# RECEPTORS OF THE OSMOREGULATING REFLEX

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One of the least-investigated mechanisms of osmoregulation is that concerning receptors which react specifically to changes in the concentration of osmotically active substances in the body fluids. Apart from several communications in which administration of hypertonic solutions was monitored by reactions of the organism not connected directly with osmoregulation [1, 2] the number of references to specific reception is extremely limited.

E. Verney [3] elicited the appropriate reflex by introduction of hypertonic solutions into the carotid artery exteriorized in a skin flap. He puts forward the suggestion that the antidiuretic reflex arises as the result of stimulation of osmoreceptors situated along the course of the internal carotid artery in the hypothalamic area and describes special histologic structures in the shape of microscopic vesicles, which, in his opinion, decrease in volume when osmotic pressure rises and increase in volume when it falls. E. Verney denies categorically the existence of osmoreceptors in other parts of the body.

However, the possibility is not excluded that osmoreceptors are extensively represented in the body along lines similar to those which apply to baro- and chemoreceptors.

The present work is concerned with an attempt to study this question.

## EXPERIMENTAL METHOD

Changes in diuresis were studied in dogs after injection of hypertonic solutions into the carotid artery exteriorized in a skin flap. Permanent ureter fistulas were made by the Pavlov-Orbeli method. The stimulating agent was NaCl solution in concentrations of 2.5-3% which was injected in 2-3 ml doses intra-arterially in a cephalad direction.

## EXPERIMENTAL RESULTS

Intra-arterial administration of hypertonic solution against the background of spontaneous diuresis not exceeding 5 ml/min per 1 $m^2$ body surface always caused its inhibition. The latter developed in the course of 10-20 minutes, sometimes reaching complete anuria. The amount of urine then began to increase, approaching the initial level (Figure 1).

This effect took place only when the hypertonic solution was injected intra-arterially. Injection of the same amount of the same solution intravenously either produced no effect at all or caused a slight increase of diuresis. Deafferentation of the carotid sinus zone did not affect the antidiuretic effect elicited by administration of hypertonic solution and, therefore, showed that this reflex was not connected with the chemoreceptors of the carotid body.

We thus confirmed E. Verney's data concerning the presence of osmoreceptors in the hypothalamic vessels.

However, inhibition of diuresis on intracarotid injection of hypertonic solution occurred consistently only

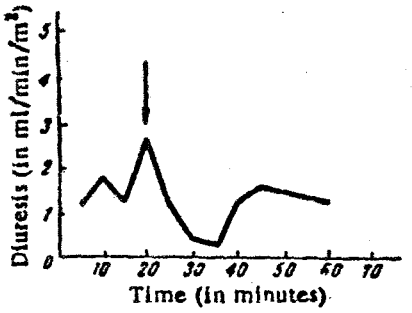


Fig. 1. Effect of intracarotic injection of hypertonic NaCl solution on spontaneous diuresis. Arrow indicates injection of 3% NaCl.

against the background of diuresis not exceeding 5 ml/min per 1 $m^2$ body surface. Injection of hypertonic NaCl solution against the background of massive or rising diuresis never elicited its inhibition. The absence of inhibition under these conditions is as consistent as its presence under conditions described above.

Figure 2 shows introduction of water (50 ml per 1 kg body weight) into the stomach, followed by growing diuresis. An intracarotid injection of 3% solution of common salt was made on the 45th minute when the diuresis had reached considerable proportions. As can be seen from Figure 2 no inhibition of diuresis occurred. Subsequently, when the excess water had been largely eliminated from the body, injection of hypertonic solution produced the usual inhibition of diuresis.

Inhibition of diuresis thus arises only at a certain level of diuresis. We suggest that this speaks in favor of extensive distribution of osmoregulators in various organs.

The phenomena observed by us are based on competitive relations between conditions created by hydration and the intra-arterial administration of hypertonic solution. Under ordinary conditions of water balance intra-arterial administration of a small amount of 3% NaCl solution proves to be adequate to ensure that "local" increase in osmotic pressure in the area supplied by the carotid artery elicits a reflex reaction, mediated by the nuclei of the hypothalamic region, from the neurohypophysis. Under conditions of water-loading the osmotic pressure of the internal medium of the body is reduced and hyperhydration of the tissues results. All the osmoreceptors in the body send afferent impulses towards the center which inhibit secretion of the antidiuretic hormone.

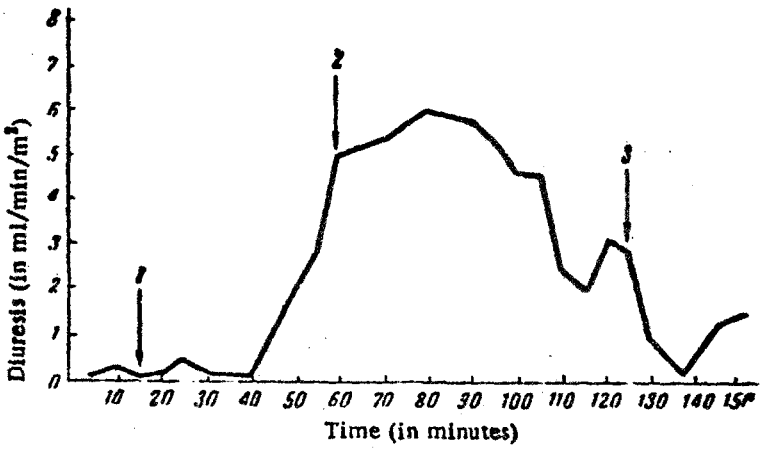


Fig. 2. Effect of injection of hypertonic NaCl solution into the common carotid artery against the background of developing water diuresis. 1) Introduction of water into the stomach; 2) administration of hypertonic solution during increasing diuresis; 3) intracarotid injection of hypertonic solution against the background of declining diuresis.

The absence of inhibition of diuresis on intracarotid injection of hypertonic solution under conditions of water-loading seen from this viewpoint can be explained as the result of predominance of reflexes from the main mass of tissue receptors over the "hypertonic" reflex from the Verney osmoreceptive zone.

In order to verify this hypothesis a series of experiments were performed on dogs in whom the main mass of interoceptors was isolated from the hypothalamic region by transection of the spinal cord. The results of this series are demonstrated in the curve of Figure 3.

Following spinal cord transection at the level of T-7 and T-8, injection of concentrated solution produced

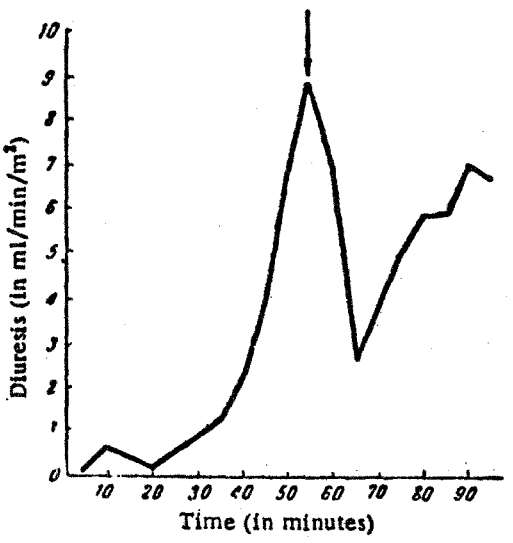


Fig. 3. Antidiuretic reaction elicited by intracarotid injection of hypertonic solution in dog with transected spinal cord. Arrow marks injection of 3% NaCl.

profound inhibition of diuresis against the background of copious urinary secretion which develops very rarely after transection of the spinal cord. In the experiment under consideration the rate of urinary excretion at the moment of injection of the hypertonic solution was 8.6 ml per 1 minute per 1 $m^2$ body surface; 10 minutes later the amount of urine fell to 2.4 ml.

Antidiuretic effect against the background of copious diuresis is more pronounced the higher the cord transection. Evidently this is determined by the fact that impairment of reflex connections between the cerebral centers and the main mass of receptors in the body is associated with assumption of a dominant role by the internal carotid artery osmoreceptive zone in the regulation of salt-water balance.

The material presented provides a basis for postulating that osmoreceptors are represented not only in the sensory formations discovered by E. Verney in the hypothalamus but are a very widely distributed type of interoreceptors in the internal organs. Osmoregulation is thus achieved reflexly as the result of the influence of afferent impulses reaching the neurohypophysis from all osmoreceptors of the body via the nuclei of the hypothalamic region.

## SUMMARY

In opposition to E. Verney's (1947) viewpoint that there is a narrow localization of osmoreceptors along a carotis interna in the hypothalamic area, the author assumes that there is a widespread distribution of receptors sensitive to variations of osmotic pressure. This assumption is based on the fact that the antidiuretic reflex, regularly repeated after intracarotid injection of 3% NaCl solution against the background of spontaneous diuresis is absent when urinary excretion is over 5 ml a minute per 1 $m^2$ of the body surface. The fact of the wide distribution of osmoreceptors is confirmed by experiments on animals with divided spinal cord in which the depression of the diuretic activity of the kidneys described above occurs with any diuresis.

## LITERATURE CITED

[1] E.A. Borshvskaia, The Physiologic Mechanisms of Thirst,* Thesis (Leningrad, 1945).

[2] K.M. Bykov, in the book: Material Concerning Physiology of Receptors* (Moscow, 1948), pp. 7-15.

[3] E. Verney, Proc. Roy. Soc. 135, 25-106 (London, 1947).

*In Russian.