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P.193 Curcumin attenuates methamphetamine-induced conditioned place preference via an inhibition of CC chemokine ligand 2 expression

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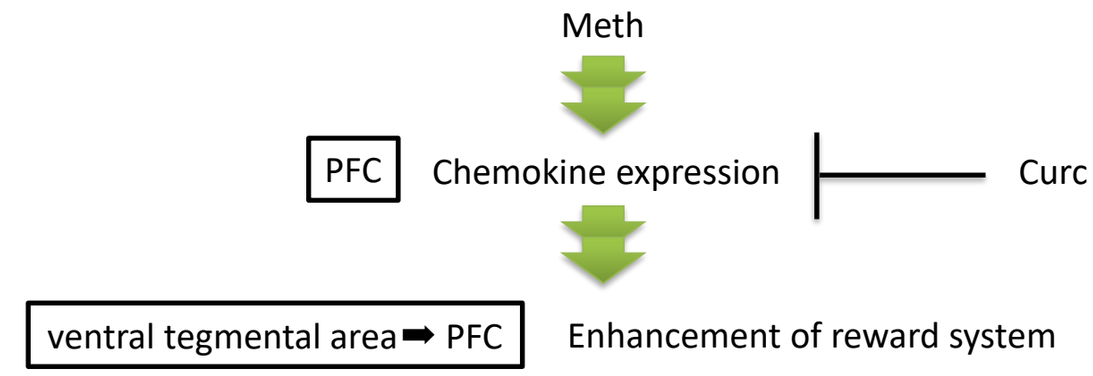
Background: Curcumin (Curc) is a natural flavonoid component and have been reported the anti-oxidant, anti-inflammatory and anti-nociceptive effects. Many clinical trials have focused on Curc as therapeutic agent in various chronic diseases, including diabetes and cancers, as well as cardiovascular, neurological and psychological diseases. Methamphetamine (Meth) is an addictive psychostimulant widely abused around the world. Meth exposure is known to promote microglial activation and production of inflammatory mediators, such as cytokines and chemokines.
Recent findings indicate that chemokine ligands play an important role in the neuroinflammation in the central nervous system (CNS). However, little is known about the relation between Meth-induced reward and inflammatory mediators. Among several chemokine ligands, CC-chemokine ligand 2 (CCL2) is derived from neurons and glial cells, and has been paid attention to the CNS effects because of its facilitative effects on neurotransmission. CCL2 acts on dopamine neurons in the substantia nigra and enhances dopamine release into the striatum. There are a lot of reports suggesting that CCL2-mediated neuroinflammation also underlies the pathogenesis of drug abuse. In addition, we previously reported that CCL2-CCR2 axis plays a crucial role in psychic dependence on Meth. In this study, we investigated the effects of Curc on Meth-induced reward, focused on CCL2.

Conclusions:



Results

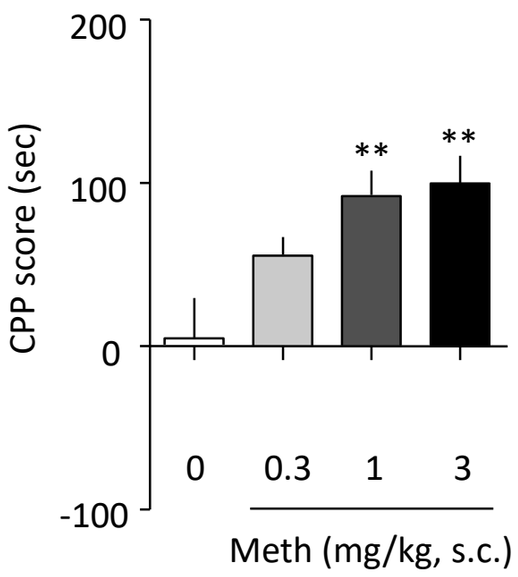
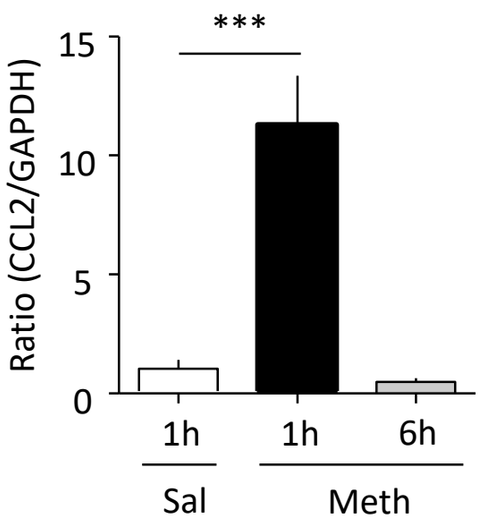
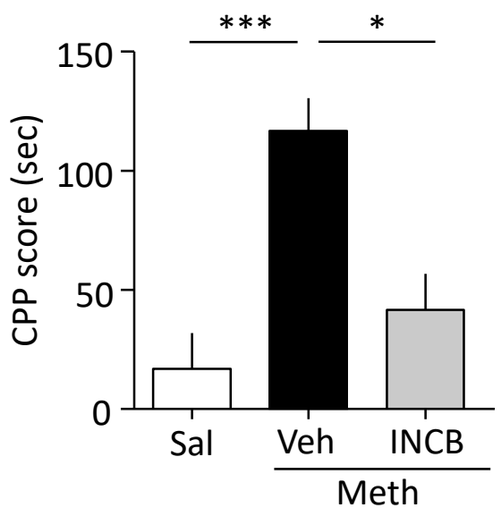


Fig.1. CPP test
Meth was administered to mice, and the place preference to Meth was evaluated by CPP test.
**P<0.01 vs control. n=9-12.



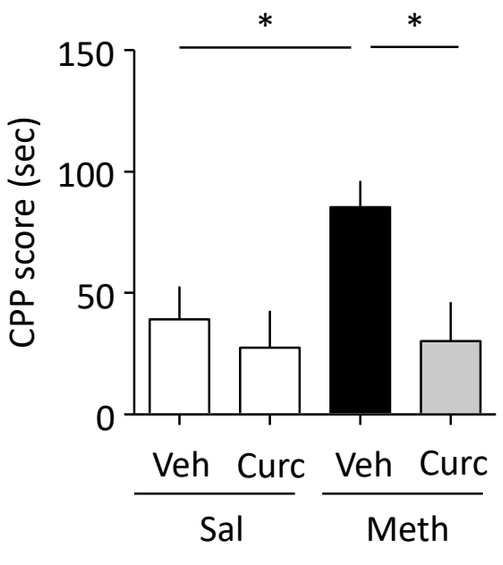
Real-time PCR

Fig.2.
Meth (3 mg/kg, s.c.) was administered to mice. On the indicated time, the PFC tissues were dissected using the brain matrix and used for real-time PCR.
***P<0.001 vs Saline (Sal). n=5-6.



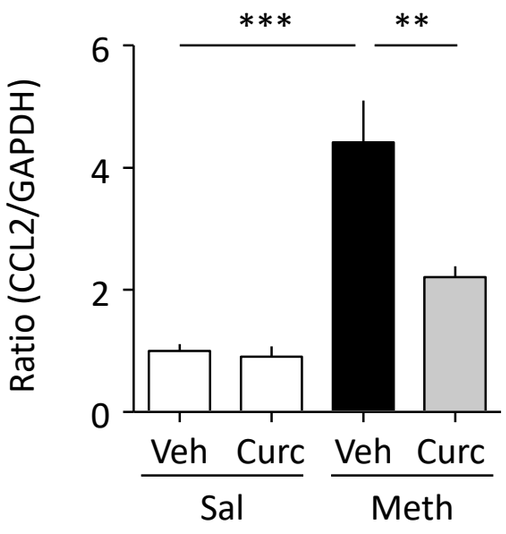
CPP test

Fig.3.
Meth (1 mg/kg, s.c.) was administered 3 times. INCB3284 (INCB; 5 mg/kg, s.c.), a CCR2 antagonist, was treated 15 min before Meth. n=8-19.



CPP test

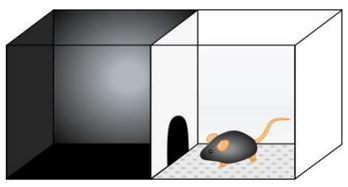
Fig.4.
Meth (1 mg/kg, s.c.) was administered 3 times. Curcumin (Curc; 50 mg/kg, i.p.) was treated 15 min before Meth and Sal administration. n=13-21.



Real-time PCR

Fig.5.
Curc (50 mg/kg, i.p.) and Meth (3 mg/kg, s.c.) was administered once a day for 3 days. The PFC tissues were dissected using the brain matrix and used for real-time PCR. n=5-6.

Method



Conditioned place preference (CPP) test:
The apparatus was consisted of two equal-sized compartment. One side of the box was white with a rough floor, and the other side of the box was black with a smooth floor.
<Pre-conditioning session>
Day1-2: mice were allowed to move freely between two boxes for 15 min.
Day3: mice were put in the apparatus like day1, and the time that mice spent in each box was measured.
<Conditioning session>
Day4: mice were administered to Meth and were kept in non-preferred box for 60 min.
Day5: mice were administered to control Sal and were kept in preferred box 60 min.
Day6-9: above conditioning processes were repeated twice.
<Post-conditioning session>
Day10: mice were put in the apparatus for 15 min as well as pre-conditioning session.
By the measurement of the time that mice spent in non-preferred box, preference to Meth was determined.
CPP score (sec) =
(the time spent in non-preferred box on day 10) – (that on day 3)