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Neurocognitive Examination of Inhibitory Control and Error Processing Mechanisms In Prescription Opioid Dependence
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Abstract
Introduction: Prescription opioid (PO) abuse is a growing public health concern worldwide as evidenced by an increasing number of opioid-related hospital admissions with a striking lack of research examining the neural basis underlying cognitive symptomatology. Drugs of abuse, through their impact on the dopaminergic system, are thought to disrupt the pre-frontal cognitive network regulating impulse control through performance monitoring and inhibition of goal-oriented behavior.

The objective of the present study is to examine neurocognitive processes in PO abusers (vs. healthy controls) by relying on the enhanced temporal resolution (1ms) of event-related potentials (ERPs) to track information processing abnormalities associated with cognitive control. Methods: In a naturalistic clinical study, 20 patients actively using prescription opioids and 20 healthy controls (matched for age, gender, educational level and smoking status) were assessed using a Go/NoGo paradigm, where the response to NoGo trials was evaluated. Results: Preliminary analysis reveals significantly (p<0.05) larger N200 and P300 amplitudes in patients (vs. controls) after successful NoGo trials. The N200 is a frontally distributed negative waveform reflecting the commencement of active inhibition, whereas the P300 is a fronto-centrally distributed positive waveform reflecting the termination of a previous inhibitory process. Following unsuccessful NoGo trials, error positivity (Pe) amplitudes were also significantly (p<0.05) increased in patients (vs. controls). The Pe is a fronto-central positive deflection component of the ERP representing the awareness of conscious error processing. Conclusions: These ERP results of altered cognitive control and error processing suggest the neural mechanisms underlying these cognitions are affected by chronic opioid abuse. Investigating the cognitive abnormalities experienced by PO abusers is an important factor in understanding the neural correlates of substance abuse and in predicting successful outcomes to ensure the best chance at long-term recovery for addicted individuals. Research funded by a Canadian Institute of Health Research (CIHR) grant.

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Knockdown Piccolo suppressed Methamphetamine-induced behavioral changes and dopamine release in the nucleus accumbens of mice
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Abstract
The Piccolo gene was identified as one increased molecular in nucleus accumbens (NAC) of mice which treated with methamphetamine (METH) continuously. Piccolo is originally reported as a Ca2+ sensor for regulating release of insulin in pancreas β cell. Piccolo is a protein of the pre-synapse, and it is comprised of domains such as PDZ, C2A or C2B mainly. The PDZ domain interacts with other pre-synapse proteins comprised of active zone.

The C2A domain is including Ca2+ binding site, and it is considered that spatial structure changes in Ca2+ binding presence. It is reported that Piccolo plays an important role in the neuronal synapse. However, function of Piccolo gene in NAc remains unclear in the drug dependence. Therefore, we investigated the physiological function of Piccolo in the NAc of mice, which were received METH treatment.

To clarify of Piccolo in the NAc, we characterized the NAc-specific knockdown mice (mi Piccolo mice) by aden-associated virus (AAV) vector including Piccolo miRNA. METH-induced locomotor activity of mi Piccolo mice was reduced compared with that of AAV-mock mice (Mock mice). The mi Piccolo mice suppressed the METH-induced CPP formation. In the microdialysis test, the mi Piccolo mice exhibited lower dopamine basal levels and tendency to decrease METH-potentiated dopamine release. These results suggested that Piccolo in the NAc regulates dopaminergic neuronal systems and METH-dependence related-behaviors.

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Pseudoginsenoside-F11 inhibits methamphetamine dependence by regulating GABAergic and opioidergic neuronal system in the nucleus accumbens of mice
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Abstract
Methamphetamine (METH) dependence is a global health and social problem, which is usually associated with serious psychiatric symptoms, and no effective therapeutic approaches have been identified. Pseudoginsenoside-F11 (PF11) is an ocatillol-type saponin that is isolated from Panax quinquefolius (American ginseng). It was shown to attenuate the pharmacological effects of morphine and METH-induced neurotoxicity in mice. However, the functional roles of PF11 in METH dependence are still unknown. In this experiment, we investigated whether PF11 would affect METH-induced abnormal behaviors and then elucidated the mechanism of its pharmacological effects on METH responses.

Results: In the conditioned place preference (CPP) test, co-administration of PF11 and METH during the conditioning phase inhibited the development of METH-induced CPP. In addition, after developing METH-induced CPP, repeated administration of PF11 for 5 days decreased the CPP compared with vehicle-treated METH withdrawal group. In the locomotor activity test, co-administration of PF11 and METH for 6 days attenuated METH-induced locomotor sensitization compared with administration of METH alone. Moreover, in vivo microdialysis analyses indicated that co-administration of PF11 and METH for 7 days prevented METH-induced extracellular dopamine (DA) increase in the nucleus accumbens (NAc). Repeated PF11 administration for 7 days increased extracellular GABA levels in the NAc, whereas single administration of PF11 did not. Furthermore, hyperlocomotion and accumbal extracellular DA
increase that induced by the infusion of μ-opioid receptor agonist DAMGO in the NAc were significantly suppressed by acute PF11 administration.

Conclusions: The present data indicate that PF11 inhibits METH-induced dependence and dopaminergic hyperfunction by regulating GABAergic and opioidergic neuronal system in the NAc of mice. And it is proposed that PF11 could be a useful compound for the therapeutic treatment of METH dependence.

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Carbachol attenuates excitatory synaptic transmission in cholinergic neurons of the laterodorsal tegmental nucleus
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Abstract
Cholinergic neurons in the laterodorsal tegmental nucleus (LDT) project to the ventral tegmental area (VTA), and changes in the activity of these neurons are thought to affect the activity of VTA dopamine (DA) neurons. We previously reported that in chronically cocaine-administered rats the activity of LDT cholinergic neurons are increased through induction of plastic changes in synaptic transmission and membrane excitability. However, it remains unclear whether acetylcholine (ACh) acts on the LDT cholinergic neurons themselves and modulates their synaptic transmission, and whether such modulatory effects, if any, are affected by chronic cocaine injection. In the present study, we addressed these issues using patch-clamp recordings in rat brain slices. Bath application of carbachol (CCh) significantly reduced the membrane input resistance and the amplitudes of evoked excitatory postsynaptic currents (eEPSCs) without affecting paired pulse ratios. These reductions were suppressed by pretreatment with scopolamine but not mecamylamine, indicating that the effects of CCh are mediated by muscarinic ACh receptors (mACHRs). Intracellular perfusion with GDPβS suppressed the CCh-induced reduction of input resistance but not eEPSC amplitudes, suggesting that the reduction of eEPSC amplitudes is not mediated by a postsynaptic G-protein signaling. Finally, the effects of CCh on eEPSC amplitudes in the LDT cholinergic neurons were not significantly different between the groups repeatedly treated with cocaine or saline. These findings suggest that ACh attenuates excitatory synaptic transmission in the LDT cholinergic neurons through mACHRs, but not through G-protein signaling, and that this effect of CCh is not affected by chronic cocaine administration.

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Characterization of nicotinic neural activities in rat medial and lateral habenula
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Abstract
Most studies have suggested a role for the medial habenula in nicotine addiction but have not assigned these effects to lateral habenula. To demonstrate the distinguished effect of nicotine on habenula between lateral and medial subnuclei, we performed an extracellular recording on various subregions of habenula with nicotine application. We found that whole region of medial habenula presented an identical nicotine-induced neuronal responses which showed a drastic excitation of medial habenula neurons followed by reduction and re-excitation. However, neuronal fields in lateral habenula presented three types of nicotine responses. One type in lateral habenula showed a dramatic excitation followed by reduction and re-excitation against the nicotine application which is similar to the nicotine-induced response in medial habenula. Another type in lateral habenula presented only a reduction of spontaneous neuronal firings for nicotine without excitation. The other type in lateral habenula showed no notable changes after nicotine application. Taken together, our findings demonstrate that lateral habenula as well as medial habenula contributes to alteration of nicotine-induced neural activity. Because the nicotine addiction has not only rewarding properties by the lateral habenula-rostromedial tegmental nucleus regulating dopamine system projection but also aversive properties by the medial habenulo-interpeduncular tract controlling serotonin system projection, the distributional differences in habenula for nicotine-induced neuronal response would be a fascinating approach to comprehend a brain function for the balance between negative and positive reward induced by nicotine. (supported by NRF-2013R1A1A057712 and NRF-2014R1A2A2A4007391)

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Spicy food preference and the HPA axis reactivity to stress in Korean social drinkers
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Abstract
Objectives: Some reports suggest that if individuals prefer spicy foods, they may be vulnerable to stress; thus, their HPA axis reactivity to stress may be abnormal. We investigated the relationship between HPA axis reactivity to stress and spicy food preference in social drinkers.

Methods: The subjects were 40 social drinkers aged above 18 years. They were exposed to stress as cold pressor test and mathematical calculations. Salivary cortisol level was measured before and after the stress and spicy food preference was measured. The subjects were divided into two groups of those who preferred spicy foods (SP, n = 20) and those who less preferred spicy foods (LP, n = 20).

Results: Repeated measures ANOVA on salivary cortisol concentration revealed a significant group by block interaction. Basal and salivary cortisol levels immediately after stress were significantly higher in SP subjects than those in LP subjects. The salivary cortisol level at 80 min after the stress decreased significantly compared to the basal salivary cortisol level in SP subjects. Salivary cortisol level 20 min after the stress increased significantly compared to the basal salivary cortisol level in LP subjects.

Conclusion: HPA axis reactivity to stress in SP subjects was more sensitive than that in LP subjects. These results suggest that HPA axis reactivity in those who prefer spicy foods may be vulnerable to stress.

Key Words: HPA axis · Stress · Spicy food preference · Vulnerability · Salivary cortisol