BRIEF COMMUNICATION

Paraventricular Nucleus Lesions in Weanling Female Rats Result in Normophagia, Normal Body Weight and Composition, Linear Growth and Normal Levels of Several Plasma Substrates

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BERNARDIS, L. L. Paraventricular nucleus lesions in weanling female rats result in normophagia, normal body weight and composition, linear growth and normal levels of several plasma substrates. PHYSIOL BEHAV 32(3) 507-510, 1984.—Female weanling rats received small (1 mAmp for 5 sec) electrolytic lesions in the paraventricular nuclei. Sham-operated rats served as controls. The rats were maintained for 42 days and body weight, linear growth, Lee Index, food intake and efficiency of food utilization were determined throughout the study. Plasma glucose, glycerol, free fatty acids, total protein and carcass fat and protein were determined at sacrifice. There was no significant difference between the lesioned and the sham-operated rats in any of the parameters measured. The findings are interpreted to mean that the PVN of the weanling rat is not functionally mature or alternatively, that there exists a sex difference in weanling rats in response to PVN lesions.

Paraventricular nucleus Food intake Body weight Body composition Food utilization
Plasma substrates Growth Obesity

ALTHOUGH the paraventricular nucleus of the hypothalamus (PVN) is primarily associated with oxytocin dynamics [16,24] its role in energy homeostasis has been suggested almost 50 years ago: Davis et al. [11] and Cleveland and Davis [9] succeeded in attenuating diabetes mellitus in cats and monkeys by lesions of the "nucleus filiformis", the older term for the PVN [19]. They also noted increased insulin sensitivity and a blunted response to adrenaline in their lesioned animals. Subsequently, Vonderahe [27] suggested that this hypothalamic structure might serve as an insulin regulating center. Soon afterwards, Heinbecker et al. [15] reported hyperphagia and obesity in dogs with lesions in the area of the PVN.

Recent evidence for a role in the PVN in energy homeostasis, i.e., food intake and obesity, indicates that its destruction in rats by electrolytic lesions [20] or its isolation by knife cuts [14] leads to hyperphagia and obesity. Furthermore, by virtue of its position in an extensive network of autonomic circuitry [23,25] the PVN is capable of influencing a great variety of autonomic functions that also extend, for instance, to cardiovascular regulation [8].

Since male and female rats that received ventromedial hypothalamic lesions (VMNL rats) shortly after weaning do not show the hyperphagia and increased body weight gains that characterize their mature counterparts [1, 2, 5] it was of interest to examine whether a similar relationship exists for the weanling rat with PVN lesions.

The data here presented show that production of small electrolytic lesions in female rats does not result in the hyperphagia and obesity that characterize the mature PVN-lesioned rat. In addition, linear growth, efficiency of food utilization and several plasma substrates are normal in weanling PVNL rats.

1This investigation was supported by VA Medical Research Funds.
Female Sprague-Dawley rats (Harlan Sprague-Dawley, Madison WI) were received shortly after weaning and accommodated in individual cages in a light cycle (L:D 12:12, light on at 0600 hr) and temperature (23°C)-controlled room and given Charles River Rat Mouse Hamster Formula and tap water ad lib. At the age of 28 days they were anesthetized with sodium hexobarbital (14 mg/100 g body weight) and received bilateral electrolytic lesions, using a direct anodal current of 1.0 mAmp that flowed for 5 seconds from the bared tip (0.2 mm) of a spar varnish-coated stainless steel electrode of 0.37 mm diameter. Sham-operated animals (electrode inserted dorsal to the PVN without current flow) served as controls.

The animals were returned to their cages and food intake was measured every other day for 42 days, but since there was no difference between PVNL and control rats in any of the measurements only the overall means are shown. Body weight and nose-tail length and Lee Index were determined every two weeks under ether anesthesia. Again, since there were no differences between PVNL rats and controls only the last measurements and the differences between the first (at operation) and last (kill) measurement are shown.

The animals were decapitated on day 43 and plasma obtained and frozen for the subsequent determination of glucose (autoanalyzer), glycerol [7], free fatty acids [17] and total protein [21]. Carcasses were eviscerated and skinned and protein [21] and lipid [12] were determined. Brains were fixed in 10% buffered formalin and processed as previously.
PARAVENTRICULAR NUCLEUS IN WEANLING RATS

TABLE 1
SOMATIC AND PLASMA SUBSTRATE DATA IN WEANLING FEMALE RATS WITH PVN LESIONS (PVNL RATS) AND THEIR SHAM-OPERATED CONTROLS (CON)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PVNL (17)*</th>
<th>CON (11)</th>
</tr>
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<tbody>
<tr>
<td>Body weight (op.) g</td>
<td>69.8 ± 1.21</td>
<td>64.9 ± 1.70</td>
</tr>
<tr>
<td>Body weight (sacr.) g</td>
<td>192.0 ± 3.47</td>
<td>198.4 ± 0.32</td>
</tr>
<tr>
<td>(\Delta) Body weight (g)</td>
<td>127.1 ± 2.07</td>
<td>133.0 ± 3.87</td>
</tr>
<tr>
<td>Body Length (op.) mm</td>
<td>243.1 ± 1.76</td>
<td>244.5 ± 1.99</td>
</tr>
<tr>
<td>Body length (sacr.) mm</td>
<td>361.9 ± 1.66</td>
<td>364.1 ± 3.39</td>
</tr>
<tr>
<td>(\Delta) Body length mm</td>
<td>118.9 ± 1.70</td>
<td>121.0 ± 2.40</td>
</tr>
<tr>
<td>Lee Index (op.) ¶</td>
<td>307.4 ± 5.59</td>
<td>301.3 ± 1.52</td>
</tr>
<tr>
<td>Lee Index (sacr.) ¶</td>
<td>301.2 ± 1.78</td>
<td>304.1 ± 1.49</td>
</tr>
<tr>
<td>Food Intake g/d</td>
<td>18.10 ± 0.32</td>
<td>18.46 ± 0.37</td>
</tr>
<tr>
<td>Efficiency of food</td>
<td>7.04 ± 0.16</td>
<td>7.20 ± 0.14</td>
</tr>
<tr>
<td>Plasma Glucose mg/dl</td>
<td>122.1 ± 1.57</td>
<td>130.0 ± 4.04</td>
</tr>
<tr>
<td>Glyceraldehyde mg/dl</td>
<td>3.88 ± 0.22</td>
<td>3.77 ± 0.27</td>
</tr>
<tr>
<td>Free Fatty</td>
<td>185.3 ± 16.48</td>
<td>219.6 ± 29.14</td>
</tr>
<tr>
<td>Acids µM/L</td>
<td>7.17 ± 0.16</td>
<td>6.76 ± 0.21</td>
</tr>
<tr>
<td>Protein g/d</td>
<td>9.62 ± 0.58</td>
<td>8.56 ± 0.68</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>10.46 ± 0.78</td>
<td>11.21 ± 0.51</td>
</tr>
</tbody>
</table>

*Number of rats per group.
\(\dagger\) (op.)—at operation (age: 28 days),—at sacrifice (age: 71 days).
\(\ddagger\) Mean ± S.E.M.
\(\ddagger\) Change between operation and sacrifice.
\(\ddagger\) Cube root of body weight (g) divided by naso-anal length (mm)\(^{10}\).

(Szentagothai et al. [26] and Bernardis [3].)

Table 1 indicates that there are no significant differences between PVNL rats and sham-operated controls in any of the parameters measured.

These findings are reminiscent of the failure to produce hyperphagia and increased body weight gains in weanling female [1] and male [2] rats with VMNL lesions. Nevertheless, weanling VMNL rats became obese. The weanling female PVNL rats in the present study, however, exhibit normal body composition.

It appears that—at least in the female rat—PVN lesions shortly after weaning fail to produce the same effect as they do in mature rats, possibly because the PVN has not functionally matured to the point that it has in the latter animal. Alternatively, the PVN may exert different functions in the weanling female from that of the weanling male rat; we are currently exploring this possibility.

Sex differences in response to hypothalamic manipulation have been reported for mature VMNL rats [10] but have been denied by other investigators [13]. We have found no differences in fat accretion between weanling male and female VMNL rats [67]. A sex difference in mature rats in response to lesions in the lateral hypothalamic area (LHA) was reported some time ago: female LHAL rats show normal body weight gains, even when large lesions are produced [18, 22, 28]. This is in striking contrast to their effect in male mature rats. It is well possible that such a sex difference exists in weanling PVNL rats.

Whereas the present communication does not define or elucidate the underlying mechanism of PVN function in the weanling as opposed to the mature rat, it shows unequivocally that destruction of this area in the weanling female rat has no effect on parameters known to reflect disruption of energy metabolism and growth.

RESULTS AND DISCUSSION

Figure 1 shows the lesion localization in a rat representative of Group 1 (PVNL rats) and indicates that the PVN was totally destroyed but that the lesions did not appreciably encroach on surrounding areas. For comparisons, a microphotograph of a sham-operated animal is also shown. Although the present lesions in their largest cross section cover the whole area of the PVN, it is conceivable and indeed likely that not all PVN neurons were destroyed.

Acknowledgement

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REFERENCES


