of the acquisition and expression of morphine CPP. Moreover, antagonism of OX2rs could facilitate extinction and may extinguish the ability of drug-related cues, implying that the antagonist might be considered as a propitious therapeutic agent to suppress drug-related behavior.

References

1. Harris, G.C., Wimmer, M., Aston-Jones, G., 2005. A role for lateral hypothalamic orexin neurons in reward seeking. Nature 437, 556–559.
2. Flores, Á., Valls-Comamala, V., Costa, G., Saravia, R., Maldonado, R., Berrendero, F., 2014. The hypocretin/orexin system mediates the extinction of fear memories. Neuropsychopharmacology 39, 2732–2741.

PM291

Synthetic cannabinoid JWH-210 induces motor impairments through the regulation of neurotransmission in tetanus toxin-treated mice

Jaesuk Yun[*,1], *Tac-hyung Lee*[1], *Yun Jeong Song*[1], *Seonhwa Seong*[1], *Young-Hoon Kim*[1], *Hye Jin Cha*[1], *Kyoung moon Han*[1], *Jisoon Shin*[1], *Hokyung Oh*[1], *Kikyung Jung*[1], *Chiyoung Ahn*[1], *Choon-gon Jang*[2], *Ji-Young Hwang*[2], *Hye-Kyung Park*[1] *and Hyung Soo Kim*[*,1]
[1]*National Institute of Drug and Safety Evaluation, Ministry of Food and Drug Safety, Osong, Cheongju, Republic of Korea,* [2]*School of Pharmacy, Sungkyunkwan University, Suwon, Republic of Korea*

Abstract

The problem of new psychoactive substances is emerging globally. Cannabinoid receptors mediate the action of synthetic cannabinoids, which are one of most abused drugs. Recently, cannabinoid receptors 1 (CB1R) have been reported to silence glutamatergic nerve terminals in cerebellar granule cells via synaptic vesicle redistribution. This study aimed to determine whether synthetic cannabinoid administration (0.1 mg/kg, 5 days) influences the development of biotoxin-induced deficit in neuronal homeostasis. We observed that JWH-210, a synthetic cannabinoid, induced motor impairment and decrement of vesicle-associated membrane proteins 2 (VAMP2) levels in the cerebellum of mice treated with tetanus toxin. Cerebellar glutamatergic neuronal homeostasis was hampered by JWH-210 administration, as evidenced by increased glutamate concentration levels in the cerebellum of the tetanus-treated mice. However, JWH-250, which has a lower CB1R binding affinity than does JWH-210 (K_i value: 1.1×10^{-7} M, and 2.6×10^{-8} M, respectively) did not exacerbate motor impairment and VMAP2 decrements in the cerebellum of tetanus-treated mice. In addition, tyrosine hydroxylase, the dopamine synthetic enzyme was downregulated in the striatum of JWH-210/Tetanus mice. These results suggest that JWH-210 may have an additive effect on the tetanus toxin-induced glutamatergic and dopaminergic neuronal dysfunction.

PM292

Possible involvement of cannabinoid CB1 receptors in behavioral impairments after withdrawal from chronic methamphetamine administration in mice.

Ryo Fukumori[1], *Catherine Ledent*[2], *Satoshi Yamada*[1], *Taku Yamaguchi*[1], *Tsuneyuki Yamamoto*[1]
[1]*Nagasaki International University, Japan,* [2]*Université Libre de Bruxelles, Belgium,*

Abstract

Objective: Endocannabinoid systems play important roles in physiological functions in the central nervous system, such as pain perception, appetite, psychomotor behavior, emotion, reward system and cognitive function. We previously reported that the involvement of cannabinoid CB1 receptors in the reinstatement of methamphetamine-seeking behaviors in rats. On the other hand, chronic administration of methamphetamine causes behavioral sensitization in rodents and human. However, the effects of withdrawal from chronic administration of methamphetamine on the cognitive deficits have been still unclear. In this study, we investigated relationship between cognitive deficits and development of behavioral sensitization by using the cannabinoid CB1 receptor knockout mice.
Method: Mice were subcutaneously administered methamphetamine at the dose of 1.8 mg/kg or saline, every other day for 30 or 60 days (15 or 30 injections). Behavioral sensitization was evaluated by locomotor activity in the open-field test. 10 or 30 days after withdrawal, the mice were tested a cognitive functions by object recognition test and sensorimotor gating function by prepulse inhibition test.
Result: In wild-type mice, locomotor activity was enhanced by the chronic administration of methamphetamine. Approach time to the novel object was decreased during withdrawal of chronic methamphetamine. In addition, prepulse inhibition of the acoustic startle response was suppressed during withdrawal of chronic methamphetamine. On the other hand, in CB1 receptor knockout mice, the locomotor activity was not enhanced by chronic administration of methamphetamine. Furthermore, CB1 receptor knockout mice were not impaired the cognitive function and prepulse inhibition by chronic administration of methamphetamine.
Conclusion: Our data suggest that activation of the cannabinoid CB1 receptors could lead to the development of behavioral sensitization and cognitive/sensorimotor gating deficits after withdrawal from chronic methamphetamine administration.

PM293

Efficacy and Safety of Aripiprazole for Maintenance Treatment of Methamphetamine Dependence Following Methamphetamine Psychosis: A Naturalistic Retrospective Study

Tuanthon Boonlue[1], *Somporn Suwanmajo*[2], *Thanarat Suansanae*[3]
[1]*Department of Pharmacy Practice, Faculty of Pharmaceutical Science, Ubonratchathani University, Ubonratchathani, Thailand* [2]*Department of Pharmacy, Princess Mother National Institute on Drug Abuse Treatment, Prathumthani, Thailand.* [3]*Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand*

Abstract

Objective: The objective was to determine the efficacy and safety of aripiprazole in the maintenance treatment of methamphetamine dependence following methamphetamine psychosis in Thai patients.
Methods: This was a retrospective chart review study in patients aged between 18–65 years with metamphetamine dependence who had been received aripiprazole (dose 2.5–15 mg/day) for at least 2 weeks after resolved from psychosis. Primary outcome was abstinence rate at 12 weeks which was assessed by urine toxicology. Adverse events were reported as secondary outcome.
Results: Forty-three patients were enrolled in this study. Most of them (58.1%) received aripiprazole 10–15 mg/day. The abstinence rate at week 2, 4, 6, 8, 10 and 12 were 90.70%, 88.10%, 78.13%, 76.47%, 91.67% and 75%, respectively. Parkinsonism was the most commonly found adverse events (11.63%), following by insomnia (6.98%), sedation (6.98%) and akathisia (4.65%).