

Alcoholism and obesity: Overlapping neuropeptide pathways? (review).

Thiele TE; Navarro M; Sparta DR; Fee JR; Knapp DJ; Cubero I. *Neuropeptides* 37(6): 321-337, 2003. (250 refs.)

Ethanol is a caloric compound, and ethanol drinking and food intake are both appetitive and consummatory behaviors. Furthermore, both ethanol and food have rewarding properties. It is therefore possible that overlapping central pathways are involved with uncontrolled eating and excessive ethanol consumption. A growing list of peptides has been shown to regulate food intake and/ or energy homeostasis. Peptides such as the melanocortins, corticotropin releasing factor, and cholecystokinin promote reductions of food intake while others such as galanin and neuropeptide Y stimulate feeding. The present review highlights research aimed at determining if ingestive peptides also regulate voluntary ethanol intake, with an emphasis on the melanocortins and neuropeptide Y. It is suggested that research directed at ingestive peptides may expand our understanding of the neurobiological mechanisms that drive ethanol self-administration, and may reveal new therapeutic candidates for treating alcohol abuse and alcoholism. Copyright 2003, Churchill Livingstone.

Body packing: The internal concealment of illicit drugs. (review).

Traub SJ; Hoffman RS; Nelson LS. *New England Journal of Medicine* 349(26): 2519-2526, 2003. (50 refs.)

This article provides an overview of the history of body-packing, and presentations to medical providers. They usually present to health care providers for one of three reasons: drug-induced toxic effects, intestinal obstruction, or medical assessment after detention or arrest. The circumstances under which the patient presents will direct the clinical assessment, laboratory evaluation, and subsequent management. Children should be evaluated in a manner similar to that used for adults, although children's protective services should immediately be consulted. It review history taking, physical exam, and diagnostic testing. Management is also reviewed: symptomatic heroin poisoning, and symptomatic poisoning with other drug, as well as asymptomatic patients, and decontamination. The article concludes with an overview of ethical issues. Copyright 2003, Massachusetts Medical Society.

Cannabinoids in multiple sclerosis: Do they have a therapeutic role?

Killestein J; Uitdehaag BMJ; Polman CH. *Drugs* 64(1): 1-11, 2004. (63 refs.)

This is an exciting time for cannabinoid research. Evidence suggests that cannabis (marijuana) can alleviate symptoms like muscle spasticity and pain in patients with multiple sclerosis (MS). Interest in the field of cannabinoids has been strengthened by the identification and cloning of cannabinoid receptors located in the central nervous system and the

peripheral immune organs, and by the discovery of the endogenous cannabinoid ligands. Cannabinoids are also efficacious in animal models of MS. However, there have been only ten published clinical reports on the use of cannabis in MS, involving 78 individuals worldwide, and the results have been equivocal. Researchers encounter a number of difficulties in designing clinical studies that use cannabinoids. From the studies reporting the use of cannabinoids in MS patients with spasticity, the somewhat better designed studies failed to demonstrate objective improvement. Therefore, convincing evidence that cannabinoids are effective in MS is still lacking. Copyright 2004, Adis International Ltd.

Cannabis use and cerebrovascular disease.

Moussouttas M. *Neurologist* 10(1): 47-53, 2004. (42 refs.)

Background: Cannabis is the most commonly abused illicit drug and is often considered innocuous. However, cases of acute onset neurologic dysfunction occurring in relation to cannabis use have been described and corresponding cerebral imaging studies have documented focal ischemic changes and vessel abnormalities. Review Summary: This article reviews all reported cases of presumed cannabis related cerebral ischemic events in the medical literature, as well as pertinent human and animal experimental studies on the cardiovascular and cerebrovascular effects of cannabis. Conclusions: Cannabis use seems to have been causally related to several instances of cerebral ischemia and infarction. Proposed etiologic mechanisms have included cerebral vasospasm, cardioembolization, and systemic hypotension with impaired cerebral autoregulation, but most of the available data points to a vasospastic process. The exact relation of cannabis to cerebrovascular disease remains to be determined. Copyright 2004, Lippincott, Williams & Wilkins.

Drinking pattern and risk of non-fatal myocardial infarction: A population-based case-control study.

Trevisan M; Dorn J; Falkner K; Russell M; Ram M; Muti P et al. *Addiction* 99(3): 313-322, 2004. (33 refs.)

Aims: Alcohol consumption has been associated with a reduced risk of heart disease incidence and mortality. However, most studies have focused on an average volume per specific time period and have paid little attention to the pattern of drinking. The aim of this study was to examine the association between various drinking patterns and myocardial infarction (MI). Design: A population-based case-control study. Methods: Participants were 427 white males with incident MI and 905 healthy white male controls (age 35-69 years) selected randomly from two Western New York counties. During computer-assisted interviews detailed information was collected regarding patterns of alcohol consumption during the 12-24 months prior to interview (controls) or MI (cases). Findings: Compared to life-time abstainers, adjusted odds ratios (ORs) and 95% confidence

interval (CI) for non-current and current drinkers were 0.66 (0.31-1.39) and 0.50 (0.24-1.02), respectively. Daily drinkers exhibited a significantly lower OR (0.41) compared to life-time abstainers. Participants who drank mainly without food had an OR of 1.49 (0.96-2.31) compared to those who drank mainly with food and 0.62 (0.28-1.37) compared to life-time abstainers. Men who reported drinking only at weekends had a significantly greater MI risk [1.91; (1.21-3.01)] compared to men who drank less than once/week, but not compared to life-time abstainers [0.91 (0.40-2.07)]. Conclusions: Our results indicate that patterns of alcohol use have important cardiovascular health implications. Copyright 2004, Society for the Study of Addiction to Alcohol and Other Drugs.

Effect of alcohol consumption on diabetes mellitus: A systematic review. (review).

Howard AA; Arnsten JH; Gourevitch MN. *Annals of Internal Medicine* 140(3): 211-219, 2004. (53 refs.)

Background: Both diabetes mellitus and alcohol consumption are prevalent in the United States, yet physicians are poorly informed about how alcohol use affects risk for or management of diabetes. Purpose: To conduct a systematic review assessing the effect of alcohol use on the incidence, management, and complications of diabetes mellitus in adults. Data Sources: English-language studies in persons 19 years of age or older that were identified by searching the MEDLINE database from 1966 to the third week of August 2003 and the reference lists of key articles. Study Selection: Two independent assessors reviewed 974 retrieved citations to identify all experimental, cohort, or case-control studies that assessed the effect of alcohol use on diabetes risk, control, self-management, adverse drug events, or complications. Data Extraction: Two independent reviewers extracted data and evaluated study quality on the basis of established criteria. Data Synthesis: Thirty-two studies that met inclusion criteria were reviewed. Compared with no alcohol use, moderate consumption (one to 3 drinks/d) is associated with a 33% to 56% lower incidence of diabetes and a 34% to 55% lower incidence of diabetes-related coronary heart disease. Compared with moderate consumption, heavy consumption (>3 drinks/d) may be associated with up to a 43% increased incidence of diabetes. Moderate alcohol consumption does not acutely impair glycemic control in persons with diabetes. Conclusions: Moderate alcohol consumption is associated with a decreased incidence of diabetes mellitus and a decreased incidence of heart disease in persons with diabetes. Further studies are needed to assess the long-term effects of alcohol consumption on glycemic control and noncardiac complications in persons with diabetes. Copyright 2004, American College of Physicians.

Family history of alcoholism and response to sweets.

Kampov-Polevoy AB; Garbutt JC; Khalitov E. *Alcoholism: Clinical and Experimental Research* 27(11): 1743-1749, 2003. (68 refs.)

Background: The relationship between a hedonic response to sweet tastes and a propensity to excessive alcohol drinking is supported by both animal and human studies. This study was

designed to test the hypothesis that the genetic risk for alcoholism as measured by a paternal history of alcoholism in young social drinkers is associated with sweet-liking, defined as rating the strongest offered sucrose solution (i.e., 0.83 M) as the most palatable during the standard sweet test. Methods: Participants were 163 subjects (39% male) without a lifetime history of alcohol or drug abuse or dependence. Eighty-one subjects had a paternal history of alcoholism (FH+), and 82 did not (FH-). Each subject rated a series of sucrose solutions for intensity of sweetness and palatability. Subjects were categorized as sweet-likers if they rated the highest sucrose concentration as the most pleasurable. Results: The estimated odds of being a sweet-liker were 2.5 times higher for FH+ than for FH- subjects. FH+ subjects disliked the tastes of the two weakest offered sucrose concentrations (0.05 and 0.10 M), whereas FH- subjects reported these tastes to be neutral. Conclusions: The results of this study support the hypothesis that sweet-liking is associated with a genetic vulnerability to alcoholism. Copyright 2003, Research Society on Alcoholism.

Fetal alcohol and drug effects. (review).

Chiriboga CA. *Neurologist* 9(6): 267-279, 2003. (130 refs.)

Background: Alcohol and drug use by pregnant women are harmful to the developing embryo and fetus. Teasing apart the specific contributions of each substance to adverse child outcome, however, proves difficult in practice. The risks to the neonate include intrauterine growth retardation, birth defects, altered neurobehavior, and withdrawal syndromes. Subsequent behavior, development, and neurologic function may also be impaired. Review Summary: Maternal cigarette smoking carries the greatest risk of impaired fetal growth of any of the substances discussed herein and has been linked to subsequent externalizing behaviors. Alcohol is a well-established teratogen. Heavy exposure to alcohol in a subset of infants is associated with fetal alcohol syndrome (FAS). Mental retardation is one of the main sequelae of alcohol exposure in utero. Fetal marijuana exposure has no consistent effect on outcome. Prenatal cocaine exposure has not been shown to have any detrimental effect on cognition, except as mediated through cocaine effects on head size. Although fetal cocaine exposure has been linked to numerous abnormalities in arousal, attention, and neurologic and neurophysiological function, most such effects appear to be self-limited and restricted to early infancy and childhood. Opiate exposure elicits a well-described withdrawal syndrome affecting central nervous, autonomic, and gastrointestinal systems, which is most severe among methadone-exposed infants. Conclusion: Most adverse effects of prenatal drug exposure are self-limited, with catch-up growth and resolution of withdrawal and of prior neurobehavioral abnormalities noted over time. The exception is alcohol, which is linked to life-long impairments (i.e., mental retardation and microcephaly) and possibly cigarette-related behavioral effects. The absence of tangible evidence of detrimental long-term cocaine effects may reflect limitations in the methodology used to identify children at greatest risk for adverse outcome. Copyright 2003, Lippincott, Williams & Wilkins.

Marijuana withdrawal in humans: Effects of oral THC or divalproex.

Haney M; Hart CL; Vosburg SK; Nasser J; Bennett A; Zubaran C; Foltin RW. *Neuropsychopharmacology* 29(1): 158-170, 2004. (39 refs.)

Abstinence following daily marijuana use can produce a withdrawal syndrome characterized by negative mood (eg irritability, anxiety, misery), muscle pain, chills, and decreased food intake. Two placebo-controlled, within-subject studies investigated the effects of a cannabinoid agonist, delta-9-tetrahydrocannabinol (THC: Study 1), and a mood stabilizer, divalproex (Study 2), on symptoms of marijuana withdrawal. Participants (n=7/study), who were not seeking treatment for their marijuana use, reported smoking 6-10 marijuana cigarettes/day, 6-7 days/week. Study 1 was a 15-day in-patient, 5-day outpatient, 15-day in-patient design. During the in-patient phases, participants took oral THC capsules (0, 10 mg) five times/day, 1 h prior to smoking marijuana (0,00, 3.04% THC). Active and placebo marijuana were smoked on in-patient days 1-8, while only placebo marijuana was smoked on days 9-14, that is, marijuana abstinence. Placebo THC was administered each day, except during one of the abstinence phases (days 9-14), when active THC was given. Mood, psychomotor task performance, food intake, and sleep were measured. Oral THC administered during marijuana abstinence decreased ratings of 'anxious', 'miserable', 'trouble sleeping', 'chills', and marijuana craving, and reversed large decreases in food intake as compared to placebo, while producing no intoxication. Study 2 was a 58-day, outpatient/in-patient design. Participants were maintained on each divalproex dose (0, 1500 mg/day) for 29 days each. Each maintenance condition began with a 14-day outpatient phase for medication induction or clearance and continued with a 15-day in-patient phase. Divalproex decreased marijuana craving during abstinence, yet increased ratings of 'anxious', 'irritable', 'bad effect', and 'tired.' Divalproex worsened performance on psychomotor tasks, and increased food intake regardless of marijuana condition. Thus, oral THC decreased marijuana craving and withdrawal symptoms at a dose that was subjectively indistinguishable from placebo. Divalproex worsened mood and cognitive performance during marijuana abstinence. These data suggest that oral THC, but not divalproex, may be useful in the treatment of marijuana dependence. Copyright 2004, Nature Publishing Group.

Maternal smoking in pregnancy, fetal development, and childhood asthma.

Jaakkola JJK; Gissler M. *American Journal of Public Health* 94(1): 136-140, 2004. (19 refs.)

Objectives. We examined the relationships among maternal smoking in pregnancy, fetal development, and the risk of asthma in childhood. Methods. We conducted a population-based cohort study, where all 58841 singleton births were followed for 7 years using nationwide registries. Results. Maternal smoking increased the risk of asthma (adjusted odds ratio = 1.35; 95% confidence interval = 1.13, 1.62 for high exposure). Low birthweight and preterm delivery increased the risk of asthma at the age of 7, whereas being small for

gestational age did not. Conclusions. Maternal smoking in pregnancy increases the risk of asthma during the first 7 years of life, and only a small fraction of the effect seems to be mediated through fetal growth. Copyright 2004, American Public Health Association.

Out-of-hospital care of critical drug overdoses involving cardiac arrest.

Paredes VL; Rea TD; Eisenberg MS; Cobb LA; Copass MK; Cagle A et al. *Academic Emergency Medicine* 11(1): 71-74, 2004. (6 refs.)

Objectives: Death from acute drug poisoning, also termed drug overdose, is a substantial public health problem. Little is known regarding the role of emergency medical services (EMS) in critical drug poisonings. This study investigates the involvement and potential mortality benefit of EMS for critical drug poisonings, characterized by cardiovascular collapse requiring cardiopulmonary resuscitation (CPR). Methods: The study population was composed of death events caused by acute drug poisoning, defined as poisoning deaths and deaths averted (persons successfully resuscitated from out-of-hospital cardiac arrest by EMS) in King County, Washington, during the year 2000. Results: Eleven persons were successfully resuscitated and 234 persons died from cardiac arrest caused by acute drug poisoning, for a total of 245 cardiac events. The EMS responded to 79.6% (195/245), attempted resuscitation in 34.7% (85/245), and successfully resuscitated 4.5% (11/245) of all events. Among the 85 persons for whom EMS attempted resuscitation, opioids, cocaine, and alcohol were the predominant drugs involved, although over half involved multiple drug classes. Among the 11 persons successfully resuscitated, return of circulation was achieved in six following EMS cardiopulmonary resuscitation alone, in one following CPR and defibrillation, and in the remaining four after additional advanced life support. Conclusions: In this community, EMS was involved in the majority of acute drug poisonings characterized by cardiovascular collapse and may potentially lower total mortality by approximately 4.5%. The results show that, in some survivors, return of spontaneous circulation may be achieved with CPR alone, suggesting a different pathophysiology in drug poisoning compared with cardiac arrest due to heart disease. Copyright 2004, Hanley & Belfus, Inc.

Surgical emergencies in the intravenous drug user. (review).

Calder KK; Severyn FA. *Emergency Medicine Clinics of North America* 21(4): 1089+, 2003. (105 refs.)

In 2000 it was estimated that approximately 6.3% of the population aged 12 or older were using illicit drugs [1]. It is a common misconception that drugs are a problem of unemployed ethnic minorities and less affluent members of society, but this is clearly not the case. Illicit drugs know no boundaries with respect to ethnicity, sex, race, or demographic group. It is estimated that 77% of illicit drug users in 2000 continued to function in the workplace [1]. The economic and social sequelae of drug abuse are immense. In 1992 drug abuse costs in the United States totaled nearly \$100 billion [2],

the majority of which came from public funds. These costs are related not only to health care issues but to more global concerns such as drug-related crime, motor vehicle accidents, interference with family caregiving, incarceration, and loss of employment [2,3]. Among illicit drug users, those who inject are at particular risk for medical complications, and many of these patients are frequent users of the local emergency department (ED) [4]. These patients are not necessarily addicts; even infrequent injection can result in severe sequelae [5]. There are a variety of proposed mechanisms for disease including contaminated delivery mechanisms, injection technique, poor hygiene, contaminated drug or drug diluents, needle sharing, impaired cell-mediated immunity, sexual promiscuity, altered mental status with impaired cough and gag reflexes, and direct toxic effects on local tissue [6-10]. Drug users are also likely to self-prescribe antibiotics, which results in alterations in their normal flora [11,12]. These patients sometimes have multiple concurrent drug-related conditions that make diagnosis and treatment more difficult. In addition, other special considerations make therapy extremely challenging such as analgesic tolerance, lack of intravenous access, poor social conditions, illiteracy, and a high likelihood of medical noncompliance. This article focuses on some of the more commonly encountered surgical complications seen in the intravenous drug user (IVDU; can mean intravenous drug user or intravenous drug use), some of which have nonspecific clinical presentations yet pose a risk for significant morbidity and mortality if not diagnosed and treated without delay. The goal is to identify clinical characteristics and laboratory and radiographic studies that are likely to aid the emergency physician (EP) in the identification of patients who warrant surgical evaluation. Copyright 2003, W.B. Saunders Co.

The effects of toluene on the central nervous system. (review).

Filley CM; Halliday W; Kleinschmidt-DeMasters BK. *Journal of Neuropathology and Experimental Neurology* 63(1): 12-12, 2004. (67 refs.)

In recent decades the organic solvent toluene (methylbenzene) has emerged as one of the best-studied neurotoxins. Long-term and intense exposure to toluene vapors in humans who abuse spray paint and related substances has led to the recognition that toluene has a severe impact on central nervous system myelin. Chronic toluene abuse produces a devastating neurological disorder, of which dementia is the most disabling component. The clinical syndrome, toluene leukoencephal-

opathy, can be detected by a combination of characteristic symptoms and signs, detailed neurobehavioral evaluation, and brain magnetic resonance imaging. In this paper, we consider the impact of toluene abuse on our society, describe the specific neurobehavioral deficits in toluene leukoencephalopathy, review the spectrum of neuroimaging findings in patients with this disorder, summarize the teratogenic effects of toluene in both humans and animal models, and offer possible explanations for the range of neuropathological damage seen in brains of individuals who chronically abuse toluene. Copyright 2004, Journal of Neuropathologists Inc.

Why is parkinsonism not a feature of human methamphetamine users?

Moszczynska A; Fitzmaurice P; Ang L; Kalasinsky KS; Schmunk GA; Peretti FJ et al. *Brain* 127(Part 2): 363-370, 2004. (34 refs.)

For more than 50 years, methamphetamine has been a widely used stimulant drug taken to maintain wakefulness and performance and, in high doses, to cause intense euphoria. Animal studies show that methamphetamine can cause short-term and even persistent depletion of brain levels of the neurotransmitter dopamine. However, the clinical features of Parkinson's disease, a dopamine deficiency disorder of the brain, do not appear to be characteristic of human methamphetamine users. We compared dopamine levels in autopsied brain tissue of chronic methamphetamine users with those in patients with Parkinson's disease and in a control group. Mean dopamine levels in the methamphetamine users were reduced more in the caudate (-61%) than in the putamen (-50%), a pattern opposite to that of Parkinson's disease. Some methamphetamine users had severely decreased dopamine levels, within the parkinsonian range, in the caudate (up to 97% dopamine loss) but not in the putamen. As the putamen and caudate subserve aspects of motor and cognitive function, respectively, our data suggest that methamphetamine users are not parkinsonian because dopamine levels are not sufficiently decreased in the motor component of the striatum. However, the near-total reduction in the caudate could explain reports of cognitive disturbances, sometimes disabling, in some drug users, and suggests that treatment with dopamine substitution medication (e.g. levodopa) during drug rehabilitation might be helpful. Copyright 2004, Oxford University Press.

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