calculated in seconds or tens of seconds the artery dilates as a result of a decrease in tone of its smooth muscles and it maintains its increased diameter as long as the blood flow in it is increased. If this increase of blood flow is maintained for a short time only, when the velocity of the blood flow falls to its initial level the diameter returns to its initial value. If the blood flow cannot return to its initial level (the presence of a chronic shunt), structural changes aimed at a lasting increase in caliber of the vessel take place in the arterial wall.

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RESPONSES OF OXYTOCINERGIC AND VASOPRESSINERGIC CELLS OF THE SUPRAOPTIC AND PARAVENTRICULAR NUCLEI OF THE RAT HYPOTHALAMUS TO REPEATED INJECTIONS OF THYROTROPHIN RELEASING HORMONE

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It has been conclusively demonstrated by immunohistochemistry that cells containing and, probably, producing thyrotrophin releasing hormone (TRH) are located in the region of the paraventricular nucleus (PVN) of the hypothalamus [10]. However, the location of these cells does not coincide with that of the main mass of Gomori-positive neurosecretory cells of PVN, whose participation in regulation of thyroid function is indicated by much, although indirect, experimental evidence [1-4]. There is also information on the direct influence of vasopressin and oxytocin on release of thyroid-stimulating hormone (TSH) by cells of the adenohypophysis [8, 11]. However, the source of the vasopressin and oxytocin in the brain may not necessarily be confined to PVN and the supraoptic nucleus (SON) of the hypothalamus [3, 5, 7]. The problem of the role of the oxytocinergic and vasopressinergic cells (OE and VE cells, respectively), of these nuclei in the regulation of thyroid gland function has not been resolved. The view is still held that OE and VE cells respond differently to the same influence, although this has not been verified experimentally. This view was confirmed by investigations which demonstrated the opposite neurotrophic effects of vasopressin and oxytocin [15]. Aside from experiments with disturbance of water metabolism [7], there have been few studies of the response of OE or VE cells [12, 14]. The writer is unaware of any investigations in which the state of the OE and VE cells was analyzed simultaneously under experimental conditions. No such investigations likewise have been undertaken when thyroid function was disturbed.

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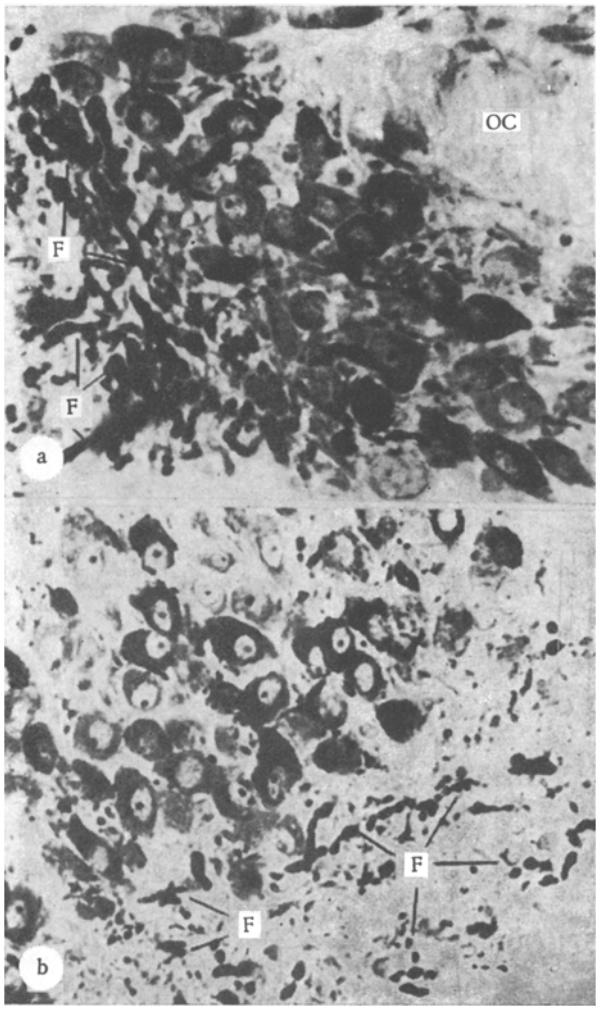

Fig. 1. Rat SON. a) Control: many fibers of supraoptico-hypophyseal tract filled with vasopressin-immunoreactive material; b) 9th day of experiment, number of fibers filled with vasopressin-immunoreactive material reduced. OC) Optic chiasma, F) fibers. Reaction with antiserum against vasopressin, counterstaining with hematoxylin. 150×.

TABLE 1. Dimensions of VE and OE Cells of SON and PVN of Hypothalamus after Repeated Injections of TRH (in μ^2)

Conditions of measurement	SON			PVN		
	cytoplasm	nucleus	nucleolus	cytoplasm	nucleus	nucleolus
			VE cells			
Control	57,6 (5)	18,0 (5)	1,45 (5)	61,7 (5)	22,3 (5)	1,35 (5)
Experiment	55,0 (3)	19,5 (3)	1,08 (4)	63,0 (5)	21,9 (5)	1,26 (5)
	4	4	0	9	11	7
	>0,05	>0,05	<0,01	>0,05	>0,05	>0,05
			OE cells			
Control	51,1 (6)	17,4 (6)	1,34 (6)	55,0 (6)	20,2 (6)	1,24 (6)
Experiment	48,7 (4)	17,5 (4)	1,1 (4)	53,5 (4)	20,4 (4)	1,49 (4)
	4,5	11	0	10,5	13	0
	>0,05	>0,05	<0,01	>0,05	>0,05	<0,01

Legend. Number of animals shown in parentheses.

In the investigation described below the response of OE and VE cells of SON and PVN of the rat hypothalamus to repeated injections of TRH was studied.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-240 g received an intramuscular injection of 1 μg synthetic TRH, dissolved in 1 ml of physiological saline, twice a day. Control animals received injections of physiological saline only. On the 9th day of the experiment, 17 h after the last injection, the animals were decapitated. The brain and thyroid gland were fixed with a mixture of picric acid and formalin in the ratio of 3:5 at 37°C for 7 days [6]. OE and VE cells of SON and PVN were revealed in frontal brain sections by the peroxidase-antiperoxidase (PAP) method, with the aid of antisera against vasopressin and oxytocin. The functional state of the cells was assessed from the dimensions of the nucleoli, a change in which is one of the most sensitive parameters of the intensity of RNA synthesis in the cell [9]. The area of cross-section of the perikaryon and of the cell nucleus also was measured. Morphometry was carried out by a photographic method with original magnification of 600. The thyroxine, triiodothyronine, and TSH levels in the rats' blood plasma were determined by radioimmunoassay. The state of the thyroid gland also was assessed according to the height of the thyrocytes. The significance of differences between the data was determined by Wilcoxon's nonparametric U test.

EXPERIMENTAL RESULTS

By the 9th day of the experiment a decrease in the number of fibers filled with vasopressin-positive and oxytocin-positive material was reduced in SON (Fig. 1). The content of neurohormones in the cytoplasm of SON cells was less distinctly changed, but pycnomorphic and darkly stained cells were more frequently found. The size of the nucleoli was significantly reduced in both VE and OE cells of SON (Table 1). Changes in the state of SON described above suggest a decrease in the intensity of synthesis of neurohormones and of their transport along the fibers.

No changes were found in the state of the VE cells or their fibers in PVN. The dimensions of the perikarya and nuclei of the OE cells of PVN were unchanged, but their nucleoli were significantly enlarged (Table 1), evidence of activation of secretion formation in these cells.

Radioimmunoassay of the blood plasma showed that by the 6th day of the experiment the TSH level was significantly raised (up to 240% compared with the control, $P < 0.01$) and it remained a little raised (110%) until the 9th day, whereas the thyroid hormone levels were lowered, both on the 6th day (tri-iodothyronine 85%, $P < 0.05$; thyroxine 85%, $P > 0.05$), and on the 9th day of the experiment (tri-iodothyronine 94%, $P > 0.05$; thyroxine 90%, $P < 0.05$; height of thyrocytes 83.7%, $P < 0.05$). A similar disparity between the TSH and thyroid hormone levels during repetitive stimulation with TSH has been described many times in the literature [13].

In the present experiments changes in OE and VE cells of SON could be identical in direction, whereas in PVN the changes in these cells were different. The reaction both OE and VE cells of SON differed from the reaction of the corresponding cells of PVN. However, the problem of whether this type of response of SON and PVN cells remains the same under all conditions still awaits investigation.

Under the present experimental conditions, when injection of TRH induced marked changes in the blood hormone levels, the difference in the response of OE and VE cells of one nucleus and the corresponding cells of the other nucleus can be explained either by unequal ability of the homonymous cells of SON and PVN to receive the same hormones, or by a difference in afferentation of the OE and VE cells of SON from that of the corresponding cells of PVN. Whereas the first hypothesis arouses fundamental misgivings, the second seems to be more likely to be correct, for a difference in the afferent innervation of SON and PVN has been demonstrated frequently [15], and our own observations show precisely that OE and VE cells of SON differ in their regulation from the corresponding cells of PVN. Furthermore, the difference in response between OE and VE cells of PVN is evidence of different afferentation of these cells within PVN itself. This hypothesis is in agreement with the results of investigations [15] showing differences in the innervation of the parvocellular and gigantocellular parts of PVN.

Depression of activity of OE and VE cells of SON after repeated injection of TRH can perhaps be explained by the nonspecific action of TRH as a neuromodulator [16] on centers regulating activity of SON, for even after a single injection of TRH the response of SON and of some parvocellular hypothalamic centers was of the same character [2]. As regards OE cells of PVN, taking account of data indicating that oxytocin reduces TSH secretion induced by injection of TRH [8], activity of OE cells of PVN in the present experiment can be interpreted as a reaction aimed at normalizing the TSH level. This hypothesis is confirmed by the decrease in the blood TSH level by the 9th day of the experiment, despite repeated injections of TRH. It can thus be tentatively suggested that it is the OE cells of PVN that participate in regulation of the TSH level.

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