3,4-Methylenedioxymethamphetamine (MDMA) impairs cognitive function during withdrawal via activation of the arachidonic acid cascade in the hippocampus

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Abstract

Background

The recreational drug ±3,4-methylenedioxymethamphetamine (MDMA; also known as "ecstasy") has unusual subjective prosocial and empathogenic effects, and has exhibited potential as an adjunct to psychotherapy in recent years. However, there has been some concern regarding possible neuropsychiatric symptoms, such as cognitive impairment and dependence, emerging after abstinence. Therefore, this study aimed to evaluate the mechanism underlying cognitive impairment during MDMA withdrawal. To achieve this, we focused on the arachidonic acid cascade, which is related to addiction to some abusive drugs.

Methods

A novel object recognition task was used to investigate cognitive function in mice. Furthermore, we quantified prostaglandin E2 during MDMA withdrawal.

Results

The recognition index significantly decreased during withdrawal after repeated administration of MDMA (10 mg/kg, i.p., once daily for 7 days), but not following co-administration of diclofenac (10 mg/kg, i.p.), a cyclooxygenase inhibitor. On day 1, following repeated MDMA treatment, prostaglandin E2 content significantly increased in the hippocampus but not in the prefrontal cortex and striatum.

Conclusions

Our findings indicate that activation of the arachidonic acid cascade at least in the hippocampus is likely involved in the development of recognition memory impairment during MDMA withdrawal. Therefore, co-use of cyclooxygenase inhibitors with MDMA may reduce concerns regarding MDMA-induced impairment of recognition memory.