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31. Effects of prenatal cocaine and heroin exposure on neuronal dendrite morphogenesis and spatial recognition memory in mice.

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34. Developing an e-learning resource in clinical risk assessment.
Search History

1. MEDLINE; exp SUBSTANCE-RELATED DISORDERS/; 190082 results.
2. MEDLINE; addict*.ti,ab; 30846 results.
3. MEDLINE; 1 OR 2; 200293 results.
4. MEDLINE; exp GREAT BRITAIN/; 259597 results.
5. MEDLINE; "United Kingdom".ti,ab; 19970 results.
6. MEDLINE; "Great Britain".ti,ab; 5453 results.
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8. MEDLINE; "Scotland".ti,ab; 9718 results.
9. MEDLINE; "Wales".ti,ab; 13517 results.
10. MEDLINE; UK.ti,ab; 48994 results.
11. MEDLINE; GB.ti,ab; 5203 results.
12. MEDLINE; ireland.ti,ab; 18758 results.
13. MEDLINE; IRELAND/; 10223 results.
14. MEDLINE; "British Isles".ti,ab; 627 results.
15. MEDLINE; "Channel islands".ti,ab; 78 results.
16. MEDLINE; 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15; 334744 results.
17. MEDLINE; 3 AND 16; 6079 results.
1. Biochemical, histopathological and clinical evaluation of delayed effects caused by methamidophos isoforms and TOCP in hens: ameliorative effects using control of calcium homeostasis.

Citation: Toxicology, December 2012, vol./is. 302/1(88-95), 0300-483X;1879-3185 (2012 Dec 8)

Author(s): Emerick GL; Ehrich M; Jortner BS; Oliveira RV; Deoliveira GH

Institution: Department of Natural Active Principles and Toxicology, School of Pharmaceutical Science, Univ Estadual Paulista - UNESP, Araraquara, SP, Brazil. glemerick@yahoo.com.br

Language: English

Abstract: This work evaluated the potential of the isoforms of methamidophos to cause organophosphorus-induced delayed neuropathy (OPIDN) in hens. In addition to inhibition of neuropathy target esterase (NTE) and acetylcholinesterase (AChE), calpain activation, spinal cord lesions and clinical signs were assessed. The isoforms (+)-, (+/-)- and (-)-methamidophos were administered at 50mg/kg orally; tri-ortho-cresyl phosphate (TOCP) was administered (500mg/kg, po) as positive control for delayed neuropathy. The TOCP hens showed greater than 80% and approximately 20% inhibition of NTE and AChE in hen brain, respectively. Among the isoforms of methamidophos, only the (+)-methamidophos was capable of inhibiting NTE activity (approximately 60%) with statistically significant difference compared to the control group. Calpain activity in brain increased by 40% in TOCP hens compared to the control group when measured 24h after dosing and remained high (18% over control) 21 days after dosing. Hens that received (+)-methamidophos had calpain activity 12% greater than controls. The histopathological findings and clinical signs corroborated the biochemical results that indicated the potential of the (+)-methamidophos to be the isoform responsible for OPIDN induction. Protection against OPIDN was examined using a treatment of 2 doses of nimodipine (1mg/kg, i.m.) and one dose of calcium gluconate (5mg/kg, i.v.). The treatment decreased the effect of OPIDN-inducing TOCP and (+)-methamidophos on calpain activity, spinal cord lesions and clinical signs. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland

CAS Registry Number: 0 (Insecticides); 0 (Organothiophosphorus Compounds); 0 (Tritolyl Phosphates); 10265-92-6 (methamidophos); 299-28-5 (Calcium Gluconate); 66085-59-4 (Nimodipine); 7440-70-2 (Calcium); 78-30-8 (tri-o-cresyl phosphate); EC 3-1-1 (Carboxylic Ester Hydrolases); EC 3-4-22 (Calpain)

Publication Type: Comparative Study; Journal Article; Research Support, Non-U.S. Gov't

2. Children's champion says more needs to be done for children whose parents misuse alcohol.

Citation: BMJ, 2012, vol./is. 345/(e6139), 0959-535X;1756-1833 (2012)

Author(s): Torjesen I

Language: English

Country of Publication: England

Publication Type: News

Subject Headings: *Alcohol-Related Disorders
Child
*Child Advocacy
England
*Health Policy
Humans
Maternal Behavior
Paternal Behavior

Source: MEDLINE


3. Evidences for a role of glutathione peroxidase 4 (GPx4) in methylmercury induced neurotoxicity in vivo.

Citation: Toxicology, December 2012, vol./is. 302/1(60-7), 0300-483X;1879-3185 (2012 Dec 8)

Author(s): Zemolin AP; Meinerz DF; de Paula MT; Mariano DO; Rocha JB; Pereira AB; Posser T; Franco JL

Institution: Campus Sao Gabriel, Universidade Federal do Pampa, 97300-000, Sao Gabriel, RS, Brazil.

Language: English

Abstract: We evaluated the activity and expression of antioxidant enzymes in the cerebellum and cortex of Swiss adult male mice exposed to methylmercury (MeHg) in drinking water (40mg/L) during 21 days. The activity of glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase (GST), catalase (CAT), superoxide dismutase (SOD) and thioredoxin reductase (TrxR) were determined spectrophotometrically. The expression (protein levels) of GPx1 and GPx4 isoforms, TrxR1 as well as heat shock protein 70 (HSP70) were evaluated using specific antibodies and normalized by actin levels. The exposure of mice to MeHg caused a significant impairment in locomotors performance in the open field test (crossings and rearing). This result was followed by a significant reduction of GPx and TrxR activities in the cerebellum and cortex when compared to untreated animals. We also observed a substantial decrease in GPx1, GPx4 and TrxR1 protein levels in the cerebellum, while in the cerebral cortex, only GPx4 and TrxR1 were decreased after MeHg treatment. The activities of the antioxidant enzymes GR, GST, CAT and SOD were increased in the cerebellum after MeHg administration to mice. In contrast, only CAT was increased in the cerebral cortex of MeHg-treated animals. The expression of HSP70 was up-regulated only in the cerebellum where MeHg-exposed mice showed a significant increase in the immunocontent of HSP70 when compared to controls. This is the first report showing a role for GPx4 in the neurotoxicity induced by MeHg in vivo. In addition, our data indicates that the selenoproteins GPx and TrxR as main targets during MeHg exposure, which may be considered in biomarker studies. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
Alcohol depletes coenzyme-Q(10) associated with increased TNF-alpha secretion to induce cytotoxicity in HepG2 cells.

Citation: Toxicology, December 2012, vol./is. 302/1(34-9), 0300-483X;1879-3185 (2012 Dec 8)

Author(s): Vidyashankar S; Nandakumar KS; Patki PS

Institution: Cell Biology and Biochemistry, Research and Development, The Himalaya Drug Company, Makali, Bangalore 562 123, India.vidyashankar77@gmail.com

Language: English

Abstract: Alcohol consumption has been implicated to cause severe hepatic steatosis which is mediated by alcohol dehydrogenase (ADH) activity and CYP(450) 2E1 expression. In this context, the effect of ethanol was studied for its influence on lipogenesis in HepG2 cell which is deficient of ADH and does not express CYP(450) 2E1. The results showed that ethanol at 100mM concentration caused 40% cytotoxicity at 72h as determined by MTT assay. The incorporation of labeled [2-(14)C] acetate into triacylglycerol and phospholipid was increased by 40% and 26% respectively upon 24h incubation, whereas incorporation of labeled [2-(14)C] acetate into cholesterol was not significantly increased. Further, ethanol inhibited HMG-CoA reductase which is a rate-limiting enzyme in the cholesterol biosynthesis. It was observed that, HMG-CoA reductase inhibition was brought about by ethanol as a consequence of decreased cell viability, since incubation of HepG2 cells with mevalonate could not increase the cholesterol content and increase the cell viability. Addition of ethanol significantly increased TNF-alpha secretion and depleted mitochondrial coenzyme-Q(10) which is detrimental for cell viability. But vitamin E (10mM) could partially restore coenzyme-Q(10) and glutathione content with decreased TNF-alpha secretion in ethanol treated cells. Further, lipid peroxidation, glutathione peroxidase and superoxide dismutase enzyme activities remained unaffected. Ethanol decreased glutathione content while, GSH/GSSG ratio was significantly higher compared to other groups showing cellular pro-oxidant and antioxidant balance remained intact. Alanine amino transferase activity was increased by 4.85 folds in cells treated with ethanol confirming hepatocyte damage. Hence, it is inferred that ethanol induced cytotoxicity in HepG2 cells due to coenzyme-Q(10) depletion and increased TNF-alpha secretion. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
N-acetylcysteine (NAC) diminishes the severity of PCB 126-induced fatty liver in male rodents.

### Citation
Toxicology, December 2012, vol./is. 302/1(25-33), 0300-483X;1879-3185 (2012 Dec 8)

### Author(s)
Lai IK; Dhakal K; Gadupudi GS; Li M; Ludewig G; Robertson LW; Olivier AK

### Institution
Interdisciplinary Graduate Program in Human Toxicology, University of Iowa, IA, United States.

### Language
English

### Abstract
Potent aryl hydrocarbon receptor agonists like PCB 126 (3,3',4,4',5-pentachlorobiphenyl) cause oxidative stress and liver pathology, including fatty liver. Our question was whether dietary supplementation with N-acetylcysteine (NAC), an antioxidant, can prevent these adverse changes. Male Sprague-Dawley rats were fed a standard AIN-93G diet (sufficient in cysteine) or a modified diet supplemented with 1.0% NAC. After one week, rats on each diet were exposed to 0, 1, or 5mumol/kg body weight PCB 126 by i.p. injection (6 rats per group) and euthanized two weeks later. PCB treatment caused a dose-dependent reduction in growth, feed consumption, relative thymus weight, total glutathione and glutathione disulfide (GSSG), while relative liver weight, glutathione transferase activity and hepatic lipid content were dose-dependently increased with PCB dose. Histologic examination of liver tissue showed PCB 126-induced hepatocellular steatosis with dose dependent increase in lipid deposition and distribution. Dietary NAC resulted in a reduction in hepatic lipid accumulation in both PCB groups. This effect was confirmed by gravimetric analysis of extracted lipids. Expression of CD36, a scavenger receptor involved in regulating hepatic fatty acid uptake, was reduced with high dose PCB treatment but unaltered in PCB-treated rats on NAC-supplemented diet. These results demonstrate that NAC has a protective effect against hepatic lipid accumulation in rats exposed to PCB 126. The mechanism of this protective effect appears to be independent
of NAC as a source of cysteine/precursor of glutathione. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland

CAS Registry Number: 0 (Antigens, CD36); 0 (Antioxidants); 0 (Polychlorinated Biphenyls); 0 (Receptors, Aryl Hydrocarbon); 57465-28-8 (3,4,5,3',4'-pentachlorobiphenyl); 616-91-1 (Acetylcysteine); 70-18-8 (Glutathione)

Publication Type: Journal Article; Research Support, N.I.H., Extramural

Subject Headings: "*Acetylcysteine/pd [Pharmacology]"
Animals
"Antigens CD36/ge [Genetics]"
"*Antioxidants/pd [Pharmacology]"
"Drug-Induced Liver Injury/et [Etiology]"
"Drug-Induced Liver Injury/pa [Pathology]"
"*Drug-Induced Liver Injury/pc [Prevention and Control]"
"Fatty Liver/ci [Chemically Induced]"
"Fatty Liver/pa [Pathology]"
"*Fatty Liver/pc [Prevention and Control]"
"Gene Expression Regulation/de [Drug Effects]"
"Glutathione/me [Metabolism]"
Injections Intraperitoneal
Male
"Organ Size/de [Drug Effects]"
"Polychlorinated Biphenyls/ad [Administration and Dosage]"
"*Polychlorinated Biphenyls/to [Toxicity]"
Rats
Rats Sprague-Dawley
"Receptors Aryl Hydrocarbon/ag [Agonists]"
Severity of Illness Index

Source: MEDLINE

6. Poisoning in young children.

Citation: Archives of Disease in Childhood, September 2012, vol./is. 97/9(831-2), 0003-9888;1468-2044 (2012 Sep)

Author(s): Anderson M

Language: English

Country of Publication: England

Publication Type: Editorial

Subject Headings: Child Preschool
*Drug Packaging
"Great Britain/ep [Epidemiology]"
Humans
Infant
"Poisoning/ep [Epidemiology]"
"*Poisoning/pc [Prevention and Control]"
"United States/ep [Epidemiology]"

Source: MEDLINE

Full Text: Available from Highwire Press in Archives of Disease in Childhood


Citation: Archives of Disease in Childhood, September 2012, vol./is. 97/9(812-7), 0003-9888;1468-2044 (2012 Sep)

Author(s): Douzgou S; Breen C; Crow YJ; Chandler K; Metcalfe K; Jones E; Kerr B; Clayton-Smith J
OBJECTIVE: A genetic opinion is frequently requested in the assessment of a child with suspected fetal alcohol spectrum disorders (FASD). We studied the outcome of genetic assessment of 80 children referred to a regional genetics centre between 2004 and 2010 to identify the value of the genetic assessment in cases of suspected FASD.

DESIGN: Retrospective case series.

PATIENTS: 80 patients, aged between 1 month and 26 years.

METHODS: Data from the medical records was abstracted, entered onto a standard study pro forma, recorded in an Excel spreadsheet and analysed using simple frequency analysis.

RESULTS: In 20% of cases fetal alcohol syndrome was confirmed at the genetic consultation. The most common facial features were thin upper lip (86.6%) and short palpebral fissures (82%). A lip-philtrum score of 4 or 5 was identified in two-thirds of cases. The most common alternative diagnosis was a chromosome disorder, representing 8.75% of the FASD referrals.

SETTING: A regional genetics service in the North West of England.

CONCLUSIONS: Genetic assessment was of particular value in excluding other diagnoses and providing information to carers. Two-thirds of the children referred were subject to a care order increasing the difficulty to obtain a family and alcohol exposure history. Classification of FASD was difficult in children under a year old when data on growth and development were limited. Structural malformations were not common in the group overall and some previously reported diagnostic signs were not found to be reliable markers of FASD. Chromosome disorders showed phenotypic overlap with FASD and are an important differential diagnosis.
Abstract: A training course on dual diagnosis was developed within the Irish forensic mental health service, to bridge the gap in the lack of training on dual diagnosis in Ireland. The course was designed for service providers within mental health and addiction services. Twenty participants involving nursing, social work, police and social welfare disciplines attended the first training course. A mixed methodology research design was adapted to describe participants' evaluation of the training course. Data were collected using multiple methods: pre- and post-test, daily evaluation and focus group interviews. Quantitative data were analysed using the spss Version 16.0 and qualitative data were analysed thematically. Findings from the pre- and post-test suggest an increase in participants' knowledge of dual diagnosis and an increase in confidence in conducting groups. Daily evaluation indicates that the course content largely met participants' needs. Finally, three themes emerged from the focus group interview: increased confidence, the training course/teaching methods and personal/organizational challenges. This study implies that service providers within mental health and addiction services benefit from inter-professional, needs and skills based courses incorporating a variety of teaching methods. The way forward for future dual diagnosis training course developments would be working in partnership with service users and carers. Copyright 2011 Blackwell Publishing.

Country of Publication: England
Publication Type: Journal Article
Subject Headings: Adult
*Diagnosis Dual (Psychiatry)
Education Nursing Continuing
Female
Humans
Ireland
Male
"Police/ed [Education]"
Program Evaluation
Social Welfare
"Social Work/ed [Education]"
Teaching
Source: MEDLINE
Full Text: Available from Wiley in Journal of Psychiatric and Mental Health Nursing

9. Steppingstone and gateway ideas: a discussion of origins, research challenges, and promising lines of research for the future.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S99-S104), 0376-8716;1879-0046 (2012 Jun)
Author(s): Anthony JC
Institution: Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, MI 48824, United States. janthony@msu.edu
Language: English
Abstract: In this discussion of contributed papers for the special issue of DAD, the author draws attention to early American laws concerning cannabis and to statements made about the epidemiology of cannabis smoking and other drug use between 1858 and the contemporary scene, with coverage of opium, heroin, tobacco, alcohol, cocaine, kava, and other drugs. He discusses these steppingstone and gateway processes in relation to political environment and in relation to scientific challenges such as uncontrolled confounding. He provides a critique of between-individual research designs, including co-twin and co-sib designs of behavior genetics, as well as imaging research, where uncontrolled confounding often exists. He highlights the epidemiologic case-crossover design and prevention research experiments as potentially valuable approaches in new directions for research on the steppingstone and gateway processes. Copyright Copyright 2012. Published by Elsevier Ireland Ltd.
10. Common and specific liability to addiction: approaches to association studies of opioid addiction.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S33-41), 0376-8716;1879-0046 (2012 Jun)

Author(s): Nielsen DA; Kreek MJ

Institution: Laboratory of the Biology of Addictive Diseases, The Rockefeller University, New York, NY 10065, USA.

Language: English

Abstract: BACKGROUND: Opioid addiction, whether to opiates such as heroin and morphine, and/or to non-medical use of opioids, is a major problem worldwide. Although drug-induced and environmental factors are essential for the liability to develop opioid addiction, the genetic background of an individual is now known also to play a substantial role.METHODS: The overall goal of this article is to address the common and specific liabilities to addiction in the context of approaches to studies of one addiction, opioid addiction. Literature on identifying genetic variants that may play a role in the development of opioid addiction was reviewed.RESULTS: A substantial number of genetic variants have been reported to be associated with opioid addiction. No single variant has been found in any of the reported GWAS studies with a substantial effect size on the liability to develop heroin addiction. It appears that there is a complex interaction of a large number of variants, some rare, some common, which interact with the environment and in response to specific drugs of abuse to increase the liability of developing opioid addiction.CONCLUSIONS: In spite of the inherent difficulties in obtaining large well-phenotyped cohorts for genetic studies, new findings have been reported that are being used to develop testable hypotheses into the biological basis of opioid addiction. Copyright Copyright 2012. Published by Elsevier Ireland Ltd.
11. Subjective effects for alcohol, tobacco, and marijuana association with cross-drug outcomes.

**Citation:** Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S52-8), 0376-8716;1879-0046 (2012 Jun)

**Author(s):** Zeiger JS; Haberstick BC; Corley RP; Ehringer MA; Crowley TJ; Hewitt JK; Hopfer CJ; Stallings MC; Young SE; Rhee SH

**Institution:** Institute for Behavioral Genetics, University of Colorado, Campus Box 447, Boulder, CO 80309-0447, USA.

**Language:** English

**Abstract:** METHODS: The cross-drug relationship of subjective experiences between alcohol, tobacco, and marijuana and problem drug use behaviors were examined. Data were drawn from 3853 individuals between the ages of 11 and 30 years of age participating in the Colorado Center on Antisocial Drug Dependence [CADD]. Subjective experiences were assessed using a 13-item questionnaire that included positive and negative responses for alcohol, tobacco, and marijuana. Lifetime abuse and dependence on these three drugs was assessed using the Composite International Diagnostic Interview, Substance Abuse Module [CIDI-SAM].RESULTS: Positive and negative subjective experience scales were similar for alcohol, tobacco, and marijuana, although the hierarchical ordering of items differed by drug. Subjective experience scales for each of the three drugs examined correlated significantly, with the strongest relationship being for alcohol and marijuana experiences. Significant associations were identified between how a person experienced a drug and abuse and dependence status for the same or different drug.CONCLUSION: Cross-drug relationships provide evidence for a common liability or sensitivity towards responding in a similar manner to drugs of abuse within and across different pharmacological classes. Published by Elsevier Ireland Ltd.

**Country of Publication:** Ireland

**CAS Registry Number:** 64-17-5 (Ethanol)

**Publication Type:** Comparative Study; Journal Article; Research Support, N.I.H., Extramural

**Subject Headings:** Adolescent
*Cannabis
"*Emotions/de [Drug Effects]"
*Ethanol
Female
Humans
Male
Questionnaires
Regression Analysis
Statistics Nonparametric
"*Substance-Related Disorders/px [Psychology]"
*Tobacco
Young Adult

12. Computer adaptive testing of liability to addiction: identifying individuals at risk.

**Citation:** Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S79-86), 0376-8716;1879-0046 (2012 Jun)

**Author(s):** Kirisci L; Tarter R; Reynolds M; Ridenour T; Stone C; Vanyukov M

**Institution:** Department of Pharmaceutical Sciences, Center for Education and Drug Abuse Research, University of Pittsburgh, 3520 Forbes Avenue, Suite 203, Pittsburgh, PA 15213, USA. levent@pitt.edu

**Language:** English
Abstract: BACKGROUND: Employed as a quantitative measure of substance use disorder (SUD) risk, the transmissible liability index (TLI) can be useful for detecting youths requiring prevention intervention. This study was conducted to develop and evaluate a computer adaptive test (CAT) version of the TLI to identifying individuals at risk for SUD. METHODS: In the first sample (N=425) of male and female subjects were recruited under aegis of the Center for Education and Drug Abuse Research in Pittsburgh, PA, USA, having a mean age of 18.8 years. A provisional CAT version of the TLI was assessed using simulation procedures. In sample 2, twins were recruited at the 2010 Twinsburg Festival in Twinsburg, OH, USA. The CAT and paper and pencil (P&P) versions of the TLI were administered to 276 twin pairs having a mean age of 19.94 years. RESULTS: The simulated CAT version of the TLI predicted cannabis use disorder 2 years after initial study with 4% less accuracy (72% vs. 68%) than P&P version but with 78% reduction of items. In the twin sample, the CAT version predicted alcohol and drug use (OR=1.7 [2.1], p<.001) with 64% and 65% accuracy (sensitivity=75% [75%] and specificity=64% [65%]). CONCLUSIONS: This study demonstrated that the CAT version of the TLI is an accurate and efficient measure of risk for SUD. The CAT version of the TLI potentially affords the opportunity for efficient screening of risk so that timely interventions can be implemented to prevent occurrence of SUDs having frequently lifelong consequences. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
Publication Type: Comparative Study; Journal Article; Research Support, N.I.H., Extramural; Twin Study; Validation Studies
Source: MEDLINE

13. Does the "gateway" sequence increase prediction of cannabis use disorder development beyond deviant socialization? Implications for prevention practice and policy.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S72-8), 0376-8716;1879-0046 (2012 Jun)
Author(s): Tarter RE; Kirisci L; Mezzich A; Ridenour T; Fishbein D; Horner M; Reynolds M; Kirillova G; Vanyukov M
Institution: Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA 15213, United States. tarter@pitt.edu
Language: English
Abstract: BACKGROUND: This study was conducted to test whether non-normative socialization mediates the association between transmissible risk measured in childhood and cannabis use disorder manifested by young adulthood, and whether the sequence of drug use initiation ("gateway", i.e., consuming legal drugs before cannabis, or the reverse) increases accuracy of prediction of cannabis use disorder. METHODS: Sons of fathers with or without substance use disorders (SUDs) related to illicit drugs were tracked from 10-12 to 22 years of age to model the association between transmissible risk for SUD, socialization (peer deviance), order of drug use initiation ("gateway" or reverse sequence), and development of cannabis use disorder. Path analysis was used to evaluate relationships among the variables. RESULTS: Non-normative socialization mediates the
association between transmissible risk measured during childhood and cannabis use disorder manifest by young adulthood. The sequence of drug use initiation did not contribute additional explanatory information to the model.

CONCLUSIONS: The order of drug use initiation does not play a substantial role in the etiology of cannabis use disorder. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
CAS Registry Number: 0 (Street Drugs)
Publication Type: Journal Article; Research Support, N.I.H., Extramural
Subject Headings: Adolescent
"*Alcohol Drinking/px [Psychology]"
Causality
Child
Fathers
Humans
Male
"*Marijuana Abuse/et [Etiology]"
"Marijuana Abuse/ge [Genetics]"
"Marijuana Abuse/px [Psychology]"
"*Marijuana Smoking/px [Psychology]"
*Peer Group
Psychiatric Status Rating Scales
Psychological Theory
Risk
"*Smoking/px [Psychology]"
*Socialization
Street Drugs
Young Adult

Source: MEDLINE

14. Imaging genetics and the neurobiological basis of individual differences in vulnerability to addiction.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S59-71), 0376-8716;1879-0046 (2012 Jun)

Author(s): Sweitzer MM; Donny EC; Hariri AR

Institution: Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260, USA. mms74@pitt.edu

Language: English

Abstract: BACKGROUND: Addictive disorders are heritable, but the search for candidate functional polymorphisms playing an etiological role in addiction is hindered by complexity of the phenotype and the variety of factors interacting to impact behavior. Advances in human genome sequencing and neuroimaging technology provide an unprecedented opportunity to explore the impact of functional genetic variants on variability in behaviorally relevant neural circuitry. Here, we present a model for merging these technologies to trace the links between genes, brain, and addictive behavior.

METHODS: We describe imaging genetics and discuss the utility of its application to addiction. We then review data pertaining to impulsivity and reward circuitry as an example of how genetic variation may lead to variation in behavioral phenotype. Finally, we present preliminary data relating the neural basis of reward processing to individual differences in nicotine dependence.

RESULTS: Complex human behaviors such as addiction can be traced to their basic genetic building blocks by identifying intermediate behavioral phenotypes, associated neural circuitry, and underlying molecular signaling pathways. Impulsivity has been linked with variation in reward-related activation in the ventral striatum (VS), altered dopamine signaling, and functional polymorphisms of DRD2 and DAT1 genes. In smokers, changes in reward-related VS activation induced by smoking abstinence may be associated with severity of nicotine dependence.

CONCLUSIONS: Variation in genes related to dopamine signaling may contribute to heterogeneity in VS sensitivity to reward and, ultimately, to

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addiction. These findings illustrate the utility of the imaging genetics approach for investigating the neurobiological basis for vulnerability to addiction. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
CAS Registry Number: 0 (Receptors, Dopamine D2)
Publication Type: Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Review
Subject Headings: Adult
"Basal Ganglia/de [Drug Effects]"
"Behavior Addictive/ge [Genetics]"
"Behavior Addictive/pp [Physiopathology]"
"Genetic Variation/ph [Physiology]"
Humans
"Impulsive Behavior/ge [Genetics]"
"Impulsive Behavior/px [Psychology]"
Individuality
Male
"Neural Pathways/pp [Physiopathology]"
*Neuroimaging
Phenotype
"Polymorphism Genetic/ph [Physiology]"
"Receptors Dopamine D2/ge [Genetics]"
"Receptors Dopamine D2/ph [Physiology]"
"Tobacco Use Disorder/ge [Genetics]"
"Tobacco Use Disorder/pp [Physiopathology]"
Source: MEDLINE

15. Nicotine dependence and comorbid psychiatric disorders: examination of specific genetic variants in the CHRNA5-A3-B4 nicotinic receptor genes.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S42-51), 0376-8716;1879-0046 (2012 Jun)
Author(s): Chen LS; Xian H; Grucza RA; Saccone NL; Wang JC; Johnson EO; Breslau N; Hatsukami D; Bierut LJ
Institution: Department of Psychiatry, Washington University, St Louis, MO 63110, USA. chenli@psychiatry.wustl.edu
Language: English
Abstract: BACKGROUND: The associations between nicotine dependence and specific variants in the nicotinic receptor CHRNA5-A3-B4 subunit genes are irrefutable with replications in many studies. The relationship between the newly identified genetic risk variants for nicotine dependence and comorbid psychiatric disorders is unclear. We examined whether these genetic variants were associated with comorbid disorders and whether comorbid psychiatric disorders modified the genetic risk of nicotine dependence. METHODS: In a case control study of nicotine dependence with 2032 subjects of European descent, we used logistic regression models to examine the pleiotropy and risk moderation. Comorbid disorders examined were alcohol dependence, cannabis dependence, major depressive disorder, panic attack, social phobia, posttraumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), conduct disorder, and antisocial personality disorder (ASPD). RESULTS: Nicotine dependence was associated with every examined comorbid psychiatric disorders, with odds ratio varying from 1.75 to 3.33. No evidence supported the associations between the genetic variants and the comorbid disorders (pleiotropy). No evidence suggested that the risks for nicotine dependence associated with the genetic variants vary with comorbid psychiatric disorders in general, but the power was limited in detecting interactions. CONCLUSIONS: The genetic risks of nicotine dependence associated with the CHRNA5-A3-B4 subunit genes are specific, and not shared among commonly comorbid psychiatric disorders. The risks for nicotine dependence associated with these genetic variants are not modified by comorbid
psychiatric disorders such as major depressive disorder or alcohol dependence. However, the power is an important limitation in studying the interplay of comorbidity and genetic variants. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
CAS Registry Number: 0 (Receptors, Nicotinic)
Publication Type: Journal Article; Research Support, N.I.H., Extramural
Subject Headings: Adult
Comorbidity
"European Continental Ancestry Group/ge [Genetics]"
Female
*Genetic Pleiotropy
*Genetic Predisposition to Disease
Humans
Logistic Models
Male
"Mental Disorders/co [Complications]"
"*Mental Disorders/ge [Genetics]"
Middle Aged
"*Receptors Nicotinic/ge [Genetics]"
Risk Factors
"*Tobacco Use Disorder/ge [Genetics]"
"Tobacco Use Disorder/px [Psychology]"
Source: MEDLINE

16. Common liability to addiction and "gateway hypothesis": theoretical, empirical and evolutionary perspective.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S3-17), 0376-8716;1879-0046 (2012 Jun)

Author(s): Vanyukov MM; Tarter RE; Kirillova GP; Kirisci L; Reynolds MD; Kreek MJ; Conway KP; Maher BS; Iacono WG; Bierut L; Neale MC; Clark DB; Ridenour TA

Institution: Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA, USA. mmv@pitt.edu

Language: English

Abstract: BACKGROUND: Two competing concepts address the development of involvement with psychoactive substances: the "gateway hypothesis" (GH) and common liability to addiction (CLA). METHOD: The literature on theoretical foundations and empirical findings related to both concepts is reviewed. RESULTS: The data suggest that drug use initiation sequencing, the core GH element, is variable and opportunistic rather than uniform and developmentally deterministic. The association between risks for use of different substances, if any, can be more readily explained by common underpinnings than by specific staging. In contrast, the CLA concept is grounded in genetic theory and supported by data identifying common sources of variation in the risk for specific addictions. This commonality has identifiable neurobiological substrate and plausible evolutionary explanations. CONCLUSIONS: Whereas the "gateway" hypothesis does not specify mechanistic connections between "stages", and does not extend to the risks for addictions, the concept of common liability to addictions incorporates sequencing of drug use initiation as well as extends to related addictions and their severity, provides a parsimonious explanation of substance use and addiction co-occurrence, and establishes a theoretical and empirical foundation to research in etiology, quantitative risk and severity measurement, as well as targeted non-drug-specific prevention and early intervention. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
Causality
*Genetic Predisposition to Disease
Humans
Risk
Social Environment
"*Substance-Related Disorders/et [Etiology]"
"Substance-Related Disorders/pp [Physiopathology]"

Source: MEDLINE


Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S87-98), 0376-8716;1879-0046 (2012 Jun)

Author(s): Ridenour TA; Meyer-Chilenski S; Reid EE

Institution: University of Pittsburgh, Department of Pharmaceutical Sciences, Center for Education and Drug Abuse Research, 3501 Terrace St., 711 Salk Hall, Pittsburgh, PA 15261, United States. tar27@pitt.edu

Language: English

Abstract: BACKGROUND: Mitigation of substance use (SU) disorder (SUD) risk factors is a common goal of prevention. Research has clarified much about risk factors including their prediction of SU/SUD, associations with other etiological variables and mediation of SU outcomes. Greater understanding of the emergence of risk factors themselves may improve prevention. For example, in lieu of experimental data, the level of resistance to change of a risk factor (its pliability) could inform "dosage" of intervention needed to reduce the risk.METHODS: Two attributes of 22 previously-documented predictors of SU/SUD were quantified: natural history (average age-related trend) and pliability (quantified using correlations between intercepts and growth parameters of hierarchical linear modeling trajectories). The longitudinal sample of 1147 8- through 16-year-olds were recruited from a northeastern summer camp for youth experiencing chronic stress due to one or more stressors (X=-2.2stressors, SD=1.41) which typically last at least one year. Half were male, 69.3% were European-American, 8.5% were African-American, and the remaining were small proportions each of other or mixed races/ethnicities.RESULTS: Average trajectories of 21 predictors correspond to increasing SUD risk with age. Predictor pliability varied greatly, ranging from extremely high for School Commitment to extremely low for Peer Pressure Susceptibility.CONCLUSIONS: Results suggest different intervention strategies may be needed to manage risk factors over the long-term. To illustrate, maintaining a high school commitment appears to require boosters whereas reducing peer pressure susceptibility appears to require high initial "dosage" with less need for boosters. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland
Publication Type: Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't
Subject Headings: Adolescent
Age Factors
Child
Female
Humans
Linear Models
Male
"*Mental Disorders/pc [Prevention and Control]"
Psychiatric Status Rating Scales
Risk Factors
*Stress Psychological
"*Substance-Related Disorders/pc [Prevention and Control]"

Source: MEDLINE
18. Index of the transmissible common liability to addiction: heritability and prospective associations with substance abuse and related outcomes.

Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S18-23), 0376-8716;1879-0046 (2012 Jun)

Author(s): Hicks BM; Iacono WG; McGue M

Institution: Department of Psychiatry, University of Michigan, 4250 Plymouth Rd, Ann Arbor, MI 48109, USA. brianhic@umich.edu

Language: English

Abstract: BACKGROUND: Substance use disorders (SUDs) are highly comorbid and exhibit a relatively late onset. As such, many behaviors and personality traits present prior to the initiation of substance use can be used to predict later SUDs. The transmissible liability index (TLI) is a quantitative measure of such behaviors that indexes the common liability to SUDs. We examined the predictive utility and heritability of the TLI in a large community twin sample.METHODS: Using the Minnesota Twin Family Study (N=2510), we estimated TLI scores from mother, child, and teacher reports of symptom and personality measures assessed at age 11. We then estimated the genetic and environmental contributions to the association between TLI scores at age 11 and composite measures of substance abuse and behavioral disinhibition (antisocial behavior) at age 17.RESULTS: For both male and female twins, TLI scores were highly heritable (.76) and exhibited moderate associations with adolescent substance abuse (r=.29) and behavioral disinhibition (r=.40). Genetic factors accounted for the association between TLI scores and the adolescent outcomes.CONCLUSIONS: Findings support the utility of the TLI as a measure of the inherited, common liability to SUDs. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland

Publication Type: Journal Article; Research Support, N.I.H., Extramural; Twin Study; Validation Studies

Subject Headings: Adolescent "*Antisocial Personality Disorder/ge [Genetics]"
"*Behavior Addictive/ge [Genetics]"
Child "*Child Behavior Disorders/ge [Genetics]"
Female Follow-Up Studies "*Genetic Predisposition to Disease/px [Psychology]"
Humans Longitudinal Studies Male Minnesota Predictive Value of Tests Psychiatric Status Rating Scales Risk Factors "*Substance-Related Disorders/ge [Genetics]"
"*Twins/ge [Genetics]"
"Twins/sn [Statistics and Numerical Data]

Source: MEDLINE


Citation: Drug & Alcohol Dependence, June 2012, vol./is. 123 Suppl 1/(S24-32), 0376-8716;1879-0046 (2012 Jun)

Author(s): Palmer RH; Button TM; Rhee SH; Corley RP; Young SE; Stallings MC; Hopfer CJ; Hewitt JK
BACKGROUND: We investigated the etiological nature of comorbid alcohol, tobacco, and cannabis DSM-IV dependence symptoms in late adolescence and young adulthood while accounting for gender differences in the magnitude of genetic and environmental influences.

METHODS: Univariate and multivariate twin modeling was used to determine the heritability of each substance and the etiology of multiple drug problems in a sample of 2484 registrants of the Center for Antisocial Drug Dependence who provided data at the second wave of an ongoing longitudinal study. We report on mean and prevalence levels of whole-life DSM-IV dependence symptoms that were assessed with the Composite International Diagnostic Interview-Substance Abuse Module. Biometrical analyses were limited to age-adjusted DSM-IV dependence symptom counts from a subset of twins that reported using alcohol, tobacco, or cannabis in their lifetime.

RESULTS: Male and female alcohol, tobacco, and cannabis DSM-IV symptoms are indicators of a heritable unidimensional latent continuous trait. Additive genetic factors explain more than 60% of the common liability to drug dependence. A larger proportion of the variation in each substance is attributable to substance-specific genetic and environmental factors.

CONCLUSIONS: These data suggest that both common and substance-specific genetic and environmental factors contribute to individual differences in the levels of DSM-IV alcohol, tobacco, and cannabis dependence symptoms. Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
of long-term exposure to ketamine on brain activity have been largely unexplored. In this study, we aimed to examine such effects on spontaneous brain dynamics measured using resting-state functional magnetic resonance imaging (fMRI). Forty-one patients with ketamine dependence and forty-four healthy control subjects were imaged with BOLD fMRI using a 3.0-Tesla Siemens scanner at the Magnetic Resonance Center of Hunan Provincial People's Hospital, analyzed with the regional homogeneity (ReHo) method. Compared with healthy controls, decreased ReHo was found in ketamine users in the right anterior cingulate cortex and increased ReHo was found in left precentral frontal gyrus (p<0.05, cluster-level corrected). We also observed negative correlations between increased ReHo in precentral frontal gyrus and estimated total lifetime ketamine consumption and ketamine craving levels. To our knowledge, this is the first study of the long-term effects of ketamine exposure on brain functional activity. Our findings indicate that ketamine dependence is associated with alterations in the functional connectivity of medial and lateral prefrontal cortices. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland

CAS Registry Number: 0 (Anesthetics, Intravenous); 0 (Psychotropic Drugs); 6740-88-1 (Ketamine)

Publication Type: Journal Article; Research Support, Non-U.S. Gov't

Subject Headings: Adult
"Anesthetics Intravenous/ae [Adverse Effects]"
"Brain/de [Drug Effects]"
"Brain/pp [Physiopathology]"
Brain Mapping
Case-Control Studies
Female
Humans
"Ketamine/ae [Adverse Effects]"
Magnetic Resonance Imaging
Male
"Psychotropic Drugs/ae [Adverse Effects]"
"Substance-Related Disorders/pp [Physiopathology]"

Source: MEDLINE

21. Differential orexin/hypocretin expression in addiction-prone and -resistant rats selectively bred for high (HiS) and low (LoS) saccharin intake.

Citation: Neuroscience Letters, July 2012, vol./is. 522/1(12-5), 0304-3940;1872-7972 (2012 Jul 26)

Author(s): Holtz NA; Zlebnik NE; Carroll ME

Institution: Department of Psychiatry, University of Minnesota, Minneapolis, MN 55455, USA. holt0324@umn.edu

Language: English

Abstract: Rats that have been selectively bred for high (HiS) saccharin intake demonstrate elevated drug-seeking behavior in several phases of addiction compared to those bred for low (LoS) saccharin intake. HiS rats also consume greater amounts of highly palatable substances compared to LoS rats; however, little is known about the neurobiological substrates moderating the divergent behaviors found between the HiS and LoS lines. Orexins are neuropeptides that have been implicated in the conditioned cue aspects of drug abuse and overconsumption of palatable substances, and differential orexin activity in the HiS and LoS phenotypes may enhance our understanding of the close relationship between food and drug reward, and ultimately food and drug addiction. The lateral hypothalamus (LH) and perifornical area (PFA) are brain regions that have been implicated in regulating feeding behavior and addiction processes, and they contain orexinergic neurons that project broadly throughout the brain. Thus, we investigated orexin and c-Fos expression in the LH and PFA using immunohistochemistry in HiS and LoS rats following either control or cocaine (15 mg/kg) injections. Results indicated that HiS rats have higher orexin-positive cell counts compared to LoS rats in both the LH and
PFA, regardless of cocaine (vs. saline) treatment. In contrast, neuronal activity indicated by c-Fos expression did not differ in either of these brain areas in HiS vs. LoS rats. These results suggest that the orexin system may be involved in aspects of genetically-mediated differences in vulnerability to compulsive, reward-driven behaviors. Published by Elsevier Ireland Ltd.

Country of Publication: Ireland
CAS Registry Number: 0 (Intracellular Signaling Peptides and Proteins); 0 (Neuropeptides); 0 (Proto-Oncogene Proteins c-fos); 0 (orexins); 50-36-2 (Cocaine); 81-07-2 (Saccharin)
Publication Type: Journal Article; Research Support, N.I.H., Extramural
Subject Headings: Animals
Breeding
Cell Count
"Cocaine/pd [Pharmacology]"
Female
Food Preferences
"Hypothalamus/cy [Cytology]"
"*Hypothalamus/me [Metabolism]"
"*Intracellular Signaling Peptides and Proteins/me [Metabolism]"
"Neurons/cy [Cytology]"
"Neurons/me [Metabolism]"
"*Neuropeptides/me [Metabolism]"
"Proto-Oncogene Proteins c-fos/me [Metabolism]"
Rats
"*Saccharin/pd [Pharmacology]"
Species Specificity
"*Substance-Related Disorders/ge [Genetics]"
Source: MEDLINE

22. A national service evaluation of the impact of alcohol on admissions to Scottish intensive care units.

Citation: Anaesthesia, October 2012, vol/is. 67/10(1132-7), 0003-2409;1365-2044 (2012 Oct)
Author(s): Geary T; O'Brien P; Ramsay S; Cook B; Scottish Intensive Care Trainees' Audit Share Group
Institution: Department of Anaesthesia, Victoria Infirmary, Glasgow, UK. t.geary@nhs.net
Language: English
Abstract: Alcohol-related disease adversely affects the outcome of critically ill patients. The burden of this in Scotland is higher than elsewhere in the United Kingdom. In a prospective observational study of all patients admitted to the 24 intensive care units in Scotland we assessed the proportion of admissions in which alcohol-related disease was implicated. Of 771 admissions, 642 (83.3%) were unplanned and 196 (25.4%) were related to alcohol. There was a significantly higher proportion of men in the alcohol-related admissions group (140 (71.4%) vs 291 (50.6%), p=0.009). This group was also significantly younger with median (IQR [range]) ages of 51 (38-63 [16-89]) vs 63 (48-73 [16-92]) years (p<0.001). The alcohol-related group had a significantly longer period of ventilation with a median (IQR [range]) of 2 (1-6 [0-176]) vs 1 (0-4 [0-136]) days (p<0.005). Admissions from an area of deprivation were more likely to be related to alcohol. Alcohol-related admissions have a significant impact on Scottish intensive care services, with an extrapolated cost of Pound8.9 million per year. Anaesthesia Copyright 2012 The Association of Anaesthetists of Great Britain and Ireland.

Country of Publication: England
Publication Type: Journal Article
Subject Headings: Adolescent
Adult
Age Factors
Aged
23. Inhibition of HSP70: a challenging anti-cancer strategy.

Citation: Cancer Letters, December 2012, vol./is. 325/2(117-24), 0304-3835;1872-7980 (2012 Dec 28)

Author(s): Goloudina AR; Demidov ON; Garrido C

Institution: Institut National de la Sante et de la Recherche Medicale, Unite Mixte de Recherche, University of Burgundy, Dijon, France.

Language: English

Abstract: HSP70 is a chaperone that accumulates in the cells after many different stresses promoting cell survival in response to the adverse conditions. In contrast to normal cells, most cancer cells abundantly express HSP70 at the basal level to resist to various insults at different stages of tumorigenesis and during anti-cancer treatment. This cancer cells addiction for HSP70 is the rational for its targeting in cancer therapy. Much effort has been dedicated in the last years for the active search of HSP70 inhibitors. Additionally, the recent clinical trials on highly promising inhibitors of another stress protein, HSP90, showed compensatory increase in HSP70 levels and raised the question of necessity to combine HSP90 inhibitors with simultaneous inhibition of HSP70. Here we analyzed the recent advancement in creation of novel HSP70 inhibitors and different strategies for their use in anti-cancer therapy. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.

Country of Publication: Ireland

CAS Registry Number: 0 (Antineoplastic Agents); 0 (HSP70 Heat-Shock Proteins); 0 (HSP90 Heat-Shock Proteins); 0 (Molecular Chaperones); 0 (Neoplasm Proteins)

Publication Type: Journal Article; Research Support, Non-U.S. Gov't; Review

Subject Headings: Animals
"Antineoplastic Agents/pd [Pharmacology]"
"*Antineoplastic Agents/tu [Therapeutic Use]"
"Apoptosis/ph [Physiology]"
"Autophagy/ph [Physiology]"
Drug Design
"Drug Resistance Neoplasm/de [Drug Effects]"

Citation: Neurology, August 2012, vol./is. 79/9(222-8), 0028-3878;1526-632X (2012 Aug 28)

Author(s): Bazelier MT; van Staa TP; Uitdehaag BM; Cooper C; Leufkens HG; Vestergaard P; Bentzen J; de Vries F

Institution: Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands.

Language: English

Abstract: OBJECTIVE: To derive a simple score for estimating the long-term risk of osteoporotic and hip fracture in individual patients with MS. METHODS: Using the UK General Practice Research Database linked to the National Hospital Registry (1997-2008), we identified patients with incident MS (n = 5,494). They were matched 1:6 by year of birth, sex, and practice with patients without MS (control subjects). Cox proportional hazards models were used to calculate the long-term risk of osteoporotic and hip fracture. We fitted the regression model with general and specific risk factors, and the final Cox model was converted into integer risk scores. RESULTS: In comparison with the FRAX calculator, our risk score contains several new risk factors that have been linked with fracture, which include MS, use of antidepressants, use of anticonvulsants, history of falling, and history of fatigue. We estimated the 5- and 10-year risks of osteoporotic and hip fracture in relation to the risk score. The C-statistic was moderate (0.67) for the prediction of osteoporotic fracture and excellent (0.89) for the prediction of hip fracture. CONCLUSION: This is the first clinical risk score for fracture risk estimation involving MS as a risk factor.
25. Protective role of glutathione reductase in paraquat induced neurotoxicity.

Citation: Chemico-Biological Interactions, August 2012, vol./is. 199/2(74-86), 0009-2797;1872-7786 (2012 Aug 30)

Author(s): Djukic MM; Jovanovic MD; Ninkovic M; Stevanovic I; Ilic K; Curcic M; Vekic J

Institution: Department of Toxicology, Faculty of Pharmacy at the University of Belgrade, Vojvode Stepe 450, 11221 Belgrade, Serbia. mirjana.djukic@pharmacy.bg.ac.rs

Language: English

Abstract: Paraquat (PQ), a widely used herbicide is a well-known free radical producing agent. The mechanistic pathways of PQ neurotoxicity were examined by assessing oxidative/nitrosative stress markers. Focus was on the role of glutathione (GSH) cycle and to examine whether the pre-treatment with enzyme glutathione reductase (GR) could protect the vulnerable brain regions (VBRs) against harmful oxidative effect of PQ. The study was conducted on Wistar rats, randomly divided in five groups: intact-control group, (n = 8) and four experimental groups (n = 24). All tested compounds were administered intrastratally (i.s.) in one single dose. The following parameters of oxidative status were measured in the striatum, hippocampus and cortex, at 30 min, 24 h and 7 days post treatment: superoxide anion radical (O2.-), nitrate (NO3-), malondialdehyde (MDA), superoxide dismutase (SOD), total GSH (tGSH) and its oxidized, disulfide form (GSSG) and glutathione peroxidase (GPx). Results obtained from the intact and the sham operated groups were not statistically different, confirming that invasive i.s. route of administration would not influence the reliability of results. Also, similar pattern of changes were observed between ipsi- and contra- lateral side of examined VBRs, indicating rapid spatial spreading of oxidative stress. Mortality of the animals (10%), within 24h, along with symptoms of Parkinsonism, after awakening from anesthesia for 2-3 h, were observed in the PQ group, only. Increased levels of O2.-, NO3- and MDA, increased ratio of GSSG/GSH and considerably high activity of GPx were measured at 30 min after the treatment. Cytotoxic effect of PQ was documented by drastic drop of all measured parameters and extremely high peak of the ratio GSSG/GSH at 24th hrs after the PQ i.s. injection. In the GR+PQ group, markedly low activity of GPx and low content of NO3- (in striatum and cortex) were measured during whole experiment, while increase value was observed only for O2.-, at 7th days. We concluded that oxidative/nitrosative stress and excitotoxicity are the most important events since the early stage of PQ induced neurotoxicity. Based on the ratio GSSG/GSH, the oxidation of GSH to GSSG is probably dominant way of GHS depletion and main reason for reduced antioxidative defense against PQ harmful oxidative effect. The GR pre-treatment resulted in the absence of Parkinson's disease-like symptoms and mortality of the rats. Additionally, oxidative/nitrosative stress did not developed, as well as almost diminished metabolism of the VBRs at 24th hours (as has been documented in the PQ group) did not occurred in the GR+PQ, suggesting a neuroprotective role for the GR in PQ induced neurotoxicity. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
Antioxidant therapy does not reduce pain in patients with chronic pancreatitis: the ANTICIPATE study.

Citation: Gastroenterology, September 2012, vol./is. 143/3(655-63.e1), 0016-5085;1528-0012 (2012 Sep)

Author(s): Siriwardena AK; Mason JM; Sheen AJ; Makin AJ; Shah NS

Institution: Hepatobiliary Surgery Unit, Manchester Royal Infirmary, Manchester, United Kingdom.

Language: English

Abstract: BACKGROUND & AIMS: We investigated whether antioxidant therapy reduces pain and improves quality of life in patients with chronic pancreatitis.

METHODS: We performed a double-blind, randomized, controlled trial that compared the effects of antioxidant therapy with placebo in 70 patients with chronic pancreatitis. Patients provided 1 month of baseline data and were followed for 6 months while receiving either antioxidant therapy (Antox version 1.2, Pharma Nord, Morpeth, UK) or matched placebo (2 tablets, 3 times/day). The primary analysis was baseline-adjusted change in pain score at 6 months, assessed by an 11-point numeric rating scale. Secondary analyses included alternative assessments of clinical and diary pain scores, scores on quality-of-life tests (the European Organization for Research and Treatment of Cancer [EORTC-QLQ-C30], Quality of Life Questionnaire-Pancreatic modification [QLQ-PAN28], European Quality of Life questionnaire [EuroQOL EQ-5D], and European Quality of Life questionnaire - Visual Analog Score [EQ-VAS]), levels of antioxidants, use of opiates, and adverse events. Analyses, reported by intention to treat, were prospectively defined by protocol.

RESULTS: After 6 months, pain scores reported to the clinic were reduced by 1.97 from baseline in the placebo group and by 2.33 in the antioxidant group but were similar between groups (-0.36; 95% confidence interval [CI], -1.44 to 0.72; P = .509). Average daily pain scores from diaries were also similar (3.05 for the placebo group and 2.93 for the antioxidant group, a difference of 0.11; 95% CI, 1.05-0.82; P = .808).

Measures of quality of life were similar between groups, as was opiate use and number of hospital admissions and outpatient visits. Blood levels of vitamin C and E, beta-carotene, and selenium were increased significantly in the antioxidant group.

CONCLUSIONS: Administration of antioxidants to patients with painful chronic pancreatitis of
predominantly alcoholic origin does not reduce pain or improve quality of life, despite causing a sustained increase in blood levels of antioxidants. Copyright Copyright 2012 AGA Institute. Published by Elsevier Inc. All rights reserved.

Country of Publication: United States
CAS Registry Number: 0 (Antioxidants)
Publication Type: Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't
Subject Headings: Adult
"Antioxidants/ae [Adverse Effects]"
"Antioxidants/tu [Therapeutic Use]"
Double-Blind Method
England
Female
Humans
Male
Middle Aged
"Pain/di [Diagnosis]"
"Pain/et [Etiology]"
"Pain/pc [Prevention and Control]"
Pain Measurement
"Pancreatitis Alcoholic/bl [Blood]"
"Pancreatitis Alcoholic/co [Complications]"
"Pancreatitis Alcoholic/di [Diagnosis]"
"Pancreatitis Alcoholic/dt [Drug Therapy]"
"Pancreatitis Chronic/bl [Blood]"
"Pancreatitis Chronic/co [Complications]"
"Pancreatitis Chronic/di [Diagnosis]"
"Pancreatitis Chronic/dt [Drug Therapy]"
Prospective Studies
Quality of Life
Questionnaires
Time Factors
Treatment Outcome

Source: MEDLINE


Citation: Annals of Epidemiology, September 2012, vol./is. 22/9(654-7), 1047-2797;1873-2585 (2012 Sep)

Author(s): White JW; Gale CR; Batty GD

Institution: Centre for the Development and Evaluation of Complex Interventions for Public Health Improvement, Cardiff University, Heath Park, Cardiff, UK. whitej11@cf.ac.uk

Language: English

Abstract: PURPOSE: High childhood IQ test scores have been associated with increased alcohol dependency and use in adult life, but the relationship between childhood IQ and illegal drug use in later life is unclear.METHODS: Participants were 6713 members of the 1958 National Child Development Survey whose IQ was assessed at 11 years and had their lifetime illegal drug use measured at 42 years of age.RESULTS: In analyses adjusted for a range of covariates, a 1 SD (15-point) increase in IQ scores was associated with an increased risk of illegal drug use in women: ever using cannabis (odds ratio [OR], 1.30; 95% confidence interval [95% CI], 1.16-1.45), cocaine (OR, 1.66; 95% CI, 1.21-2.27), amphetamines (OR, 1.50; 95% CI, 1.22-1.83), amyl nitrate (OR, 1.79; 95% CI, 1.30-2.46) and "magic mushrooms" (OR, 1.52; 95% CI, 1.18-1.98). Associations were of lower magnitude in men.CONCLUSIONS: In this cohort, high childhood IQ was related to illegal drug use in adulthood. Crown Copyright Copyright 2012. Published by Elsevier Inc. All rights reserved.
Impact of pre-enlistment antisocial behaviour on behavioural outcomes among U.K. military personnel.

Citation: Social Psychiatry & Psychiatric Epidemiology, August 2012, vol./is. 47/8(1353-8), 0933-7954;1433-9285 (2012 Aug)

Author(s): Macmanus D; Dean K; Iversen AC; Hull L; Jones N; Fahy T; Wessely S; Fear NT

Institution: Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, King's College London, PO23, De Crespigny Park, Denmark Hill, London, SE5 8AF, UK. deemacmanus@hotmail.com

Language: English

Abstract: PURPOSE: Concern has been raised over alleged increases in antisocial behaviour by military personnel returning from the deployment in Iraq and Afghanistan. U.S.-based research has shown that post-deployment violence is related not only to combat experience, but also to pre-enlistment antisocial behaviour (ASB). This study aimed to examine the association between pre-enlistment ASB and later behavioural outcomes, including aggression, in a large randomly selected U.K. military cohort.

METHODS: Baseline data from a cohort study of 10,272 U.K. military personnel in service at the time of the Iraq war in 2003 were analysed. The associations between pre-enlistment ASB and a range of socio-demographic and military variables were examined as potential confounders. Logistic regression analyses were performed to examine the relationship between pre-enlistment ASB and military behavioural outcomes such as severe alcohol use, violence/aggression and risk-taking behaviour, controlling for confounders.

RESULTS: 18.1% were defined as having displayed pre-enlistment ASB. Pre-enlistment ASB was significantly associated with factors such as younger age, low educational achievement, male gender, non-officer rank, Army personnel, being a regular, increasing time spent on the deployment and having a combat role. Pre-enlistment ASB was associated with increased risk of negative behavioural outcomes (severe alcohol misuse, outbursts of anger or irritability, fighting or assultative behaviour and risk-taking behaviour), after controlling for confounders, suggesting that such background information may identify individuals who are more vulnerable to subsequent behavioural disturbance.

CONCLUSION: The results of this study suggest that those already demonstrating ASB prior to joining the military are more likely to continue on this trajectory, thus emphasising the importance of considering pre-enlistment behaviour when exploring the aetiology of aggression in military personnel.

**Citation:** Alcohol & Alcoholism, July 2012, vol./is. 47/4(423-7), 0735-0414;1464-3502 (2012 Jul-Aug)

**Author(s):** Coulton S; Newbury-Birch D; Cassidy P; Dale V; Deluca P; Gilvarry E; Godfrey C; Heather N; Kaner E; Oyefeso A; Parrott S; Phillips T; Shepherd J; Drummond C

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**Language:** English

**Abstract:**
AIMS: To examine the feasibility and acceptability of alcohol screening and delivery of brief interventions within criminal justice settings.METHODS: A quantitative survey of those aged 18 or over in English criminal justice settings (three custody suites within police stations, three prisons and three probation offices).MEASUREMENTS: The Fast Alcohol Screening Test (FAST) and a modified version of the Single Alcohol Screening Question (M-SASQ) were compared with the Alcohol Use Disorders Identification Test (AUDIT) as the 'gold standard'. Participants completed a health status questionnaire (EQ5D), questions on service utilization and the Readiness to Change Questionnaire. Questions relating to the acceptability and feasibility of delivering brief interventions and about perception of coercion were included.FINDINGS: Five hundred and ninety-two individuals were approached and 251 were eligible. Of these, 205 (82%) consented to take part in the study. The mean AUDIT score was 19.9 (SD 13.5) and 73% scored 8 or more on AUDIT. A higher percentage of those approached in the probation setting consented to take part (81%: prison 36%, police setting 10%). Those scoring AUDIT positive were more likely to be involved in violent offences (36.5 vs 9.4%; P < 0.001) and less likely to be involved in offences involving property (27.7 vs 45.3%; P = 0.03). Three quarters of the sample (74%) reported that they would not feel coerced to engage in an intervention about their alcohol use. FAST and M-SASQ had acceptable screening properties when compared with AUDIT with area under the curves of 0.97 and 0.92, respectively.CONCLUSIONS: The results confirm that there is a major problem with alcohol use in the criminal justice system and this impacts on health and criminal behaviour. Of the three criminal justice settings, probation was found to be the most suitable for screening. Participants were positive about receiving interventions for their alcohol use in probation settings.
30. Exposure to liquid detergent capsules: a study undertaken by the UK National Poisons Information Service.

Citation: Clinical Toxicology: The Official Journal of the American Academy of Clinical Toxicology & European Association of Poisons Centres & Clinical Toxicologists, September 2012, vol./is. 50/8(776-80), 1556-3650;1556-9519 (2012 Sep)

Author(s): Williams H; Bateman DN; Thomas SH; Thompson JP; Scott RA; Vale JA

Institution: NPIS (Birmingham Unit), City Hospital, Birmingham, UK.

Language: English

Abstract: OBJECTIVE: To ascertain the reported toxicity of liquid detergent capsules. METHODS: Between 1 March 2008 and 30 April 2009 the UK National Poisons Information Service collected prospectively 647 telephone enquiries relating to liquid detergent capsules. RESULTS: The majority of enquiries (96.1%) concerned children of 5 years of age or less. Exposure to these products occurred mainly as a result of ingestion alone (n = 518; 80.1%), with eye contact alone (n = 61; 9.4%), and skin contact alone (n = 7; 1.1%) being less common; multiple routes of exposure were involved in 61 (9.4%) enquiries. Following ocular exposure, conjunctivitis with or without eye pain (n = 61), eye pain alone (n = 11) and keratitis (n = 4) developed; in one case the keratitis persisted for nine days, though recovery occurred in all cases as far as is known. The most common features reported following ingestion alone were nausea and vomiting (n = 143), followed by coughing (n = 21). Eleven children less than 2 years of age also developed drowsiness. A rash occurred in nine patients where ingestion was considered to be the route of exposure, probably due to topical contact with the capsule. Seven children aged 3 or less were exposed via the dermal route alone and developed rash (n = 4), irritation (n = 2), chemical burn (n = 2), and paresthesia (n = 1). CONCLUSIONS: Ocular exposure may lead to conjunctivitis and keratitis; recovery is to be expected in all cases within 7-10 days. Ingestion may also result in drowsiness. Greater consumer awareness is required to reduce injury from liquid detergent capsules, particularly that involving the eye. Parents have a vital role to play in ensuring that these products are stored safely at all times.
31. Effects of prenatal cocaine and heroin exposure on neuronal dendrite morphogenesis and spatial recognition memory in mice.

Citation: Neuroscience Letters, August 2012, vol./is. 522/2(128-33), 0304-3940;1872-7972 (2012 Aug 1)

Author(s): Lu R; Liu X; Long H; Ma L

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Language: English

Abstract: Cocaine and heroin are psychoactive substances frequently used by woman abusers of childbearing age. In this study, we used in utero electroporation labeling technique and novelty recognition models to evaluate the effects of prenatal exposure of mice to cocaine or heroin on the morphological development of cortical neurons and postnatal cognitive functions. Our results showed that prenatal cocaine exposure increased dendrite outgrowth, and prenatal heroin exposure decreased dendrite length and branch number in pyramidal neurons in the somatosensory cortex. Furthermore, although no effects of prenatal cocaine or heroin exposure on novel object recognition were observed, offspring prenatally exposed to cocaine exhibited no exploration preference for objects placed in novel locations, and mice prenatally exposed to heroin showed a reduced tendency of exploration for objects in novel locations. These data demonstrate that maternal cocaine or heroin administration during pregnancy causes morphological alterations in pyramidal neurons in the somatosensory cortex and suggest that prenatal administration of addictive substances may impair short-term spatial memory in adult offspring. Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
Mice Inbred ICR
Morphogenesis
Pregnancy
"*Prenatal Exposure Delayed Effects/pa [Pathology]"
"Prenatal Exposure Delayed Effects/px [Psychology]"
"*Psychotropic Drugs/to [Toxicity]"
Recognition (Psychology)
Space Perception

Source: MEDLINE

32. DRD2/ANKK1 TaqIA and SLC6A3 VNTR polymorphisms in alcohol dependence: association and gene-gene interaction study in a population of Central Italy.

Citation: Neuroscience Letters, August 2012, vol./is. 522/2(103-7), 0304-3940;1872-7972 (2012 Aug 1)

Author(s): Mignini F; Napolioni V; Codazzo C; Carpi FM; Vitali M; Romeo M; Ceccanti M

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Language: English

Abstract: Dopamine is a neurotransmitter whose functions are mediated by five receptors expressed in several organs and tissues. Dopaminergic system dysfunctions are involved in the etiology or treatment of several pathological conditions, including drug addiction. Alcohol dependence (AD) is a widespread psychiatric disorder, affecting 5.4% of the general population lifetime. Family and twins studies support the role of a genetic component in AD. Since dopamine neurotransmission has been shown to be involved in drug reward, related genes are plausible candidates for susceptibility to AD. Here, we evaluated both the DRD2/ANKK1 TaqIA (rs1800497) and SLC6A3 40 bp-VNTR SNP and gene-gene interaction analysis in AD patients from a population of Central Italy. The study design was a case-control. In total, 280 alcoholic subjects (213 men and 67 woman) and 280 age- and sex-matched control subjects were recruited for this study. Case subjects met the DSM-IV criteria for AD and they are free from any psychiatric co-morbidities. Controls were subjects who had non-alcohol problem either never drank; those who have smoked at least one pack of cigarettes per day for at least 1 year were excluded. Genotyping was performed by allele-specific PCR and RFLP-PCR. SLC6A3 40 bp 3'UTR-VNTR displays no association with AD. DRD2/ANKK1 TaqIA genotype distribution is significantly associated to AD (O.R.=1.551, p=0.023), with A1* allele displaying an O.R.=1.403 (p=0.029). Gene-gene interaction analysis using three-way contingency table analysis by a log-linear model yielded no significant result. Our study in a population of Central Italy extends and confirms previous results and, for the first time, tested the gene-gene interaction between SLC6A3 and DRD2 in AD. Copyright Copyright 2012 Elsevier Ireland Ltd. All rights reserved.
33. The detection of the urinary metabolites of 3-[(adamantan-1-yl)carbonyl]-1-pentyllindole (AB-001), a novel cannabimimetic, by gas chromatography-mass spectrometry.

Citation: Drug Testing & Analysis, June 2012, vol./is. 4/6(519-24), 1942-7611 (2012 Jun)

Author(s): Grigoryev A; Kavanagh P; Melnik A

Institution: Bureau of Forensic-Medical Expertise, Forensic-Chemical Division, Belgorod, Russia.

Language: English

Abstract: 3-[(Adamantan-1-yl)carbonyl]-1-pentyllindole (AB-001), a synthetic cannabimimetic, was identified in head shop products in Ireland in 2010. German authorities also reported it to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) via the Early Warning System (EWS) in 2011. As indole-derived cannabimimetics, such as JWH-018, JWH-073, and JWH-250, undergo extensive metabolism, it was expected that AB-001 would behave similarly. To include it in our toxicological screening protocols, we have identified its urinary metabolites in humans following oral administration. The major metabolites were found to be adamantane mono-hydroxylated and adamantane mono-hydroxylated/N-dealkylated products. No parent compound was found in urine, and metabolites were detectable for up to 160[THIN SPACE]h following administration.

Country of Publication: England

CAS Registry Number: 0 (3-((adamantan-1-yl)carbonyl)-1-pentyllindole); 0 (Cannabinoids); 0 (Indoles); 281-23-2 (Adamantane)

Publication Type: Journal Article

Subject Headings: "*Adamantane/aa [Analogs and Derivatives]"
"Adamantane/me [Metabolism]"
"Adamantane/ur [Urine]"
Administration Oral Adult
"Cannabinoids/ad [Administration and Dosage]"
"Cannabinoids/me [Metabolism]"
"*Cannabinoids/ur [Urine]"
Female
"*Gas Chromatography-Mass Spectrometry/mt [Methods]"
Humans Hydroxylation
"Indoles/me [Metabolism]"
"*Indoles/ur [Urine]"
Ireland Male Middle Aged
"*Substance Abuse Detection/mt [Methods]"
Time Factors

Source: MEDLINE

34. Developing an e-learning resource in clinical risk assessment.

Citation: Nursing Management (Harrow), September 2012, vol./is. 19/5(26-9), 1354-5760;1354-5760 (2012 Sep)
This article describes a project in which computer-centred technology was used to deliver clinical risk assessment training to staff in a specialist addictions unit. The difficulty in releasing staff from already stretched services led to the development of an in-house e-learning tool designed to bridge the gap between standardised risk assessment training and the requirements of staff who work in addictions services. The e-learning tool was developed on a small budget and is fairly rudimentary, but has been well received by staff, although they do not regard it as a replacement for classroom-based teaching. This was a pilot project that aimed to develop the resource and consider its use as a method of future training delivery.