



Effects of agmatine on nicotine-evoked behavioral responses in rats

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Abstract:

Agmatine [2-(4-aminobutyl)guanidine], is a novel endogenous ligand at α_2 -adrenoceptors, imidazoline and N-methyl-D-aspartate receptors, as well as a nitric oxide synthase inhibitor. The present study tested whether agmatine (5–40 mg/kg, *sc*) modulated the locomotor, sensitizing, and discriminative stimulus effects of nicotine in male Wistar rats. Agmatine (10–40 mg/kg) affected neither the basal locomotor activity, nor the nicotine (0.4 mg/kg, *sc*)-evoked hyperactivation. A challenge with saline or nicotine (0.4 mg/kg, *sc*) on day 10 to rats treated repeatedly (for 5 days) with nicotine (0.4 mg/kg, *sc*; and exposed to experimental chambers), resulted in the expression of nicotine-evoked conditioned hyperlocomotor response or behavioral sensitization. Given on day 10, agmatine at a dose of 40 mg/kg (but not 20 mg/kg) attenuated nicotine-induced conditioned hyperactivity. However, when this dose was administered to the nicotine-sensitized rats, agmatine failed to alter the effect of the challenge dose of nicotine. In rats trained to discriminate nicotine (0.4 mg/kg, *sc*) from saline in a two-lever water-reinforced fixed ratio 10 task, agmatine (20 or 40 mg/kg) did not substitute for the training dose of nicotine. In combination studies, pretreatment with agmatine (5–40 mg/kg) did not affect the nicotine (0.4 mg/kg) discrimination and the fixed dose of agmatine (20 mg/kg) did not change the effects of the lower doses of nicotine (0.05–0.2 mg/kg).

Our pharmacological analyses indicate that agmatine does not affect the locomotor, sensitizing, or subjective effects of nicotine. However, these data do show an inhibitory effect of agmatine over the expression of nicotine-induced conditioned hyperlocomotion.

Key words:

agmatine, nicotine, drug discrimination, locomotor activity, rat, sensitization
