

## Cocaine-induced conditioned place preference and locomotor response are distinctively regulated by glutamate and dopamine receptor signaling in the prefrontal cortex

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The dopamine (DA) D1 receptors in the nucleus accumbens (NAc) is implicated in cocaine-induced conditioned place preference (CPP), which is driven by the cocaine-associated cue. However, the effect of the cocaine-associated cue on DA release in the prefrontal cortex (PFC) has little been studied. The present study examined the effects of cocaine-associated cues on the extracellular DA levels in the NAc and PFC using *in vivo* microdialysis. Furthermore, the role of D1, D2, and ionotropic glutamate receptors in cocaine (7.5 mg/kg i.p.)-induced CPP, locomotor and DA release were investigated. Cocaine-associated cues increased DA levels in the PFC, but unexpectedly had no effects on DA levels in the NAc. Pharmacological inhibition of D1 and D2 receptors and chemogenetic inhibition of D1 receptor-expressing cells by Gi-DREADD in the PFC during the cocaine conditioning procedure suppressed the cocaine-induced locomotor response, but did not affect the CPP. Pharmacological modulation of ionotropic glutamate receptors by antagonists and agonists in the PFC suppressed the cocaine-induced CPP, but did not affect the locomotor response. The DA response to the cocaine-associated cue in the PFC was abolished by pharmacological inhibition of ionotropic glutamate receptors, but not of D1 or D2 receptors.

The present results demonstrate that the cocaine-induced CPP and locomotor response are induced by the distinct neural pathways in the PFC mediated through ionotropic glutamate receptor and DA receptor signaling, respectively.