BRIEF COMMUNICATION

Effects of Septal Lesions on Shock Thresholds in Weanling Male and Female Rats

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STEWART, J., S. ATKINSON AND D. CYGAN. Effects of septal lesions and gonadectomy on shock thresholds in weanling male and female rats. PHYSIOL. BEHAV. 19(5) 693–696, 1977. — Twenty-four-day old weanling male and female rats were either lesioned in the septal area, gonadectomized, lesioned and gonadectomized, or untreated. Tests for reactivity to electric shock were conducted at 26 and at 40 days of age. Neither males nor females showed any effect of the lesions as measured by flinch and jump thresholds to electric shock immediately following surgery; both male and female lesioned groups showed a significant lowering of thresholds when tested at 40 days of age. The effects of septal lesions on response to electric shock were dissociated from the effects on hyperemotionality measured over the same period of time after the lesions, and appeared to have their effect independent of the sex or hormonal condition of the animals.

PHILLIPS and Deol [9] have reported a sex difference in the response of 25-day old rats to lesions of the septal nuclei. In their experiment female rats showed hyperemotionality immediately following surgery and lasting over several days, whereas males showed no comparable change in emotional reactivity.

In other experiments from the same laboratory [6, 9, 10], it was found that although hyperemotionality could be obtained in weanling males, the effects of septal lesions were transient compared to those lasting at least three weeks in adult males. Furthermore, it was found that the reduced hyperemotionality in weanling males was dependent on the presence of androgens in neonatal life, while, paradoxically, its appearance in adult animals was dependent on the presence of testicular hormones in the prepubertal period.

These findings in prepubertal rats provide a stimulus for investigating the possibility that the septal nuclei are involved in the mediation of sex differences in behavior and that the functions of the septal nuclei interact with those of gonadal hormones. Previous studies in adult animals showed that food and water consumption of male and female rats were differentially affected by septal lesions [5,7], but that the effects of septal lesions on footshock thresholds were not sex dependent [3]. Bengelloun, Nelson, Zent and Beatty [2] have also found no sex dependent effects of septal lesions on open-field behavior and on active and passive avoidance responding in adult male and female rats lesioned at 100 days of age. They studied sex differences in these behaviors in animals gonadectomized prepuberally and as adults, and found the effects of sex and gonadectomy to be similar in control and septally lesioned animals; the variable, lesion, did not interact with either sex or gonadectomy.

In order to test for the generality of the differential effects of septal lesions on hyperemotionality found by Phillips and Deol [9] in prepubescent male and female rats, we have been studying the effects of septal lesions in 24-day old rats on other behaviors. The present report is concerned with the effects of septal lesions on reactivity to electric shock in intact and gonadectomized, male and female animals.

METHOD

Fifty-four male and 38 female Wistar rats from Canadian Breeding Farms were used in these experiments. The animals arrived at the laboratory at 21 days of age and were housed two or three rats of the same sex and treatment in standard laboratory cages. Food and water were available at all times.

In the first experiment, 24 male and 24 female rats were
used. At 24 days of age, six animals of each sex were assigned to one of four treatment conditions and were either gonadectomized, lesioned in the septal area, gonadectomized and lesioned, or untreated. Between 26 and 27 days of age, and again between 40 and 42 days of age all animals were tested for flinch and jump thresholds. Two of the male groups lost one animal each before testing began.

Two additional groups of eight male rats each, one lesioned in the septal area, and one anesthetized only, were operated at 24 days of age. These groups were tested for flinch and jump thresholds only once, between 40 and 42 days of age, and thus served as control groups for the possible effects of repeated testing.

In a second experiment, 14 male and 14 female rats were used. As before, at 24 days of age, eight males and eight females were lesioned in the septal area, the others were anesthetized but otherwise untreated. One animal from each of the lesioned groups died following surgery. In addition to the tests for flinch and jump threshold given between 26 and 27 days of age and again between 40 and 42 days of age, these animals were tested for hyperemotionality once before, and several times following, surgery.

Surgical and histological procedures: the gonadectomies and brain lesions were carried out when the animals were 24-25 days of age under chloral hydrate anesthesia (300 mg/kg of a 60 mg/ml solution, injected intraperitoneally). Bilateral electrolytic lesions were made in the septal area.

Using a flat skull position, following the Sherwood and Timiras atlas for developing rats [12], the coordinates were 1.0 mm anterior to Bregma, 0.75 mm lateral from midline, and 4.5 mm ventral from the dura. An anodal direct current of 2 mA for 10 sec was delivered via a 254 μ diameter stainless steel electrode. An injection of bicillin was given each animal following surgery.

At the end of the experiment the lesioned animals were overdosed with ether and perfused with 0.9% saline followed by 10% Formalin. The brains were kept in 10% Formalin for a week. Sufficient frozen sections were cut at 40 μ to allow reconstruction of the lesions. Sections were stained with thionin. Examples of the lesions can be seen in Fig. 1. There were no group differences in the apparent size and location of the lesions.

Flinch-jump threshold tests: for each of these tests, an animal was placed in a 30 x 30 x 30 cm Grason-Stadler rat chamber with a grid floor connected to a Grason-Stadler Shock generator with grid scrambler. The animal was given six alternating ascending and descending series of 10 half-sec shocks with a 30-sec intershock interval and a two-min interseries interval. Current ranges established in pilot testing led to the use of the series 0.05, 0.06, 0.08, 0.10, 0.13, 0.16, 0.20, 0.25, 0.30 and 0.40 mA for the 26–27 day old rats, and of the series 0.06, 0.08, 0.10, 0.13, 0.16, 0.20, 0.25, 0.30, 0.40 and 0.50 mA for the 40–42 day old rats.

![Fig. 1. Examples of the extent of damage to septal nuclei in three different animals. No. 50 represents a typical lesion found in the great majority of animals. No. 45 and 36 are the two atypical, less extensive lesions.](image-url)
SEPTAL LESIONS IN WEANLING MALE AND FEMALE RATS

One of three possible responses was recorded for each current level in each series – no response, flinch (rigidity, slight paw movement), and jump (body movement, 3 or 4 paws lifting off the grid, and possible vocalization). The flinch threshold was the lowest current level at which the animal flinched on 5 out of 6 occasions; the jump threshold was the current level at which the animal jumped on 5 out of 6 occasions. Mean thresholds were calculated for flinch and jump thresholds for each of the sexes in each of the conditions.

Hyperemotionality tests: all animals from the second experiment were tested for hyperemotionality. Tests were run prior to surgery at 24 days of age, the day following surgery at 25 days of age, and at 26, 32 and 40 days of age. Three measures of hyperemotionality were recorded: resistance to capture (scored from 0, no response, to 4, leaps from cage, struggles and bites), startle response to tap on back (scored from 0, no response, to 4, leaps into air and moves off rapidly), and number of consecutive startle responses before three consecutive non-responses (maximum of 20). These three scores could be combined to give an overall hyperemotionality score with a maximum of 28 for each animal.

RESULTS AND DISCUSSION

Table 1 presents the mean flinch and jump thresholds for the eight groups of the first experiment tested at 26 and at 40 days of age. Two points are noteworthy. First, in unlesioned animals there was, as expected, an increase in thresholds between 26 and 40 days of age [1,8]. Second, there was no obvious effect of lesioning the septal nuclei on reactivity to shock immediately following surgery; only at the 40-day test did the effect of the lesion become apparent.

Three-way (sex x gonadectomy x lesions) analyses of variance were carried out on the threshold across for flinch and for jump separately on the data obtained at 26 and 40 days of age. At 26 days, neither jump nor flinch scores were affected by lesions. The only significant effect for the jump scores was sex, F(1,38) = 5.19; p<0.05. It can be seen from Table 1 that the mean jump thresholds for females were slightly but consistently lower in all conditions.

<table>
<thead>
<tr>
<th>SEX</th>
<th>GONADS</th>
<th>LESION</th>
<th>N</th>
<th>36 DAY OLD</th>
<th>40 DAY OLD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FLINCH</td>
<td>JUMP</td>
</tr>
<tr>
<td>F</td>
<td>Intact</td>
<td>Control</td>
<td>6</td>
<td>.105</td>
<td>.225</td>
</tr>
<tr>
<td>F</td>
<td>Ovex</td>
<td>Control</td>
<td>6</td>
<td>.117</td>
<td>.245</td>
</tr>
<tr>
<td>F</td>
<td>Intact</td>
<td>Septal</td>
<td>6</td>
<td>.128</td>
<td>.277</td>
</tr>
<tr>
<td>F</td>
<td>Ovex</td>
<td>Septal</td>
<td>6</td>
<td>.100</td>
<td>.275</td>
</tr>
<tr>
<td>M</td>
<td>Intact</td>
<td>Control</td>
<td>5</td>
<td>.168</td>
<td>.370</td>
</tr>
<tr>
<td>M</td>
<td>Cast</td>
<td>Control</td>
<td>6</td>
<td>.122</td>
<td>.230</td>
</tr>
<tr>
<td>M</td>
<td>Intact</td>
<td>Septal</td>
<td>5</td>
<td>.113</td>
<td>.260</td>
</tr>
<tr>
<td>M</td>
<td>Cast</td>
<td>Septal</td>
<td>6</td>
<td>.115</td>
<td>.266</td>
</tr>
</tbody>
</table>

The only significant finding for the flinch scores at 26 days was the sex x gonadectomy x lesion interaction, F(1,38) = 6.95; p<0.02. The contributing factors to this interaction seemed to be a small, but nonsignificant sex difference (males having higher thresholds than females), and a more marked, but nonsignificant sex x lesion interaction, F(1,38) = 3.52; p<0.07. In which males had higher thresholds than females when unlesioned, but did not differ from females when lesioned.

At 40 days of age the effects of septal lesions on both dependent measures were highly significant (for jump threshold, F(1,38) = 46.85; p<0.0001; and for flinch threshold F(1,38) = 23.27; p<0.0001). Lesioned animals had lower thresholds than unlesioned animals.

The effects of septal lesions on the flinch and jump thresholds at 40 days of age were found even in animals tested for the first time at this age. The mean flinch thresholds for the two additional groups of nonlesioned and lesioned males were 0.270 and 0.102, respectively. This difference was found to be significant, t(14) = 2.83, p<0.02. For jump, the mean thresholds were 0.438 and 0.176 for the nonlesioned and lesioned groups (t(14) = 4.00, p<0.002). This finding indicates that the differences observed between the effects of septal lesions on flinch and jump thresholds at 26 and at 40 days of age cannot be accounted for in terms of repeated testing.

The results from the second experiment in which lesioned and nonlesioned male and female groups were again tested for flinch and jump thresholds were similar to those of the first experiment. At 26 days of age neither jump nor flinch scores were affected by lesions. However, no significant sex difference was apparent for either flinch or jump scores: Flinch: Male-no lesion ñ = 0.080, male-lesion ñ = 0.085, female-no lesion ñ = 0.095, female-lesion ñ = 0.089; Jump: male-no lesion ñ = 0.266, male-lesion ñ = 0.239, female-no lesion ñ = 0.276, female-lesion ñ = 0.239. At 40 days of age the effect of septal lesions on both flinch, F(1,21) = 8.28; p<0.01, and jump, F(1,21) = 11.70; p<0.005, were significant. Again, lesioned animals had lower thresholds than unlesioned animals.

Thus, there is no evidence from these tests of response to electric shock that male and female rats are differentially affected by septal lesions made at 24 days of age. In fact, neither males nor females showed any effect of the lesion as measured by response to electric shock immediately following surgery, whereas both showed a marked effect when tested at 40 days of age. These results stand in contrast to the effect of the septal lesions on hyperemotionality and on hyperreactivity to handling noted in the course of running the first experiment and measured formally in the second.

The results from the tests for hyperemotionality are shown in Table 2 as overall combined scores. The pattern of results was similar for each of the individual response measures; unlike the responses to electric shock, the hyperemotionality scores were highest immediately following the lesions at 25 days of age and fell to near control levels by 40 days of age. While both males and females showed a considerable degree of hyperemotionality initially, it tended to be less and to disappear more rapidly among males. In the case of resistance to capture this sex difference was significant over days, F(1,12) = 8.93; p<0.01.

The results of these experiments, showing a clear contrast between the effects of septal lesions on hyperemotionality and the effects on response to electric shock,
TABLE 2
MEAN COMBINED HYPEREMOTIONALITY SCORES FOR NON-LESIONED AND SEPTALLY LESIONED MALE AND FEMALE RATS IN THE SECOND EXPERIMENT

<table>
<thead>
<tr>
<th>SEX</th>
<th>LESION</th>
<th>N</th>
<th>24 POST TRE</th>
<th>40 POST TRE</th>
<th>27 TESTS</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>CONTROL</td>
<td>6</td>
<td>0.16</td>
<td>0.33</td>
<td>0.33</td>
<td>6</td>
</tr>
<tr>
<td>F</td>
<td>SEPTAL</td>
<td>7</td>
<td>18.28</td>
<td>7.43</td>
<td>7.43</td>
<td>7</td>
</tr>
<tr>
<td>M</td>
<td>CONTROL</td>
<td>6</td>
<td>0.16</td>
<td>0.16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>M</td>
<td>SEPTAL</td>
<td>7</td>
<td>18.28</td>
<td>7.71</td>
<td>7.71</td>
<td>7</td>
</tr>
</tbody>
</table>

Add support for the view that the mechanisms underlying hyperreactivity are different from those underlying other dysfunctions involving the response suppression systems [4]. Furthermore, our results would seem to be in agreement with those of Bengelloun et al. [2] that septal lesions have their effects on shock-induced behaviors independent of sex or hormonal condition, and lead us to conclude with them that differences in septal function probably do not underlie sex differences in behaviors such as responsiveness to electric shock.

REFERENCES