



## Effects of serotonin (5-HT)<sub>1B</sub> receptor ligands on cocaine-seeking behavior in rats

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### Abstract:

Numerous data indicated a significance for the brain dopaminergic pathways in the behavioral effects of cocaine, however recent research also demonstrated involvement of serotonin (5-HT) neurotransmission and particularly 5-HT<sub>1B</sub> receptors in the reinforcing, discriminative stimulus and sensitizing effects of cocaine. In order to substantiate a role of these receptors in incentive motivation for cocaine, we used the extinction/reinstatement model to examine the effects of the 5-HT<sub>1B</sub> receptor ligands on reinstatement of extinguished cocaine-seeking behavior and food-taking behavior. Rats trained to self-administer cocaine (0.5 mg/kg/infusion) subsequently underwent extinction procedures. They were then tested for the cocaine-primed or cocaine-associated cue-induced reinstatement of extinguished cocaine-seeking behavior. Other groups of rats were trained to self-administer food (sweet milk), and after extinction they were tested for the reinstatement of food-taking behavior induced by contingent food presentation. The 5-HT<sub>1B</sub> receptor antagonists SB 216641 (2.5–7.5 mg/kg) and GR 127935 (2.5–10 mg/kg) dose-dependently attenuated the cocaine (10 mg/kg)- and cocaine-associated cue-induced reinstatement of cocaine-seeking behavior whereas they failed to alter reinstatement of food-taking behavior. The 5-HT<sub>1B</sub> receptor agonist CP 94253 (2.5 or 5 mg/kg) combined with a subthreshold priming dose of cocaine (2.5 mg/kg) potentiated reinstatement of the drug seeking-behavior, but inhibited cocaine seeking induced by a submaximal dose (10 mg/kg) of cocaine or the cocaine-associated cue. Moreover, the 5-HT<sub>1B</sub> receptor agonist attenuated reinstatement of food-taking behavior. Facilitatory effect of CP 94253 on cocaine-seeking behavior and its inhibitory effect on food-taking behavior were blocked by SB 216641, but its inhibitory effect on cocaine-seeking behavior remained unaffected by this 5-HT<sub>1B</sub> receptor antagonist. Our results indicate that tonic activation of 5-HT<sub>1B</sub> receptors is involved in cocaine- and cue-induced reinstatement of cocaine-seeking behavior and that the inhibitory effects of 5-HT<sub>1B</sub> receptor antagonists on these phenomena are directly related to motivational aspects of cocaine abuse. The facilitatory 5-HT<sub>1B</sub> receptor-mediated effect of the 5-HT<sub>1B</sub> receptor agonist on cocaine seeking may be related to the earlier reported enhancement of the rewarding properties of cocaine, while its inhibitory effect on cocaine-seeking behavior, unrelated to the 5-HT<sub>1B</sub> receptor activation, may result from a general reduction of motivation.

### Key words:

5-HT<sub>1B</sub> receptors, cocaine-seeking, food taking, rats

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