REVISTA ESPAÑOLA DE FISIOLOGIA, **43**, (3), 345-350, 1987

Effects of Nucleus Accumbens Lesions in Rats on Spatial Preference in an Open Field*

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(Received on September 29, 1986)

D. MIR and E. PEREZ-LUCENA. *Effects of Nucleus Accumbens Lesions in Rats on Spatial Preference in an Open Field.* Rev. esp. Fisiol., 43 (3), 345-350, 1987.

Selective lesions placed in three different regions of the nucleus accumbens were performed to assess their effects on spatial preference in the rat. Histological verification allowed to establish three groups of lesioned animals: medial, intermediate and lateral. Sham operations involved all procedures except the passing of a current. All animals were tested once prior to operation and twice postoperatively. Sherman's directionality score (DS) was adopted. Positive values indicate right side preference and negative ones leftward bias. Statistical analysis revealed that rats used in this study showed a nonsignificant spontaneous right side preference in the open field (DS = +0.08). Medial and intermediate lesions increased the right side bias (DS = +0.37), whereas lateral lesioned animals reversed their preoperative rightward bias and showed a significant left side preference (DS = −0.48). These results suggest a participation of the nucleus accumbens in spatial preference and are considered to be due to the well known uneven distribution of the afferent and efferent fiber systems within the nucleus.

Key words: Nucleus accumbens, Spatial preference, Cerebral asymmetry, Lateralization, Open field.

The nucleus accumbens is a neostriatal structure which has attracted much interest in recent years because of its possible role as a functional interface between the basal ganglia and the limbic system (6). It should be emphasized here that nucleus accumbens shows several neurobiological right-left asymmetries (1, 10); as well as a non-homogenous organization since its several systems of afferent and efferent fibers are unevenly distributed within the nucleus (4, 5, 8).

The present study was undertaken to assess whether selective lesions placed in three different regions of the nucleus accumbens could interact with the brain inherent lateralization and therefore modify spatial preference in an open field;

* Supported by a grant from the Spanish CAICYT (1048/84).

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and if possible effects might depend on the area lesioned within the nucleus.

Materials and Methods

Subjects. — Fifty four adult male Wistar rats weighing 270-300 g at the beginning of the experiments were used. They were housed individually in a room kept at a constant temperature (22 ± 1°C) and maintained on 12 h light-dark cycle (light 8:00-20:00). Animals had free access to food and water.

Spatial preference in the open field. — Animals were tested in an open field apparatus (100 × 100 cm) with its floor divided into 16 equal squares by thin lines. The field was bordered by 40 cm side walls and illuminated by a 60 W lamp suspended 80 cm above the center. An L-shaped barrier was placed in a corner of the field, thus creating a square cell into which each animal was put at the beginning of the observation period (12). After 30 s the barrier was removed (regardless of rat's position) and a 5 minute observation period began. The L-shaped barrier was randomly placed in the different corners of the field. Initial and subsequent movements (deambulation bouts) during each observation period were recorded as R when the rat moved along the right-hand wall and as L when it was along the left-hand wall. The directionality score (DS) to evaluate the spatial preference in the open field was adopted from SHERMAN *et al.* (12). In their formula the numerator is the number of right wall deambulations minus the number of movements in which the animal moved along the left wall, and the denominator is the square root of the total number of deambulation bouts made [(R-L)/√R+L]. Positive values indicate right side preference and negative ones leftward bias. To illustrate the scoring procedure, if the sequence of deambulation bouts during a five minute run was R R R L R R L R L, the directionality score would be +1.0 [(6-3)/√9]. Each rat was studied in the open field during three observation periods. The first was carried out during the week before surgery (preoperative observation), once the animals had adapted to the laboratory for 8-10 days. The two remaining observation periods were performed during the second and the third week after operation (postoperative observations 1 and 2). All testing was carried out during the light phase of the light/dark cycle.

Surgery, histology and statistical analysis. — All surgery was performed under thiopenthal anesthesia (40 mg/kg, ip). Standard stereotaxic procedures were carried out in a DKI instrument. Stereotaxic coordinates were 2.2 mm anterior to bregma, 7.0 mm below skull surface, and ±0.7, ±1.2 and ±1.7 mm from midline for medial, intermediate and lateral lesions (7). Bilateral electrolytic lesions were made with a Cibertec lesion maker by passing a 2 mA direct current for 15 s through a 300 μm stainless steel electrode, isolated with teflon except for 0.5 mm at the tip. A silver-silver chloride cathode was introduced through the caudal end of the surgical wound under the rat's neck skin. Sham operations involved all surgical procedures except that the electrode tip was lowered to 1 mm above nucleus accumbens and no current was passed. At the end of the experiments the brain of each animal was prepared for histology by perfusing the anesthetized rat with saline and formaline solutions. Frozen coronal sections 50 μm thick were mounted and stained with cresyl violet. The location and extent of the lesions were verified under microscope examination (Leitz Dialux 20), photographed and transferred by camara lucida to the most appropiate plate of the PAXINOS and WATSON atlas (7). The results were statistically analyzed with the nonparametric Kruskal-Wallis test on an IBM PC-XT.

Results

Histology. — Histological examination of the brain in sham operated animals only showed a slight gliosis along electrode tracts, therefore all of them were included in the control group (n = 15). The lesions were found to be located entirely within the nucleus accumbens limits in thirty animals, whereas adjacent structures were also affected in nine rats which were excluded from analysis. The location of the lesions allowed to establish three groups of lesioned animals: medial (n = 11), intermediate (n = 8) and lateral (n = 11). Coronal sections of the brain of three animals with representative lesions of the nucleus accumbens are shown in fig. 1. Microscopic verification showed that anterior commissure was spared and its tissue was intact, even when lesions were close to its medial limit, in the rats included in the lateral group (rat F9 in fig. 1).

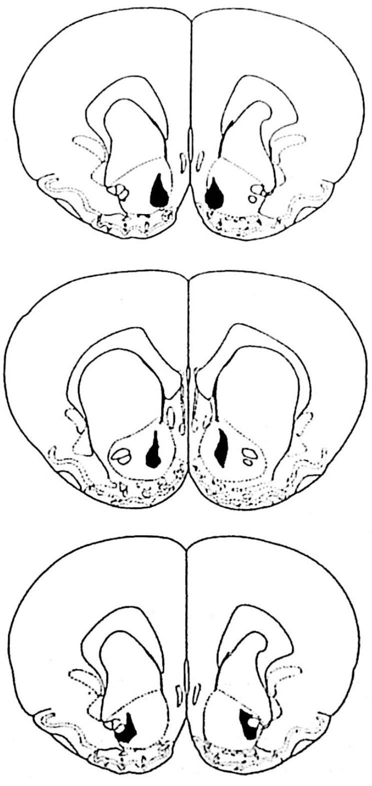

Fig. 1. *Lesions in representative animals.* (A) rat E2 medial; (B) rat F2 intermediate; (C) rat F9 lateral. Stereotaxic diagrams from PAXINOS and WATSON (7).

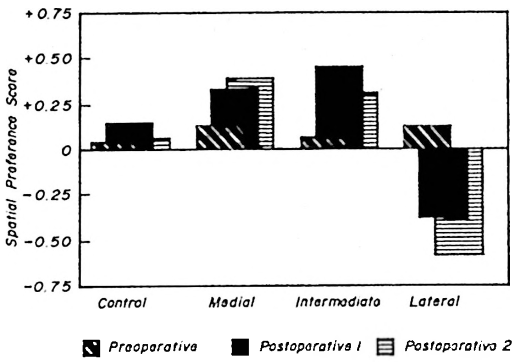

Fig. 2. *Spatial preference in the open field.* Animal groups: control, medial, intermediate, lateral. Observation periods: preoperative, postoperative 1 and 2. Spatial preference score: positive values, ride side preference; negative, leftward bias. Statistical significance: Lateral differed from the other three groups ($p < 0.05$) in both postoperative observations.

Spatial preference in the open field. — All experimental groups showed a slight rightward bias before operation (fig. 2). Nevertheless the mean spatial preference score for all experimental animals and for each group did not differ significantly from zero, indicating that the rats used in these experiments showed a non significant spontaneous right side preference in the open field (mean directionality score ± standard error of the mean for preoperative observation were: all experimental animals +0.08 ± 0.01; control group +0.04 ± 0.01; medial +0.12 ± 0.02;

intermediate +0.06 ± 0.03; lateral +0.12 ± 0.01). Whereas control animals maintained their slight rightward bias after surgery (+0.14 ± 0.01; +0.06 ± 0.01), medial and intermediate animals increased their spatial right-sided preference, but statistical significance was not reached when compared to the control group (medial +0.33 ± 0.03; +0.39 ± 0.02 and intermediate +0.45 ± 0.06; +0.31 ± 0.02). On the contrary, animals lesioned in the lateral part of the nucleus accumbens reversed their slight bias to the right and showed such an increased spatial preference to the left that they differed significantly ($p < 0.05$) from the other three groups in both postoperative observations (−0.38 ± 0.02; −0.59 ± 0.03). The mean directionality score for pooled data from medial and intermediate lesioned animals in the two postoperative observation periods was +0.37 whereas it was −0.48 for lateral lesioned rats. It is noteworthy that described changes in the spatial preference score in lesioned rats were observed without a significant increase either in the total number of squares entered or in the deambulation bouts frequency.

Discussion

Recent studies have reported much evidence of functional lateralization in the brain of variety of nonhuman species. Research findings during the past years have shown numerous morphological, biochemical and behavioral asymmetries in the rat's brain. Postural/motor asymmetries studied included spatial preference in an open field, spatial preference in swimming behavior, side preference in a T-maze, paw preference in reaching for food, level preference in a two-lever operant chamber, bias in induced circling behavior and tail pinch-induced asymmetries (1-3, 9-13).

Open field observation was chosen because it is a rapid and easy test to perform, requires minimal equipment, results are objective and quantifiable; and, normal Wistar rats without any preliminary training reliably show locomotor activity once placed in the field. To evaluate spatial preference it was considered that DENENBERG's group directionality score was the most appropriate procedure (12). Based on the score used to determine ear advantage in dichotic listening tests, it has been widely included in studies of postural/motor asymmetries (1, 2, 12, 13). Nevertheless, while DENENBERG's group and others (1, 2, 12) only recorded the initial direction of movement, spatial preference was evaluated in this study throughout the observation periods as done by WEST *et al.* in their swim test (13).

Directionality score analysis revealed that rats used in this study showed a nonsignificant spontaneous right side preference in the open field. The score for all experimental animals before surgery only indicated a slight rightward bias. Until recently there appeared to be no population asymmetry for spatial preference in rats, however GLICK and ROSS have reported right side bias for rotation and for lever preference in an operant situation (3) WEST *et al.* in a swim test (13), in both studies Sprague-Dawley rats were used. On the contrary, DENENBERG's group has shown leftward bias in some of their experiments with Wistar rats in the open fiels (2, 12). This study suggests that the existence of a population asymmetry for spatial preference in rats is not a firmly established fact; and contrary to what has been reported (2) the different strains of rats do not display a consistent side preference.

That bilateral and symmetrical lesions of a forebrain structure had an effect on spatial preference is interpreted as due to the fact that nucleus accumbens right-left asymmetries normally interact with the rat's brain inherent lateralization. To the best of the authors' knowledge there is only one other instance of such an interaction reported, that of ROSS and GLICK (11) who showed that bilateral frontal cortical lesions had opposite effects on right-sided versus left-sided rats, which they interpreted as due to a lateralized modulation role for the frontal cortex.

The fact that results depended upon the lesioned region is considered to be due to the well known uneven distribution of both the afferent and efferent fiber systems within the nucleus accumbens. The hippocampal and thalamic projections share a closely parallel distribution within medial and intermediate nucleus accumbens, whereas afferents coming from amygdala, perirhinal and prefrontal cortex innervate the lateral accumbens (6, 8). On the other hand it has been established that the medial nucleus accumbens projects mainly to the limbic circuitry whereas its lateral part projects more directly to extrapyramidal structures (4). The obtained results, therefore, seem to confirm the hypothesis that the dichotomy in the connections of the nucleus accumbens has functional consequences which must be further investigated.

Resumen

Se evalúan los efectos de lesionar tres zonas distintas del núcleo accumbens en ratas sobre la preferencia espacial en un campo abierto. El estudio histológico establece tres grupos de animales lesionados: mediales, intermedios y laterales. En las intervenciones control se siguió todo el procedimiento experimental excepto que no se pasa corriente por el electrodo. Todos los animales se estudian una vez antes de la intervención y dos tras ella. Se adopta el índice de direccionalidad de Sherman (DS). Los valores positivos indican preferencia hacia la derecha y los negativos a la izquierda. El estudio estadístico manifiesta que las ratas empleadas en esta experimentación muestran una preferencia espacial espontánea no significativa hacia la derecha (DS = +0,08). Las lesiones mediales e intermedias incrementan la preferencia hacia la derecha (DS = +0,37), mientras que las laterales invierten la preferencia preoperatoria hacia la derecha y originan una preferencia significativa hacia la izquierda (DS = −0,48). Estos resultados sugieren la participación del núcleo accumbens en la preferencia espacial y se consideran debidos a la bien conocida desigual distribución dentro del núcleo accumbens de sus sistemas de fibras aferentes y eferentes.

Palabras clave: Núcleo accumbens, Preferencia espacial, Asimetría cerebral, Lateralización, Campo abierto.

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