AN ELECTROPHYSIOLOGICAL INVESTIGATION INTO THE AFFERENT CONNECTIONS OF THE THYROID GLAND WITH THE CENTRAL NERVOUS SYSTEM

N. A. Adamovich

From the Laboratory of Electrophysiology (Head – V. E. Delov) of the I. P. Pavlov Institute of Physiology (Director – Academician K. M. Bykov) of the Academy of Sciences of the USSR, Leningrad

(Received December 11, 1957. Presented by Academician K. M. Bykov)

The question of the afferent connections of the thyroid gland with the central nervous system has so far received little attention. In morphological papers are described various forms of receptor endings both in the parenchyma of the gland and in the walls of the blood vessels [1, 4, 5, 7, 8, 9 and others]. However their functional importance in the activity of the thyroid gland has not yet been explained.

The purpose of the present investigation was to establish by an electrophysiological method the presence of afferent impulsation from the receptors of the thyroid gland during the action of various agents on this organ.

Electrophysiological data in respect of afferent signals from the receptors of the thyroid gland are not available, with the exception of a brief reference in the paper by Andrew [6]. This author observed an outburst of impulses in the superior laryngeal nerve during mechanical stimulation of the thyroid gland. On the basis of this observation he put forward the view that mechanoreceptors were present in the thyroid gland.

EXPERIMENTAL METHOD

Experiments were carried out on 90 adult cats weighing from 2.5 to 5 kg. An intramuscular injection of a solution of sodium amytal in a dose of 70-80 mg/kg body weight was given to each animal. A longitudinal skin incision was made in the neck. The thyroid gland was exposed by retraction of the sternothyroid, sternohyoid and cricothyroid muscles to the side. The topography of the thyroid nerve was very variable and in some cases it could not be found. For taking a lead of the afferent impulses the nerve branch which was isolated along the course of the thyroid artery was usually utilized. This branch was divided at the point where the thyroid artery emerged from the carotid. The peripheral end of the branch was seized in a ligature and laid on silver electrodes, the distance between the electrodes being 3-4 mm. The potentials of the afferent impulses were passed through an amplifier to a cathode ray oscillograph. The frequency characteristic curve of the amplifier was rectilinear between 10 and 1500 cps.

EXPERIMENTAL RESULTS

In the majority of the experiments with no form of action on the thyroid gland afferent impulses were not present in the thyroid nerves (Fig. 1, a, e). In a series of experiments the impulses took the form of irregular rapid oscillations with an amplitude of 5 to 50 μv (Fig. 1, c, g). During local warming of the thyroid gland by application of cotton wool soaked in warm (about 40°C) physiological saline, in all the experiments afferent impulses were found to appear, or those already in existence were strengthened (Fig. 1, b, d, f). The stream of impulses lasted until the cotton wool became cool. In some of the experiments grouping of impulses to the rhythm of the pulse beats was sometimes observed in response to warming the gland, which may indicate some connection between these impulses and the vascular receptors. Each group consisted of 2-8 separate

oscillations (Fig. 1, h). During warming of the thyroid gland, in addition to relatively rapid variations in the potential, impulses were observed which were characterized by slower oscillations in the form of biphasic waves with an amplitude of 10 to 20 μ v, in single phases (Fig. 1, f). Potentials of this type were found earlier in impulses from receptors lying in the walls of the intestine [3] and the stomach [2].

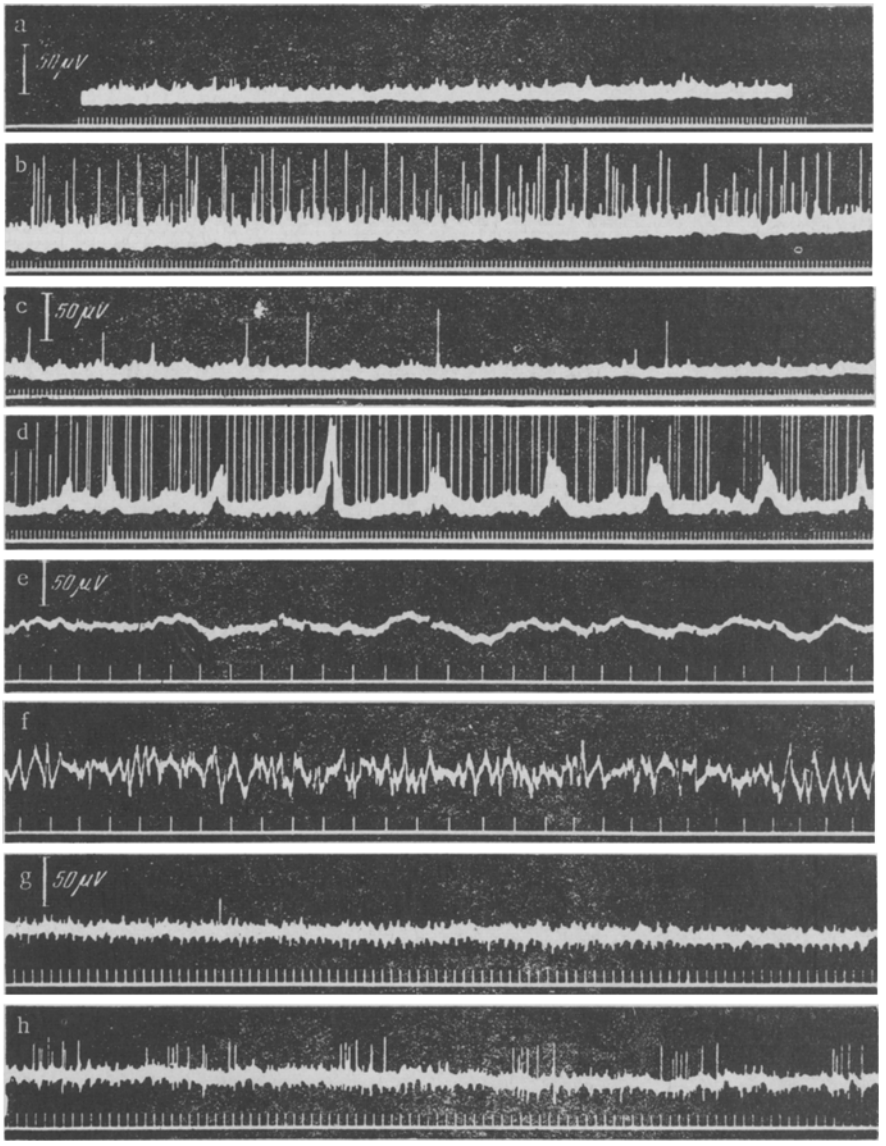

Fig. 1. Electrical activity in the peripheral end of the thyroid nerve before and during warming of the thyroid gland. a, c, e, g) Before warming; b, d, f, h) during warming of the gland. In this and all subsequent illustrations the time marker records 0.02 seconds.

In the next series of experiments the action of a series of drugs which alter the state of the blood supply to the thyroid gland was studied – a 10% solution of caffeine, histamine in a dilution of $1 \cdot 10^{-5}$ and adrenalin in a dilution of $1 \cdot 10^{-4}$. These solutions were injected into the thyroid artery in the course of the blood flow in a volume of 0.5 - 1 ml. In order to prolong the action of the agent on the receptors of the gland during injection of the solution, the blood flow in the thyroid gland was artifically slowed by means of partial ligation of the carotid artery above the origin from it of the thyroid artery.

During injection of a 10% solution of caffeine into the thyroid artery, afferent impulses arose every time even though they had previously been absent. The maximum intensity of this impulsation was reached on the 2nd-3rd minute after injection of caffeine, when reddening of the gland was observed in consequence of vasodilatation. In Fig. 2, a before injection of caffeine complete absence of afferent impulses was observed. Forty-five seconds after injection of 0.5 ml of a 10% solution of caffeine isolated potentials were observed with an amplitude of 100 μ v. Two minutes after the injection of caffeine the frequency of the potentials was considerably increased (Fig. 2,b). This effect of increase in afferent impulsation in the nerves of the gland was observed for a period of 8-10 minutes after injection of caffeine.

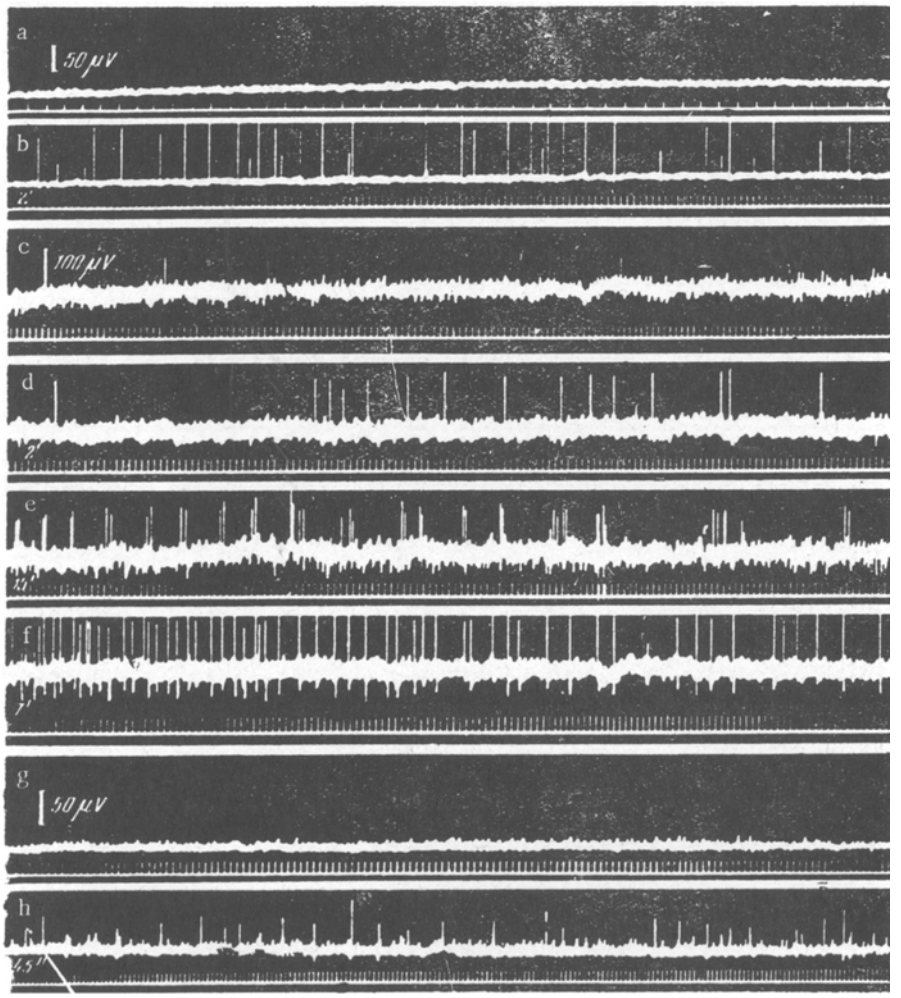

Fig. 2. Electrical activity in the peripheral end of the thyroid nerve before and after injection of caffeine, histamine and adrenalin into the thyroid artery. a) Before injection of caffeine; b) 2 minutes after injection of caffeine; c) before injection of histamine; d) 2 minutes after injection of histamine; e) 15 minutes after injection of histamine; f) 7 minutes after a second injection of histamine; g) before injection of adrenalin; h) 45 seconds after injection of adrenalin.

During injection of histamine also the amplitude and frequency of the potentials were increased.

Whereas before injection of histamine (Fig. 2, c) single oscillations with an amplitude of 25-30 μ v were rarely observed, after injection into the blood stream of 0.06 ml of histamine in a dilution of $1 \cdot 10^{-5}$ both the frequency and the amplitude of the potentials rose (Fig. 2, d). They were sometimes found to be grouped together in the rhythm of the contractions of the heart. The effect of intensification of the impulses was more

prolonged than with injection of caffeine, and it could be registered even 15 minutes after the injection of histamine (Fig. 2, e). A futher injection of histamine into the thyroid artery was again accompanied by increase in the frequency of the impulses (Fig. 2, f).

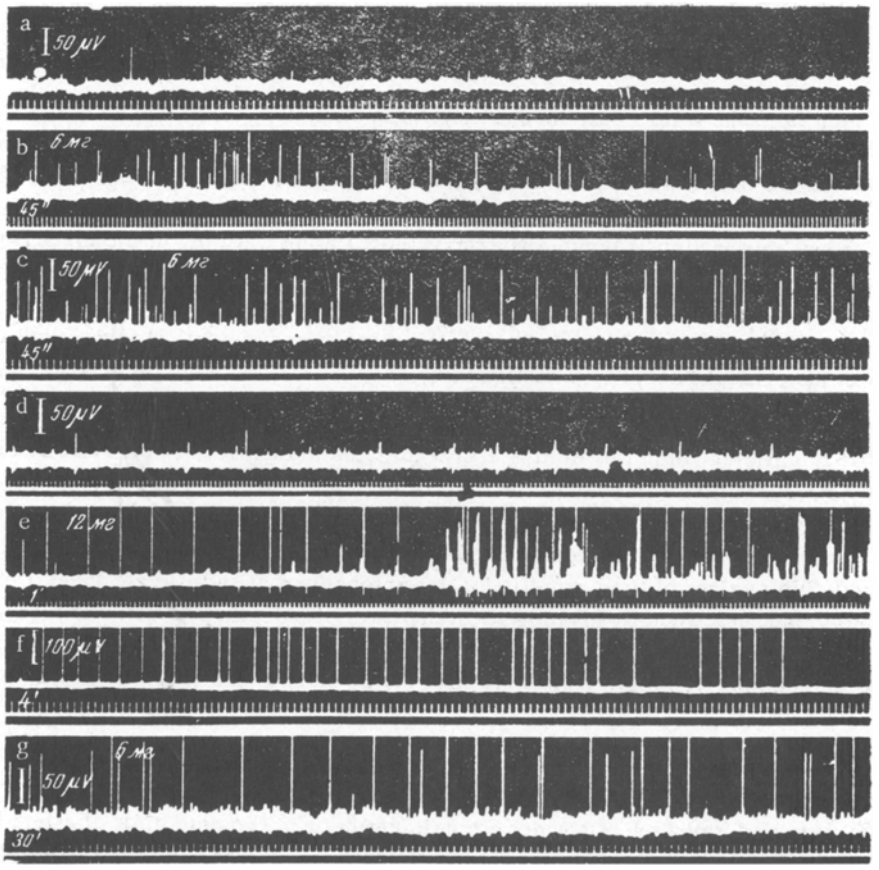

Fig. 3. Electrical activity in the peripheral end of the thyroid nerve before and after injection of thyrotropic hormone into the thyroid artery. a) Impulses before injection of the hormone; b) 45 seconds after the injection of 6 mg of thyrotropic hormone; c) 45 seconds after a second injection of the hormone in a dose of 6 mg; d) before injection of hormone; e) 1 minute after injection of 12 mg of the hormone; f) 4 minutes after the same injection with a reduction of the amplification by one half; g) impulses 30 minutes after injection of the hormone.

The action of adrenalin was considerably weaker than those of caffeine and histamine. Forty-five seconds after injection of 0.5 ml of adrenalin in a concentration of 10^{-4} into the thyroid artery a brief appearance of afferent impulses, previously absent, was observed (Fig. 2, h, g). After the injection of adrenalin a less frequent and less regular rhythm of impulses was noted in the thyroid nerve than under the influence of caffeine and histamine. From $1\frac{1}{2}$ – 2 minutes after the injection of adrenalin the impulses completely ceased.

In the next series of experiments the influence of a solution of thyrotropic hormone in 0.7% saline was studied. In all the experiments in which thyrotropic hormone was injected, the appearance of afferent impulses or the intensification of previously existing impulses before the action of the hormone was observed in the thyroid nerve. After injection of 6 mg of hormone an increase in the frequency of the potentials always took place and was accompanied by an increase in their amplitude (Fig. 3, a, b). This effect was observed for a period of 3-4 minutes. A futher injection of 6 mg of the hormone caused a more appreciable increase in the frequency of the impulses (Fig. 3, c) and the appearance of new oscillations, whose amplitude reached 200-220 μ v. The appearance of oscillations of this form was observed during repeated injection of thyrotropic

hormone or by increasing its dose to 12 mg. Thus in Fig. 3, d may be seen predominance of potentials with an amplitude of 25-30 μ v. One minute after injection of 12 mg of thyrotropic hormone into the thyroid artery oscillations of such a high amplitude were seen that their apices were cut off (Fig. 3, e). When the degree of amplification was reduced by half, it could be seen that their amplitude reached 200-220 μ v (Fig. 3, f).

If the time of action of the hormone on the receptors of the gland is prolonged by delaying its passage into the general circulation by means of partial clamping of the veins of the thyroid gland, the effect of intensification (increase of frequency and of amplitude) of the afferent impulsation can be observed to last for 30 minutes after the injection of 6 mg of thyrotropic hormone (Fig. 3, g). Without clamping of the veins the impulses after injection of 6 mg of the hormone returned to their original level after 4-5 minutes.

As may be seen from the results described, afferent impulses from the receptors of the thyroid gland were frequently absent before the action of certain agents. Such impulses always appeared, however, when the gland was warmed. This feature may suggest that during an acute experiment the thyroid gland was subjected to cooling, as a result of which the metabolic rate was diminished, the vessels were constricted and the functional state of the receptors of this particular organ was aggravated. During warming of the gland, not only was there local dilatation of the vessels and increase in the blood flow, but the metabolic processes in the tissues were speeded up. In consequence of this there was an increase in the excitation of the receptors of the organ, leading to a greater synchrony of their action (see Fig. 1). Increased synchronization of the work of the receptors during warming was also brought about by intensification of the variations in pulse pressure, which act as a natural stimulus for the vascular receptors.

The fact that the afferent impulses from the thyroid gland mainly reflect the state of its blood vessels is demonstrated by our experiments in which injections of caffeine, histamine and adrenalin were given. In the experiments where thyrotropic hormone was injected we observed in addition to an increase in the frequency of the potentials of the relatively rapid afferent impulses, the appearance also of specific potentials characterized by extremely high values of their amplitude. It is probable that in this case special receptors situated in the tissues of the gland, described by histologists in the form of bulb-shaped formations [8], are subjected to stimulation. However it is not impossible that there is an increase in amplitude on account of the synchronization of action of the receptors which are connected with the activity of the vascular apparatus of the thyroid gland.

SUMMARY

Experiments were performed on cats under amytal anesthesia. The potentials of afferent impulses due to various actions upon the thyroid gland, were registered in the nerve supplying the thyroid gland. Three types of afferent impulse potentials were revealed: relatively slow low voltage oscillations (in heating the gland), quick oscillations with the amplitude from 10 to 100 μ v (in heating the gland) and in injection of substances into the thyroid artery (caffeine, histamine, adrenalin, and thyrotropic hormone), and quick oscillations with the amplitude of 200-220 μ v in introduction of thyrotropic hormone into the thyroid artery.

LITERATURE CITED

[1] V. I. Akimov, Collected Transactions of the Clinic of the Surgical Faculty of Lvov Medical Institute,* pp. 149-156, Lvov, 1947.

[2] V. E. Delov, O. N. Zamiatina and P. A. Kiselev, Scientific Conference on the Physiology and Pathology of Digestion* Transactions. pp. 67-69, Tartu, 1957.

[3] O. N. Zamiatina, Fiziol. Zhur. SSSR 43, 5, 441-448 (1957).

[4] R. Maiman-Pines, Sovet. Nevropatol. Psikhiatr. i Psikholog. 2, 8-9, 85-90 (1933).

[5] E. I. Tarakanov, Problemy Endokrinol. i Gormonoterap. 5, 75-84 (1955).

[6] B. L. Andrew, J. Physiol. 1956, v. 133, pp. 420-432.

[7] J. F. Nonidez, Am. J. Anat. 1935, v. 57, p. 135-169.

[8] L. Pines, Ztschr. ges. Neurol. u. Psychiatr. 1929, Bd. 118, S. 552-561.

[9] N. A. Popow, Ztschr. ges. Neurol. u. Psychiatr. 1927, Bd. 110, S. 383-397; 1928, Bd. 115, S. 131-157.

*In Russian.