Effect of Ventromedial Hypothalamic Lesions on Development of Adrenal-Regeneration Hypertension in Weanling Female Rats

Regeneration of the adrenal cortex in the uninephrectomized rat given saline to drink is accompanied by the development of an acute form of hypertensive vascular disease. When adrenal regeneration is prevented by hypophysectomy or by administration of corticosterone the hypertension fails to develop, thereby indicating the dependence of this form of hypertension on the functional integrity of the pituitary-adrenal axis. The physiologic function of this latter system is, in turn, dependent upon the development of an acute form of hypertensive vascular disease in adult rats after ablation of the ventromedial hypothalamus, since placement of electrolytic lesions in the hypothalamus is followed by evidence of disturbed adrenocortical activity. It seemed reasonable to suppose, therefore, that hypothalamic lesions might exert an influence on the development of adrenal-regeneration hypertension. Initial experiments demonstrated that placement of bilateral ventromedial lesions in young-adult animals inhibited the development of adrenal-regeneration hypertension when the hyperphagia, which regularly occurs in adult rats after ablation of the ventromedial nuclei, was prevented by pair-feeding with sham-operated control animals. The present study was done to determine the influence of ventromedial nuclear ablation on adrenal-regeneration hypertension in weanling rats in which hyperphagia does not occur as a result of such hypothalamic lesions.

Materials and methods. Weanling female Charles River rats were uninephrectomized and uniaudrenalectomized, divided into 4 groups and treated as follows: group 1 rats received no further treatment. Group 2 rats had bilateral electrolytic lesions placed in the ventromedial hypothalamus as described previously. Group 3 rats had the left adrenal enucleated. Group 4 rats had both left adrenal enucleation and electrolytic ablation of ventromedial nuclei performed 5 days apart. Adrenal enucleation was performed first in 17 rats whereas ventromedial lesions were placed first in 14 animals. All operations were done under ether anesthesia.

The animals were caged singly in a room kept at 22.5 °C with 12 h light and 12 h dark cycles. A synthetic diet (4.2 Cal/g, 0.8% NaCl) and 1% saline as drinking fluid were provided ad libitum. Food and saline intake were measured weekly and the total sodium consumption computed. Body weight and systolic blood pressure were measured under light ether anesthesia at weekly intervals and at the end of the experiment.

After 6 weeks the rats were killed by decapitation, blood collected and plasma obtained for sodium and potassium determination by flame-photometry. Organs were removed, fixed in 10% formalin and weighed. Pituitaries were examined under a dissecting microscope for possible mechanical or thermal damage. The hypothalamic lesions were localized on cresyl violet-stained sections and composite diagrams constructed of the lesions common to the rats of each group (Figure 1).

Data was analyzed according to students t test. Differences between standard errors of the mean having a P value < 0.05 are considered significant and < 0.01 are considered highly significant.

Results. Terminal systolic blood pressure: Figure 2 shows that rats with hypothalamic lesions (group 2) had a significantly lower blood pressure (P < 0.02) than untreated controls (group 1) and that rats bearing regenerating adrenals (group 3) developed highly significant hypertension (P < 0.01). However, the presence of bilateral ventromedial lesions prevented to a highly significant

Terminal body weights (g) and relative organ weights (mg/100 g body weight)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of animals</th>
<th>Final body weight g</th>
<th>Heart mg%</th>
<th>Kidney mg%</th>
<th>Thymus mg%</th>
<th>Adrenal mg%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>187 ± 5*</td>
<td>391 ± 9</td>
<td>732 ± 25</td>
<td>315 ± 18</td>
<td>19.1 ± 1.2</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>175 ± 8</td>
<td>404 ± 11</td>
<td>700 ± 17</td>
<td>305 ± 9</td>
<td>18.3 ± 0.8</td>
</tr>
<tr>
<td>3</td>
<td>37</td>
<td>193 ± 3</td>
<td>449 ± 12</td>
<td>768 ± 29</td>
<td>293 ± 11</td>
<td>17.5 ± 0.9</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>200 ± 8</td>
<td>405 ± 12</td>
<td>719 ± 38</td>
<td>228 ± 14</td>
<td>15.6 ± 1.1</td>
</tr>
</tbody>
</table>

* Standard error of the mean.

Fig. 2. Caloric intake, sodium intake and terminal systolic blood pressure. Group 1, controls; group 2, bilateral electrolytic lesions in the ventromedial hypothalamus; group 3, adrenal-enucleation; group 4, adrenal enucleation and ventromedial hypothalamic lesions. In the sodium intake graph the dietary sodium consumption is represented by the lower part of each bar and the sodium intake from the drinking fluid is shown as the open part of each bar. The vertical line at the top of the bars indicates the standard error of the mean.

degree (P < 0.001) the elevation of blood pressure in the rats of group 4 which also bore regenerating adrenals.

Sodium consumption and caloric intake: sodium intake was slightly reduced (P < 0.02) in group 2 because of a smaller consumption of saline drinking solution. There was no significant difference in caloric consumption between any of the groups (Figure 2). Plasma sodium and potassium: plasma sodium levels in groups 2, 3 and 4 were very significantly higher (P < 0.01) than in group 1 (Figure 3). In contrast, plasma potassium was significantly higher (P < 0.05) than control levels in the rats with hypothalamic lesions (groups 2 and 4), and very significantly lower (P < 0.01) in the rats with adrenal-regeneration hypertension (group 3). The difference between the values for group 3 and group 4 was highly significant (P < 0.01) in the rats with adrenal-regeneration hypertension (group 3). The difference between the heart weights of groups 3 and 4 was highly significant (P < 0.01). The weight of the kidney was largest in group 3 but differed significantly from other groups only in the case of group 2. The adrenal weight of rats with ventromedial lesions (group 2) was unchanged from control values (group 1) but the weight of the regenerated adrenal was significantly less (P < 0.05) in group 4 than in group 3. It is of interest, therefore, that significant (P < 0.01) thymic involution occurred only in group 4.

Discussion. The results of this experiment clearly support previously published observations in young-adult rats, that the development of adrenal regeneration hypertension is inhibited by placement of electrolytic lesions in the ventromedial nuclear region of the hypothalamus. How this is brought about remains a matter for speculation. It is apparent from both the present and previous experimental results that the hypotensive effect of ventromedial nuclear ablation cannot be explained by differences in either caloric or sodium chloride consumption, since these parameters were the same in rats which became hypertensive and in those which did not. However, this does not mean that the mechanism is unrelated to the electrolyte metabolic status of the lesioned animals. Elevated plasma potassium levels have been reported in...