern of activity, consisting of an initial depression in locomotion followed by hyperactivity, appeared in 59% of the rats. ACTH1-24 elicited SD in 13% of the rats tested. Neither the dosage of ACTH1-24 nor the strain of rats influenced the occurrence of SD and the incidence of ACTH-induced grooming behavior. SD induced by KCl also resulted in excessive grooming comparable to that induced by ACTH1-24. In the case of KCl-induced SD, grooming began directly after the injection of KCl and was frequently interrupted by short periods of locomotion. ACTH-induced grooming had a later onset and episodes of stretching and yawning were observed. It can be concluded that the behavioral effects of the injection of DAME are unspecific responses to SD and seizure activity. However, ACTH-induced grooming is not solely a byproduct of SD, since it occurred also in the absence of SD.

Nickolson, V. J., H. van Riezen, et al. (1984). "Response changes after repeated low apomorphine: dopamine autoreceptor desensitization or learning?" Psychopharmacology (Berl) 83(2): 188-93.
Repeated injection of rats with low doses of apomorphine (APO), which selectively interact with dopamine (DA) autoreceptors, caused a change in yawning responses that suggests initial low-APO-induced desensitization of DA autoreceptors, followed by a long-lasting rebound hypersensitivity. Repeated treatment with low APO followed by open-field testing, however, yielded totally different results. APO accelerated intrasession response decrement and upon repeated administration enhanced the intersession response decrement. Both for yawning and open-field behavior, the response change after the second dose of APO was only evident when the first as well as the second APO injection were followed by exposure of the rat to the same test situation. These results indicate that response changes after repeated treatment with low APO are not due to a simple DA-agonist-induced change in receptor sensitivity but that drug experience combined with environmental influences play a decisive role.

Mogilnicka, E., C. G. Boissard, et al. (1984). "Effects of apomorphine, TL-99 and 3-PPP on yawning in rats." Neuropharmacology 23(1): 19-22.
Dopaminergic agonists, apomorphine (APO) (0.025-0.25 mg/kg, s.c.), TL-99 (0.5-3 mg/kg, s.c.) and 3-PPP (0.15-10 mg/kg, s.c.) elicited yawning in rats and the dose-response curves of all 3 compounds showed a bell-shaped form. Haloperidol (0.02 mg/kg, s.c.) reduced the yawning induced by DA-agonists to about 50%. The potencies of the DA-agonists in inducing yawning were APO greater than TL-99 greater than 3-PPP (comparable to potencies obtained in other in vivo tests, determining DA-ergic activity). The findings support the validity of the yawning phenomenon as a screening test for DA-agonists. Additionally, it was found that apomorphine induced yawning was significantly and dose-dependently enhanced by the beta-agonist, formoterol. This effect was counteracted by scopolamine, not changed by metergoline and further increased by l-propranolol. These data support the hypothesis of cholinergic involvement in yawning and indicate a role, though unclear at present, of beta-receptors in this behaviour.

Hylander, W. L. (1984). "Stress and strain in the mandibular symphysis of primates: a test of competing hypotheses." Am J Phys Anthropol 64 (1): 1-46.
The primary purpose of this study was to test various hypotheses about symphyseal stress in primates. First, those patterns of symphyseal strain that would be associated with various hypothetical patterns of symphyseal stress were formulated. Then these hypothetical patterns of stress and strain were tested by comparing the formulated bone strain pattern with actual in vivo symphyseal bone strain patterns. Patterns of in vivo symphyseal bone strain were determined by bonding rosette and/or single-element strain gages to the midline of the middle and lower third of the labial aspect of the symphysis of six adult Macaca fascicularis. Following recovery from the anesthetic, bone strain was recorded during mastication, incision, and isometric biting. Symphyseal bone strain was also recorded during yawning, licking, and threat behaviors. The data suggest that during the power stroke of mastication, the macaque symphysis is predominately sheared dorsoventrally and/or twisted about a transverse axis and bent by lateral transverse bending of the mandibular corpora. During lateral transverse bending of the mandibular corpora, the labial aspect of the macaque symphysis experiences compressive bending stress, while the lingual aspect experiences tensile bending stress. During the opening stroke of mastication and during other jaw opening behaviors, the macaque symphysis is bent by medial transverse bending of the mandibular corpora. At this time the labial aspect of the symphysis experiences tensile bending stress, while its lingual aspect experiences compressive bending stress. During both the power and opening strokes of mastication, the macaque mandible is bent in the plane of its curvature, and therefore the mandible acts as a curved beam. This is important because it results in elevated levels of stress along the lingual aspect of the macaque symphysis, particularly during the power stroke of mastication. During the power stroke of incision, the local effects of the bite force are unknown; however, at this time the lower half of the macaque symphysis is both sheared dorsoventrally and bent due to twisting of the mandibular corpora about their long axes. The results of this stress analysis have implications for understanding the mechanical attributes of symphyseal structure. In order to counter dorsoventral shear, the most important symphyseal attribute is to have adequate cross-sectional area of bone in the plane of the applied stress. In contrast, both the cross-sectional area of bone and symphyseal shape is important in order to counter stress effectively during symphyseal torsion and the three symphyseal bending regimes.(ABSTRACT TRUNCATED AT 400 WORDS)

Harrison, W., J. Stewart, et al. (1984). "Unusual side effects of clomipramine associated with yawning." Can J Psychiatry 29(6): 546.

Gower, A. J., H. G. Berendsen, et al. (1984). "The yawning-penile erection syndrome as a model for putative dopamine autoreceptor activity." Eur J Pharmacol 103(1-2): 81-9.
The efficacy of several drugs to elicit yawning and penile erections were determined in rats. The dopamine agonists, N-propylnorapomorphine, apomorphine, pergolide, (+/-)-3-PPP, TL-99 and N,N-dipropylamino-5,6-dihydroxy-1,2,3,4-tetrahydronaphthalene (N,N-dipropyl A-5,6-DTN) all elicited yawning accompanied by an increase in spontaneous penile erections. The potencies of these drugs in causing yawning closely resemble published data concerning their actions in biochemical tests reputedly indicative of autoreceptor activity. In contrast, SK&F 38393, A-5,6-DTN and clonidine produced no yawning and few or no penile erections. Although physostigmine also caused yawning, the effect was not accompanied by penile erections. Studies with the optical isomers of 3-PPP showed that (+)-3-PPP was considerably more potent than (-)-3-PPP. Haloperidol antagonised dopamine agonist-induced yawning and penile erections. Apomorphine-induced yawning and penile erections were also antagonised by sulpiride and atropine but not by domperidone. The suitability of elicitation of the combined syndrome of yawning plus penile erections as useful behavioural model for dopamine autoreceptor agonists is discussed.

Genedani, S., M. Bernardi, et al. (1984). "Effect of alpha-difluoromethylornithine (DFMO) on the behavioral syndrome induced by intracerebroventricular injection of ACTH 1-24, in rats." Neuropeptides 4(3): 247-50.
Stretching-yawning syndrome (SYS) and penile erections (PE) are typical components of the behavioral picture induced by intracerebroventricular (i.c.v.) injection of ACTH 1-24. The present study shows that pretreatment with alpha-difluoromethylornithine (DFMO), and irreversible inhibitor of mammalian ornithine decarboxylase (ODC), antagonizes these behavioral effects in a dose-dependent way, in rats. These results suggest that ODC and polyamines may play a role in the transduction and transmission of receptor-mediated signals.

Edery, H., G. Porath, et al. (1984). "Activity of novel aminocannabinoids in baboons." J Med Chem 27(10): 1370-3.
The axial and equatorial isomers of 7-(methylamino)hexahydrocannabinol (1 and 2) and 7-(dimethylamino)hexahydrocannabinol (3 and 4) were prepared by reductive amination of the corresponding cannabinoid aldehydes. The amines caused some tranquility in baboons but did not evoke the typical cannabimimetic syndrome caused by psychoactive cannabinoids. However the axial amines (1 and 3) but not the equatorial ones (2 and 4) caused bouts of scratching and yawning. The latter is a rare pharmacological effect hitherto not observed with other cannabinoids.

Anias, J., B. Holmgren, et al. (1984). "Circadian variation of yawning behavior." Acta Neurobiol Exp (Wars) 44(4): 179-86.

van Someren, V. and J. K. Stothers (1983). "A critical dissection of obstructive apnea in the human infant." Pediatrics 71(5): 721-5.
It is universally accepted that with the cessation of airflow, the infant is technically apneic, but the significance of such respiratory "pauses" remains a matter of discussion. Central apnea is easily recognized, but the absence of airflow with continued "respiratory" movements is commonly interpreted as obstructive apnea. The respiratory pattern of individual normal and abnormal infants was studied in depth. Airflow was monitored using a recently devised facial plate thermistor system; chest movement was recorded by measuring changes in thoracic impedance. On several occasions, esophageal pressure was also recorded as was expired CO2. Using the above systems, it was confirmed that mouth breathing in the infant is confined to periods of crying or yawning, and that many "obstructive" episodes merely represent straining against a closed glottis during movement.

Serra, G., M. Collu, et al. (1983). "Hypophysectomy prevents yawning and penile erection but not hypomotility induced by apomorphine." Pharmacol Biochem Behav 19(16): 917-9.
A small dose of apomorphine (25 or 50 micrograms/kg, SC) induced repeated episodes of yawning, penile erection, genital grooming and a decrease in locomotor activity in rats. Hypophysectomy almost completely abolished yawning, penile erection and genital abolished yawning, penile erection and genital grooming but failed to modify the hypomotility induced by apomorphine. These results suggest that pituitary hormones are directly or indirectly involved in the apomorphine-induced yawning, penile erection and genital grooming but not in the sedative response to this drug.

Ramabadran, K. (1983). "Naloxone-precipitated abstinence in mice, rats and gerbils acutely dependent on morphine." Life Sci 33 Suppl 1: 385-8.
Acute dependence on a single dose of morphine in mice, rats and gerbils was assessed by observing several signs of abstinence precipitated by various doses of naloxone, diprenorphine and Mr 2097. In mice and rats acutely dependent on morphine, naloxone,

diprenorphine and Mr 2097 precipitated dose-dependently the signs of abstinence such as jumping, urination, teeth chattering, chewing, paw shakes, head shakes and ptosis. In these two species, the precipitation of these signs were mediated by stereospecific opiate receptors, as Mr 2096, the non-antagonistic isomer of Mr 2097, did not precipitate any of them. In gerbils acutely dependent on morphine, naloxone precipitated urination, teeth chattering, chewing, paw shakes, head shakes, "wet dog" shakes, yawning and writhing. In naive animals of all three species, the opioid antagonists produced varying degrees of "abstinoid" signs. The precipitated withdrawal might be the result of "abstinoid" effects superimposed on real abstinence signs. High doses of naloxone and diprenorphine showed a regression of "abstinoid" signs probably because of interfering morphinomimetic properties. The present data indicate that these three rodents may be successfully employed in the rapid identification of drugs to produce morphine-like dependence or to precipitate withdrawal.

Protais, P., I. Dubuc, et al. (1983). "Pharmacological characteristics of dopamine receptors involved in the dual effect of dopamine agonists on yawning behaviour in rats." Eur J Pharmacol 94(3-4): 271-80.
Increasing doses of apomorphine (APO) induced the dose-dependent appearance of yawns in rats at doses up to 0.1 mg X kg-1 and their disappearance from 0.1 to 0.6 mg X kg-1. A similar biphasic effect on yawning was observed with increasing doses of n-propyl norapomorphine, piribedil, S 584, bromocriptine, lergotrile, lisuride, CQ 32084 and L-DOPA. APO, n-propyl norapomorphine, piribedil and CQ 32084 had similar ED50 on the induction of sniffing and on the disappearance of yawns. All the neuroleptics tested antagonized the yawns induced by 0.1 mg X kg-1 APO. Increasing doses of haloperidol, chlorpromazine, mezilamine, metoclopramide and thioridazine made the yawns reappear in rats injected with 0.6 mg X kg-1 APO. The ID50 were similar to those for the antagonism of sniffing. On the other hand, increasing doses of clozapine, (+/-)- or (-)-sulpiride, veralipride and DAN 2163 did not make the yawns reappear in rats injected with 0.6 mg X kg-1 APO although sniffing was antagonized. These results are discussed in terms of the ability of sulpiride, veralipride and DAN 2163 to distinguish between the dopamine (DA) receptors involved in the appearance of yawns at low doses of DA agonists and in their disappearance at higher doses. The decreased APO-induced yawning observed concomitantly with increased sniffing in rats with 6-hydroxydopamine-lesioned olfactory tubercles suggests that yawning and sniffing could be mutually exclusive.

McLean, J. D., R. G. Forsythe, et al. (1983). "Unusual side effects of clomipramine associated with yawning." Can J Psychiatry 28(7): 569-70.
Although there have been previous reports of decreased sexual capacity as a side effect of antidepressants (1-3), the authors know of no previous records of increased capacity of the type described in the following reports, or of reports of side effects associated with yawning. Observation of unusual yawning-associated side effects is now reported, in order to alert clinicians to a possible side effect that can influence patient-compliance with the prescribed medication regimen.

Lanari, A. and O. Delbono (1983). "[The yawning and stretching sign in hemiplegics]." Medicina (B Aires) 43(3): 355-6.

Handa, J., Y. Nakasu, et al. (1983). "Transient cerebral ischemia evoked by yawning: an experience after superficial temporal artery--middle cerebral artery bypass operation." Surg Neurol 19(1): 46-50.

Gray, L. P. (1983). "The relationship between the 'superior constrictor swallow', clicking of the ears and ear disease." J Laryngol Otol 97 (12): 1121-8.
A normal modified type of swallow is described, the function of which is to open the pharyngotympanic tube. It is associated with clicking of the ears. The tensor veli palatini, the levator palatini and the superior constrictor muscles appear to be the muscles involved, as it can occur without swallowing or movement of the tongue, or speaking. This modified swallow has been called the 'superior constrictor swallow', and it is demonstrated by productions of typical frames from a cine film. Sniffing, yawning and normal swallowing can occur with or without opening of the pharyngotympanic tubes, but this normal modified swallow (SCS) must be initiated to produce opening of the tubes. The change in middle-ear pressures with clicking is well shown with tympanometry. Modified swallow, largely involving the inferior constrictor muscle, may also occur.

Goldberg, R. L. (1983). "Sustained yawning as a side of imipramine." Int J Psychiatry Med 13(4): 277-80.
The occurrence of sustained yawning, uncoupled from sedation but caused by psychotropic medication, has been noted infrequently in the literature. This case report suggests the possibility of an association between imipramine and sustained yawning. Mechanisms of action for this yawning are proposed and a treatment strategy is offered.

Edery, H. (1983). "Models to predict cannabinoid-induced disturbances." Arch Toxicol Suppl 6: 91-103.
The most commonly used animal models to evaluate the psychoactivity of cannabinoids have been reviewed. The need for suitable models is acute considering the present interest to develop drugs based on the cannabinoid moiety but preferably dissociated from psychoactivity. Conceivably, a satisfactory assay should show features of cannabinoid-induced disturbances relevant to man as well as sensitivity, specificity and simplicity. These requisites seemed better fulfilled in the monkey model. Various lines of evidence have demonstrated the close pattern of the behavioural response to psychoactive and inactive cannabinoids in man and monkeys. Rhesus monkeys showed development of tolerance and withdrawal symptoms, which have been frequently reported in humans after prolonged exposure to cannabinoids. The exposure was reported also to cause in monkeys alterations of electrical activity and organic damage in deep brain structures. The monkey model has been particularly useful to determine the relative potency of naturally occurring cannabinoids and metabolites, which was adequately compared to that in man, and to establish the structural requirements for psychoactivity in large series of synthetic new compounds. In addition it appeared that rhesus monkeys react similarly to man with respect to proposed antidotes against cannabinoids. Four newly synthetized amino-cannabinoids were tested in baboons. All these compounds were virtually void of typical cannabinoid psychoactivity but two trans-analogs differed from the cis-analogs in that they provoked bouts of vigorous scratching and yawning. This unusual drug-effect, at difference from scratching alone has not been previously observed after administration of cannabinoids. In this presentation some terms of cannabis terminology have been discussed.

Deviche, P. (1983). "Stereotyped behavior affected by peripheral and intracerebroventricular apomorphine administration in pigeons." Pharmacol Biochem Behav 18(3): 323-6.
In pigeons, peripheral injection of apomorphine HCl (1.5 mg) produced a rapid pecking response while intracerebroventricular administration of the drug (60 micrograms) was ineffective in this respect. Both peripheral and to a larger extent central treatment with apomorphine stimulated another activity, that is headshaking. The frequency of other behavioral patterns was either decreased (preening) or unaffected (yawning, stretching) following both treatments. Together with previous studies, these data suggest that (a) apomorphine stimulates pecking in pigeons by activating dopaminergic mechanisms lying in brain areas situated away from the ventricles; (b) dopaminergic mechanisms situated in periventricular regions may take part in the control of some patterns, e.g. headshaking, and (c) other activities do not appear to depend directly on these mechanisms.

Baggio, G. and F. Ferrari (1983). "The role of dopaminergic receptors in the behavioral effects induced by lisuride in male rats." Psychopharmacology (Berl) 80(1): 38-42.
Lisuride increased the incidence of stretching and yawning (SY) as well as of penile erection (PE) and elicited stereotyped behavior (SB), aggressive behavior and mounting in male rats, depending on the dose used. SY was prevented by two dopaminergic antagonists, haloperidol and sulpiride, but not by methysergide, a serotoninergic antagonist, while PE was antagonized by all three drugs. With regard to SB, aggressive behavior and mounting, all three were suppressed by haloperidol; sulpiride, while partially antagonizing aggressiveness, failed to affect SB and mounting; methysergide did not significantly influence any of the three. This suggests that lisuride principally affects the dopaminergic system. Although further detailed studies are required to elucidate which type of the complex population of DA-receptors is involved in each kind of behavior, we suggest that SY at least is due to the activation by lisuride of presynaptic DA-receptors.

Anlezark, G. M., D. H. Blackwood, et al. (1983). "Comparative assessment of dopamine agonist aporphines as anticonvulsants in two models of reflex epilepsy." Psychopharmacology (Berl) 81(2): 135-9.
The anticonvulsant action of various aporphine derivatives that act on dopamine receptors has been investigated in two genetically determined animal models--DBA/2 mice with sound-induced seizures and baboons Papio papio with photically-induced seizures. Protection against the clonic and tonic phases of the seizures response in DBA/2 mice was seen for 15-60 min after (-)2,10,11-trihydroxy-N-n-propylnoraporphine (1.25 mg/kg) and (-)10,11-methyl-enedioxy-N-n-propylnoraporphine (0.625-1.25 mg/kg) and for 30-60 min after (-)2,10,11-trihydroxyaporphine (31.25 mg/kg). Short-lasting protection (up to 30 min) was seen following (-)2,10,11-trihydroxy-N-ethyl-noraporphine (1.25-6.25 mg/kg). Changes in audiogenic seizure susceptibility were accompanied by piloerection, ptosis and loss of spontaneous locomotor and exploratory behaviour. No protection was seen after (-)norapomorphine (0.05-18.75 mg/kg). All the compounds (including norapomorphine) significantly lowered rectal temperature, although the time course of this effect was often longer than that of protection against audiogenic seizures. In baboons, marked reductions in photomyoclonic responses were seen following (-)10,11-methylenedioxy-N-n-propylnoraporphine (0.25 mg/kg, lasting up to 2h); (-)2,10,11-trihydroxy-N-n-propylnoraporphine (0.5-2.5 mg/kg, lasting up to 7 h); (-)2,10,11-trihydroxyaporphine (5 mg/kg, duration of action 1-4 h) and (-)2,10,11-trihydroxy-N-ethylnoraporphine (6.25 mg/kg, lasting 2 h). Little change in responsiveness followed administration of (-)norapomorphine 1.25 or 6.25 mg/kg. Changes in photosensitivity were accompanied by yawning and pupil dilatation. (-)10,11-Methylenedioxy-N-n-propylnoraporphine (0.5-6.25 mg/kg) was also administered orally in baboons.(ABSTRACT TRUNCATED AT 250 WORDS)

Urba-Holmgren, R., B. Holmgren, et al. (1982). "Pre- and post-synaptic dopaminergic receptors involved in apomorphine-induced yawning." Acta Neurobiol Exp (Wars) 42(2): 115-25.

Trulson, M. E., J. W. Brandstetter, et al. (1982). "Behavioral effects of quipazine in the cat." Eur J Pharmacol 78(3): 295-305.
Administration of quipazine to cats elicits a number of behaviors, such as limb flicking abortive grooming, investigatory behavior

and hallucinatory-like behavior, which we have previously proposed as an animal behavioral model for studying the actions of LSD and related hallucinogens. While recent studies have indicated that these model behaviors may not be totally specific for hallucinogenic drugs, the model can still be useful for studying drug action. Quipazine (0.5-5.0 mg/kg i.p.) produced significant increases in limb flicking, abortive grooming, investigatory behavior, hallucinatory-like behavior grooming, head and body shakes, staring and yawning. These behavioral changes persisted for 1-6 h, depending on the dose of quipazine employed. Administration of quipazine (5.0 mg/kg per day) for 5 consecutive days produced no significant tolerance effect on any of these model behaviors. These quipazine induced behavioral changes were potentiated by pretreatment with apomorphine, and partially blocked by pretreatment with haloperidol. Quipazine-induced behavioral changes were potentiated by prior serotonin depletion with p-chlorophenylalanine, and completely blocked by pretreatment with a monoamine oxidase inhibitor or the serotonin precursor, L-5-hydroxytryptophan. These quipazine-induced behavioral changes were also blocked by pretreatment with the serotonin receptor blockers, cinnanserin, methysergide or cyproheptadine. The mechanism of action of quipazine, as well as the neuropharmacology of the limb flick model, is discussed in the content of these studies with serotonergic and dopaminergic drugs.

Serra, G., W. Fratta, et al. (1982). "Cycloheximide prevents apomorphine-induced yawning, penile erection and genital grooming in rats." Eur J Pharmacol 86(2): 279-82.

Apomorphine (50 micrograms/kg) induced repeated episodes of yawning, penile erection and genital grooming in rats. A dose of cycloheximide, which inhibited brain protein synthesis by 50% totally prevented apomorphine-induced yawning and reduced by approximately 50% the occurrence of episodes of penile erection and genital grooming. However, this treatment failed to modify the stereotyped behaviour induced by 200 micrograms/kg of apomorphine. These results suggest that protein synthesis is required for the behavioural effects of small doses of apomorphine.

Phoenix, C. H. and K. C. Chambers (1982). "Sexual behavior in adult gonadectomized female pseudohermaphrodite, female, and male rhesus macaques (Macaca mulatta) treated with estradiol benzoate and testosterone propionate." J Comp Physiol Psychol 96(5): 823-33.

Studies were made of the sexual behavior of 22 gonadectomized adult rhesus macaques (Macaca mulatta) given no hormonal treatment, treated with estradiol benzoate (EB, 20 microgram/day), and treated with testosterone propionate (TP, 10 mg/day). Experimentally produced female pseudohermaphrodites (hermaphrodites, n = 6), long-term castrated males (n = 9), and ovariectomized females (n = 7) were given 36 pair tests of 10-min duration with ovariectomized, estrogen-primed female partners. Twelve tests were given under each treatment condition. Yawning was the only behavior that showed a significant effect across treatments for hermaphrodites and females; the yawning rate was greater with TP treatment. The number of tests during which hermaphrodites showed erections increased significantly under TP treatment. One hermaphrodite mounted, but none achieved intromission or ejaculated. Males displayed several significant treatment effects, including increased mounting, intromitting, and ejaculating frequencies under TP treatment. The EB had little effect on any of the behaviors in any group. Rates of aggression and grimacing were greater among hermaphrodites than among males and females. Males displayed significantly greater rates of sexual behavior than hermaphrodites or females. As infants and juveniles, these hermaphrodites had displayed social and sexual behavior characteristic of males, but as mature adults, their behavior and responsiveness to testosterone at a dose capable of activating a high level of sexual behavior in castrated males gave little evidence of masculinization.

Mulley, G. (1982). "Associated reactions in the hemiplegic arm." Scand J Rehabil Med 14(3): 117-20.

Of 40 stroke patients attending a rehabilitation department, 32 (80%) had associated reactions affecting the hemiplegic arm. These involuntary movements nearly always occurred in association with yawning and less frequently with stretching, coughing, sneezing and laughing. In many patients the pattern of these reactions differed from previous descriptions. In the majority of patients they raised false hopes about the recovery of arm function, but sometimes they were a cause of distress. All 8 patients who did not have associated reactions had some voluntary movement of the affected arm and 4 of them had very useful manipulative function. By contrast, 25% of those with associated reactions had no voluntary arm movement and only 2 (6%) had very useful hand function. Involuntary arm movements are common in hemiplegia and those involved in care of stroke patients should be aware of them.

Karasawa, J., Y. Kuriyama, et al. (1982). "[Monitoring system of cerebral blood flow and cerebral metabolism. Part II. Relationship between internal jugular O2 tention and cerebral blood flow (author's transl)]." No To Shinkei 34(3): 239-45.

Changes of PjO2 values of internal jugular vein were monitored in patients with various types of cerebrovascular disease. The significance of PjO2 monitoring was evaluated. 1) Control value of PjO2 in thirteen normal control cases was 36.7 +/- 1.9 mmHg (mean +/- SD). 2) Limit of brain hypoxia showing no neurological sign and symptom in patients with occlusive cerebrovascular disease was studied by the stepwise reduction of arterial blood pressure, using drip infusion of trymetaphan camsylate, under the careful monitoring of signs and symptoms and monitoring of PjO2 and EEG. Appearance of signs and symptoms of brain hypoxia were checked by yawning and EEG slowing. At the time of the appearance of brain hypoxia PjO2 was 28.6 +/- 3.2 mmHg. 3) CO2 reactivity of CBF was studied in patients with occlusive cerebrovascular disease. Relation between PaCO2 and PjO2 was as follows; PjO2 = 0.68 . PaCO2 + 7.55 4) Within 24 hours after the onset of stroke, ipsilateral PjO2 of the cases with disturbance of consciousness was lower than that of the cases without disturbance of consciousness, which might indicate the significant decrease of CBF in the former cases. During 3rd to 7th day after the onset the cases with disturbance of consciousness showed the significant elevation of PjO2, which might indicate the reduction of cerebral metabolism. 5) The elevation of ipsilateral PjO2 were well correlated to the degree of hemispheric brain swelling. 6) During general convulsion, high level of PjO2 values were observed. 7) PjO2 values were inversely correlated to the hemoglobin values after blood transfusion, which was mainly due to the decrease of CBF by high content of hemoglobin.

Ide, M., A. Kataoka, et al. (1982). "[New accompaning signs and symptoms of adrenoleukodystrophy. --Adrenoleukomyeloneuropathy with hypoparathyroidism, cerebral calcification, and frequent yawning--(author's transl)]." Rinsho Shinkeigaku 22(2): 112-9.

Dubuc, I., P. Protais, et al. (1982). "Antagonism of the apomorphine-induced yawning by "atypical" neuroleptics." Neuropharmacology 21(11): 1203-6.

In relatively small doses, the four "atypical" neuroleptics, sulpiride, clozapine, thoiridazine and mezilamine were effective antagonists of apomorphine-induced yawning in rats. Of the four drugs, used in doses which inhibited apomorphine-induced yawning almost completely, only clozapine also antagonized yawning induced by physostigmine. Therefore it appears that the antagonism of this effect of apomorphine, already reported for classical neuroleptic agents, is also shown by "atypical" ones. By combining apomorphine- and physostigmine-induced yawning, it is possible to assess the anticholinergic component in the antagonism of this effect of apomorphine and this may be of value for the understanding of the mechanisms underlying the "atypical" character.

Yamada, K. and T. Furukawa (1981). "The Yawning elicited by alpha-melanocyte-stimulating hormone involves serotonergic-dopaminergic-cholinergic neuron link in rats." Naunyn Schmiedebergs Arch Pharmacol 316(2): 155-60.

Rodriguez-Sierra, J. F., E. Terasawa, et al. (1981). "Testosterone potentiation of the effectiveness of ACTH1-24 on the induction of the stretch-yawning syndrome (SYS) in male guinea pigs." Horm Behav 15(1): 77-85.

Robe, L. B., D. S. Gromisch, et al. (1981). "Symptoms of neonatal ethanol withdrawal." Curr Alcohol 8: 485-93.

Neonatal withdrawal symptoms in 15 cases of fetal alcohol syndrome with maternal intoxication at time of delivery, reported in 9 studies, are compared with symptoms reported in 138 cases of neonatal narcotic withdrawal. Seen frequently in ethanol but rarely in narcotic withdrawal are abdominal distention and opisthotonos. Seen frequently in narcotic but rarely in ethanol withdrawal are high pitch cry, frequent yawning, excessive sucking, mottling of the skin, excoriation, nasal stuffiness, excess sweating, sleeplessness and diarrhea. Seen frequently in both are increased muscle tonicity and tremors; however, convulsions are rare in narcotic yet are fairly frequent in neonatal ethanol withdrawal.

Marini, J. L. (1981). "Serotonergic and dopaminergic effects of yawning in the cat." Pharmacol Biochem Behav 15(5): 711-5.

The serotonergic agents LSD (0.01-0.05 mg/kg) and lisuride (0.025 and 0.05 mg/kg) elicited a high frequency of limb flicking in the cat after IP doses; LSD, but not lisuride, elicited a significantly increased frequency of yawning as well. In combination, LSD plus lisuride (0.025 mg/kg each) gave additive frequencies of limb flicking, but the frequency of yawning was half that after LSD alone. The dopamine agonist apomorphine had no significant effect on either yawning or limb flicking over the dose range 0.006 to 3.2 mg/kg. Pretreatment of cats with 1.0 mg/kg of apomorphine (but not with 0.05 mg/kg) significantly reduced the frequency of yawning elicited by 0.01 or 0.025 mg/kg of LSD, but had no effect on limb flicking. The dopamine antagonist haloperidol had no effect on limb flicking at doses from 0.008 to 0.512 mg/kg, but produced a significantly increased frequency of yawning at 0.256 mg/kg, an effect antagonized by lisuride administration. Given that lisuride has more potent dopamine agonist properties than LSD, these results are consistent with serotonergic elicitation of yawning, dopaminergic inhibition of yawning, and with their concomitant interaction in the expression of drug-induced yawning in the cat. The behavioral pharmacologies of limb flicking and yawning are different in this species.

Macapinlac, M. P. and J. A. Olson (1981). "A lethal hypervitaminosis A syndrome in young monkeys (Macacus fascicularis) following a single intramuscular dose of a water-miscible preparation containing vitamins A, D2 and E." Int J Vitam Nutr Res 51(4): 331-41.

Large intramuscular doses of a water-miscible preparation of vitamin A (500,000 I.U. retinyl acetate/ml), vitamin E (50 I.U./ml) and vitamin D2 (50,000 I.U./ml) were administered to young monkeys (Macacus fascicularis) weighing 1-1.8 kg. At vitamin A doses equivalent to 200 mg retinol/kg or higher, early signs of acute toxicity included yawning, apparent drowsiness, nausea and vomiting, head shaking, neck hyperextension, motor hyperactivity and coordination. These immediate signs were first noted 3-35 minutes after injection. Following apparent recovery at 1-2 hrs, longer term signs of toxicity, such as decreased activity, malaise, drowsiness, loss of appetite, loss of weight, and itchiness of the skin, appeared within 1-6 days, depending on the dose. Monkeys receiving the highest lethal doses became progressively weaker, showed labored breathing, lapsed into a coma, lost simple reflexes and then died. Respiratory failure usually preceded the cessation of heart beat. In some monkeys on a lower but lethal dose, death was preceded by generalized convulsive seizures. The time of onset of the first sign and survival time were inversely proportional to the dosage, but in individual monkeys no correlation existed

between onset time and survival time. Female monkeys seemed to succumb faster to a lethal dose than male monkeys. All animals receiving the equivalent of 300 mg retinol/kg died. Under the conditions used, the LD50 was estimated to be 168 mg retinol (560 000 I>U.) per body weight.

Fratta, W., Z. L. Rossetti, et al. (1981). "Reciprocal antagonism between ACTH1-24 and beta-endorphin in rats." Neurosci Lett 24(1): 71-4.
ACTH1-24 and beta-endorphin simultaneously injected at 5-10 microgram dose into the lateral ventricle, reciprocally suppress most of their respective behavioural effects (stretching-yawning syndrome, sexual excitement and hyperalgesia for ACTH1-24 and catalepsy and analgesia for beta-endorphin). The results obtained support the hypothesis that ACTH1-24 and beta-endorphin might interact antagonistically at CNS level.

Deviche, P. and J. D. Delius (1981). "Short-term modulation of domestic pigeon (Columbia livia L.) behaviour induced by intraventricular administration of ACTH." Z Tierpsychol 55(4): 335-42.
The behavioural responses induced in adult domestic pigeons by intraventricular injections of 0 to 6 IU of ACTH 1-39 are reported. The frequency of 10 different behaviour patterns was recorded for 90 min after administration of the peptide. The effect that was induced was complex, the frequency of some patterns increasing (yawning, headshaking, body shaking, wing-flapping), or some others decreasing (feeding, one-wing stretching, eye closing) or remaining unchanged (preening). The frequency of several patterns was maximal during the first 30 min following the injections but this was shown in some cases to be independent on the hormone administration.

Berendsen, H. H. and V. J. Nickolson (1981). "Androgenic influences on apomorphine-induced yawning in rats." Behav Neural Biol 33(1): 123-8.

Beckmann, H. and R. Zimmer (1981). "[An ethological interpretation of stereotypy induced by environmental stimulus (author's transl)]." Arch Psychiatr Nervenkr 230(1): 81-9.
Stereotyped behavior in the schizophrenic patient is described, provoked by yawning or fragments of this act in the environment. It consists of elements that, in an ethological sense are reminiscent of activities which increase vigilance and cleanse the body. It is suggested that yawning brings about a certain 'mood transfer' which induces this kind of specific stereotyped behavior. The adequacy of an ethological interpretation of these symptoms of disease is briefly discussed.

Yamada, K. and T. Furukawa (1980). "Direct evidence for involvement of dopaminergic inhibition and cholinergic activation in yawning." Psychopharmacology (Berl) 67(1): 39-43.
A behavioral study was performed in an attempt to understand the neurological mechanism involved in yawning in rats. Intraperitoneal injections of low doses (0.25 mg/kg) of apomorphine, which preferentially activate presynaptic dopamine autoreceptors, elicited yawning. Whereas apomorphine, at a high dose of 2 mg/kg, produces stereotypy which has been thought to be mediated by stimulation of postsynaptic dopamine receptors. The yawning and stereotypy did not occur simultaneously in the rat. The apomorphine-induced yawning was completely inhibited by pretreatment with fluphenazine (9 mg/kg, IM) or scopolamine (0.5 mg/kg IP), but markedly increased by reserpine (5 mg/kg, SC), however it was not affected by methylscopolamine (0.5 mg/kg, IP). Both physostigmine (0.2 mg/kg, IP), an indirect acetylcholine agonist, and pilocarpine (4 mg/kg, IP), a direct acetylcholine agonist, also induced yawning. This was abolished by scopolamine (0.5 mg/kg, IP) and increased by reserpine (5 mg/kg, SC). Fluphenazine (9 mg/kg, IP) did not affect the pilocarpine-induced yawning but increased the physostigmine-induced yawning. The results indicate that apomorphine elicits yawning by stimulating presynaptic dopamine receptors, and that dopaminergic inhibition and cholinergic activation are concomitantly involved in the yawning.

Yamada, K. and T. Furukawa (1980). "behavior of rats and mice administered active metabolites of fluphenazine, 7-hydroxy-fluphenazine and fluphenazine-sulfoxide." Arch Int Pharmacodyn Ther 248(1): 76-85.
We investigated the effects of 7-hydroxy-fluphenazine and fluphenazine-sulfoxide, main metabolites of fluphenazine (FZ), on behavior of mice and rats. These metabolites inhibited open-field behavior and methamphetamine-induced hyperactivity, lowered body temperature, and elicited catalepsy in mice, as did FZ-2HCl, FZ-enanthate and FZ-decanoate. After intramuscular administration, the onset of action of FZ-enanthae, FZ-decanoate and their metabolites was somewhat delayed compared to findings with FZ-2HCl, and the duration of FZ-enanthate and FZ-decanoate lasted longer than that of FZ-2HCl and metabolites. FZ-metabolites decreased stereotypy induced by a high dose (4 mg/kg, i.p.) of apomorphine and yawning elicitedby a low dose (0.25 mg/kg i.p.) of apomorphine in rats. The results suggest that 7-hydroxy-FZ and FZ-sulfoxide exert their psychotropic actions by blocking pre- and postsynaptic dopamine receptors and that formation of active metabolite may affect theprolonged therapeutic action of depot-type preparations of FZ.

Holmgren, B. and R. Urba-Holmgren (1980). "Interaction of cholinergic and dopaminergic influences on yawning behavior." Acta Neurobiol Exp (Wars) 40(3): 633-42.

Holmgren, B., R. Urba-Holmgren, et al. (1980). "Sex hormone influences on yawning behavior." Acta Neurobiol Exp (Wars) 40(2): 515-9.

Bauer, G., F. Gerstenbrand, et al. (1980). "Involuntary motor phenomena in the locked-in syndrome." J Neurol 223(3): 191-8.
Several involuntary movements were observed in patients who were totally immobile except for vertical gaze due to bilateral pyramidal transverse lesion at the pontine or midbrain level. In those conscious locked-in patients extensor spasms and flexor spasms could be elicited by nonspecific stimulation. Mimic pain reactions, pathological crying, and primordial screaming ("cat crying') were also noted. Other motor patterns were whining, moaning, groaning, sighing, and yawning. The pathophysiological implications of these observations are discussed.

Wood, P. L., D. L. Cheney, et al. (1979). "Modulation of the turnover rate of hippocampal acetylcholine by neuropeptides: possible site of action of alpha-melanocyte-stimulating hormone, adrenocorticotrophic hormone and somatostatin." J Pharmacol Exp Ther 209(1): 97-103.
The intraventricular injection of alpha-melanocyte-stimulating hormone (alpha-MSH), adrenocorticotrophic hormone (ACTH1--24) or somatostatin increases the acetylcholine turnover rate (TRACh) in the hippocampus of rats. Two to 3 weeks after surgical transection of the projections from the cingulum of the entorhinal cortex to the hippocampus the injections of these peptides can still activate hippocampal TRACh. alpha-MSH, ACTH1--24 and somatostatin also increase hippocampal TRACh when injected two to 3 hr after section of the fimbria. In contrast, the intraseptal administration of these peptides fails to change the hippocampal TRACh. The results suggest that the increase in hippocampal TRACh elicited by the three polypeptides may be caused by their interaction with receptors located in the hippocampus. Moreover, the data exclude the possibility that these peptide receptors may be located in septum or in other telencephalic areas that contain neurons projecting to the hippocampus. In addition, this study shows that the septal-hippocampal cholinergic pathway is necessary to elicit a specific stretching-yawning syndrome described by Ferrari et al. (Ann. N.Y. Acad. Sci. 104: 330--345, 1963) after injection of alpha-MSH or ACTH1--24.

Urba-Holmgren, R., B. Holmgren, et al. (1979). "Serotonergic modulation of yawning." Pharmacol Biochem Behav 11(3): 371-2.
Yawning induced by intraperitoneal (IP) injection of physostigmine (0.15 mgKg-1), in infant or adult rats is potentiated by Lu 10-171 (0.5-10 mgKg-1), a selective serotonin uptake inhibiting drug, which, by itself does not induce yawning. This effect is counteracted by metergoline (5-10 mgKg-1, IP) which blocks serotonin postsynaptic receptors. It is suggested that serotonin may exert a positivie modulating effect on yawning.

Rollison, R. D., W. S. Wiggins, et al. (1979). "Drug-induced yawning successfully treated with pimozide." Arch Neurol 36(4): 253.

Rollinson, R. D. and B. S. Gilligan (1979). "Postanoxic action myoclonus (Lance-Adams syndrome) responding to valproate." Arch Neurol 36(1): 44-5.
A patient with postanoxic action myoclonus (Lance-Adams syndrome) was severely disabled with this movement disorder. Valproate sodium was administered orally, with complete resolution of the myoclonus. This favorable response has been maintained for two years. Excessive yawning, the only side effect encountered, was dose related and was abolished with the addition of pimozide to the drug regimen.

Lehmann, H. E. (1979). "Yawning. A homeostatic reflex and its psychological significance." Bull Menninger Clin 43(2): 123-6.

Lanthorn, T. H. and R. L. Isaacson (1979). "Stretching and yawning: a role of glutamate." Psychopharmacology (Berl) 65(3): 317-8.
Systemic injection of GDEE (glutamate diethyl ester), an antagonist of glutamate and aspartate receptors, induces stretching and yawning in rats. This was not accompanied by excessive grooming. Coupled with previous work these findings give evidence that a glutamatergic mechanism is involved in stretching and yawning.

Heloe, B. and L. A. Heloe (1979). "Frequency and distribution of myofascial pain-dysfunction syndrome in a population of 25-year-olds." Community Dent Oral Epidemiol 7(6): 357-60.
Interviews on the occurrence of Myofascial Pain-Dysfunction (MPD) Syndrome were held with a group consisting of 246 individuals 25 years of age. Every fifth interviewee said she/he had experienced clicking/crepitation from the TMJs. Five percent had felt pain when opening the mouth wide and 3% while chewing, yawning or talking. These frequencies of symptoms were much like those found in a probability sample of the total adult population in Norway and a probability sample of elderly Norweigians. In the present study, 28% said they had some or much headache recently. These symptoms varied with background characteristics, especially with sex. There was also a relationship between headache and MPD-symptoms. By combining the effect of the variables sex and headache upon the frequency of reported clicking/crepitation, it was tripled.

Crumley, R. L. (1979). "The opercular syndrome--diagnostic trap in facial paralysis." Laryngoscope 89(3): 361-5.
We describe a patient with a left facial paralysis and hemotympanum following left parieto-occipital skull trauma. The initial admission diagnosis of intratemporal facial nerve injury secondary to temporal bone fracture was incorrect. Normal facial movements during

involuntary activity (yawning, laughing at a joke) and focal seizure activity on the paralyzed side of the face, seen subsequently, indicated the site of lesion as supranuclear. The diagnosis of opercular syndrome was made. This syndrome can result when the contralateral frontal lobe is injured. Supranuclear weakness of muscles supplied by the hypoglossal or spinal accessory nerves is also present. Unlike other central paralyses, the facial paralysis in operculum syndrome may not demonstrate "forehead sparing" and consequently it may be mistaken for a peripheral paralysis. The neuroanatomic basis for the syndrome is discussed. Signs and symptoms are outlined to help the otolaryngologist avoid this diagnostic pitfall.

Banks, W. F., J. C. Saunders, et al. (1979). "Olivocochlear bundle activity recorded in awake cats." Otolaryngol Head Neck Surg 87(4): 463-71.
Multi-unit activity was recorded in awake cats from the crossed olivocochlear bundle (COCB). Miniature stainless stell concentric electrodes were chronically implanted onto the floor of the fourth ventricle of six animals. There was no activity at the electrode tip in anesthetized animals, while in awake cats a great deal of unit activity could be seen. A correlation between COCB activity and ongoing behavioral activity such as scratching, grooming, yawning, or orientation could not be established. It was found, however, that the multi-unit responses in the COCB statistically increased their firing rate during acoustic stimulation, and a 500-Hz tone was found to be most effective. The electrode locations were histologically confirmed. The present results are similar to other data that describe unit activity in the olivocochlear bundle of decerebrate cats. The capacity to record from this fiber tract in awake animals, however, provides a new tool for studying the peripheral efferent pathway of the auditory system.

Woodman, G. F. (1978). "Shortcomings of the NHS: a yawning chasm." Br Med J 2(6145): 1158.

Wood, P. L., D. Malthe-Sorenssen, et al. (1978). "Increase of hippocampal acetylcholine turnover rate and the stretching-yawning syndrome elicited by alpha-MSH and ACTH." Life Sci 22(8): 673-8.

Slimp, J. C., B. L. Hart, et al. (1978). "Heterosexual, autosexual and social behavior of adult male rhesus monkeys with medial preoptic-anterior hypothalamic lesions." Brain Res 142(1): 105-22.
Bilateral radiofrequency lesions were made in the medial preoptic-anterior hypothalamic (MP-AH) area of 6 adult male rhesus monkeys; 5 sham-lesioned subjects served as controls. Behavioral analysis consisted of observations on copulatory behavior, yawning, masturbation and some aspects of social behavior. MP-AH lesions reduced or completely eliminated the display of manual contacts of the partner, mounts, intromissions and ejaculations without interfering with masturbation. Yawning, a sexually dimorphic behavior, was not affected either, Measure of several social behaviors indicated no evidence of social withdrawal or other aberrance of social interactions, which might have led to the decline in heterosexual behavior. The results with regard to copulatory behavior were consistent with the effects of MP-AH lesions in rats, cats and dogs. In rhesus monkeys it appears as though the MP-AH region is specifically involved in the mediation of heterosexual copulation and is not vital to the performance of other forms of male sexual activity such as masturbation. Also the MP-AH is not critical for the display of all sexually dimorphic behaviors. The types of behavioral change in MP-AH lesioned subjects differed to some extent from those following castration, indicating that the effects of the lesions cannot be explained as basically that of functional castration.

Holmgren, B. and R. Urba-Holmgren (1978). "Ontogeny of two cholinergically mediated central effects: stereotyped yawning and potentiation of head-shaking." Acta Neurobiol Exp (Wars) 38(1): 11-23.

Evans, E. B. (1978). "Yawning in pharyngeal obstruction." Br Med J 1(6110): 443-4.

Donovan, B. T. (1978). "The behavioural actions of the hypothalamic peptides: a review." Psychol Med 8(2): 305-16.
Recent work has shown that the hypothalamic peptides commonly associated with the control of pituitary function have important behavioural actions of possible psychiatric significance. Thus, vasopressin, ACTH and like peptides may influence memory processes, and ACTH and MSH given intracranially induce a peculiar stretching and yawning syndrome accompanied by penile erection and ejaculation. Thyrotrophic hormone-releasing factor potentiates behavioural excitation, somatostatin is depressive, while luteinizing hormone-releasing hormone facilitates sexual behaviour and the newly identified endorphins are markedly opioid in character. These and other activities of the hypothalamic peptides are reviewed and assessed alongside the clinical information available.

Cowan, A. (1978). "Cholinergic link in yawning." Nature 271(5641): 187-8.

Urba-Holmgren, R., R. M. Gonzalez, et al. (1977). "Is yawning a cholinergic response?" Nature 267(5608): 261-2.

Mogilnicka, E. and V. Klimek (1977). "Drugs affecting dopamine neurons and yawning behavior." Pharmacol Biochem Behav 7(4): 303-5.
Drugs stimulating the dopamine (DA) neurons in different ways (apomorphine, piribedil, amphetamine, nomifensine, L-DOPA) given in low doses (not producing behavioral excitation) induced yawning in rats. Blockade of DA receptors with neuroleptics counteracted DA-agonists induced yawning which may indicate a dopaminergic component of this behavior.

Gschwend, J. (1977). "[Yawning in a case with transsecting glioma of the pons (author's transl)]." Fortschr Neurol Psychiatr Grenzgeb 45 (12): 652-5.
A patient with ponsglioma got completely tetraplegic and plegic in all muscles innervated by the caudal brainstem nerves (locked-in syndrome). He could not open or close the mouth, but he was able to yawn. It is concluded that the motivation of yawning stems from the sleep inducing system in the region of the raphe-nuclei and is projected directly to the nuclei of the caudal brainstem nerves.

Stastny, F. and Z. Rychter (1976). "Quantitative development of choroid plexuses in chick embryo cerebral ventricles." Acta Neurol Scand 53 (4): 251-9.
Quantitative development of choroid plexuses in cerebral ventricles of chick embryos was investigated by means of the planary projection of the choroid plexuses from the time the plexuses reached a consistent flattened structure. Choroid plexuses in the lateral cerbral ventricles were studied from day 6, the plexus in the third cerebral ventricle from day 8, and the plexus in the fourth cerebral ventricle from day 11 of incubation. Regardless of the microscopic origin of these choroid plexuses, their development reached a growth maximum on day 15 of incubation, after which there was a slight regression. The regression was gradual in the plexus of the third cerebral ventricle but a transient enlargement of plexuses in the laternal and in the fourth cerebral ventricle was observed between days 18 and 19. The enlargement of choroid plexuses in the lateral cerebral ventricles was caused by a flattening of the villi, whereas that of the plexus in the fourth cerebral ventricle was caused by thinning and yawning of the villi. The area of choroid plexuses in the lateral cerebral ventricles was six or seven times larger than the sum of the areas of the remaining choroid plexuses.

O'Brien, C. P., T. Testa, et al. (1976). "Conditioning in human opiate addicts." Pavlov J Biol Sci 11(4): 195-202.
Eight volunteers maintained on daily methadone participated in a classical conditioning procedure to determine which if any of the elements of narcotic withdrawal could be conditioned; The unconditioned stimulus was the injection of a small dose of naloxone. The unconditioned response was a brief precipitated withdrawal syndrome. The conditioning stimulus was a tone, odor, and injection of saline. Conditioning was successful in the pilot study in 5 of 8 subjects. The conditioned response consisted of tearing, yawning, lacrimation, systolic blood pressure increase, respiratory irregularities and subjective feelings of narcotic withdrawal sickness (nausea, muscle aches, chills). A second group of 8 subjects showed, in addition to the above, evidence of conditioning of heart rate, respiratory rate, respiratory, rate and skin temperature decrease. These laboratory findings support the clinical reports of a conditioned withdrawal syndrome and suggest ways to improve treatment results by detecting and extinguishing or modifying conditioned responses.

Heymer, A. and C. A. de Ferret (1976). "[Ethology of the Mediterranean blenny Blennius rouxi Cocco 1833]." Z Tierpsychol 41(2): 121-41.
The Mediterranean blenny Blennius rouxi has been studied mainly in the Banyuls-sur-Mer region. Data on its behaviour have been obtained by skin diving, SCUBA diving and observations in captivity. At Banyuls-sur-Mer Blennius rouxi lives at a depth of 1 to 42m. As an exception among Mediterranean blennies, Bl. rouxi feeds by grazing off the substrate. Algae, sponges and polychaetes (Sedentaria) are the main components of its food (HEYMER and ZANDER, in press). We could not confirm that the colouration, a white body with a conspicuous dark horizontal band, can be regarded as a signal of cleaning activity in statu nascendi. The male male have a spatial territory in which they occupy haptic holes. The female female lead a vagabond life and actively join the male male in their territories during the breeding season. Head nodding is an agonistic behaviour against other female female and has an attractive significance for spawning-motivated female female. The male male threaten with a widely opened mouth (threat yawning). Our data and observations on the ethology of Bl. rouxi are discussed and compared with those known of Bl. sphinx, Bl. incognitus, and Bl. zvonimiri, its nearest relatives.

Hayward, J. N. and K. Pavasuthipaisit (1976). "Vasopressin released by nicotine in the monkey." Neuroendocrinology 21(2): 120-9.
The objective of this study was to determine the effects of i.v. nicotine on plasma arginine vasopressin (AVP), plasma osmolality, and behavior in the conscious monkey. Adult, female, chronically prepared monkeys (Macaca mulatta) were studied with i.v. infusion of 5% dextrose and water in control experiments without change in parameters. Nicotine infusion (100 mug/kg/min) in 14 experiments produced a significant increase in plasma AVP from control levels of 0.6 +/- 0.5 muU/ml to end-of-infusion levels of 35 +/- 17 muU/ml (p less than 0.001). During the 15-20 min of nicotine infusion, a behavioral sequence of restlessness, yawning, retching, salivation and chewing accompanied AVP release. Plasma osmolality remained unchanged. Pretreatment of the monkeys with promethazine (Phenergan) and diphenhydramine (Benadryl) at 1-5 mg/kg reduced both the plasma AVP increase and the behavioral effects. These results provide conclusive evidence that nicotine can release large amounts of AVP in the monkey.

Graybiel, A. and J. Knepton (1976). "Sopite syndrome: a sometimes sole manifestation of motion sickness." Aviat Space Environ Med 47(8):

873-82.
Drowsiness is one of the cardinal symptoms of motion sickness; therefore, a symptom-complex centering around "drowsiness" has been identified which, for convenience, has been termed the sopite syndrome. Generally, the symptoms characterizing this syndrome are interwoven with other symptoms but under two circumstances the sopite syndrome comprises the main or sole overt manifestation of motion sickness. One circumstance is that in which the intensity of the eliciting stimuli is closely matched to a person's susceptibility, and the sopite syndrome is evoked either before other symptoms of motion sickness appear or in their absence. The second circumstance occurs during prolonged exposure in a motion environment when adaptation results in the disappearance of motion sickness symptoms, except for responses characterizing the sopite syndrome. Typical symptoms of the syndrome are: 1) yawning, 2) drowsiness, 3) disinclination for work, either physical or mental, and 4) lack of participation in group activities. Phenomena derived from an analysis of the symptomatology of the sopite syndrome are qualitatively similar but may differ quantitatively from abstractions derived in other motion sickness responses. One example is the sometimes unique time course of the sopite syndrome. This implies that the immediate eliciting mechanisms not only differ from those involved in evoking other symptoms, but, also, that they must represent first order responses. Diagnosis is difficult unless the syndrome under discussion is kept in mind. Prevention poses a greater problem than treatment.

Dunn, A. J., P. M. Iuvone, et al. (1976). "Neurochemical responses of mice to ACTH and lysine vasopressin." Pharmacol Biochem Behav 5(Suppl 1): 139-45.
Subcutaneous administration of ACTH 1-24 to mice increased the incorporation of [3H]lysine into brain and liver proteins, an effect which resembled that due to footshock. Corticosterone administration did not mimic these effects. ACTH 4-10 increased the [3H]lysine incorporation into brain or liver. These results are consistent with ACTH mediating the effects of footshock. However, dexamethasone decreased the brain responses to both footshock and ACTH, but while the liver response to ACTH was blocked, the footshock response was only diminished. This suggests a neural component in the response of the liver and possibly the brain. Intraventricular administration of ACTH 1-24 or ACTH 4-10 (D-phe), but not ACTH 4-10, increased [3H]lysine incorporation into brain protein. These neurochemical responses parallelled a distinctive pattern of behavior characterized by stretching, yawning and excessive grooming. Treatment for 3 days with long-acting preparations of ACTH 4-10, ACTH 4-10 (D-phe) or ACTH 1-24 increased the conversion of [3H]tyrosine into dopamine but not norepinephrine, alpha-MSH, beta-MSH or LVP had no such effect. Similar treatment with ACTH 4-10 or ACTH 1-24 increased striatal tyrosine hydroxylase activity measured in vitro, but did not significantly alter the enzyme activity from other brain regions. We conclude that ACTH peptides can stimulate protein and dopamine metabolism in mouse brain and that LVP has no such effects.

Delius, J. D., B. Craig, et al. (1976). "Adrenocorticotropic hormone, glucose and displacement activities in pigeons." Z Tierpsychol 40(2): 183-93.
The possibility that displacement activities might be consequences of stress-induced humoral responses was investigated. Adrenocorticotropic hormone and glucose were injected into the brain ventricles of unrestrained domestic pigeons. ACTH leads to an increased frequency of yawning and headshaking and glucose to a decrease in arousal. It is concluded that these behavioural responses correspond partly with the displacement activities shown by birds. The role of the cerebrospinal fluid as a mediator of behaviourally active substances is discussed.

Barbeau, A., M. Gonce, et al. (1976). "Neurologically active peptides." Pharmacol Biochem Behav 5(Suppl 1): 159-63.
This paper reviews recent evidence that a number of small peptides found in the brain are active in the central nervous system and behaviorally. Attention is focused on MSH/ACTH 4-10, alpha- and beta-MSH, and the prohormone beta-LPH, as they produce a syndrome of yawning and stretching. Studies with substance P and mainly with MIF-I are also reviewed. It is shown that substance P is an excitatory transmitter or modulator in the dorsal spinal cord with that MIF-I has antiparkinson properties. It is concluded that many polypeptides have direct actions on the central nervous system independent of their neuroendocrine properties.

Sakai, K. and Y. Takahashi (1975). "Driving and subsidiary behavior of taxi drivers working alternate-day shifts." J Hum Ergol (Tokyo) 4(2): 115-27.
A field study on taxi drivers working alternate-day shifts of prescribed duration of 16 hr of work revealed that most of them actually worked longer for 16 hr 50 min on the average, starting from 7:00 and ending later than 2:00. The mean hourly income greatly increased in hours later than 22:00 due to the increased fare per hire and higher speed, so that these hours were regarded by the drivers as the most important period of the day. This resulted in retarded mean bedtime of 5:31 after the shift end and in reduced sleep. The total rate of subsidiary activities of the drivers decreased during the middle of the day, but increased towards the shift end. Those activities having a relatively low rate at the beginning, such as subsidiary lower limb movements, shoulder-neck movements, and yawning, remarkably increased in the late evening and midnight hours. These activities increased even during frequent driving operations and tended to relate with each other, often recurring in bursts especially while feeling drowsy. The incentive wage system of the drivers thus accounts not only for the extraordinarily long working hours but also for intensified night work.

Ostrea, E. M., Jr., C. J. Chavez, et al. (1975). "A study of factors that influence the severity of neonatal narcotic withdrawal." Addict Dis 2(1-2): 187-99.
1. History is unreliable in assessing maternal drug habit. Morphine was detected in significant amounts in maternal and fetal urine regardless of whether the mother was on a methadone program or whether she denied any use of heroin during the last trimester of pregnancy. 2. Infants born to drug-addicted mothers were, in general, of birthweight normal and appropriate for gestational age (i.e., greater that 10th percentile). The infants born to mothers on a methadone clinic program had a higher birthweight compared to those whose mothers were not on any methadone program. 3. In order of frequency, the signs and symptoms of withdrawal were: central nervous system manifestations-fist sucking, irritability, tremors, sneezing, high-pitch cry, hypertonia; vasomotor in the form of stuffy nose; and gastrointestinal in the form of sweating, diarrhea, vomiting and yawning. Convulsions were not noted. No death occurred. 4. The severity of neonatal narcotic withdrawal did not correlate with the infant's gestational age, APGAR, sex or race; nor with maternal age, parity, duration of heroin addiction or duration of methadone intake. Also, it did not correlate with the total morphine level measured either in infant's or mother's urine or in cord blood. The serum levels of calcium and glucose were normal and identical in either mild or severe withdrawal. 5. The severity of neonatal withdrawal correlated significantly with the methadone dose per day of the mother (in initial, final or average dose). A maternal methadone dose of more than 20 mg per day was associated with a higher incidence of moderate to severe withdrawal in their babies. As a corollary, it was also noted that infants whose mothers were on a high methadone dose (i.e., greater than 20 mg per day) had a greater postnatal weight loss despite a significantly higher birthweight initially, and stayed in the hospital longer. 6. Finally, the modification of the environment to reduce external stimuli to the infant born to a drug-dependent mother, does not prevent or diminish the severity of neonatal narcotic withdrawal. Thus, there is no need to manage these infants in a special nursery.

O'Brien, C. P., T. J. O'Brien, et al. (1975). "Conditioning of narcotic abstinence symptoms in human subjects." Drug Alcohol Depend 1(2): 115-23.
Clinical evidence suggests the possibility of conditioning of narcotic abstinence symptoms. Addicts report subjective and objective signs of withdrawal/craving when exposed to certain stimuli. This may partially explain the high rate of relapse to drug seeking behavior when treated addicts return to their home environment. Conditioning of narcotic abstinence symptoms was produced experimentally in five of eight volunteer subjects. Brief naloxone precipitated abstinence was the unconditioned response. The conditioned stimulus was a tone and odor. After an average of seven training trials, the tone and odor produced a conditioned abstinence response. The conditioned response consisted of subjective components (feelings of sickness, nausea, cramps, craving) and objective components (yawning, tearing, rhinorrhea, irregular respiration and transiently increased blood pressure). These laboratory findings support the anecdotal evidence regarding the existence of conditioned abstinence phenomena.

Luttenberger, F. (1975). "[The problem of yawning in reptiles]." Z Tierpsychol 37(2): 113-37.
Yawning in reptiles was investigated in field observations of various lizard and tortoise species and in laboratory experiments with the tortoises Testudo h. hermanni and Emys orbicularis. In the experiments the animals' reactions to various conditions of temperature, air O2 and CO2 content, fatigue and hunger, were tested. Yawning and related or similar motor patterns are described and discussed.

Jurko, M. F. and O. J. Andy (1975). "Post-lesion yawning and thalamotomy site." Appl Neurophysiol 38(1): 73-9.
Yawning during hyperventilation occurred in certain patients post-thalamotomy. It was found that all of the lesions which elicited yawning (during the routine recording of electroencephalograms) were localized to the medial portion of the center-median nucleus. Yawning was noted to persist up to 3(1/2) years post surgery. Another group of patients who yawned when hyperventilated were patients with a history of a recent head injury who showed post-traumatic behavioral changes. Patients in both groups were young. There was no direct relationship between yawning and EEG abnormality. It was suggested that yawning during hyperventilation may serve as a sign of brain damage, especially at the brain stem level, in young patients.

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