



Effects of GABA_B receptor agonists on cocaine hyperlocomotor and sensitizing effects in rats

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Abstract:

The present study was designed to find out whether pharmacological activation of GABA_B receptors played a role in cocaine sensitization. To this end, male Wistar rats were injected with baclofen or 3-aminopropyl(methyl)phosphinic acid (SKF 97541), the potent and selective GABA_B receptor agonists. The rats, which were repeatedly (for 5 days) administered with cocaine (10 mg/kg) and then challenged with cocaine (10 mg/kg) after 5-day withdrawal period, showed significantly higher locomotor hyperactivity in comparison with the effect observed in saline-pretreated and cocaine challenged rats. Baclofen (1.25, 2.5 and 5 mg/kg), administered for 5 days prior to cocaine, dose-dependently attenuated cocaine sensitization. When injected in the same treatment regimen, SKF 97541 (0.03 mg/kg) reduced the development of cocaine sensitization. To examine the effects of baclofen and SKF 97541 on the expression of cocaine sensitization, the drugs were given acutely before a challenge dose of cocaine (10 mg/kg) on day 10. Either baclofen (2.5 and 5 mg/kg) or SKF 97541 (0.1 mg/kg) decreased sensitization to cocaine. Our findings implicate a role of GABA_B receptors in locomotor responses to cocaine. More specifically, they show that stimulation of GABA_B receptors exerted inhibitory actions on acute locomotor responses to cocaine and on the expression of cocaine sensitization, what may offer a therapeutic potential of GABA_B receptor agonists in the treatment of cocaine dependence.

Key words:

cocaine, baclofen, SKF 97541, behavioral sensitization, locomotor activity
