Conclusions: Aripiprazole demonstrated its efficacy in maintaining abstinence from metamphetamine use in Thai patients with metamphetamine dependence following metamphetamine psychosis. It was found to be safe and well tolerated.
Keyword: methamphetamine, aripiprazole, dependence, abstinence

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Association between polymorphism of COMT gene and domestic violence in Han and Uygur on alcoholics in Xinjiang

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Abstract
Objective: The domestic violence may be related a number of neurotransmitters, and its associated gene, especially polymorphism of catecholamine-O-methyltransferase(COMT) gene, and gene expression. Herein, we sought to investigate the association between COMT gene rs4680、rs4818 polymorphism and domestic violence in Han and Uygur on alcoholics in Xinjiang.
Methods: The methods of PCR and Direct PCR sequencing were conducted to detect rs4680 and rs4818 single nucleotide polymorphism loci of COMT gene in 208 domestic violence perpetrators and 180 normal controls. The association between the polymorphisms and violent behavior was analyzed with SPSSl7.0. The SHEsis program was applied to perform the combined effect analysis of the paired SNPs.
Results: The frequency of the genotypes and alleles of rs4680 and rs4818 polymorphisms in the domestic violence group were not statistically different from those in the normal control group(P>0.05).The two groups were divided in Han and Uygur ethnic group. The frequency of the genotypes and alleles of rs4680 and rs4818 polymorphisms in the domestic violence Uygur and Han ethnic group were not statistically different from those in the normal control group(P>0.05). The results in Han and Uygur ethnic group of the combined effect analysis showed that rs4818-rs4680 in the domestic violence group were not statistically different from those in the normal control group(P>0.05).
Conclusion: COMT gene rs4818、rs4680 polymorphism may be not associated with domestic violence on alcoholics in Xinjiang.
Key words Domestic violence (DV); Violent behavior; catecholamine-O-methyltransferase (COMT); alcoholic.

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Association between autism susceptibility candidate 2 haplotypes and alcohol dependence in a Japanese population

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Abstract
The autism susceptibility candidate 2 (*AUTS2*) gene has been implicated in multiple neurological disorders including autism. Recent genome-wide analysis has indicated that the *AUTS2* gene is involved in the regulation of alcohol consumption. Therefore, we hypothesized that *AUTS2* might be associated with the development of alcohol dependence, and focused on two single nucleotide polymorphisms (rs6943555 and rs9886351) in the *AUTS2* gene, which have been studied extensively. In this exploratory study, we compared the genotype and allele frequencies of two polymorphisms in the *AUTS2* gene between patients with alcohol dependence and healthy control subjects living in a Japanese provincial prefecture. We also examined whether or not the haplotypes consisting of these polymorphisms are related to alcohol dependence. The subjects of this study consisted of 64 patients with alcohol dependence (male: 50, female: 7, not available: 7; 57.34±10.18 years) and 75 unrelated healthy people (male: 23, female: 52; 35.36±9.06 years). The *AUTS2* genotypes were determined by the polymerase chain reaction (PCR) - restriction fragment length polymorphism (RFLP) method. The study was approved by the ethics committees of the Tokyo Metropolitan Institute of Medical Science and Azabu University. No significant differences in the genotype and allele frequencies of the polymorphisms *AUTS2* rs6943555 and rs9886351 were found between alcohol dependence and control subjects. On the other hand, the frequencies of the *AUTS2* haplotypes were significantly different between them (p = 0.0187), and the patients with alcohol dependence showed a higher frequency of the rs6943555 and rs9886351 A-A haplotype as compared with the control group (26.73% of patients, 15.03% of controls). This suggests that the rs6943555 and rs9886351 A-A haplotype might affect the vulnerability to alcohol dependence pathogenesis. Further studies are needed to confirm the reproducibility of the results of this study with increased numbers of subjects.

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SORCS2 regulates alcohol withdrawal severity and excitatory synaptic transmission

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Abstract

Objective: Efforts to promote the cessation of harmful alcohol use are hindered by the affective and physiological components of alcohol withdrawal (AW), which can include life-threatening seizures. Although previous studies of AW and relapse have highlighted the critical importance of the N-methyl-D-aspartate receptor (NMDAR) subunit GluN2B and the detrimental role of stress, little is known about genetic risk factors. We therefore conducted genetic and neurobiological studies to identify and characterize novel risk loci.

Methods: We performed a genome-wide association study (GWAS) of AW symptom count in uniformly assessed subjects with histories of serious AW, followed by additional genotyping in independent subjects, and bioinformatic analyses. We used genetically modified mouse neuronal cultures to conduct electrophysiological and pharmacological studies of neurobiological systems implicated by the GWAS.

Results: The top association signal for AW severity was in sortilin-related gene *SORCS2* on chromosome 4 (European-American meta-analysis n = 1,478, P = 4.3 x 10^{-9}), and the same risk allele also predicted more severe clinical outcomes in seizure disorder patients participating in a randomized trial of anticonvulsant effectiveness (n = 654, P = 3.2 x 10^{-3}). In humans, *SORCS2* is most highly expressed in the nervous system, and bioinformatic analyses showed that the *SORCS2* risk haplotype disrupts transcription factor (TF) binding motifs within a stress hormone-regulated enhancer element active in human hippocampus. In mouse hippocampal preparations, we demonstrate that SorCS2 is a key regulator of GluN2B-mediated synaptic responses.

Conclusion: These translational findings identify new synaptic regulatory processes, and provide novel targets for managing the aversive consequences of abrupt alcohol cessation.

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High-dose zolpidem dependence and detoxification from withdrawal symptoms using diazepam

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Abstract

Objective of the study: Zolpidem is a nonbenzodiazepine hypnotic for the treatment of insomnia, and known as a relatively safe medication. However, there have been several case reports of zolpidem abuse and dependence these days. Even though some withdrawal symptoms like seizures can occur, there was no standard detoxification method until now.

Methods used: We reviewed the previous researches about high-dose zolpidem addiction and proposed treatment, and the clinical case.

Summary of results: A high dose of zolpidem has similar pharmacologic properties as the rest of benzodiazepines, even though the usual dose of zolpidem has a selectivity to type 1 benzodiazepine receptor. So, some cases of high-dose Zolpidem dependence can be treated by conventional benzodiazepines, such as diazepam. Actually, diazepam tends to be avoided because of complicated pharmacological properties and potential risks like respiratory suppression, iatrogenic dependence. But diazepam is still one of candidate medication for managing withdrawal symptoms of benzodiazepine dependence, and also, nonbenzodiazepine hypnotics in the clinical setting.

Conclusions reaches: We report a rare case of high-dose addiction and successful detoxification by cross-titration with diazepam.

Key words: addiction, dependence, detoxification, diazepam, withdrawal, zolpidem.

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Dissociable effects of cannabinoids on anticipatory and consummatory reward processing

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Running title: 'cannabis and musical reward'

Abstract

Reward processing can be parsed into dissociable components of anticipation (e.g. wanting) and consummation (e.g. liking). Dysfunctional reward anticipation is a transdiagnostic pathology spanning depression, schizophrenia and addiction. The rewarding effects of cannabis may be caused by its primary psychoactive constituent, delta-9-tetrahydrocannabinol (THC). Cannabidiol (CBD) is another cannabis constituent that can inhibit some effects of THC. This study had the following objectives: 1) to investigate the acute effects of cannabis on reward anticipation and consummation, 2) to establish whether these effects are blocked by CBD.

Across 3 sessions, 16 healthy cannabis users inhaled vaporized cannabis preparations containing 8mg THC, 8mg THC + 10mg CBD, and placebo. Reward consummation was indexed using functional Magnetic Resonance Imaging, evidenced by greater signal whilst listening to classical music versus scrambled sound. Regions of interest were selected from a meta-analysis of music-evoked emotion, and all results were False Discovery Rate corrected. Reward anticipation was recorded using the visual analogue scale 'want to listen to music'; post-hoc tests were Bonferroni-corrected.

Analysis of consummatory reward showed that cannabis containing THC only reduced activation in bilateral temporal gyrus (right: p=0.005, left: p=0.008), right hippocampus (p=0.025), right amygdala (p=0.025), right insula (p=0.026) and right medial orbitofrontal cortex (OFC, p=0.033). Cannabis containing THC and CBD did not alter signal in any regions. Across all scans, OFC activation correlated with subjective pleasure ratings (r(48)=0.463, p<0.001). Both types of cannabis increased reward anticipation to a similar extent (THC: p=0.001, THC+CBD: p=0.006).

Reward anticipation is primed by cannabis, regardless of its CBD content. By contrast, cannabis reduces neural activation to reward consummation, and this effect is blocked by CBD. These