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BRIEF COMMUNICATION

Rotation and Postural Deviation Elicited by Microinjections of Dopamine Into Medial and Lateral Regions of Dorsal Striatum

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JOYCE, J. N. AND C. VAN HARTESVELDT. *Rotation and postural deviation elicited by microinjections of dopamine into medial and lateral regions of dorsal striatum.* PHARMACOL BIOCHEM BEHAV 21(6) 979–981, 1984.—Unilateral microinjections of DA (25 μg/0.25 μl) into several medial to lateral regions of the dorsal striatum of female rats produced both contralateral postural deviation and rotation. However, injections of DA into the medial striatum were more effective in producing rotation than postural deviation, whereas the opposite was the case for lateral striatal injections.

Dopamine Postural deviation Rotation Striatum Rat

SEVERAL investigators have reported that microinjections of dopamine (DA) into the dorsal striatum of the rat produce contralateral postural deviation and rotation [1, 2, 7, 14]. However, these two behaviors are affected differentially by estrogen treatment and do not covary in magnitude across the estrous cycle of the rat [8,9]. These results suggest that separate DA-sensitive neural systems mediate the two behaviors. These findings are consistent with other results indicating that different DA-sensitive behaviors can be mediated by separate subregions of the striatum [4, 5, 6, 13]. The purpose of this investigation was to analyze the effects of microinjections of DA into different zones of the dorsal striatum on postural deviation and rotation.

METHOD

Subjects

This experiment employed 17 female Long-Evans hooded rats which weighed 180–220 g at the beginning of the experiment. They were housed individually and maintained on a 12:12 light:dark cycle (lights on, 0800–2000). Vaginal smears were taken twice daily (1000 hr, 1600 hr) and each day of the estrous cycle was determined with reference to the day of estrus. The rats were part of a more extensive investigation concerning changes in magnitude of intrastriatal DA-induced behaviors across the estrous cycle [9].

Surgery and Drug Injection

Under sodium pentobarbital (W. T. Butler Co.) anesthesia the rats were implanted bilaterally with permanent cannulae. Guide cannulae were constructed from 21 ga stainless steel tubing, and the injection cannulae were constructed using 27 ga tubing. The injection cannulae terminated 3.0 mm below the guide cannulae. The guide cannulae were located stereotaxically such that the injection cannulae were aimed for the anterior dorsal striatum using coordinates previously derived [7]. Stainless steel stylets, made from closed 27 ga tubing, kept the guide cannulae patent when the animals were not being injected intracerebrally.

The intracerebral application of a drug was made by injecting the drug solution through the 27 ga cannula which was connected by polyethylene tubing to a Hamilton syringe mounted on a Sage syringe pump (Orion Research). The injection of 0.25 μl of drug solution was made at a constant rate of 0.5 μl/min, and the injection cannula remained in place for an additional 30 sec after completion of the drug injection. For the intrastriatal injection, DA (Sigma) was dissolved in the phosphate buffer solution at a final concentration of 25 μg/0.25 μl and a pH of 7.4. The phosphate buffer solution was 140 mM sodium phosphate dibasic/7.0 mM sodium phosphate monobasic solution. The control drug (VH) was the phosphate buffer adjusted to a pH of 7.4 with glacial acetic acid.

Behavioral Testing

After drug administration the rats were placed into a circular clear Plexiglas observation chamber, 34 cm in diameter and 30.5 cm in height, and observed for 40 min. The duration of postural deviation and the number of 1/4 rotations that occurred both contralaterally and ipsilaterally to the side of intrastriatal injection were recorded. Postural deviation is a quantitative measure of the amount of time the animal spends producing behaviors to the environment ipsilateral and contralateral to the side of the intrastriatal injection. The amount of time the rats deviated contralateral and ipsilateral to the side of the intrastriatal injection was recorded continuously by the observer using a two pole switch connected in series to a time clock and a rack of cumulative counters. The cumulative durations of postural deviation and number of 1/4 rotations were recorded every 5 min for 40 min. Rats were administered the drug on diestrus days 1 and 2 between 0900–1500 hr. Rats were administered both DA and VH separated by a 4 day interval. The experimenters were blind to the categorization of the cannula placement at the time of behavioral testing.

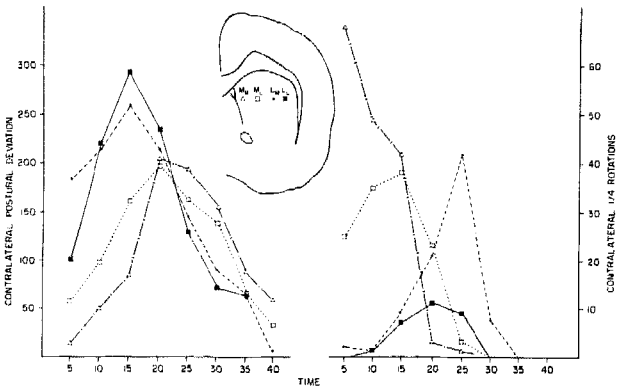

FIG. 1. The effects of unilateral microinjections of DA into medial or lateral striatum on postural deviation (left panel) and 1/4 rotations (right panel) over the 40 minute session. Postural deviation scores represent the difference between contralateral and ipsilateral deviation in 0.01 minutes. Mm=medial aspect of the medial region, n=4; Ml=lateral aspect of the medial region, n=4; Lm=medial aspect of the lateral region, n=4; and Ll=lateral aspect of the lateral region, n=5.

Histology

After behavioral testing, rats were administered an overdose of sodium pentobarbital and perfused intracardially with 0.9% saline followed by 10% formalin. The brains were placed in a 20% sucrose-10% formalin mixture for at least 24 hr. The brains were frozen, sectioned at 30 μm, stained with cresyl violet, and the locations of the cannula tips verified.

Data Analysis

The dorsal striatum was divided into 4 equal medial to lateral regions. The medial region was subdivided into medial (Mm) and lateral (Ml) aspects, as was the lateral region (Lm and Ll). Animals were grouped together by cannula placement based on the medial to lateral placement of the injection cannulae in the dorsal striatum. The magnitudes of postural deviation and rotation to intrastriatal DA were analyzed for group (region) differences. To obtain a measure of the magnitude of contralateral postural deviation for each injection, the time spent ipsilateral was subtracted from the time spent contralateral to the side of the intracerebral injection (difference score). A dominant direction index was also obtained for the number of 1/4 rotations by subtracting the number of 1/4 rotations ipsilateral from the number contralateral to the side of the intracerebral injection. An analysis of covariance with sequence (8 levels) as the quantitative covariable was run to determine whether there were overall differences between sites of injection (4 groups). The difference scores were then analyzed for differences between groups for each 5 min block of the total 40 min observation period (sequence).

RESULTS

The results for the postural deviation response to intrastriatal injection of DA are shown in the left panel of Fig. 1, grouped by medial-lateral placement of injection cannulae. Injections of DA into the two most lateral regions of the dorsal striatum (Ll+Lm) produced contralateral postural deviation with an earlier onset than did injections into the two most medial regions (Mm+Ml). Groups Ll and Lm had significantly greater contralateral deviations than groups Ml and Mm at 5, 10 and 15 min after the intrastriatal DA injection ($p<0.01$). Medial striatal injections produced a response greater than that for lateral striatal injections at a later time point (30 min, $p<0.01$). The changes in the magnitude of the postural deviation response to intrastriatal DA at any site were due entirely to changes in the magnitude of the contralateral postural deviation response and not due to changes in the minimal ipsilateral deviation response. This result suggests that DA injected into medial striatum had its effect on postural deviation after bulk flow to the lateral striatum.

The right panel of Fig. 1 shows the rotational response to DA injected into the dorsal striatum, grouped by medial-lateral placement of injection cannulae. In contrast to the postural deviation response, the rotational response was most effectively elicited from the medial striatum. Injection of DA into the most medial dorsal striatum (Mm) produced a rotational response with the shortest latency and greatest magnitude of effect. Group Mm had a significantly greater response than all other groups at 5 and 10 min after injection ($p<0.01$), and groups Mm and Ml are different from all other groups at 15 min after injection ($p<0.01$). Injections of DA more laterally had a reduced effect, and the response had a longer latency. Thus, group Lm had significantly greater rotation than all other groups only at 25 min after injection, and group Ll had less than all other groups. The changes in the magnitude of the rotational response to intrastriatal DA, regardless of site of injection, were due to changes in the magnitude of contralateral rotations, suggesting that the most effective sites for eliciting rotation are in the medial dorsal striatum.

DISCUSSION

We have previously argued that contralateral postural deviation is a measure of contralateral orientation to stimuli [7], a measure which is sensitive to manipulations of striatal DA [12]. The region most sensitive to DA augmentation of postural deviation is the dorsal lateral striatum. The lateral striatum has been proposed as the critical region involved in

the loss of contralateral orientation to stimuli after striatal DA denervation [4, 5, 6, 13]. While Dunnett and associates [4, 5, 6] have argued that the ventrolateral striatum is the most critical region, a large part of the lateral striatum may be involved in sensorimotor orientation. Consistent with that hypothesis, after DA denervation, recovery of orientation induced by an acute injection of apomorphine is associated with normalization of 2-deoxy-glucose uptake in the lateral striatum [11].

The evidence that the sites most sensitive for DA-induced postural deviation are located more laterally in the striatum than sites most sensitive for DA-induced rotation is consistent with other reports of functional heterogeneity within the striatum. However, it might be argued that the rotational response to medial striatal injections of DA is due to spread of the drug into the ventral striatum (nucleus accumbens) to induce activity with a concomitant induction of postural deviation from the dorsal striatum [10]. For several reasons this appears unlikely. First, after intrastriatal injection of DA there is very little spread of the drug ventrally [15]. Second, with medial striatal injections of DA, postural deviation occurs after the rotational response and therefore the behaviors are not temporally correlated. Third, in a separate paper we have shown that estrogen modulation of rotation, following dorsal striatal injection of DA or amphetamine, can be dissociated from the hormonal modulation of locomotor activity induced by injection of amphetamine into nucleus accumbens [8]. We therefore conclude that postural deviation and rotation are independent behaviors mediated by different regions of the striatum.

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