The Effect of Ablation of the Area Postrema on Water and Electrolyte Metabolism in Dogs*

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With 5 Figures

The clinical syndrome of "cerebral salt wasting", documented by Peters and his co-workers (Peters and coll., 1950; Welt and coll., 1952), has generally been observed in patients with diffuse cerebral disease. A few cases have been reported, however, in which the syndrome was present with pathological processes localized to the brain stem (Welt and coll., 1952; Cort, 1954; unpublished case cited by Wise, 1956).

It was with this fact in mind that one of us (Wise, 1956) studied the effect of bipolar stimulation of the medulla oblongata in dogs. In preliminary experiments with this technique, increased excretion of water, sodium and potassium was observed in 5 of 10 dogs tested. Subsequent studies (Wise and Ganong, unpublished) confirmed this observation, and it was also noted that the effective stimuli were localized to the region just rostral to the obex, near the area postrema.

It is of interest in this regard that Claude Bernard reported over 100 years ago that pique of the "median eminence of the floor of the fourth ventricle" slightly cephalad to his well known "glycosuria point" led to polyuria without the appearance of sugar in the urine (Bernard, 1856). Little attention was paid to this observation, but recently Clemente, Sutin and Silverstone (1957) reported increased electrical activity in the region of the area postrema after the intravenous injection of hypertonic solutions. The latter investigators suggested, on the basis of this result, that this region might subserve an osmoreceptor function.

Because of these observations, it was felt that studies of salt and water metabolism after ablation of the area postrema would be of interest. The following experiments were undertaken to study sodium and potassium excretion in dogs after destruction of this region, and the response of such animals to salt and water loading and deprivation.

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Materials and Methods

The area postrema was destroyed electrolytically under direct vision in adult male mongrel dogs. Anesthesia was induced with pentobarbital sodium administered intravenously. Exposure of the region was obtained by performing a suboccipital craniectomy, opening the dura and elevating the cerebellum. A 2 milliamperc direct current was delivered to the area by an electrode which was moved over its surface for approximately 2 minutes. In another group of dogs the area postrema was exposed as described above, but no current was applied to the region. A third group of 6 dogs was subjected to craniectomy and the dura opened without tearing the posterior medullary velum. The results obtained in these groups of animals were compared to results obtained in comparable normal dogs. Postoperatively, they were maintained on a commercial dog food for at least 3 weeks before studies were performed. At the end of the experiment, all animals that had had operations were autopsied (see below). The time between operation and autopsy depended on the particular tests performed in each dog. It was 106 to 126 days in 4 dogs, but 28 to 79 days in all others. There was no evidence that any of the physiological responses changed with time after the first 3 weeks.

Examination of the serially sectioned brains showed that tearing the posterior medullary velum was associated with moderate damage to the area postrema in some instances. For analysis of the data, therefore, the damage to the area postrema was graded by comparison with serial sections of the area in 2 normal dogs, and the dogs were divided into 3 groups: 1. Area postrema lesions: 16 dogs with 50% or more of the area postrema destroyed, weight 5.6 to 16.0 kg. 2. Control group 1: 8 dogs in which less than half the area postrema was destroyed, including all dogs in which the posterior medullary velum had been detached at operation, even though the area postrema seemed intact, weight 7.5 to 22.0 kg. 3. Control group 2: 6 dogs in which the posterior medullary velum had not been torn, weight 7.5 to 22.0 kg.

The following studies were performed in these groups of animals:

A. Electrolyte and water metabolism on normal salt intake. 8 dogs with the lesions of the area postrema and 5 control group 1 dogs were fed a diet containing 40 mEq. of sodium and 8 mEq. of potassium per day for 2 days. Two 24-hour urine specimens were obtained and blood samples were drawn at the beginning and end of the 48-hour period. The details of making up the diet with Lonalac* and the handling of the specimens have been published previously (Daily and Ganong, 1958). From these specimens the sodium, potassium and water excretion per 24 hours were calculated and the serum sodium and potassium levels determined. 15 normal dogs were similarly studied.

B. Response to salt loading (conscious dog). 8 dogs with lesions of the area postrema, 5 control group 1 dogs and 15 normal dogs were given 2 ml./kg. of 15% sodium chloride (5.13 mEq./kg. of sodium) intravenously. This procedure was carried out after 2 days on the 40 mEq. sodium diet. The dogs' bladders were emptied before the injection and urine samples were obtained 3 hours later. Blood samples were collected before and 3 hours after injection. After these specimens had been obtained, the dogs were fed the daily amount of the diet and the study terminated with another urine and blood sample at the end of the 24-hour period. Determination of the sodium and potassium content of these specimens permitted

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* Ken-L-Ration, Quaker Oats Company, Chicago, Illinois, USA.
** Mead Johnson and Company, Evansville, Indiana, USA.