THE INFLUENCE OF EFFERENT NERVES TO THE THYROID GLAND ON THYROID FUNCTION

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 50, No. 10, pp. 3-7, October, 1960
Original article submitted December 31, 1959

Published data concerning the importance of the innervation of the thyroid gland for its function are contradictory. Recently, however, more and more investigators have come to the conclusion that the efferent nerves to the thyroid gland are vasomotor, and have no direct secretory function [3, 4, 5].

In view of these data, we were interested in finding out how the thyroid gland, when it is deprived of its nervous connections, functions under conditions of so-called emotional excitation.

Our premise was that if the nervous component in the transmission of cortical impulses to the periphery is of substantial physiological significance, the secretory activity of the denervated gland under these conditions ought to differ radically from the normal.

EXPERIMENTAL METHODS

Eight dogs with denervated thyroids were used in these experiments. The controls were three unoperated animals. The thyroid glands were denervated in the standard way. All the nerve branches from the superior laryngeal nerve, the superior cervical ganglion, and the recurrent nerve to the thyroid gland were excised over a length of 1-2 cm. The blood vessels supplying the thyroid were carefully painted (until they turned white) with 5% phenol. Experiments were performed on these animals 1-4 weeks after the operation. The level of radioiodine (I^{131}) in the thyroid was taken as the indicator of its functional state. We shall not describe in detail the method used for determing radioiodine in the thyroid gland in the whole animal while the latter is working in the conditioned reflex chamber, since we have set forth this method in earlier publications [1, 2].

The functional state of the central nervous system was altered by the presentation of conditioned defense stimuli. Conditioned reflexes were developed to the sound of a metronome at 120 beats per minute. The unconditioned stimulus was an electrical current from an inductorium. The conditioned stimulus was given at five-minute intervals, ten times in each experimental session. The conditioned stimulus was applied alone for 20 sec each time. I^{131}, 0.7 μC/kg, was given by mouth, with milk. The experiments were performed 72 hr after the administration of I^{131}. Thyroid gland radioactivity was determined after each conditioned stimulus and for four hours after the last conditioned stimulus was applied.

EXPERIMENTAL RESULTS

The reactions of normal and denervated thyroid glands to conditioned defense stimuli were studied. The experiments showed that these stimuli elicit the release of hormones from both innervated and denervated thyroids. As may be seen from the data shown in Table 1, in all the experiments we found a sizable drop in the I^{131} level in the denervated thyroid gland. These experiments give evidence that thyroid glands deprived of their nervous connections lose none of their capacity to react to impulses originating in the central nervous system. It can not be said, however, that the reactions of denervated glands are in no way different from those of normal glands. We noted several characteristic features in the reactions of glands deprived of their innervation.

First, the reactions of denervated glands were of greater amplitude than those of intact glands. As is apparent from the figure, denervated thyroids reacted to defense-conditioned stimuli with a marked reduction in the level of radioactivity. At the same time, these reactions were distinguished by their low mobility, in that they displayed very slight variations in the level of radioactivity during the course of an experiment.

Secondly, the reactions of denervated thyroids lasted longer than those of normal glands. It was observed that the level of radioactivity of the denervated gland, after a 44.4% reduction at the outset of an experiment, thereupon remains constant throughout the entire experiment (4-5 hr), showing only slight variations in one direction or another. The reactions of normal thyroids

TABLE 1. Effect of Conditioned Defense Activity on Radioiodine Content in Dog Thyroid After Denervation*

Date of experiment, 1959	Radioactivity in intervals following individual conditioned stimuli — number of preceding conditioned stimulus										Radioactivity following conditioned stimulation — time (minutes)							
	1	2	3	4	5	6	7	8	9	10	15	45	75	105	135	165	195	225
Aug. 21	—24.1	—23.5	—29.9	—28.2	—26.9	—19.3	—23.4	—24.5	—24.9	—26.6	—27.3	—26.3	—27.1	—22.7	—20.3	—21.9	—22.4	—22.4
" 25	—39.3	—21.5	—36.4	—36.6	—32.9	—34.5	—35.4	—35.0	—36.7	—	—36.0	—35.5	—37.9	—36.2	—39.7	—36.7	—38.2	—34.5
" 27	—42.5	—41.9	—41.9	—40.9	—37.1	—40.5	—35.8	—38.1	—42.9	—37.7	—38.5	—30.6	—35.0	—33.8	—31.8	—35.8	—33.4	—33.8
" 22	—26.8	—22.5	—21.8	—15.6	—23.1	—21.8	—22.0	—21.4	—22.5	—24.2	—18.2	—21.2	—19.9	—20.7	—21.6	—20.3	—22.0	—21.4
" 24	—23.3	—26.9	—23.3	—30.5	—20.4	—33.2	—34.8	—39.5	—30.5	—34.8	—19.1	—33.2	—17.5	—36.8	—25.3	—27.3	—29.9	—29.9
" 26	—41.0	—45.7	—37.8	—35.1	—39.8	—46.1	—45.7	—39.0	—42.3	—44.5	—39.0	—43.0	—41.4	—42.3	—40.6	—44.1	—39.0	—35.1
Sept. 8	—32.9	—46.5	—38.9	—37.9	—39.2	—35.8	—39.4	—37.5	—33.4	—31.9	—41.7	—45.3	—40.6	—37.9	—41.1	—42.4	—37.0	—
" 10	—33.2	—32.4	—33.6	—30.8	—17.3	—18.3	—19.5	—26.4	—22.0	—	—24.3	—15.1	—12.7	—19.7	—15.9	— 8.2	—	—
" 12	—44.4	—43.5	—44.4	—45.3	—45.9	—42.3	—45.9	—43.7	—42.3	—47.2	—43.1	—41.2	—43.5	—44.4	—46.5	—46.0	—44.0	—44.4

*Results of experiments are expressed as percent of initial radioactivity.

TABLE 2. Effect of Conditioned Defense Activity on Radioiodine Content in Normal Dog Thyroid*

Date of experiment, 1959	Radioactivity in intervals following individual conditioned stimuli — number of preceding conditioned stimulus										Radioactivity following conditioned stimulation — time (minutes)						
	1	2	3	4	5	6	7	8	9	10	15	45	75	105	135	165	195
Sept. 9	—12.0	—18.0	— 9.8	—13.5	—10.7	— 7.2	— 2.3	— 4.8	— 8.5	— 3.9	— 3.9	— 4.8	— 5.7	— 3.9	— 3.2	—	—
" 11	—26.7	—21.8	—20.0	— 9.6	—14.7	—15.4	— 8.3	— 6.9	— 8.7	— 5.5	— 8.0	—10.5	— 9.1	—11.5	—12.6	— 9.8	—
" 16	—27.8	—26.6	—33.0	—27.8	—15.0	—22.5	—14.7	—20.5	—11.3	—21.2	— 7.4	— 8.9	— 9.8	—12.5	—16.8	—13.5	— 8.3
" 20	— 9.0	—11.7	— 9.5	— 7.4	—10.6	— 8.4	— 6.8	— 5.7	— 4.1	— 3.6	— 6.3	+ 2.9	— 5.7	— 5.7	— 4.1	— 9.0	— 7.9
" 22	— 9.0	—16.0	—17.1	—13.1	—11.9	—15.4	— 9.0	—10.2	—20.0	— 5.0	—28.7	—10.2	+ 0.2	— 2.7	— 2.7	— 3.2	— 3.8
" 24	—32.2	—22.3	—28.5	—28.3	—24.1	—28.5	—18.5	—24.1	—27.3	—12.9	—11.7	— 3.6	—11.0	— 1.7	— 5.8	— 5.8	—
Oct. 16	—20.9	—18.9	—25.4	—22.7	—30.1	—27.9	—30.0	—23.6	—28.4	—27.7	—32.7	—26.9	—30.4	—23.8	—32.2	—30.4	—29.3
" 19	— 8.8	— 5.8	— 2.8	— 5.8	— 8.3	— 8.3	— 5.3	— 9.8	— 9.8	—11.3	—16.9	—11.8	—11.3	—10.8	—14.4	—13.9	—14.9
" 19	— 3.6	+ 0.3	— 8.4	— 8.8	— 8.8	—15.7	—15.4	—18.8	—19.8	—	—15.7	—11.2	— 9.8	—12.6	+ 9.5	+ 7.0	+ 9.5
" 21	—17.8	—17.4	—20.0	—17.8	—20.4	—22.6	—20.7	—20.0	—22.6	—11.9	—23.8	—17.4	—14.1	—20.7	—17.1	—13.4	—11.1

*Results of experiments are expressed as percent of initial radioactivity.

were different; as a rule, their radioactivity level approached the normal physiological range by 1-2 hr after the end of conditioned stimulation, and only occasionally remained low for longer periods. Thus the experiments showed that the reactions of denervated glands differ from normal in having greater amplitudes and less lability.

With regard to the mechanism of this phenomenon, it should be observed that with the setup used in these experiments the question is complicated by the presence of the vasomotor innervation of the thyroid. Since there unquestionably exists an intimate relation between the gland's blood supply and its secretory activity, the change in the diameter of its vessels and the counsequent filling withblood after denervation of the gland must naturally affect the secretion process. And if we try to understand what it is in the reaction of the denervated gland that depends on the damage to the vasomotor fibers, it seems to us that, first and foremost, the inertness and extreme duration of the reaction must be attributed to this cause.

It is known that vasomotor reactions are especially pronounced in emotional excitation, and can not be without effect on organ activity. And in this case we may assume that the monotonous and drawn-out character of reactions observed after denervation is to be understood from this standpoint.

In the experiments on intact animals we often observed large variations in the level of radioactivity of the gland; we saw that during the course of an experiment the radioactivity of the gland first fell, then returned to the original level. This is well shown in the experiments of September 9, 11, 16, and 22, all of which are presented in Table 2. It is not impossible that these variations in thyroid activity during the defense reaction reflect the participation of vasomotor fibers. It is no coincidence that after denervation of the gland these variations almost completely disappeared.

The reactions of denervated glands, as we have indicated above, were more marked than those of intact glands. We felt that the cause of this phenomenon lies in the sensitization of denervated thyroid cells to epinephrine.

If this hypothesis is correct, then a reduction of the blood epinephrine concentration should cause a weakening of the reaction of denervated thyroids.

In order to limit the entrance of epinephrine into the blood, after denervating the thyroids we performed a second operation in which we completely removed the adrenal gland on one side and excised portions 1-2 cm long of the large and small splanchnic nerves, to eliminate reflex secretion of epinephrine.

As may be seen from the figure, under the influence of the conditioned defense stimuli the thyroid glands of these animals secrete less actively into the blood than do the glands of animals after the first operation. The figure shows that the maximum change in the radioactivity of the thyroid gland after the first operation is -47.2%, and in dogs after both operations it is only -18%. This fact confirms our hypothesis that the reaction of denervated thyroids seen in these experiments is the result of sensitization of the gland cells to epinephrine.

Our experiments showed that the efferent nerves to the thyroid gland ensure the completest possible adaptation of the gland to altered environmental conditions.

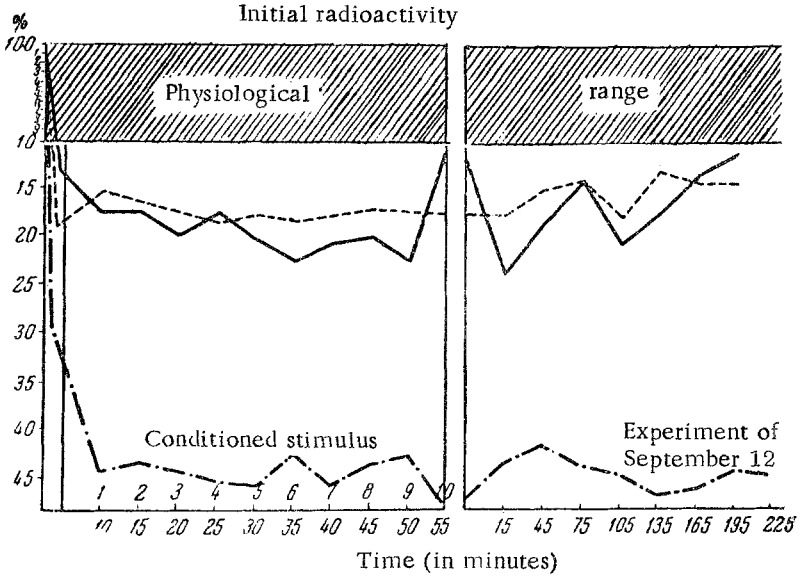

Figure. The effect of conditioned defense activity on radioiodine content in dog thyroid. —— normal; ---- after denervation on the thyroid gland and one adrenal, and extirpation of the other adrenal; —·—· after denervation of the thyroid gland.

SUMMARY

The author studied the reaction of the denervated thyroid gland to conditioned defense stimuli. The functional state of the gland was determined from changes in its content of radioactive iodine (I^{131}). Experiments on dogs with denervated thyroids showed that after denervation cortical influences still reach the thyroid gland. But the reaction of the denervated thyroid is different from that of the normal thyroid: it is more pronounced and more prolonged than normal.

Dogs subjected to a second operation-removal of one adrenal gland and denervation of the other-reacted in a manner suggesting that the response of denervated thyroids is due to sensitization of the gland cells to epinephrine, as well as to denervation of the blood vessels of the thyroid.

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