

# Library Watch

substance use  
medical aspects

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## Substance abuse vaccines

Orson FM; Kinsey BM; Singh RAK; Wu Y; Gardner T; Kosten TR. *Annals of the New York Academy of Sciences* 1141(Addiction Reviews 2008): 257-269, 2008. (68 refs.)

Conventional substance-abuse treatments have only had limited success for drugs such as cocaine, nicotine, methamphetamine, and phencyclidine. New approaches, including vaccination to block the effects of these drugs on the brain, are in advanced stages of development. Although several potential mechanisms for the effects of antidrug vaccines have been suggested, the most straightforward and intuitive mechanism involves binding of the drug by antibodies in the bloodstream, thereby blocking entry and/or reducing the rate of entry of the drug into the central nervous system. The benefits of such antibodies on drug pharmacodynamics will be influenced by both the quantitative and the qualitative properties of the antibodies. The sum of these effects will determine the success of the clinical applications of antidrug vaccines in addiction medicine. This review will discuss these issues and present the current status of vaccine development for nicotine, cocaine, methamphetamine, phencyclidine, and morphine. Copyright 2008, New York Academy of Sciences.

## Abuse of amphetamines and structural abnormalities in the brain.

Berman S; O'Neill J; Fears S; Bartzokis G; London ED. *Annals of the New York Academy of Sciences* 1141(Addiction Reviews 2008): 195-220, 2008. (133 refs.)

We review evidence that structural brain abnormalities are associated with abuse of amphetamines. A brief history of amphetamine use/abuse and evidence for toxicity is followed by a summary of findings from structural magnetic resonance imaging (MRI) studies of human subjects who had abused amphetamines and children who were exposed to amphetamines in utero. Evidence comes from studies that used a variety of techniques including manual tracing, pattern matching, voxel-based, tensor-based, or cortical thickness mapping, quantification of white matter signal hyperintensities, and diffusion tensor imaging. Ten

studies compared controls to individuals who were exposed to methamphetamine. Three studies assessed individuals exposed to 3-4-methylenedioxymethamphetamine (MDMA). Brain structural abnormalities were consistently reported in amphetamine abusers, as compared to control subjects. These included lower cortical gray matter volume and higher striatal volume than control subjects. These differences might reflect brain features that could predispose to substance dependence. High striatal volumes might also reflect compensation for toxicity in the dopamine-rich basal ganglia. Prenatal exposure was associated with striatal volume that was below control values, suggesting that such compensation might not occur in utero. Several forms of white matter abnormality are also common and may involve gliosis. Many of the limitations and inconsistencies in the literature relate to techniques and cross-sectional designs, which cannot infer causality. Potential confounding influences include effects of pre existing risk/protective factors, development, gender, severity of amphetamine abuse, abuse of other drugs, abstinence, and differences in lifestyle. Longitudinal designs in which multimodal datasets are acquired and are subjected to multivariate analyses would enhance our ability to provide general conclusions regarding the associations between amphetamine abuse and brain structure. Copyright 2008, New York Academy of Sciences.

## Adverse clinical outcomes associated with elevated blood alcohol levels at the time of burn injury.

Silver GM; Albright JM; Schermer CR; Halerz M; Conrad P; Ackerman PD et al. *Journal of Burn Care & Research* 29(5): 784-789, 2008. (34 refs.)

Elevated blood alcohol content (BAC) on admission is associated with poorer outcomes, larger burns and more inhalation injury. This study's purpose was to examine the effects of alcohol through a matched case-controlled study, measuring early and extended markers of clinical outcomes. The hypothesis was that patients with an elevated admission BAC would require more resuscitation and have a longer hospital stay. Admissions 16 to 75 years of age with 15 to 75% TBSA and admission BACs were identified. Patients with BAC >30 mg/dl (BAC+, cases) were matched

with patients with undetectable BAC (BAC-, controls), according to age, sex, TBSA, inhalation injury and mechanism. Screening identified 258 patients, 146 with admission BACs. Twenty-seven had a BAC 2: 30 mg/dl. There were 24 matched pairs. At 24 hours, BAC+ group had larger acute physiology and chronic health evaluation 11 scores (23.33 vs 18.75,  $P < .05$ ), fluid requirements (5.25 vs 3.82 L (cc/kg/TBSA),  $P < .05$ ), and base deficit (11.15 vs 7.15,  $P < .05$ ). The duration of mechanical ventilation (14.85 vs 4.23 days,  $P < .05$ ), intensive care unit length of stay (22.85 vs 9.38,  $P < .05$ ), hospital length of stay (28.95 vs 15.68,  $P < .05$ ), and mean hospital charges (\$239,507 vs \$144,598,  $P < .05$ ) were increased in the BAC+ patients. Despite matched baseline injury characteristics, elevated BAC was associated with poorer short term and extended clinical outcomes, illustrating the impact of alcohol intoxication on physiologic derangement after burn injury. Copyright 2008, Lippincott, Williams & Wilkins.

#### **Ammonia release from heated 'street' cannabis leaf and its potential toxic effects on cannabis users.**

Bloor RN; Wang TS; Spanel P; Smith D. *Addiction* 103(10): 1671-1677, 2008. (27 refs.)

**Aims:** To use selected ion flow tube mass spectrometry (SIFT-MS) to analyse the molecular species emitted by heated 'street' cannabis plant material, especially targeting ammonia. **Materials and methods:** Samples of 'street' cannabis leaf, held under a UK Home Office licence, were prepared by finely chopping and mixing the material. The samples were then heated in commercially available devices. The air containing the released gaseous compounds was sampled into the SIFT-MS instrument for analysis. Smoke from standard 3% National Institute on Drug Abuse (National Institute on Drug Abuse) cannabis cigarettes was also analysed. **Findings:** For 'street' cannabis, ammonia was present in the air samples from the devices at levels approaching 200 parts per million (p.p.m.). This is compared with peak levels of 10 p.p.m. using National Institute on Drug Abuse samples of known provenance and tetrahydrocannabinol content (3%). Several other compounds were present at lower levels, including acetaldehyde, methanol, acetone, acetic acid and uncharacterized terpenes. **Conclusions:** Awareness of the risks of inhaling the smoke directly from burning cannabis has led to the development of a number of alternative methods of delivery, which are claimed to be safer than direct smoking. Ammonia at toxic levels is produced from heating 'street' cannabis in these commercially available devices. Thus, the use of these devices to deliver 'street' cannabis is now open to

question and further research is needed to investigate their safety. Copyright 2008, Society for the Study of Addiction to Alcohol and Other Drugs.

#### **Correlations of maternal buprenorphine dose, buprenorphine, and metabolite concentrations in meconium with neonatal outcomes.**

Kacinko SL; Jones HE; Johnson RE; Choo RE; Huestis MA. *Clinical Pharmacology & Therapeutics* 84(5): 604-612, 2008. (39 refs.)

For the first time, relationships among maternal buprenorphine dose, meconium buprenorphine and metabolite concentrations, and neonatal outcomes are reported. Free and total buprenorphine and norbuprenorphine, nicotine, opiates, cocaine, benzodiazepines, and metabolites were quantified in meconium from 10 infants born to women who had received buprenorphine during pregnancy. Neither cumulative nor total third-trimester maternal buprenorphine dose predicted meconium concentrations or neonatal outcomes. Total buprenorphine meconium concentrations and buprenorphine/norbuprenorphine ratios were significantly related to neonatal abstinence syndrome (NAS) scores  $>4$ . As free buprenorphine concentration and percentage free buprenorphine increased, head circumference decreased. Thrice-weekly urine tests for opiates, cocaine, and benzodiazepines and self-reported smoking data from the mother were compared with data from analysis of the meconium to estimate in utero exposure. Time of last drug use and frequency of use during the third trimester were important factors associated with drug-positive meconium specimens. The results suggest that buprenorphine and metabolite concentrations in the meconium may predict the onset and frequency of NAS. Copyright 2008, Nature Publishing Group.

#### **Drug users seeking emergency care for soft tissue infection at high risk for subsequent hospitalization and death.**

Binswanger IA; Takahashi TA; Bradley K; Dellit TH; Benton KL; Merrill JO. *Journal of Studies on Alcohol and Drugs* 69(6): 924-932, 2008. (41 refs.)

**Objective:** Although soft tissue infections are common among injection drug users (IDUs), little is known about the health outcomes among those who seek care for these infections. Emergency department visits are an important point-of-health-care contact for IDUs. In this prospective cohort study, we aimed to determine the hospitalization and mortality rates and factors associated with hospitalization or death among IDUs seeking emergency care for soft tissue infection. **Method:** Participants were English-speaking IDUs, 18

years of age and older. who sought initial care for soft tissue infection in an urban emergency department. We conducted semistructured interviews, identified hospitalizations from hospital records, and identified deaths using the National Death Index. Cox proportional hazards regression was used to investigate associations between baseline characteristics and hospitalizations or death. Results: Of 211 eligible patients, 156 (74%) participated (mean age = 42 years). There were 255 subsequent hospitalizations over a mean of 3.9 years follow-up. The hospitalization rate was 42 hospitalizations per 100 person-years (95% confidence interval [CI]: 38-48). The mortality rate was 2.0 per 100 person-years (95% CI: 1.1-3.7). Factors associated with increased risk for hospitalization or death included living on the street or in a shelter (adjusted odds ratio [AOR] = 1.75, 95% CI: 1.10-2.79), being recently incarcerated (AOR = 1.90, 95% CI: 1.05-3.44), and having insurance (AOR: 1.98, 95% CI: 1.22-3.23). Conclusions: IDUs who sought care in the emergency department for soft tissue infections were at high risk for subsequent hospitalization and death. Visits for soft tissue infections represent missed opportunities for preventive care. Copyright 2008, Alcohol Research Documentation.

**Eye malformations in children with heavy alcohol exposure in utero.**

Flanigan EY; Aros S; Bueno MF; Conley M; Troendle JF; Cassorla F et al. *Journal of Pediatrics* 153(3): 391-395, 2008. (35 refs.)

Objective: To determine whether children who do not develop fetal alcohol syndrome (FAS) despite heavy alcohol exposure are at risk for eye abnormalities. Study design: We screened 9628 pregnant women and identified 101 women who were drinking  $\geq 2$  oz of absolute alcohol per day and 101 nondrinking control women. We followed 43 exposed and 55 control offspring between age 4 and 9 years, performing masked standardized ophthalmologic examinations. Results: The groups did not differ in their rates of impaired visual acuity, refractory errors, ptosis, epicanthal folds, or short palpebral fissures. Biomicroscopy examination was normal in all exposed subjects; cataracts were detected in 2 control subjects (4%) but in no exposed subjects. Arterial tortuosity was seen in 7 exposed subjects (16%) and in 8 control subjects (15%). Optic nerve hypoplasia was not detected in any subject. Conclusions: Previous research has found that children with FAS have a high incidence of serious ophthalmologic defects; our data indicate that the risk is limited to children with FAS and does not extend to children exposed to high levels

of alcohol prenatally who do not develop FAS. Eye examinations are unlikely to clarify the diagnosis in children suspected of having alcohol-related damage. Copyright 2008, Elsevier Science.

**Gray matter volume abnormalities and externalizing symptoms in subjects at high risk for alcohol dependence.**

Benegal V; Antony G; Venkatasubramanian G; Jayakumar PN. *Addiction Biology* 12(1): 122-132, 2007. (61 refs.)

Reduced right amygdala volumes have been reported in young, alcohol-naive subjects at high risk (HR) for alcohol dependence. The differences in brain morphometry have been associated with an excess of externalizing behaviors in these subjects. This may reflect a neurobiological vulnerability to alcohol dependence. Existing Magnetic Resonance Imaging (MRI) studies on these subjects have examined only a few, pre-selected brain regions using the manual regions of interest (ROI) approach. MRI of HR subjects (n = 20) and age, sex, and handedness-matched low-risk (LR) subjects (n = 21) were analyzed using optimized voxel-based morphometry and ROI approach. The externalizing symptoms of these subjects and their fathers were measured using the Semi-Structured Assessment for the Genetics of Alcoholism. HR subjects had significantly smaller volumes of superior frontal, cingulate and parahippocampal gyri, amygdala, thalamus and cerebellum. These gray matter volumes correlated negatively with externalizing symptoms scores. Subjects at HR for alcoholism have reduced volumes of critical areas of brain gray matter, which are associated with increased externalizing symptoms. These represent key endophenotypes of alcoholism. Copyright 2007, Blackwell Publishing.

**Neuropsychological characteristics of Italian children with fetal alcohol spectrum disorders.**

Aragon AS; Coriale G; Fiorentino D; Kalberg WO; Buckley D; Gossage JP et al. *Alcoholism: Clinical and Experimental Research* 32(11): 1909-1919, 2008. (67 refs.)

Background: Children with fetal alcohol spectrum disorders (FASD) display many problems ranging from deficits in intelligence to behavioral difficulties. Thus, many studies have aimed at defining the neuropsychological characteristics of children with FASD. The current article describes the neuropsychological characteristics of Italian children with severe diagnosis within FASD and compares them with controls. It was expected that intellectual functioning, language comprehension, academic skills,

and inattention/hyperactivity would discriminate children with FASD from randomly selected peers without FASD. Methods: This article presents data from a second cohort of children examined in 2005 as part of an in-school epidemiological study of FASD in Italy. Of 80 children, 23 diagnosed with a FASD, and 57 randomly selected control children from the same first-grade classes, participated. After screening for FASD via growth and dysmorphology, the children were administered a test of general intelligence (WISC-R) as well as tests of nonverbal reasoning (Raven Colored Progressive Matrices), language comprehension (Rustioni), academic achievement (IPDA), and problem behavior (Disruptive Behavior Disorder Rating Scale). Results: Children diagnosed with a FASD achieved lower scores than control children on Verbal, Performance, and Full Scale IQ. Profile analysis of the WISC-R indicates overall differences between the groups. However, some intact functioning within the FASD group was found, as the Similarities and Vocabulary subtests were similar to the controls. After an alpha adjustment to 0.004, the Block Design, Object Assembly, and Mazes subtests were significantly different from controls. On tests of nonverbal reasoning, language comprehension, and academic achievement, the children with a FASD scored significantly lower. Moreover, teachers rated children with a severe diagnosis within FASD as showing more inattentive symptoms than controls, while hyperactive/impulsive characteristics among children with a FASD were comparable with the control children. Significant correlations between head circumference, child dysmorphology, WISC-R, and Raven CPM scores are also reported. Conclusions: This study indicates that a sample of Italian children with a FASD, when compared with control children, display poorer functioning on measures of general intelligence, nonverbal reasoning, academic achievement, and teacher-rated problem behaviors. The findings also contribute to the formulation of a neuropsychological profile of children diagnosed with a FASD. Copyright 2008, Blackwell Publishing.

#### **Neurotoxic effects of ecstasy on the thalamus.**

de Win MML; Jager G; Booij J; Reneman L; Schilt T; Lavini C et al. *British Journal of Psychiatry* 193(4): 289-296, 2008. (42 refs.)

Background: Neurotoxic effects of ecstasy have been reported, although it remains unclear whether effects can be attributed to ecstasy, other recreational drugs or a combination of these. Aims: To assess specific/independent neurotoxic effects of heavy ecstasy use and contributions of amphetamine, cocaine and cannabis as part of The Netherlands XTC Toxicity

(NeXT) study. Method: Effects of ecstasy and other substances were assessed with H-1-magnetic resonance spectroscopy, diffusion tensor imaging, perfusion weighted imaging and [I-123]2 beta-carbomethoxy-3 beta-(4-iodophenyl)-tropane ([I-123]beta-CIT) single photon emission computed tomography (serotonin transporters) in a sample (n=71) with broad variation in drug use, using multiple regression analyses. Results: Ecstasy showed specific effects in the thalamus with decreased [I-123] beta-CIT binding, suggesting serotonergic axonal damage; decreased fractional anisotropy, suggesting axonal loss; and increased cerebral blood volume probably caused by serotonin depletion. Ecstasy had no effect on brain metabolites and apparent diffusion coefficients. Conclusions: Converging evidence was found for a specific toxic effect of ecstasy on serotonergic axons in the thalamus. Copyright 2008, Royal College of Psychiatry.

#### **Substance abuse and withdrawal in the critical care setting.**

Tetrault JM; O'Connor PG. *Critical Care Clinics* 24(4): 767+, 2008. (97 refs.)

Substance use is common among individuals admitted to the critical care setting and may complicate treatment of underlying disorders. It is imperative for the critical care team to have a high index of suspicion for substance intoxication and withdrawal. This article reviews the epidemiology of substance use in this population and the treatment of common withdrawal syndromes. General principles regarding the management of substance withdrawal syndromes include general resuscitative measures, use of a symptom-triggered approach, and substitution of a long-acting replacement for the abused drug in gradual tapering dose. The authors stress the importance of long-term planning as part of the overall treatment protocol beyond the acute presentation. Copyright 2008, W B Saunders.

#### **Tai-Kang-Ning, a Chinese herbal medicine formula, alleviates acute heroin withdrawal.**

Kang L; Li B; Gao L; Li SX; Wang D; Hu M et al. *American Journal of Drug and Alcohol Abuse* 34(3): 269-276, 2008. (15 refs.)

The efficacy and safety of Tai-Kang-Ning (TKN) capsule, a traditional Chinese medicine formula, for the treatment of acute heroin withdrawal syndrome were investigated by conducting a double-blind, double-dummy, positive-controlled, and randomized trial. Sixty-four patients with acute heroin withdrawal syndrome were recruited. These patients were treated with either TKN or lofexidine in a fixed schedule of

doses for 10 days. The results indicate that both treatments significantly reduced withdrawal symptoms by day 3, but there was no significant difference overall between lofexidine and TKN in efficacy or safety. These results demonstrate that TKN is effective in the treatment of moderate-to-severe acute heroin withdrawal syndrome with mild adverse effects. Copyright 2008, Marcel Dekker Inc.

**The association of ADH and ALDH gene variants with alcohol drinking habits and cardiovascular disease risk factors.**

Husemoen LLN; Fenger M; Friedrich N; Tolstrup JS; Fredriksen SB; Linneberg A. *Alcoholism: Clinical and Experimental Research* 32(11): 1984-1991, 2008. (59 refs.)

Background: Genetic variation in ethanol metabolism may have an influence on both alcohol drinking habits and the susceptibility to health effects of alcohol drinking. Such influences are likely to bias exposure-disease associations in epidemiologic studies of health effects of alcohol drinking. In a Caucasian population, we examined the association of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) genetic variants with alcohol drinking habits, biomarkers of alcohol exposure, and risk factors for cardiovascular disease. Methods: The study population consisted of 1,216 Danish men and women aged 15-77 years participating in a health examination in 1998. The health examination included a self-administered questionnaire (alcohol drinking habits), a physical examination (blood pressure), and various blood tests [alanine aminotransferase (ALAT), erythrocyte mean corpuscular volume (E-MCV), and lipids]. ADH and ALDH gene variants were determined by standard techniques. Data were analyzed by regression analyses adjusted for relevant confounders. Results: Self-reported alcohol drinking was significantly associated with increasing levels of ALAT, E-MCV, high-density lipoprotein cholesterol, and blood pressure. The ALDH1b ala69val variant was associated with nondrinking and total alcohol intake. The ALDH2 promoter variant was associated with binge-drinking, and the ALDH1b1 ala69val polymorphism was associated with diastolic blood pressure. We did not find any statistically significant interactions between any of the gene variants and alcohol consumption in relation to the various outcomes. Conclusions: In this Caucasian population sample, we found evidence to support that genetic variation in ethanol metabolism may influence drinking habits, but no statistically significant gene-environment interactions. More large-scale epidemiologic studies are needed to confirm these results and to further investigate genetic

susceptibility to the effects of alcohol drinking. Copyright 2008, Blackwell Publishing.

**The validity of the laboratory marker combinations DOVER and QUVER to detect physician's diagnosis of at-risk drinking.**

Bentele M; Kriston L; Clement HW; Harter M; Mundle G; Berner MM. *Addiction Biology* 12(1): 85-92, 2007. (36 refs.)

Especially in situations where it might be favorable for the patient to dissimulate the existing alcohol problem, 'objective' laboratory tests can be helpful. In this study we report validation of the two combinations DOVER (DOctor VERified) and QUVER (QUestionnaire VERified) of the biological markers percent carbohydrate-deficient transferrin (%CDT) and gamma-glutamyl-transferase (gamma-GT) to detect patients that have been identified by their physicians with at-risk drinking behavior. Fifty-eight general practitioners (GPs) participated at two study sites in South-West Germany. Patients filled in a questionnaire that included the alcohol use disorders identification test (AUDIT) and gave a blood sample. The GP recorded his/her assessment about the presence of an alcohol-related disorder in the patient. Receiver operating characteristics (ROC) analyses of the marker combinations DOVER and QUVER were performed. A total of 2940 patients participated in the study, of which 2496 completed data sets that could be used for further analysis. The area under the curve (AUC) of 79.5% for DOVER and 77.2% (QUVER) are in a higher range than the values for gamma%CDT (75.7%) or gamma-GT (72.5%) and %CDT (64.5%) and suggest superiority of the proposed marker combinations. Cross-validation results were almost identical with 76.6% and 73.3% for DOVER and QUVER, respectively. Our analysis demonstrated that the combination of the markers gamma-GT and %CDT with the physician's judgement of the condition as reference was superior to the use of single markers. Copyright 2007, Blackwell Publishing.

**Trazodone for sleep disturbance after alcohol detoxification: A double-blind, placebo-controlled trial.**

Friedmann PD; Rose JS; Swift R; Stout RL; Millman RP; Stein MD. *Alcoholism: Clinical and Experimental Research* 32(9): 1652-1660, 2008. (43 refs.)

Background: Trazodone is a commonly prescribed off-label for sleep disturbance in alcohol-dependent patients, but its safety and efficacy for this indication is unknown. Methods: We conducted a randomized, double-blind, placebo-control trial of low-dose trazodone (50 to 150 mg at bedtime) for 12 weeks

among 173 alcohol detoxification patients who reported current sleep disturbance on a validated measure of sleep quality or during prior periods of abstinence. Primary outcomes were the proportion of days abstinent and drinks per drinking day over 6-months; sleep quality was also assessed. Results: Urn randomization balanced baseline features among the 88 subjects who received trazodone and 85 who received placebo. The trazodone group experienced less improvement in the proportion of days abstinent during administration of study medication (mean change between baseline and 3 months: -0.12; 95% CI: -0.15 to -0.09), and an increase in the number of drinks per drinking day on cessation of the study medication (mean change between baseline and 6 months, 4.6; 95% CI: 2.1 to 7.1). Trazodone was associated with improved sleep quality during its administration (mean change on the Pittsburgh Sleep Quality Index between baseline and 3 months: -3.02; 95% CI: -3.38 to -2.67), but after it was stopped sleep quality equalized with placebo. Conclusions: Trazodone, despite a short-term benefit on sleep quality, might impede improvements in alcohol consumption in the postdetoxification period and lead to increased drinking when stopped. Until further studies have established benefits and safety, routine initiation of trazodone for sleep disturbance cannot be recommended with confidence during the period after detoxification from alcoholism. Copyright 2008, Research Society on Alcoholism.

**Treatment for amphetamine psychosis. (review).**

Shoptaw SJ; Kao U; Ling WW. *Cochrane Database of Systematic Reviews* 4(e-article CD003026): 4, 2008. (39 refs.)

Background: Chronic amphetamine users may have experience of paranoia and hallucination. It has long been believed that dopamine antagonists, such as chlorpromazine, haloperidol, and thioridazine, are effective for the treatment of amphetamine psychosis. Objectives: To evaluate risks, benefits, costs of treatments for amphetamine psychosis. Search strategy: MEDLINE (1966-2007), EMBASE (1980-2007), CINAHL (1982-2007), PsychINFO (1806-2007), CENTRAL (Cochrane Library 2008 issue 1), references of obtained articles. Selection criteria: All randomised controlled and clinical trials (RCTs, CCTs) evaluating treatments (alone or combined) for people with amphetamine psychosis Data collection

and analysis: Two authors evaluated and extracted the data independently. Dichotomous data were extracted on an intention-to-treat basis in which the dropouts were assigned as participants with the worst outcomes. The Relative Risk (RR) with the 95% confidence interval (95% CI) was used to assess the dichotomous data. The Weighted Mean Difference (WMD) with 95% CI was used to assess the continuous data. Main results: The comprehensive searches found one randomised controlled trial of treatment for amphetamine psychosis meeting the criteria for considering studies. The study involved 58 participants and compared the efficacy and tolerability of two antipsychotic drugs, olanzapine (a newer antipsychotic) and haloperidol (a commonly used antipsychotic medication used as a control condition), in treating amphetamine-induced psychosis. The results show that both olanzapine and haloperidol at clinically relevant doses were efficacious in resolving psychotic symptoms, with the olanzapine condition showing significantly greater safety and tolerability than the haloperidol control as measured by frequency and severity of extrapyramidal symptoms. Authors' conclusions: Only one RCT of treatment for amphetamine psychosis has been published. Outcomes from this trial indicate that antipsychotic medications effectively reduce symptoms of amphetamine psychosis, the newer generation and more expensive antipsychotic medication, olanzapine, demonstrates significantly better tolerability than the more affordable and commonly used medication, haloperidol. There are other two studies that did not meet the inclusion criteria: for this review. The results of these two studies show that agitation and some psychotic symptoms may be abated within an hour after antipsychotic injection. Whether this limited evidence can be applied for amphetamine psychotic patients is not yet known. The medications that should be further investigate are conventional antipsychotics, newer antipsychotics and benzodiazepines. However, naturalistic studies of amphetamine psychotic symptoms and the prevalence of relapse to psychosis in the presence of amphetamine, are also crucial for advising the development of study designs appropriate for further treatment studies of amphetamine psychosis. Copyright 2008, John Wiley & Sons Ltd.