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BRIEF COMMUNICATION

Postural Asymmetry and Lateralized Rotation in Normal Rats Administered Apomorphine

HENRY SZECHTMAN[1] AND MICHELE PISA

Departments of Neurosciences and Psychiatry, McMaster University
1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5

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SZECHTMAN, H. AND M. PISA. *Postural asymmetry and lateralized rotation in normal rats administered apomorphine.* PHARMACOL BIOCHEM BEHAV **25**(3) 689–691, 1986.—The study examines the hypothesis that the direction of circling exhibited by normal rats administered apomorphine reflects a drug-induced bias to use one specific hindleg for stepping and the other one for postural support. Results indicate that a majority of rats injected with this dopamine receptor agonist do show an asymmetry in the usage of the hindlegs (postural bias). However, the side of more frequent steppings does not predict the direction of circling. Moreover, postural bias may exist without lateralized circling. It is suggested that lateralized circling and postural asymmetry are two of several biases induced by apomorphine that may coexist in individual rats.

Circling Rotational behaviour Apomorphine Dopamine Posture Lateralization of function

STUDIES of behavioural lateralization in rats suggest that their brains have an asymmetrical organization. For instance, the preference of rats to turn in a particular direction in a T-maze or to circle in a specific direction in a rotometer after injections of amphetamine or apomorphine, have both been linked to an interhemispheric asymmetry of striatal dopamine [3]. It is not yet understood, however, whether motor, sensory [10], sensorimotor [6] or attentional [7,8] mechanisms account for these directional asymmetries. In the present study we examined the possible role of a motor mechanism, namely an asymmetry of postural support. Specifically, we determined whether apomorphine-treated rats consistently use one hindleg for postural support and the other hindleg for stepping during turning, and whether the side of this postural asymmetry is related to the direction of rotation. The results indicate that apomorphine can induce an asymmetry in the usage of the hindlegs for postural support. However, the direction of this asymmetry does not appear to be related to the direction of the rotational asymmetry.

The hypothesis that a drug-induced postural asymmetry may result in a directional bias has been advanced previously [5] for rats with unilateral lesions of the nigrostriatal dopamine system [12]. In particular, since the striatum appears to control motor initiation on the contralateral side [1,5], it has been proposed that when one of the striata is preferentially activated by amphetamine or apomorphine, then the contralateral legs move more readily than the ipsilateral legs, resulting in contralateral turning [5]. Presumably, the hindleg on the ipsilateral side of the activated striatum steps less because it serves to bear weight during rotation [11]. A similar motor mechanism might underlie the directional asymmetry induced by dopaminomimetic drugs in non-lesioned rats. Therefore, we measured whether the hindlegs of rats treated with the dopamine receptor agonist apomorphine consistently differ in the number of steps performed during turning, and examined whether this asymmetry is related to the direction of rotation.

METHOD

Seventeen male Sprague-Dawley (Canadian Breeding Farms) rats weighing 360–460 g at the start of the experiment were used. They were injected subcutaneously under the nape of the neck with 1.25 mg/kg of apomorphine hydro-

[1]Requests for reprints should be addressed to Dr. Henry Szechtman, Department of Neurosciences, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5.

chloride, and tested for 1 hr in a hemispheric bowl (60 cm diameter) made of transparent Perspex and placed over a flat glass surface. A mirror, inclined 45° relative to the base of the rotometer, permitted a bottom view of the rat's behaviour, which was recorded continuously on a video cassette recorder. The number of circles (clockwise and counterclockwise) and the number of steps performed by each hindleg were counted during the playback of video records. Circling and stepping were scored by different observers and on separate occasions. A rat was considered to have performed one circle when its pelvis and middle torso completed 8 consecutive 45° turns in the same direction (measured using the Eshkol-Wachman Movement Notation, 1=45 deg) [2,11]. A step was counted whenever the rat lifted a hindpaw off the floor. The behaviour of the rats was analyzed during 20 time samples of 1 min each, at intervals of 3 min, from 3 to 60 min after drug injection. For each rat, the consistency of the postural and the rotational asymmetries over time was statistically evaluated by paired t-tests of the difference between number of steps performed by the right and the left hindlegs (the measure of postural asymmetry), and the difference between clockwise and counterclockwise rotations (the measure of lateralized turning) in the 20 time samples.

RESULTS AND DISCUSSION

Figure 1 (top) indicates that of the 17 animals tested, 14 rats (82%) stepped significantly more frequently with one of their hindlegs: 8 rats stepped more often with the left hindleg and 6 rats with the right one. Therefore, a majority of non-lesioned rats administered apomorphine showed an asymmetry in the usage of their hindlegs during turning.

Figure 1 (bottom) indicates that 5 of 17 rats (28%) exhibited a statistically significant lateralization of rotation: 3 rats had a bias for counterclockwise circling and 2 rats for clockwise circling. Thus, in contrast to the high incidence of postural asymmetry, only a minority of rats showed rotational asymmetry.

It appears that side of postural bias and direction of lateralized circling are not coupled. Inspection of Fig. 1 reveals that of 9 rats which stepped more frequently with the left hindleg, 4 rats circled more often to the left (counterclockwise) and 5 rats to the right (clockwise); of the 8 rats which stepped more often with the right hindleg, 6 circled to the right and 2 to the left. The association between side of postural asymmetry and direction of circling was not statistically significant ($p>0.1$, Fisher's exact probability test). A similar lack of statistically significant association was obtained when Fisher's test was applied to the group of rats with a significant rotational asymmetry, or to the group of rats with a significant postural bias. Therefore, there is no clear association between the side of postural bias and the direction of rotational asymmetry.

The lack of coupling may be related to the variety of stepping patterns that apomorphine-treated rats utilize in a rotometer. Specifically, we observed both forward and backward patterns of stepping with the non-weight bearing leg. It is possible, therefore, that different rats predominantly stepped either forward or backward with their non-weight bearing hindleg, thus predominantly turning either towards or away from the side of postural support.

The results also fail to support the hypothesis that a reliable postural asymmetry is consistently related to a reliable rotational asymmetry:

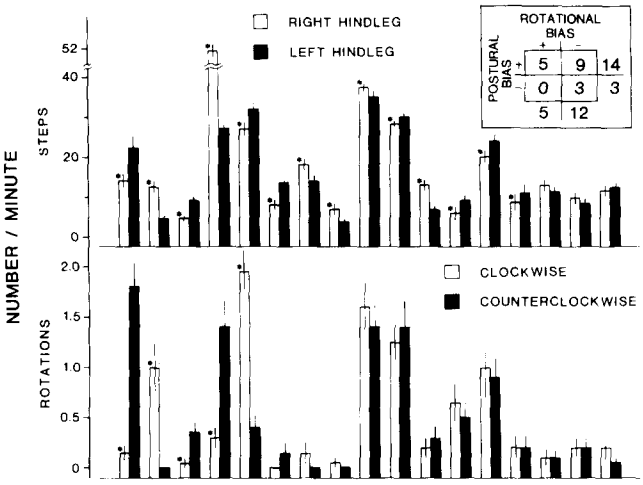

FIG. 1. Lateralization of posture (top row) and rotation (bottom row) in each of the 17 rats administered apomorphine (1.25 mg/kg). Each bar represents the mean (±SEM) of 20 one-min observations taken at 3 min. intervals. For each rat, paired t-tests were used to evaluate the statistical significance of the difference between number of steps performed by the right and the left hindlegs (the measure of postural asymmetry), and the difference between clockwise and counterclockwise rotations (the measure of lateralized turning). Asterisks indicate statistically significant asymmetries ($p<0.05$ or less, two-tailed probability). The inset summarizes the incidence of rats with (+) or without (−) statistically significant lateralizations of rotation and posture. A test of independence indicated no significant association between the two phenomena ($p=0.32$, Fisher's exact probability).

Figure 1 (inset) indicates that among the 14 rats with a reliable postural asymmetry only 5 rats showed a reliable rotational asymmetry. The null hypothesis of no association between the two types of asymmetries was not rejected ($p=0.21$, binomial test). Furthermore, a test of independence indicated no significant association between presence or absence of reliable postural asymmetry and presence or absence of reliable rotational asymmetry (Fig. 1, inset; $p=0.32$, Fisher's exact probability). Thus, it does not appear that at the dose of apomorphine tested there is a necessary causal relation between the two phenomena.

In summary, the present findings indicate that a majority of non-lesioned rats treated with apomorphine show an asymmetry of postural support, and that the side of this motor bias does not predict the direction of apomorphine-induced circling. Therefore, the results do not support the hypothesis that in non-lesioned rats the direction of lateralized rotation reflects a drug-induced preference to use one specific hindleg for stepping and the other one for postural support. Furthermore, our findings show that a postural asymmetry may exist without lateralized turning. Since apomorphine can also induce an asymmetry of attention [7,8] that is not related to lateralized rotation [9], a number of behavioural asymmetries including asymmetries of posture, turning, and attention, may be found in individual rats. The presence of different combinations of such functional asymmetries may account for some inter-individual variations in the behavioural response to apomorphine, and may be related to the multiple asymmetries in brain metabolic activity observed by others [4].

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