Normal and amphetamine-induced rotation of rats on a flat surface

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Recent work in this laboratory has revealed a possible neutroanatomical and neurochemical basis for spatial preferences. Such a basis was initially suggested by the accidental finding that (+)-amphetamine induces circling behaviour or rotation in normal rats (Jerussi & Glick, 1974). Previously rotation has been reported only in rats with unilateral lesions of the nigrostriatal system (e.g. Ungerstedt & Arbuthnott, 1970). As the rotation in lesioned rats was attributable to an asymmetry between the intact and lesioned nigrostriatal systems, it was postulated that rotation in normal rats might analogously reflect an intrinsic nigrostriatal asymmetry. And indeed, it was subsequently determined that normal rats had a significant asymmetry in striatal dopamine content. Striatal dopamine concentrations of normal rats previously tested in a T-maze were found to be lower in the striatum ipsilateral to a side preference than in the striatum contralateral to a side preference (Zimmerberg, Glick & Jerussi, 1974). Following (+)-amphetamine, the asymmetry in striatal dopamine increased and rats rotated toward the side with the lower concentration of dopamine (Glick, Jerussi & others, 1974). The direction of rats' rotation after (+)-amphetamine was found to be correlated with rats' side preferences in a two-lever operant task (Glick & Jerussi, 1974) and in a T-maze (Zimmerberg & others, 1974). Although these and other results (Zimmerberg & Glick, 1974, 1975) strongly indicate that rotation, in normal as well as in lesioned animals, is an exaggerated or stereotyped form of spatial behaviour, the phenomenon of rotation *per se* in normal animals has been questioned. Because the rotation studies in normal animals have always been conducted in a spherical apparatus (Greenstein & Glick, 1975) whereas lesioned animals are known to rotate on a flat surface (Glick, Jerussi & Fleisher, 1976a), it has been proposed that rotation in normal animals is an artifact of hyperactivity such that 'hyperactive rats in a spherical bowl will follow the shape of the container' (Cohn, Cohn & Taylor, 1975). We have already shown that rotation cannot be attributed to hyperactivity and that rotation and activity are inversely related (Glick, Zimmerberg & Greenstein, 1976c). A close relation, if not identical in mechanism, between rotation in normal and lesioned animals has also been demonstrated since unilaterally caudate lesioned rats rotate more if the lesion is made ipsilateral rather than contralateral to the preoperative direction of rotation (Jerussi & Glick, 1975; Glick, 1976). We now report that, in normal rats, amphetamine will induce rotation on a flat surface as well as in a bowl and that when monitored continuously for 24 h normal rats rotate without any drug.

The subjects were eight naive female Sprague Dawley rats about 3 months old and ∼250 g. Each rat was tested twice for rotation following the same dose (1·0 mg kg^{-1}) of (+)-amphetamine sulphate. The two tests were conducted a week apart. For the first test, four rats were individually placed in a spherical (30·5 cm in diameter) opaque Plexiglas 'rotometer' (Greenstein & Glick, 1975) and four rats were individually placed in a square (30·5 cm × 30·5 cm) Plexiglas box (with a flat grid floor) enclosed in a sound-attenuated cubicle. In each apparatus, a flexible wire, which harnessed the animal, was connected to a shaft which activated a photoelectric position sensing device that differentiated between incomplete and full (360°) rotations (Greenstein & Glick, 1975). For the second test, each rat was placed in the other apparatus, i.e. rats previously tested in the spherical bowl were now tested in the square box and vice-versa. Full rotations to the left and right were always recorded automatically by a printout counter. Rats were injected intraperitoneally 15 min after their placement in an apparatus. Left and right rotations during the pre- and post-injection periods were separately totalled and the net rotational difference (i.e. rotations in the dominant direction minus rotations in the opposite direction) was determined for each rat. An index (i.e. % dominance) of the consistency of each rat's directional preference independent of variations in the total number of rotations was also determined by the following formula: rotations in the dominant direction × 100/total rotations.

The mean net rotations h^{-1} with (+)-amphetamine (1 mg kg^{-1}) were 42·3 ± 9·1 (s.e.) for the bowl and 36·7 ± 10·4 for the flat surface. The corresponding figures for % dominance were 89·5 ± 4·1 and 85·1 ± 5·6. There were no significant differences at $P>0.1$ (paired *t*-test) between the data obtained in the bowl-shaped 'rotometer' and the flat-surfaced box. Moreover, both net rotations and % dominance were significantly correlated ($r = 0.71$ and 0·83, respectively, $P<0.05$) from apparatus to apparatus. The rotatory effects of (+)-amphetamine were also comparable to those obtained in previous studies (Glick, Crane & others, 1975; Jerussi & Glick, 1975; Jerussi & Glick, 1976) with the rotometer.

Before this study, we had tentatively concluded that 'the spherical nature of the apparatus seemed to be an important factor in eliciting rotation at low doses of

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(+)-amphetamine' (Jerussi & Glick, 1974). The presumed advantage of the sphere was only partly attributed to the supposition that an enclosed apparatus should eliminate distracting environmental influences (Glick & others, 1976a). In view of the present results, it appears now that there is no real advantage of the sphere *per se* and that isolation in any enclosed apparatus provides the one sufficient condition for observing drug-induced rotation in the normal animal. A sphere merely represents a simple and pragmatic way of providing such an environment.

If, as our previous studies demonstrate (Glick & others, 1975; Glick & others, 1974; Zimmerberg & others, 1974), there is a striatal dopamine asymmetry in normal rats, it might be expected that rats should rotate without any drug. However, the very little rotation occurring in the hour following a saline injection was generally discounted as random movement (Jerussi & Glick, 1974, 1975). Also ignored were the data obtained during the 15 min pre-injection period which was viewed as time for the rat to adjust to the apparatus. After testing more than 100 rats with (+)-amphetamine (1·0 mg kg^{-1}), we decided to analyse the pre-injection data. Although net rotations per 15 min averaged only about 4, there was a relation between the pre- and post-injection data. That is, 70% of all rats tested had net rotations in the pre-injection period that were in the same direction as their rotations following the injection of (+)-amphetamine (significant association at $P<0{\cdot}001$, χ-square test). This result suggested that normal rats might make significant numbers of net rotations without any drug if the period of observation was very long. Accordingly, four drug-naive rats were individually placed in the enclosed Plexiglas box (see above) for four successive days; food and water were always available and rotation was recorded continuously. Each rat rotated consistently, i.e. the direction of net rotations was the same on each of the four days. Mean net rotations per rat per 24 h (beginning 10:00 a.m.) were 42·5. Subsequently, when twelve additional rats were tested continuously for several days and then administered (+)-amphetamine (1·0 mg kg^{-1}, i.p.), net rotations for the 24 h preceding drug administration were in the same direction and quantitatively correlated ($r = {\cdot}87$, $P<0{\cdot}001$) with net rotations in the hour following drug administration. Thus we now have evidence that rotation or turning in circles is a normal component of the behavioural repertoire of the rat. A complete 360° turn appears to be the logical result of an intrinsic and persistent side preference (Zimmerberg & others 1974; Glick, Jerussi & Zimmerberg, 1976b).

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