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BRIEF REPORT

Impairments in Sodium Appetite after Lesions of Gustatory Thalamus: Replication and Extension[1]

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Rats received electrolytic lesions centered in the gustatory subnucleus of the ventral posterior complex of the thalamus. They were tested for impairments of the ability to increase sodium chloride intake after depletion of body sodium or treatment with the mineralocorticoid desoxycorticosterone. Tests were administered either within a few weeks or after 2 months postoperative recovery to test a hypothesis suggested by previous studies that the decremental effect of the lesions would appear only after a latent period. This hypothesis was refuted by the results—the thalamic lesions resulted in highly significant impairments of sodium intake at either time period. An additional finding was that a particular type of general feeding impairment previously attributed to subthalamic damage also occurs after thalamic lesions.

The work reported here continues a program aimed at tracing the neural systems mediating sodium appetite in the rat (Wolf, 1968; Wolf, 1971a; Wolf, DiCara, and Braun, 1970). Recently, we were confronted with a perplexing finding. In an earlier study (Wolf, 1968), we found that lesions in the gustatory region of the thalamus (centered in the subnucleus defined by Benjamin and Akert, 1959) resulted in significant impariments in sodium appetite. In a later study concerned with identifying hypothalamic pathways for sodium appetite (Wolf, 1971a), lesions were aimed at the caudal subthalamus ventral to the gustatory region of the thalamus. The lesions were quite large and extended dorsally into the thalamus to substantially overlap the region of the effective thalamic lesions of the prior study. However, these

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subthalamic centered lesions caused no observable impairment of sodium appetite. (Note that the term "sodium appetite" is used for convenience to refer to regulatory sodium intake and "impairments" referred to in the text are not meant to imply specific loss of motivation as opposed to other critical functions.)

One potentially important difference between the two studies was that the rats with thalamic lesions were not tested for sodium appetite until 2-3 months after induction of the lesion, while the rats with subthalamic lesions were generally tested within 2-3 weeks following induction of the lesions. It seemed quite conceivable that the decrement resulting from the thalamic damage does not appear immediately following the lesion but is dependent on delayed secondary changes in neural functioning. Harvey and Lints (1965) found delayed behavioral effects of brain lesions attributable to gradual depletion of serotonin and associated central denervation supersensitivity. Cowen (1970) has described anterograde and retrograde transneural degenerative processes which have a long time course and may be responsible for long latency behavioral disruptions.

On the other hand, it is possible that the effect of the thalamic lesions is not reliable, for we were quite concerned in that study with the finding that about 30% of the lesioned rats showed no indication of impaired sodium appetite even though their lesions were indistinguishable from those of rats which manifested a total impairment. The present study investigates the effect of lesions in the thalamic gustatory region on sodium appetite tested within 2-3 weeks and after 2 months following lesioning.

Sixty-two adult male rats of several standard strains were used. They weighed between 300 and 400 g at the time of lesioning. Lesions were induced by passing anodal DC through stereotaxically guided 00-gauge stainless-steel insect pins insulated except for 0.3 mm at the tip. The coordinates for the gustatory region with bregma and lambda at the same horizontal plane were 3.5–4.0 mm posterior to bregma, 6.0-6.5 mm below the midsaggital sinus, and 1.4 mm lateral to the midline. The current intensity was 0.8 mA for 3-12 sec. In order to avoid damage to the corda tympani nerve, the ear bars were inserted in holes drilled into the sides of the skull just below lambda.

Rats which did not eat or drink after the lesions were tube fed and given wet palatable food until recovery of normal food and water intake. At the completion of the experiments, the rats were sacrificed, and the brains prepared for histologic analysis as described elsewhere (Wolf, 1971b). Successive groups of rats were run until a sufficient number with lesions acceptable for inclusion in either the experimental or control groups were obtained. Generally several unoperated rats were run concurrently. Twenty rats with bilaterally symmetrical lesions centered in the thalamic gustatory relay were included in the experimental groups. Ten rats with unformed, unilateral, or small assymetric lesions were included in the control groups with 10 normal

unoperated rats. Data from 13 rats with accessory brain damage or with large poorly localized lesions were discarded. All decisions based upon histological criteria were made without knowledge of behavioral results. The remaining 9 rats died within a week after surgery subsequent to severe weight loss despite daily food and fluid intubation.

It should be noted that the procedure of including only rats with accurately placed bilaterally symmetrical lesions in the experimental groups as used here and in our previous studies (Wolf, 1968; Wolf, 1971a) is carried out for the purpose of minimizing uninterpretable intragroup variability and allowing a more objective and precise analysis of the relations between specific tissue damage and behavioral change. There is a substantial and largely unavoidable margin of subjectivity in the analysis of lesion data (Wolf and DiCara, 1969). The utilization of only "clean" lesions and the analysis of individual rather than grouped histologic and behavioral data serve to minimize misinterpretation and potential experimenter bias. Of the rats with unacceptable lesions, those with minimal tissue damage provide an ideal control for the operative procedure. In the present analysis the data of the rats with minimal lesions of the unoperated rats were combined in a mixed control group, since their results were essentially identical and no relevant data were lost thereby. Finally, it is important to note that the data of the 13 lesioned rats which were discarded from the study were carefully analyzed. They yielded no data which would bear upon the conclusions from the present results and provided no other interpretable information.

Eight experimental and eight control rats comprising the Long Recovery Group were tested for sodium appetite after a 2-month postoperative recovery period. The rationale and conditions for the tests have been described in detail elsewhere (Wolf, 1968) and only a brief description will be given here. About 2 months after lesioning, the rats were given a 0.50 *M* NaCl solution, 0.30 *M* KCl solution, and distilled water *ad lib* in separate graduated tubes with metal drinking nozzles which protruded through the fronts of the individual cages about 3 cm apart. The positions of the solutions remained constant during each of the two phases of the experiment but were changed between the phases. The food was condensed milk, given in a beaker attached to one corner of the front of the cage. Fluid and food intake and body weight were measured daily. After a few days of adaptation when total intake of salt solutions was less than 2 ml per day and intake of water was more than 5 ml per day, the rats were injected subcutaneously with 2.5 ml of 1.5% formalin to induce sodium depletion. (This procedure has subsequently been discontinued for reasons described elsewhere, Wolf, McGovern, and DiCara, 1974.) Two days after formalin injection, the relative positions of the 3 solutions were changed and a few days later, when intake stabilized and met the above criterion, the rats were injected subcutaneously with 5.0 mg of desoxycorticosterone acetate (DOCA) on each of 3 successive days. Three

successive DOCA injections are administered because its natrorexigenic effect becomes gradually more consistent across animals and less variable with the successive injections. The measures of sodium appetite are the difference in sodium chloride intake between the day before and the day following formalin injection and between the day before the first and the day following the final (third) DOCA injection.

Twelve experimental and 12 control rats comprising the Short Recovery Groups were tested for sodium appetite under the following conditions described in detail elsewhere (Wolf, 1971a). The test was administered within a few days after the rats recovered the ability to eat condensed milk and to ingest water from a standard drinking tube. Generally, the testing was completed and the rats were sacrificed within 2-3 weeks after brain lesioning. The short recovery test was identical to the first phase of the long recovery tests, except that the KCl solution was omitted in order to minimize the time to learn the fluid discrimination. Thus the rats were given 0.50 *M* NaCl, distilled water, and condensed milk until intake stabilized, and were then injected with formalin. The experiment was terminated 2 days after formalin injection.

Figure 1 shows sections near the centers of the lesions for individual lesioned rats of the Long Recovery Group (Fig. 1a) and the Short Recovery Group (Fig. 1b). The lesions were all similarly placed—centered in the caudal half of the thalamic taste relay. The lesions destroyed the medial tip of the medial lemniscus and invaded the subthalamus and ventromedial nucleus ventrally and the parafascicular nucleus dorsally. Note that the lesions of the Long Recovery Group appear smaller than those of the Short Recovery Group. This is due to the contraction which occurs during prolonged postoperative recovery periods (Wolf and DiCara, 1969).

Recovery of the ability to ingest dry food and drink water from a metal drinking nozzle occurred from 1 day to 1 month following lesioning. Rats with larger lesions tended to show more severe feeding and drinking deficits than those with smaller lesions although this relationship was quite variable. The pattern of recovery of feeding and drinking closely resembled that following lesions of the caudal subthalamus and ventral thalamus described in detail elsewhere (Wolf, 1971a). Briefly, the rats attempt to ingest food but appear to have impairments of sensori-motor coordinative mechanisms necessary for food ingestion. They have obvious difficulty eating hard food pellets and licking water from a spout. These results indicate that this pattern of feeding impairments which we previously termed "prerubral syndrome" may be more related to thalamic than to subthalamic systems.

After recovery of normal feeding and drinking, when the lesioned rats were offered the salt solutions and water, they generally learned the discrimination and began to avoid the salt solutions almost totally within 3 days. The control rats generally learned the discrimination within 2 days but there were

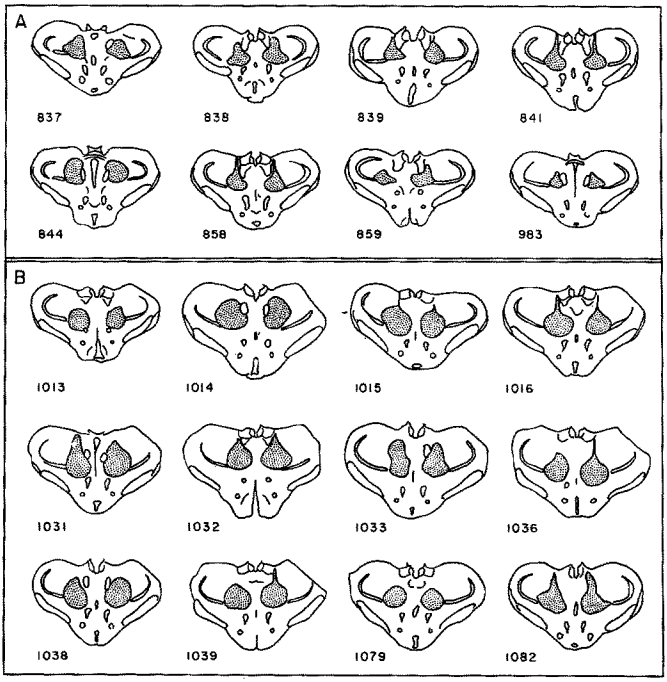

Fig. 1. Projection drawings of sections near centers of lesions at level of thalamic gustatory relay for individual rats of Long Recovery (A) and Short Recovery (B) experimental groups. Lesions are represented by shaded areas which include central cavity and surrounding area of gliosis.

large individual differences (1-8 days) in both groups, and the differences between experimental and control rats did not approach statistical significance. While it is known that rats with lesions of the thalamic gustatory region show decrements in taste discrimination, such decrements may not be apparent when very strong taste stimuli such as the present hypertonic salt solutions are used (Oakley and Pfaffmann, 1962).

The left side of Table 1 shows the changes in sodium and water intake after formalin and DOCA treatments in the Long Recovery Groups. KCl and milk intake are not shown since KCl intake was not affected by either treatment in either group, and milk intake was slightly diminished by formalin and unaffected by DOCA treatment in both groups. The average increases in sodium intake after either formalin or DOCA treatment were significantly diminished in the experimental group ($p < .02$ for formalin and $p < .01$ for DOCA). The experimental rats tended to manifest smaller increases in water intake than the control rats but these differences did not reach statistical significance.

TABLE 1

Changes in Sodium and Water Intake in Long- and Short-Recovery-Period Tests for Individual Rats with Lesions of the Thalamic Gustatory Relay and for Respective Control Groups

Long recovery period					Short recovery period		
	Change in Na (mEq)		Change in H_2O (ml)			Change in Na (mEq)	Change in H_2O (ml)
Experimental Rat #	after formalin	after DOCA	after formalin	after DOCA	Experimental Rat #	after formalin	after formalin
837	9.0	8.0	20	5	1013	0.5	1
838	0	0	-2	8	1014	0	16
839	3.5	4.0	6	0	1015	0	-11
841	0	0	14	6	1016	0	11
844	3.0	6.0	12	15	1031	0	-3
858	-0.5	7.0	6	-4	1032	3.4	28
859	0	1.5	2	1	1033	3.3	12
983	0	0	20	4	1036	3.0	13
					1038	0	4
					1039	1.9	7
					1079	0.5	8
					1082	5.0	22
$\bar{x}$	1.9	3.3	9.8	4.4	$\bar{x}$	1.5	9.0
SD	3.0	3.2	7.6	5.4	SD	1.7	10.2
Control group $N = 8$					Control group $N = 12$		
$\bar{x}$	5.7	8.9	14.8	12.9	$\bar{x}$	6.9	20.0
SD	2.2	3.3	3.3	9.7	SD	3.7	15.0

The data of the Short Recovery Groups are shown on the right side of Table 1 and are similar to those of the Long Recovery Groups. The increase in sodium intake after formalin was significantly diminished in the experimental group ($p < .001$) and, while there was an attenuation of the normal increase in water intake after formalin, this difference between the groups was not significant.

Two apparently distinct but possibly related problems emerge from this study and our previous research. First, there is a clear bimodal distribution of the effect of thalamic lesions on sodium appetite; when an impairment occurs, it is generally total but some rats with typically effective lesions (e.g., 837, 844, 1032, 1082) show little impairment (see also Wolf, 1968). Second, under identical testing conditions and postoperative recovery periods, lesions centered in the thalamic gustatory relay cause a highly significant impairment of sodium appetite (Short Recovery Group), while larger lesions centered in the subthalamus but including the gustatory relay cause no impairment (Wolf, 1971a).

The phenomenon of all-or-none bimodal effects of lesions may be much more common than is apparent from the literature, for such effects are not revealed by the usual modes of analysis of lesion data wherein only group averages are utilized. Such bimodal effects may be due to individual differences in the central mechanisms utilized in the tests, or they may indicate a particular type of structure and function of the lesioned area. In the present case, the tendency toward an all-or-none effect of the thalamic lesions suggests the hypothesis that there is a diffuse gustatory region of the thalamus which transmits messages whose effectiveness is not related to their intensity, so that undefined peripheral tissue spared by subtotal lesions can transmit sufficient information to stimulate an otherwise intact and normally functioning consummatory system.

The latter hypothesis allows us to relate the bimodal effect to the problem of the differential effects of the thalamic and subthalamic lesions. There is, in fact, evidence that the gustatory region of the thalamus extends beyond the limits of the classically defined nucleus (Norgren and Leonard, 1973) and encompasses a rostro-dorsal region which appears more extensively damaged by the thalamic than by the subthalamic lesions. A quite different hypothesis is also apparent, however. The thalamic and subthalamic regions may have counterbalancing excitatory-inhibitory functions so that destruction of both regions masks the disruptive effect of destruction of the thalamic region alone—such masking effects have been observed in other brain systems (Meyer, Johnson, and Vaughn, 1970).

Finally, one must consider the possibility that the lesion effects are unrelated to the gustatory system. First, neocortical ablations which result in extensive retrograde cell degeneration in the thalamic gustatory nucleus cause little impairment of sodium appetite (Wolf, DiCara, and Braun, 1970).

Secondly, other important systems are damaged by the thalamic lesions. Of relevance in this regard are the ascending reticular pathway to the intralaminar nuclei and the ascending noradrenergic pathways to the hypothalamus and forebrain. According to the map of Ungerstedt (1971), the dorsal noradrenergic pathway passes through the region destroyed by the caudal poles of the present lesions. The subthalamic lesions of our prior study would have destroyed both the dorsal and ventral pathways which, one might speculate, may have counterbalancing functions as discussed above.

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