Pharmacology Biochemistry & Behavior, Vol. 13, pp. 743–745. Printed in the U.S.A.

Postural Asymmetry and Directionality of Rotation in Rats

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Received 27 March 1980

MYSLOBODSKY, M. S. AND H. BRAUN. *Postural asymmetry and directionality of rotation in rats.* PHARMAC. BIOCHEM. BEHAV. 13(5) 743–745, 1980.—The hypothesis [12] that the direction of postural asymmetry can predict rotational side preferences caused by amphetamine, was tested. Postural asymmetry of male and female Wistar rats was assessed using four tests: (a) tail suspension, (b) tail holding, (c) tail pinch, and (d) walking on a narrow path. The tests were conducted prior to and after (+)-amphetamine (1 mg/kg, IP) administration. Rotational directionality was assessed in a rotometer. None of the tests predicted the direction of circling. The findings suggest that there is a multitude of systems contributing to asymmetric posture.

Postural asymmetry Rotation Nigrostriatal system

THERE is considerable experimental evidence indicating an involvement of nigrostriatal dopaminergic activity in postural asymmetry and circling behavior in rodents. Unilateral neostriatal depletion of dopamine has been shown to result in circling behavior directed away from a more active side (away from the lesion side with apomorphine and towards the lesion with amphetamine [13,14]). Some observations suggest that rotation is more closely related to mechanisms of amphetamine-induced stereotyped behavior than to locomotor activity. Specifically, Pycock and Marsden [12] hypothesized that postural asymmetry, reflecting an imbalance of nigrostriatal dopaminergic activity, converts locomotion, depending in part on dopamine release in the nucleus accumbens, to turning in circles.

Injection of amphetamine to intact rats has been shown to produce consistent rotation either to the left or to the right side [5] and it was interpreted as an indication of an intrinsic hemispheric asymmetry in dopamine receptor activity accentuated by drugs. Indeed, while the dopamine contents of the right and left striata in intact rats were found to differ by 10–15%, this difference reached 25% after administration of amphetamine. Therefore, the rotation directionality of normal rats conforms with the law established for lesioned animals, i.e. under amphetamine they circle away from the side with higher dopamine content.

On the basis of these findings one would anticipate that normal rotation is organized by the same "two-component system" [12], where the asymmetry of posture is responsible for the directionality of locomotion. While planning a replication study in normal rats we paid attention to the fact that Pycock and Marsden [12] assessed posturing while the rat was circling in a rotometer. Since the degree of posturing has been found to strongly correlate with the intensity of circling, it is quite natural that the latter may have confounded the postural response. In fact, informal observations in our laboratory showed that naive judges were unable to agree upon the preferred direction of postural asymmetry or upon its intensity when the rat was observed after amphetamine administration in a large space and not in the rotometer.

It was important to find a system of assessment of postural imbalance independent of rotational locomotion. Four such tests and their correlation with rotation produced by (+)-amphetamine in normal rats are described.

METHOD

Subjects

The subjects were twenty male and female Wistar rats (200 g). Animals were singly housed and had free access to food and water. They were maintained under controlled experimental conditions with a 12 hour light-dark cycle.

Procedure

Four postural tests were conducted with each rat before and after amphetamine administration.

Tail suspension test. A rat suspended by its tail displays an asymmetric posture in an attempt to restore normal position of the head. The directionality of posturing was assessed while the animal was held by the tail, 2 cm from its end, in the air for 15 sec.

Tail holding test. The test was conducted in a box 42×30×36 cm with an opening for a tail held outside the box. With one hand the rat was gently restrained to prevent lateral deviations of the head while the other hand restrained the

[1]Supported in part by a gift from H. Pardee and A. and E. Spiegel Family Foundation. We thank Ms. R. Tomer and Ms. I. Weiner for their assistance with the manuscript.

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TABLE 1

POSTURAL ASYMMETRY TEST BEFORE AND AFTER AMPHETAMINE (1 mg/kg IP) ADMINISTRATION

Sample	N	Rotation directionality prediction (pre-/post-drug) Tail Suspension	Tail Holding	Tail Pinch	Walking
Female	10	0.6/0.4 (0.8)	0.6/0.7 (0.9*)	0.8/0.8 (1.0*)	0.6/0.8 (0.8)
Male	10	0.5/0.7 (0.7)	0.4/0.7 (0.9*)	0.6/0.6 (0.9*)	0.6/0.7 (1.0*)
Total	20	0.5/0.5 (0.7)	0.5/0.7 (0.9*)	0.7/0.7 (0.9*)	0.6/0.7 (0.9*)

Values represent the proportions of unidirectional trials (pre-/post-drug). Numbers in parentheses refer to reliability of the tests as assessed before and after amphetamine and expressed in proportions of unidirectional responses. The null hypothesis that we are likely to get the same directionality in postural responses, retests and circling behavior with $p=0.50$ against the alternative $p>0.50$ is rejected at a level of significance of $*p>0.05$ [2].

tail. When the rat's body was released, a pressure was simultaneously applied to the tail. A typical response was a fast lateral deviation of the head towards the root of the tail.

Tail pinch test. A miniature clip was placed at the tail 3–4 cm from its end. A typical response is a prompt and tight postural asymmetry in an attempt to reach the source of the pain and to bite the clip. The amount of time spent by the rat curved in one vs. the other direction was assessed during 15 min of the test period.

Walking test. A rat, placed on a wooden "bridge" 2 cm wide and 1 m long displays several behavioral responses: depth exploration, slow walking with lateral exploration, attempts to change the directionality of movement, etc. The directionality of postural asymmetry was assessed irrespective of the behavior exhibited.

Each test (except for the tail pinch, which was assessed once), was conducted three times and the dominant directionality was defined as two postural asymmetries in the same direction. Thereafter (+)-amphetamine (1 mg/kg, IP) was administered and the directionality of rotation was assessed for 30 min. Immediately after the rotation session the entire battery of tests was rerun in a counterbalanced fashion.

RESULTS

The findings of the study are summarized in Table 1. As can be seen in the table, in none of the tests conducted in either the drug or non-drug condition, did the animals show postural adjustment in the direction of rotation. However, part way through the present series of experiments, it was noted that the incidence of postural turns in the direction of rotation was higher in female rats. A separation of the female sample confirmed that during the tail pinch they more often curved the body in the direction of circling, irrespective of whether they were tested before or after amphetamine administration. There was also a better correspondence in females between the direction of the asymmetric posture in the walking test and that of circling, albeit only under amphetamine (Table 1). However, this correspondence in both tests was marginally statistically significant ($p=0.055$).

DISCUSSION

Current hypothesis assumes that postural asymmetry reflects an imbalance within the nigrostriatal dopaminergic system (see Introduction). However, even the tail-pinch test, which is known to elicit behaviors that are probably dependent upon the nigrostriatal dopaminergic system or other transmitter systems acting agonistically to dopamine [1,15], failed to predict the directionality of rotation. In view of these findings one may suggest that the postural response should be initiated and sustained by a variety of brain systems which enter different temporary dynamic "constellational" interactions for controlling specific behaviors. A corollary to this conjecture is that some or most of the controlling systems may have an imbalance slightly tipped in different directions.

Indeed, dopamine is not the only asymmetrically localized transmitter in the brain. A compounded nature of brain laterality has been postulated recently on the basis of circumstantial evidence [8] and directly demonstrated with the (1,2-^{3}H) desoxy-d-glucose technique [6]. Some of the lateralized systems may actually antagonise and overrule dopamine-based asymmetry in a variety of experimental conditions. A deterioration of tail suspension test predictability under (+)-amphetamine may suggest such a possibility. The operation of non-dopaminergic neurons which mediate posture and circling behavior in a manner opposite to the nigrostriatal system has been demonstrated in experiments with intranigral injections of kainic acid [10]. This system probably uses γ-aminobutyric acid (GABA) as a transmitter substance [3]. A possibility of the asymmetric regulation of posture and attention by the pallidum, the major outflow of the GABA system, has been demonstrated recently [7].

There is no doubt that the vestibular and cerebellar assistance is also important in the postural adjustment. Both systems seem to contribute in displacement of the body in the walking and, especially, tail suspension tests. Very little is known, at the present time, of the measure of imbalance within this system. Complex asymmetric responses were obtained during unilateral stimulation of the cerebellar dentate nucleus: a (^{3}H)-dopamine release in the contralateral caudate was paralleled by its reduction in the ipsilateral caudate [9]. Although the vestibular system asymmetry has been found recently by Douglas *et al.* [4], the details of this study have yet to be published. In any event vestibular influences may cause asymmetric response via vestibular projections to the caudate [11]. Whatever final picture may emerge, the complex circuitry, which is beginning to show some contours, suggests that the nigrostriatal system is by no means a simple relay mechanism or a final station destined for other sensory and motor centers, and there are probably more than two systems contributing to asymmetric posture.

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