



Modulatory role of 5-HT_{1B} receptors in the discriminative signal of amphetamine in the conditioned taste aversion paradigm

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Abstract:

Drugs of abuse, such as amphetamine (AMPH), share the ability to activate the mesolimbic dopamine (DA) system. The behavioral effects of AMPH are largely mediated by increased DA neurotransmission in the nucleus accumbens. However, there is evidence that serotonin (5-hydroxytryptamine – 5-HT) systems may regulate forebrain DA function. We examined the role of 5-HT_{1B} receptors on the discriminative stimulus properties of AMPH using conditioned taste aversion (CTA) as the drug discrimination procedure. Male Wistar rats were deprived of water and trained in the CTA procedure. They received the administration of AMPH (1.0 mg/kg) before a 10 min period of access to saccharin solution and followed by an injection of LiCl; on alternate days, rats received saline before and after the access to saccharin solution. In generalization and combination tests, the training dose of AMPH was substituted by 5-HT_{1B} receptor ligands RU24969 (5-HT_{1B} agonist: 0.1, 0.3 and 1.0 mg/kg), CP94253 (5-HT_{1B} agonist: 1.0, 3.0 and 5.6 mg/kg) and GR127935 (5-HT_{1B} antagonist: 0.3, 1.0 and 3.0 mg/kg) or a combination of RU24969 (0.1, 0.3 and 1.0 mg/kg), CP94253 (1.0, 3.0 and 5.6 mg/kg) or GR127935 (0.3, 1.0 and 3.0 mg/kg) with AMPH (0.3 mg/kg) or GR127935 (0.3, 1.0 and 3.0 mg/kg) and CP94253 (5.6 mg/kg) with AMPH (0.3 mg/kg). The results showed that 5-HT_{1B} agonists RU24969 and CP94253 produced partial generalization of 48% and 60%, respectively, and the 5-HT_{1B} antagonist GR127935 neither substituted for AMPH nor affected the discriminative cue of AMPH; however, when RU24969 or CP94253 were administered in combination with AMPH, they increased the discriminative cue of AMPH. This effect was reversed by the administration of 5-HT_{1B} antagonist GR127935. These data suggest that 5-HT_{1B} receptors play a modulatory role in the discriminative cue of AMPH.

Key words:

amphetamine, drug discrimination, 5-HT_{1B} receptors
