both adult and weanling rats with ventromedial lesions[16], and in the present experiment plasma sodium was elevated as well. In contrast, the rats bearing a regenerating adrenal had elevated plasma sodium and depressed plasma potassium levels. The net effect of these plasma electrolyte changes was an increased Na/K ratio in the rats with a regenerating adrenal (group 3) and a normal Na/K ratio in the rats with both a regenerating adrenal and ventromedial lesions (group 4).

Although these findings do not clarify the mechanism whereby ventromedial nuclear ablation affects the development of adrenal-regeneration hypertension, they do call to mind the reports of MENEELY, BALL and YOUMANS[17] and MENEELY and BALL[18] that administration of potassium chloride can ameliorate the hypertension which accompanies high sodium chloride consumption in the rat.

[16] L. L. BERNARDIS, A. MOLTENI, B. PATTERSON and F. R. SKELTON, Acta Neurovegetativa, in press (1967).
[17] G. R. MENEELY, C. O. T. BALL and J. B. YOUMANS, Ann. intern. Med. *47*, 263 (1957).
[18] G. R. MENEELY and C. O. T. BALL, Proc. Coun. high Blood Press. Res. *6*, 65 (1958).

Zusammenfassung. Ventromedial hypothalame Läsionen hemmen die NNR-Regenerations-Hypertonie. Dabei ist nicht eine Verschiebung in der Nahrungs- oder Elektrolyt-Aufnahme verantwortlich[19,20].

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Eating and Drinking Induced by Cerebral-Ventricular Injections in Rats with Lesions in the Lateral Hypothalamus

Normal, satiated rats, when injected in the lateral ventricle of the brain with small quantities of pentobarbital sodium or 5% saline at 10 µl/min for 10 min, show a temporary eating response. Hyperphagic rats with lesions in the ventromedial area of the hypothalamus exhibit the same response to the pentobarbital sodium injection but do not eat following the 5% saline injection[1]. Drinking is caused by an injection of 2 or 5% saline at about 10 µl/min in the lateral ventricle of either normal or hyperphagic rats[1,2], apparently as a result of hypertonicity acting on osmoreceptors in the hypothalamus.

Rats suffering from aphagia and adipsia following lesions in the lateral hypothalamus often recover from these deficits in a few days or weeks if the animals are maintained by forced feeding and watering. RODGERS, EPSTEIN and TEITELBAUM[3] have presented rather conclusive evidence that the aphagia and adipsia are temporary motivational deficits and have described 4 stages of recovery. In stage I, the rats are both aphagic and adipsic. In stage II, the rats are anorexic and adipsic (e.g. the animals eat small quantities of wet, chocolate chip cookies). In stage III, the rats remain adipsic, but eat enough voluntarily to maintain their body weight. In stage IV, the animals drink water and eat normal laboratory food. These animals often still remain 'prandial drinkers' in that they drink only if receiving food.

In contrast to normal rats, rats with lesions in the lateral area who have then recovered from aphagia and adipsia do not respond to insulin-induced hypoglycemia by eating[4]. They lack many of the normal water regulation functions and will not drink to regulate body water following hyperthermia, increased serum osmolarity, or water deprivation[5]. They do not compensate for an induced sodium deficiency[6]; nor can they be induced to drink by intracranially administered carbachol[6].

We have studied, in rats recovering from lateral lesions, the responses to injections of pentobarbital sodium and 5% saline at 5 µl/min for about 4 min. We have not been able to induce aphagic rats to eat by intraventricular injections until they eat voluntarily, nor can they be induced to drink by intraventricular injections of a hypertonic solution until they drink voluntarily.

Female Charles River albino rats (220–270 g) were lesioned in the lateral area of the hypothalamus (stereotaxic coordinates of BERNARDIS and SKELTON[7] for the ventromedial nuclei with the substitution of 1.8–2.0 mm for the lateral coordinates). The rats were then cannulated in the lateral ventricle in a manner similar to that of MABEL, BAILE and MAYER[1]. The accuracy of this method of cannula placement was confirmed with the following tests: (1) histological location of Indian ink infused through the cannula; (2) elicitation of eating in normal rats infused with 65 mg/ml pentobarbital sodium at the rate of 5 µl/min; (3) elicitation of drinking in normal rats infused with 5% saline at 5 µl/min.

[1] J. A. MABEL, C. A. BAILE and J. MAYER, Lancet *7461*, 472 (1966).
[2] L. J. HERBERG, Q. Jl exp. Psychol. *14*, 8 (1962).
[3] W. L. RODGERS, A. N. EPSTEIN and P. TEITELBAUM, Am. J. Physiol. *208* (2), 134 (1965).
[4] A. N. EPSTEIN and P. TEITELBAUM, 22nd Int. Physiol. Congr. Leiden, Abstr. 361 (1962).
[5] G. WOLF and D. QUARTERMAIN, Am. J. Physiol. *212*, 113 (1967).
[6] G. WOLF and N. E. MILLER, Science *143*, 585 (1964).
[7] L. L. BERNARDIS and F. R. SKELTON, Am. J. Anat. *116*, 69 (1965).

Fourteen rats which remained aphagic and adipsic for more than 3 days were periodically tested with infusions of pentobarbital sodium at 65 mg/ml. Pressure, monitored during the pentobarbital infusions, served as a check that the cannula was still open.

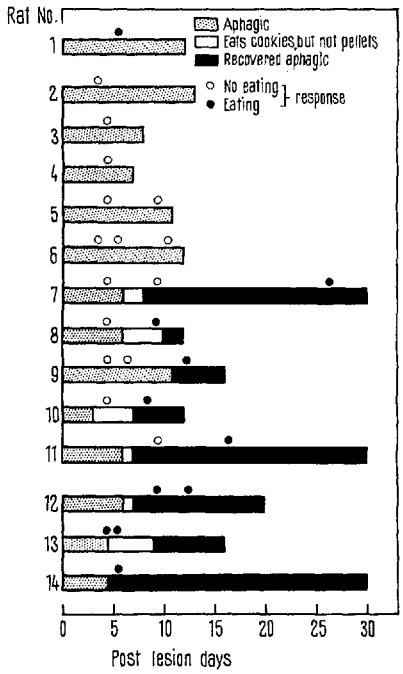

Fig. 1. The results of the infusion of pentobarbital into the lateral ventricle of rats lesioned in the lateral hypothalamus. o, test period in which there was no eating response; •, test period in which there was an eating response.

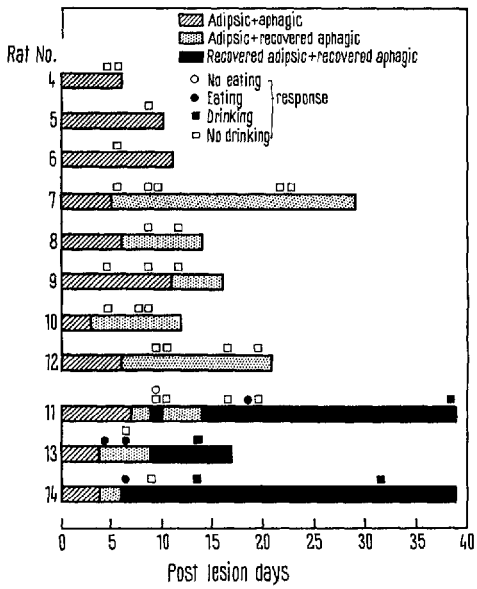

Fig. 2. The results of the infusion of hypertonic saline and pentobarbital into the lateral ventricle of rats lesioned in the lateral hypothalamus. o, test period with pentobarbital in which there was no eating response; •, test period with pentobarbital in which there was an eating response. Pentobarbital tests are shown only for those rats which recovered from adipsia. □, test period with 5% saline at 5 µl/min during which there was no response; ■, test period with 5% saline during which there was a drinking response.

The results for those rats infused with pentobarbital sodium in the lateral ventricle were (Figure 1): (1) 27 of 30 normal animals ate; (2) one of 8 unrecovered aphagics ate; (3) all of the 8 recovered aphagics ate. The pattern of recovery of the eating response to pentobarbital sodium was: 2 of 3 ate cookies but not pellets; 3 of 4 had started eating pellets within the last 3 days; 1 of 2 had started drinking water on the third day after eating pellets and was tested on that third day; all eventually recovered the response.

The results of the infusions of 5% saline into the lateral ventricles were (Figure 2): (1) all of 8 normals drank; (2) none of 9 unrecovered adipsic rats drank (in 11 of 21 tests the rats had recovered from aphagia); (3) all of 3 recovered adipsic rats drank (these 3 recovered the drinking response by the fourth day, by the eigth day, and by sometime following the twentieth day, after voluntary drinking).

Our work would suggest that rats with lesions in the lateral areas cannot be readily induced to eat by intraventricular injections of pentobarbital sodium, unless the rats are in at least stage II and probably stage III of recovery. The drinking response to similar injections of 5% saline at 5 µl/min is not readily produced until the rats reach stage IV of recovery.

The rats we studied, following lesions in the lateral hypothalamus, definitely recovered some of the normal eating and drinking responses. However, other deficits observed in the 'aphagic and adipsic' rat are not compensated for as they recover[4,8]. In particular, near lethal doses of hypertonic NaCl solutions administered either i.p. or intragastrically by EPSTEIN and TEITELBAUM did not cause drinking in 'recovered aphagic' rats. It thus appears that there are control mechanisms that disappear following the induction of lesions and reappear, at least in part, as the animals recover[9].

Résumé. Par des lésions bilatérales hypothalamiques on a rendu des rats aphagiques et adipsiques. Durant la période de convalescence, on a injecté dans le ventricule latéral du pentotal de sodium (ce qui normalement fait manger les animaux) et une solution saline hypertonique (qui normalement les fait boire). On a trouvé qu'après les lésions les rats ne réagissent que lorsqu'ils sont redevenus capables de manger et de boire spontanément.

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[8] A. N. EPSTEIN and P. TEITELBAUM in *Thirst* (Ed. M. J. WAYNER; Pergamon Press, New York 1964), p. 395.

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