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Rapid communication

7-OH-DPAT produces place conditioning in rats

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Abstract

The rewarding properties of the putative dopamine D_3 receptor-selective agonist, 7-OH-DPAT ((±)-2-dipropylamino-7-hydroxy-1,2,3,4-tetrahydronaphthalene hydrobromide), were investigated using a place conditioning paradigm consisting of three phases: preconditioning (three undrugged exposures to an apparatus consisting of two visually distinct compartments); conditioning (four pairings of one compartment with drug); and test (one undrugged exposure to the same apparatus). Rats received either saline, amphetamine (2.0 mg/kg), or 7-OH-DPAT (0.5, 2.0 or 5.0 mg/kg) during conditioning. Amphetamine and 7-OH-DPAT produced a place preference.

Key words: 7-OH-DPAT ((±)-2-dipropylamino-7-hydroxy-1,2,3,4-tetrahydronaphthalene hydrobromide); Place conditioning; Dopamine D_3 receptor

The rewarding properties of drugs acting at the dopamine D_1 or D_2 receptor families have been well characterised using the place conditioning paradigm. Both the D_1-like agonist SKF 38393 and the D_2-like agonist bromocriptine, as well as amphetamine, produce a place preference that can be attenuated with either D_1- or D_2-like antagonists (for a review, see Beninger, 1993). Until recently, there have been no compounds that are relatively selective for any of the newly identified dopamine receptor subtypes; therefore, nothing is known about their possible role in place conditioning.

Recently, (±)-2-dipropylamino-7-hydroxy-1,2,3,4-tetrahydronaphthalene hydrobromide (7-OH-DPAT) has been shown to bind to D_3 receptors with subnanomolar affinity; its affinity at D_2, D_4 and D_1 receptors is approximately 100-, 1000- and 10 000-fold lower, respectively (Lévesque et al., 1992). Hence, the present study evaluated the effect of the putative D_3 agonist, 7-OH-DPAT, on place conditioning.

Forty-four male Wistar rats (Charles River, Canada) weighing from 200–250 g at the beginning of the experiment were individually housed in wire mesh cages in a temperature-controlled (21 ± 1°C) room maintained on a 12 h light/dark cycle. Experimental sessions were conducted approximately 2–4 h into the light cycle. Lab chow and water were always available in the home cage.

Place conditioning was conducted as previously described (Hoffman and Beninger, 1989) in an apparatus consisting of two visually distinct compartments connected by a tunnel. Briefly, testing consisted of three phases: preconditioning, conditioning and test carried out over 14 consecutive days. Each subject received three 15-min undrugged preconditioning sessions, one per day, during which they were placed in one of the two compartments and given access to the entire apparatus. Each subject then received eight 30-min conditioning sessions. Saline injections were paired with one compartment on odd days, while drug injections were paired with the other compartment on even days. Drug injections (1.0 ml/kg) consisted of either 0.9% saline ($n = 8$), 2.0 mg/kg (+)-amphetamine ($n = 12$), or 0.5, 2.0 or 5.0 mg/kg 7-OH-DPAT ($n = 8$). 7-OH-DPAT (Research Biochemical, USA) was dissolved in distilled water and administered s.c. 30 min prior to conditioning; (+)-amphetamine (Smith, Kline and French, Canada) was dissolved in 0.9% saline and administered i.p. 5 min prior to conditioning. Following conditioning, each rat received one test session, identical to the

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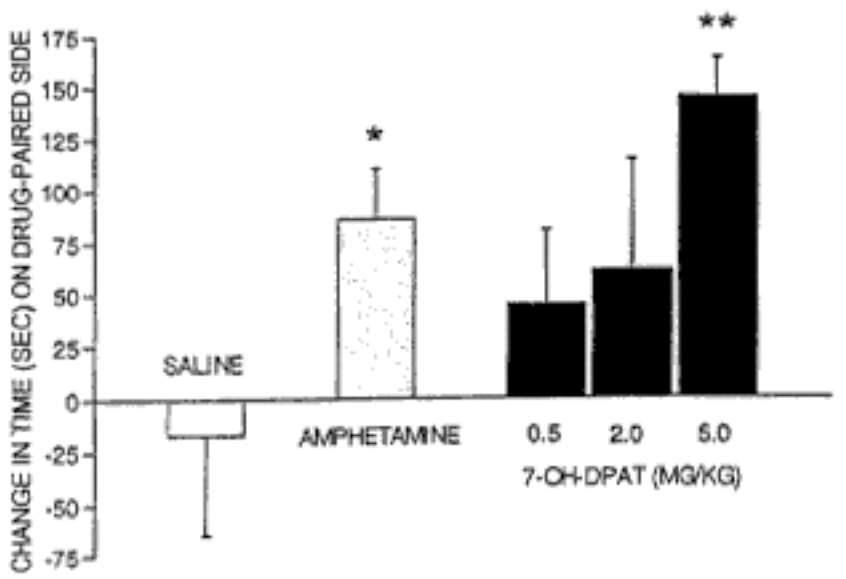

Fig. 1. Change (±S.E.M.) in time (s) spent in the drug-paired compartment from the preconditioning phase to the test phase. Significantly different from saline. $^{*}P < 0.05$; $^{**}P < 0.01$.

preconditioning sessions. The amount of time spent in each compartment was recorded during the preconditioning and test phases.

Difference scores were calculated by subtracting the mean amount of time spent in the drug-paired compartment during the three preconditioning sessions from the time during the test phase (Fig. 1). A significant increase in time was interpreted as evidence for the establishment of a place preference. In planned comparisons each drug group was compared to saline. The change in time spent in the drug-paired compartment was significantly greater than that of saline for subjects that received amphetamine, and 5.0 mg/kg 7-OH-DPAT during the conditioning phase, $t_{18} = -2.12$, $P < 0.05$ and $t_{14} = 3.13$, $P < 0.01$, respectively; the increases were not significant for 0.5 and 2.0 mg/kg 7-OH-DPAT, $P > 0.05$.

These results suggest that the D_3 receptor may be involved in reward. This is in agreement with the recent report by Caine and Koob (1993) that cocaine self-administration is modulated through dopamine D_3 receptors. However, as Large and Stubbs (1994) have cautioned, the D_2-D_3 receptor subtype specificity of 7-OH-DPAT is small, even under the best possible binding assay conditions. Further studies will characterise the effects of D_1- and D_2-like receptor antagonists on 7-OH-DPAT-produced place conditioning. However, as previous studies have shown that these receptors interact (Beninger, 1993; White and Hu, 1993), results would not provide conclusive evidence concerning the role of dopamine D_3 receptors in reward. New, specific compounds are eagerly awaited.

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