The Effect of Lateral Hypothalamic Lesions in Weanling Rats Bearing Lesions in the Ventromedial Hypothalamic Nuclei (37000)

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Weanling rats with bilateral lesions in the ventromedial hypothalamic nuclei have been shown to develop both hypertriglyceridemia and hyperinsulinemia in the presence of normal food intake (1, 2). These findings are associated with decreased growth and increased deposition of fat (1). It has been suggested that both the hypertriglyceridemia and hyperinsulinemia (3, 4) might be mediated via a connection between the ventromedial and ventrolateral hypothalamus with involvement of the parasympathetic nervous system (5). If this were correct, lesions in the lateral hypothalamus should interrupt efferent pathways and eliminate the observed metabolic alterations. The present studies were undertaken to see what effect lesions of the lateral hypothalamus would have on the hypertriglyceridemia and hyperinsulinemia resulting from lesions in the ventromedial hypothalamus.

Materials and Methods. Weanling male Sprague-Dawley rats were accommodated in individual cages under standard conditions and given Teklad Lab Chow and tap water *ad libitum*. At the age of 26 days they were anesthetized with hexobarbital (Evipal, Winthrop), 14 mg/100 g body weight, and inserted into a stereotaxic instrument (Baltimore Instrument Co.). Stainless steel electrodes (0.25 mm diam and spar varnish coated except for the tip) were inserted into the ventromedial nuclei (VMN) using previously established coordinates (6). In 2 groups a current of 1.5 mA was passed for 10 sec to produce lesions in the VMN. In a third group there was no current flow. Five days thereafter the rats were anesthetized with Evipal for the following operations: Group 1 received bilateral lesions in the lateral hypothalamic area (LHA) using the same size electrodes and lesion parameters as for the VMN lesions. groups 2 and 3 had the electrode inserted bilaterally in the LHA without current flow. A fourth group had LHA lesions placed prior to VMN lesions but all rats died subsequently due to anorexia. Thus, they are not included in the data.

All rats were maintained on Lab Chow and tap water *ad libitum*. Food intake was measured during the period between the two operations and after the second operation. Ten days after the second operation the rats were anesthetized with ether, weighed and measured (naso–anal length and nose–tail length) for the assessment of linear growth change and obesity index (1). On the following day they were decapitated, heparinized trunk blood was collected, chilled immediately, centrifuged and the plasma was frozen for subsequent determination of triglycerides (7) and insulin (8). The brains were fixed in 10% buffered formalin and lesion localization was performed as previously described (9). Rats with asymmetrical lesions and injury to the median eminence or with lesions that extended beyond the ventral border of the brain were excluded from the final statistical analysis.

Results. Lesions in the area of the lateral hypothalamic area did not eliminate either the hypertriglyceridemia or the hyperinsulinemia produced by lesions in the area of the ventromedial nucleus (Table I). This occurred despite the fact that food intake during the latter stages of each experiment was the same for each group and that plasma glucose remained unaltered in all groups. The decrease in food intake seen in the VMN group prior to lesion of the LHA has been reported previously (10). A similar, but not significant hypophagia was seen in the VMN-LHA group.

TABLE I. Effect of Lesions in the Lateral Hypothalamic Area (LHA) in Weanling Rats with Lesions in the Ventromedial Nucleus (VMN).[a]

	VMN + LHA (15)	VMN (9)	Control (6)
Insulin (μU/ml)	57 ± 7[e]	71 ± 10[e]	22 ± 5
Triglyceride (mg/100 ml)	65 ± 5[b]	76 ± 9[c]	44 ± 5
Glucose (mg/100 ml)	116 ± 5	120 ± 4	123 ± 3
Food intake (g)			
Before LHA	14.6 ± 2.1	12.6 ± 2.0[d]	21.0 ± 1.0
After LHA	21.5 ± 1.8	20.8 ± 2.4	22.7 ± 0.7
ΔBody wt (g)	64 ± 8	61 ± 10	82 ± 1
ΔBody length[g] (mm)	34 ± 3[f]	32 ± 5[f]	61 ± 2
Obesity index[h]	325 ± 4[d]	327 ± 4[f]	307 ± 2

[a] Results expressed as mean ± SEM; number of animals per group is given in parentheses.

[b] Significance of difference from control: $p < .05$; [c] $p < .02$; [d] $p < .01$; [e] $p < .005$; [f] $p < .001$.

[g] Nose-tail.

[h] Obesity index (l) $(wt)^{1/3}$/naso-anal length $\times 10^4$.

The somatic parameters listed in Table I are consistent with previous results observed in VMN rats: significant decrease in body length, slight but insignificant decrease in body weight and significant increase in obesity index (1).

Discussion. The present data confirm the previously reported hypertriglyceridemia and hyperinsulinemia in rats with hypothalamic obesity due to bilateral destruction of the ventromedial nuclei. Bilateral lesions of the lateral nuclei, placed 5 days after destruction of the ventromedial hypothalamic area, did not eliminate either the hypertriglyceridemia or hyperinsulinemia. These findings do not support the possibility that the efferent pathways involved in the development of either hypertriglyceridemia or hyperinsulinemia include a connection between the ventromedial and lateral hypothalamus. Although this experiment indicates that the syndrome, once produced by lesions in the ventromedial nucleus, cannot be eliminated by a subsequent lesion of the lateral hypothalamus, it is still possible that a lesion of the lateral area might prevent the occurrence of the syndrome by a subsequent VMN lesion.

Since the parasympathetic pathways previously postulated as one possibility (3) appear eliminated by the present data, the sympathetic pathways must be considered. Such an influence might be exerted along longitudinal fiber bundles, for example the dorsal longitudinal fasciculus of Schütz, connecting the hypothalamus with the midbrain and the autonomic centers in the neuroaxis (5, 11, 12).

Summary. Lateral hypothalamic lesions in weanling rats bearing lesions in the ventromedial hypothalamic nuclei (VMN) did not eliminate the hypertriglyceridemia, hyperinsulinemia or changes in somatic parameters associated with VMN lesions. In conjunction with previous data, the present findings suggest that altered sympathetic nervous system activity, subsequent to ventromedial hypothalamic destruction, is important in the development of the syndrome of hypothalamic obesity.

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