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BRIEF COMMUNICATION

Effects of Intrastriatal and Intracortical Scopolamine on Behavior in Rats

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CHAMBERS, L. K. AND C. VAN HARTESVELDT. *Effects of intrastriatal and intracortical scopolamine on behavior in rats.* PHARMACOL BIOCHEM BEHAV 21(3) 471–473, 1984.—The anticholinergic drug scopolamine (20 μg, 30 μg, 40 μg) or its vehicle was injected unilaterally into the dorsal anterior striatum or overlying rostral neocortex in rats in order to examine the role of each region in contralateral postural deviation and stereotyped rearing. Scopolamine-induced contralateral deviation was observed in all subjects with striatal injections ($p<0.01$), and was of the same magnitude at all dose levels. Intracortical scopolamine did not induce contralateral deviation. However, stereotyped rearing was elicited from both the striatum and neocortex ($p<0.01$) at the two highest dose levels of scopolamine. Thus the mechanisms for contralateral deviation and stereotyped rearing differ both with respect to brain region and drug sensitivity.

Scopolamine Striatum Neocortex Postural deviation Rearing Rat

CHOLINERGIC mechanisms in the striatum have been implicated in a variety of behaviors. Two behaviors which can be elicited by injection of anticholinergic drugs directly into the striatum are stereotyped rearing [6] and (after unilateral injection) contralateral deviation or circling [1]. However, since the neocortex overlying the striatum has a cholinergic input and cholinergic receptors [2,4], it is possible that some of the drugs injected into the striatum spread up the cannula to the neocortex [5] and elicited the behavior due to its effects there.

The present experiment was carried out in order to determine the answers to several questions raised by previous studies. First, is either contralateral deviation or stereotyped rearing elicited exclusively from the striatum, or do cholinergic mechanisms in the neocortex play a role? Second, what is the relationship underlying these two behaviors? In the previous experiment on contralateral deviation [1] there was no mention of rearing; and the group measuring scopolamine-elicited stereotyped rearing [6] gave their injections bilaterally and had no opportunity to observe contralateral deviation. In order to resolve these questions we injected the anticholinergic drug scopolamine unilaterally into the striatum and neocortex at several dose levels, and measured both postural deviation and stereotyped rearing simultaneously in the same subjects.

METHOD

Subjects

The subjects were 18 Long Evans hooded male rats weighing 300–450 g at the beginning of the experiment. Each rat was implanted bilaterally in the anterior dorsal striatum or neocortex with a 21 ga stainless steel guide cannula fitted with a removable 27 ga stylet. One week of recovery was allowed before experimental testing.

Drugs

Scopolamine hydrochloride (SCOP, Sigma) was given at doses of 20, 30, and 40 μg in 0.25 μl of a 0.5 M sodium phosphate buffer at pH 7.4. The vehicle (VEH) was this buffer at pH 7.4

Drug Injection Procedures

Intracerebral applications were made through 27 ga injection cannulae at a constant rate of 0.5 μl/min and the injection cannulae remained in place for 30 sec after the drug injection, after which the stylets were replaced.

Experimental Procedure and Behavioral Observation

Subjects were placed in the observation chamber (a circular clear Plexiglas chamber, 34 cm in diameter and 30.5 cm in height) and allowed to habituate for 30 min prior to any observation session. They were then removed, injected unilaterally with VEH, and replaced in the chamber for the 30 min observation session. Four hours later the above procedure was repeated except that one of the three doses of SCOP was injected instead of VEH.

During the observation session subjects were monitored

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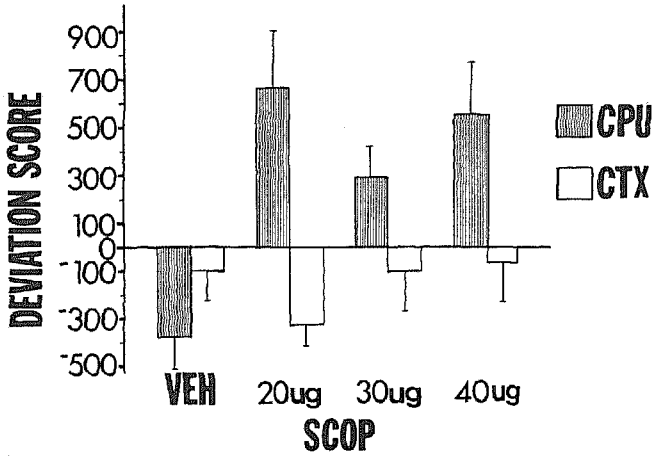

FIG. 1. Postural deviation scores for unilateral intrastriatal and intracortical injections of scopolamine across dose levels. The ordinate represents the average difference score for postural deviation expressed in 0.01 min. Bars represent the mean overall deviation score for each group±S.E.M.

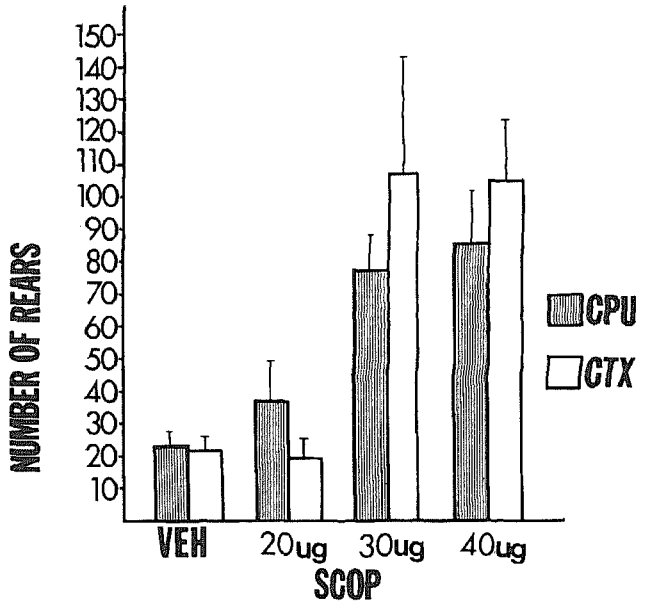

FIG. 2. Rearing scores for unilateral intrastriatal and intracortical injections of scopolamine across dose levels. Bars represent mean number of rears recorded in the 30 min session±S.E.M.

for both postural deviation and rearing. The duration of postural deviation in either direction was continuously recorded on time clocks. For statistical analysis, the amount of time Ss deviated ipsilateral was subtracted from the amount of time spent deviated contralateral to the site of drug injection. Thus, positive scores reflect predominantly contralateral behavior. A rear was counted whenever the subject was supported on the two hind legs alone and was not in the grooming posture.

Each subject received one VEH/SCOP injection (of the same dose) in each of its two cannulae, thereby giving two data points. For each dose at each site, N-6. One week's time elapsed between tests.

Histology

Subjects were administered an overdose of sodium pentobarbital and perfused intracardially with 0.9% saline followed by 10% formalin. After treatment with 20% sucrose-10% formalin mixture for 24 hr, the brains were frozen, sectioned at 30 μm, stained with cresyl violet, and the locations of the cannula tips verified. Mean locations for the CPU subjects were +3.0 mm with respect to bregma, +2.2 mm lateral to midline and 4.3 mm below the brain surface. Mean locations for the CTX subjects were +3.2 mm with respect to bregma, +2.4 mm lateral to bregma and 1.3 mm below the brain surface [10].

RESULTS

The postural deviation data were analyzed with a factorial ANOVA for repeated measures, which revealed a significant effect of site (CPU vs. CTX), $F(1,30)=17.18$, $p<0.01$. Intracaudate injection sites produced consistent contralateral deviation to all doses of SCOP, whereas CTX injection sites did not (Fig. 1). There were no other significant effects.

The rearing data under VEH conditions were analyzed with a factorial ANOVA which revealed no significant differences between any of the groups. The VEH scores for all CTX subjects were then collapsed and treated as one group, as were VEH scores for CPU subjects. A factorial ANOVA for repeated measures was then performed yielding a significant main effect of dose, $F(3,64)=22.52$, $p<0.01$. Post hoc tests (Fisher's LSD) revealed no significant differences between the 30 and 40 μg SCOP groups or between the VEH and 20 μg SCOP groups. Both the 30 and 40 μg SCOP groups had significantly higher rearing scores than the VEH and 20 μg SCOP groups, Fisher's LSD (df=64), critical value=15.92, $p<0.01$ (Fig. 2).

DISCUSSION

The results of the present experiment confirm and extend previous work using atropine [1,6] which indicated that mechanisms underlying both postural deviation and stereotyped rearing are, in part, cholinergic. In the present experiment another anticholinergic drug, scopolamine, elicited both behaviors. Contralateral deviation was elicited from the striatum but not the overlying neocortex, showing that the cholinergic mechanism underlying this response is in the striatum, as are dopaminergic mechanisms governing postural deviation. The drug doses all elicited comparable postural deviation, indicating that even the lowest dose was well above the threshold for this behavioral response.

In contrast to the results on postural deviation, we found that stereotyped rearing could be elicited by unilateral injection of scopolamine into either the striatum or the overlying neocortex, and thus rearing elicited by anticholinergic drugs is not mediated exclusively the the striatum. Several additional pieces of data indicate that postural deviation and rearing have different underlying mechanisms and are not on a dose-response continuum. The threshold for scopolamine-induced rearing was higher than that for contralateral postural deviation, but the responses were independent of one another. Intracortical scopolamine elicited stereotyped rearing but not postural deviation. Intrastriatal scopolamine

elicited postural deviation but not rearing at the lowest dose, and elicited both responses at the highest doses. Since cholinergic neurons within the striatum are local circuit neurons and cortical cholinergic input comes largely from the ventral pallidus or nucleus basalis [2,4] there is an anatomical basis for the different behaviors elicited by an anticholinergic drug in these two brain regions.

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