Pharmacology Biochemistry & Behavior, Vol. 22, pp. 341–342, 1985. © Ankho International Inc. Printed in the U.S.A. 0091-3057/85 $3.00 + .00

BRIEF COMMUNICATION

The D1 Dopamine Receptor Antagonist, SCH 23390 Reduces Locomotor Activity and Rearing in Rats

DIANE C. HOFFMAN AND RICHARD J. BENINGER

Department of Psychology, Queen's University, Kingston K7L 3N6 Canada

Received 30 July 1984

HOFFMAN, D. C. AND R. J. BENINGER. *The D1 dopamine receptor antagonist, SCH 23390 reduces locomotor activity and rearing in rats.* PHARMACOL BIOCHEM BEHAV 22(2) 341–342, 1985.—Dopamine receptors have been found to be of at least two types, and interest has focused on the possible differential role played by each in the control of behavior. The recent finding that SCH 23390 selectively blocks D1 receptors has provided a new tool. To examine the contribution of D1 receptors to locomotor activity and rearing, rats were injected SC with doses of 0.01, 0.1 and 1.0 mg/kg and monitored for 3 hr in photocell cages. SCH 23390 suppressed both behaviors in a dose-dependent fashion. These results suggest that D1 receptors participate in dopamine's control of locomotor activity and rearing.

SCH 23390 D1 receptor antagonist Locomotor activity and rearing

AT least two different receptor subtypes for the central neurotransmitter, dopamine (DA) have been differentiated: D1 receptors stimulate the enzyme, adenylate cyclase whereas D2 receptors do not [6]. Interest has focused on determining the possible behavioral functions of each receptor. This research has been greatly facilitated by the development of specific DA antagonists which make it possible to selectively block one receptor subtype and observe the behavioral consequences.

The new drug, SCH 23390 [R-(+)-8-chloro-2,3,4,5-tetrahydro-3-methyl-5-phenyl-1H-3-benzazepine-7-ol] appears to be a selective D1 receptor antagonist. Thus, in low doses it blocks DA-stimulated adenylate cyclase in the rat brain but is very weak in displacing [^{3}H]-spiperone or [^{3}H]-haloperidol binding [4,5]. Behavioral effects include selective suppression of avoidance responding in rats and blocking of apomorphine-induced stereotypy and methamphetamine-induced lethality in aggregated mice; however, in contrast to most other neuroleptics, SCH 23390, up to doses of 300 mg/kg PO in rats, does not produce catalepsy [5]. Recently, some controversy has arisen regarding this last point as Carboni *et al.* [3] reported SCH 23390 to be cataleptogenic in small doses (ED50=0.053 mg/kg, SC) whereas Barnett *et al.* [1], using three behavioral tests, concluded that SCH 23390 produced little or no catalepsy.

The latter observations are interesting and suggest that D1 receptors may not be involved in the extra-pyramidal motor functioning mediated by DA transmission (cf. [2]). This suggestion was investigated systematically in the present experiment; using SCH 23390, the role of D1 receptors in locomotor activity and rearing was assessed.

METHOD

Subjects

Twelve experimentally naive male Wistar rats (250–300 g) were individually housed in a temperature controlled environment on a 12 hr light (0600 to 1800)/dark cycle. Animals had free access to food and water for the duration of the study.

Drugs

SCH 23390 (Schering-Plough Corp.) was suspended in Tween 80 and distilled water yielding an injection volume of 1.0 ml/kg. Saline was used for vehicle control injections.

Apparatus

Locomotor activity and rearing were monitored in six activity chambers (41×51×37 cm) each equipped with two tiers of infrared emitters and detectors. The lower tier (5 cm high) recorded horizontal locomotion while the upper tier (15 cm high) recorded rearing. Each chamber was located in an insulated wooden sound attenuating box. Data collection was controlled by a single board microcomputer variably interfaced with a screen or printing terminal.

Procedure

All rats received a 60-min pre-exposure to the activity chambers. Beginning on the next day, 4 three-hour test sessions occurred from 0900 to 1200 hr every fourth day. Each rat was injected SC with either saline, 0.01, 0.1 or 1.0 mg/kg

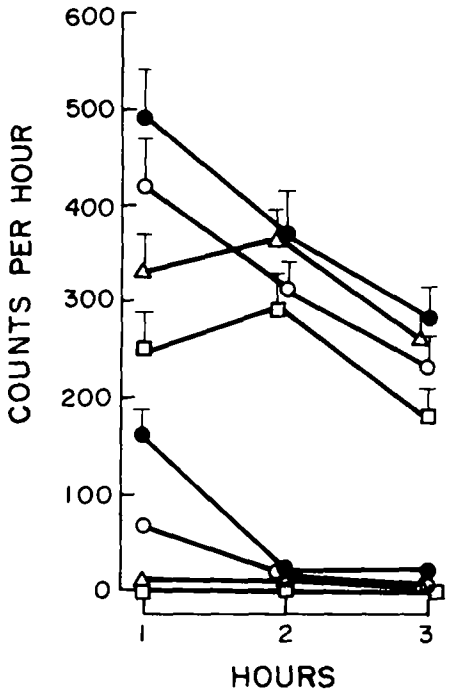

FIG. 1. Mean (±SEM) counts per hr over 3 hr for locomotor activity (upper 4 lines) and rearing (lower 4 lines) of rats treated with saline (●) or SCH 23390: 0.01 (○), 0.1 (△), 1.0 (□) mg/kg.

SCH 23390, 1 hr prior to these sessions. Each animal received the four doses in a different order, yielding a counterbalanced design.

RESULTS

As shown in Fig. 1, SCH 23390 produced a dose-dependent decrease in locomotor activity and rearing, both effects being especially evident in the first hr of testing (the second hr postinjection). This description was supported by analyses of variance yielding significant main effects of dose on locomotor activity, $F(3,33)=4.64$, $p<0.01$, and rearing, $F(3,33)=44.7$, $p<0.01$.

Further tests of simple main effects of dose in the first hr were significant for both locomotor activity and rearing, $F(3,33)=5.05$, $p<0.01$ and $F(3,33)=39.85$, $p<0.01$, respectively. Post hoc individual comparisons (Dunnett) showed that the effect of the highest dose of SCH 23390 on locomotion was significantly different from saline, $d(4,33)=3.33$, $p<0.05$, while the effects of 0.1 mg/kg approached significance, $d(4,33)=2.43$, $p<0.10$. For rearing, post hoc tests showed that each dose was significantly different from saline in the first hr ($p<0.01$).

DISCUSSION

The results showed that SCH 23390 suppressed locomotor activity and rearing in a dose-dependent manner, the effect being greatest for the highest dose during the first hr of testing. These observations provide evidence supporting a role for D1 receptors in at least some of the locomotor functions mediated by DA neurotransmission. Since little research has been published on SCH 23390, it is difficult to rule out completely the possible involvement of the D2 receptor in mediating the behavioral changes. This seems unlikely, however, in view of the reported D1 specificity of SCH 23390 [4,5], and the exceptionally low dose-effects (especially on rearing) observed in the present study and by Iorio *et al.* [5]. These results are of particular note as it has been suggested that the D1 receptor is a dopaminoceptive site in search of a function [7]. Future research with SCH 23390 may lead to a further characterization of the behavioral function of the D1 receptor.

ACKNOWLEDGEMENTS

SCH 23390 was the generous gift of Schering-Plough Corp. This study was supported by grants from the Natural Sciences and Engineering Research Council and the Ontario Ministry of Health to RJB.

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