ANALYSIS OF THE ROLE OF THE AUTONOMIC NERVES OF THE THYROID GLAND IN ITS ACTIVITY

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M. G. Amiragova

Institute of Normal and Pathological Physiology of the AMN SSSR, Moscow
(Presented by Active Member AMN SSSR V. V. Parin)
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In a previous investigation [5] we showed that in normal conditions of activity of the organism the processes of formation and secretion of hormones in animals after denervation of the thyroid take place at the same intensity as before the operation. However, when increased demands are made on the thyroid, especially in the course of defensive conditioned-reflex activity, the denervated gland reacts to these influences by a more intensive and prolonged secretion than the intact thyroid.

The object of the present investigation was to examine the causes of the inadequate secretion of the denervated thyroid during changes in the functional state of the central nervous system.

EXPERIMENTAL METHOD

Experiments were conducted on 9 dogs. The functional state of the central nervous stystem in the animals was modified by the application of defensive conditioned stimuli. A positive conditioned reflex was produced to the sound of a metronome giving 120 beats per minute and an inhibitory conditioned reflex to the sound of a metronome giving 60 beats per minute. The unconditioned stimulus was an electric current from an induction coil. The conditioned stimuli were applied 10 times in an experiment at intervals of 5 min. The isolated action of the conditioned stimulus lasted 20 sec. The indicator of the functional state of the thyroid was its content of radioactive iodine (I^{131}), given to the animals by mouth with milk (0.5 μCi/kg) 72 h before the start of the experiment. The radioactivity of the thyroid was determined after the application of each conditioned stimulus and for a period of 4 h until the termination of its effect.

The method of investigation of radioiodine in animals during work in the conditioned reflex chamber has been described in our earlier papers [2, 3]. The thyroid glands were denervated in the usual manner. The animals were used in the experiment 1-4 weeks after the operation. Adrenalin (crystalline) and noradrenalin were injected intravenously in a dose of 10 μg/kg, and thyrotropic hormone intravenously in a dose of 25 i.u./kg body weight. These substances were given to intact dogs and to dogs after denervation of the thyroid.

At the end of the investigation the dogs were sacrificed and a histological analysis was made of the nervous apparatus of the thyroid by Kampos' method.

EXPERIMENTAL RESULTS

The excessively intensive and prolonged reaction of the denervated thyroid gland to defensive stimuli observed in our previous investigations [5] bore a great resemblance to the reactions of denervated structures. However, before the reaction of the denervated thyroid could be so classified, it was necessary to show that the gland, when deprived of its nerve supply, reacts to its natural chemical stimuli (adrenalin, noradrenalin, and thyrotropic hormone) more strongly than the intact gland. To examine this problem special investigations were carried out. Experiments showed that the level of radioactivity of the denervated thyroid changed after the injection of adrenalin by approximately the same degree as in the animals with the intact gland, although in the intact animals the reaction to adrenalin appeared more quickly—15 min after injection of the drug, compared with 30 min after injection in the animals with the denervated gland (Fig. 1, A). Clearly, therefore, the reaction of the denervated thyroid to adrenalin was essentially indistinguishable from the reaction of the intact glands.

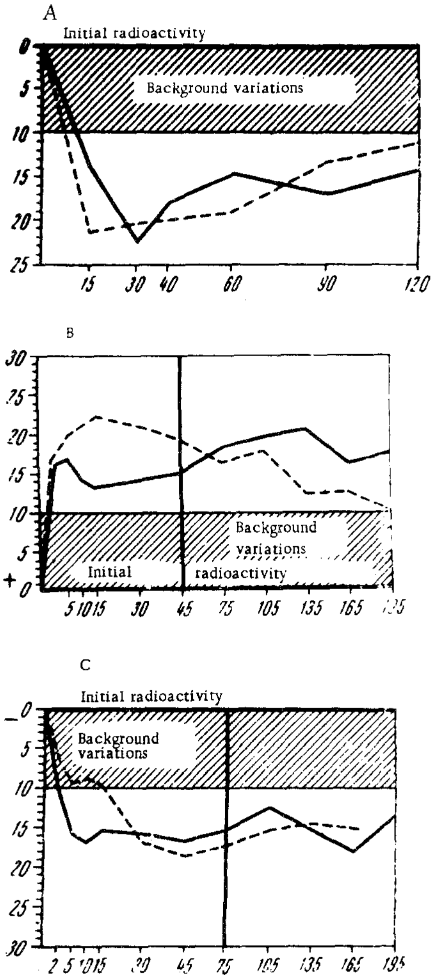

Fig. 1. Effect of adrenalin (A), noradrenalin (B), and thyrotropic hormone (C) on the secretion of the hormones of the intact and denervated gland. For A and B the broken line represents the radioactivity of the intact gland and the continuous line the radioactivity of the denervated thyroid. For C the broken line represents the radioactivity of the denervated gland and the continuous line the radioactivity of the intact gland. Along the axis of abscissas—time (in min) after injection of the radioisotope; along the axis of ordinates—changes in radioactivity (in % of initial level).

After injection of noradrenalin into the intact animals the radioactivity of the thyroid rose immediately and reached a maximum in 20 min, after which the content of radioiodine in the gland feel gradually and returned to its initial level after 3 h (Fig. 1, B).

The curve of radioactivity of the denervated thyroid was slightly different. The level of radioactivity of the gland rose immediately after the injection of noradrenalin, after 5 min it began to fall, and after 15 min it gradually rose again and reached its maximum only after 135 min; it then fell gradually, but did not reach its original level. In both cases the maximal effect was approximately the same.

The experiments in which noradrenalin was injected showed that the intact gland reacts to this substance in the same way as the denervated thyroid; in the latter case the maximal reaction takes slightly longer to develop than in the former.

After injection of thyrotropic hormone (Fig. 1, C) into the intact animals the radioactivity of the gland fell after 5 min; the maximal reaction developed at the 10th minute and, after a few fluctuations of the level of radioiodine in the gland, the reaction gradually approximated to the initial level. The reaction of the denervated gland was more even. The initial effect after injection of thyrotropic hormone appeared in 30 min and the maximal effect in 45 min, after which the curve of radioactivity gradually approximated to the initial level. Hence, as in the preceding investigations, the denervated gland reacted to the injected substances later than the normal gland. The intensity of the reaction was the same in both cases.

The results of these investigations are in agreement with corresponding data in the literature. It has been found, for example, that thyrotropic hormone acts on thyroid gland tissue independently of its sympathetic innervation, and the identical reaction of the denervated and intact thyroid gland to thyrotropic hormone has been demonstrated [7, 8, 10, 11]. Similar results have also been obtained in relation to the action of adrenalin [1, 9].

Hence, judging by the results of our experiments and by the data in the literature, the reaction of the denervated gland to adrenalin, noradrenalin, and thyrotropic hormone is indistinguishable from the reaction of the intact gland. This indicates that the thyroid gland is not one of those structures whose sensitivity is increased after denervation.

In this case, what physiological mechanisms are responsible for such an excessive reaction of the denervated gland to defensive stimuli? We know that processes of both stimulation and inhibition are concerned in the maintenance of equilibrium between the organism and the outside world, and that the process of inhibition determines the finest degrees of the relationship between organism and environment. If this view is adopted as the basis for the analysis of the present problem, it may be assumed that the secretion of the denervated gland, triggered off by stimuli from the central nervous system by means of humoral transmission links, subsequently continues autonomously, without any form of influence to determine its intensity and duration.

In order to test this hypothesis a special series of experiments was undertaken to investigate the effect of inhibitory stimuli on the function of the denervated thyroid.

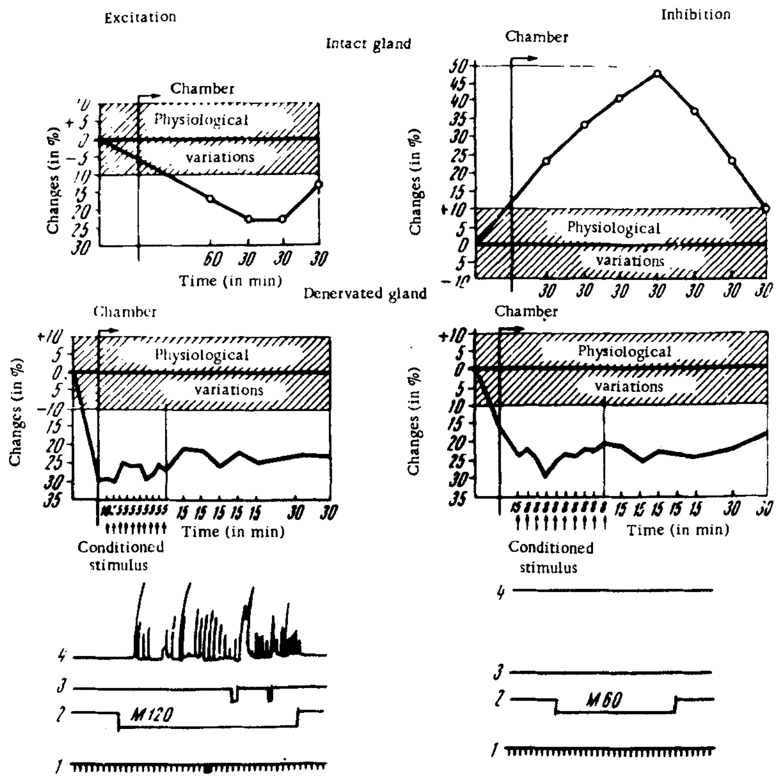

Fig. 2. Effect of excitation and inhibition of the central nervous system on the secretion of hormonal iodine by the intact and denervated gland. 1) time marker (in sec); 2) stimulation marker (conditioned stimulus M_{120}); 3) stimulation marker (electric current); 4) recording of defensive motor reflex.

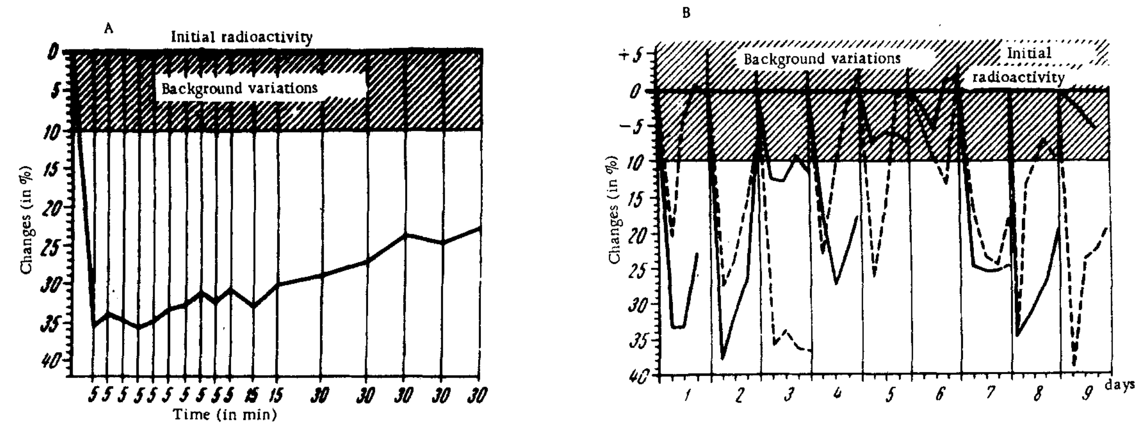

Fig. 3. Secretion of the denervated thyroid gland. A) during overstress of the process of stimulation; B) during conflict between excitation and inhibition. Continuous line—first period of conflict, broken line—second period of conflict.

We have previously shown [4, 6] that under the influence of a conditioned inhibitory stimulus the secretion of the intact gland is depressed. Changes of this type in the secretion of the thyroid gland have also been found in the case of overstress of stimulation, or of conflict between the fundamental nervous processes, or under the influence of sodium amytal—in other words, during the action of factors leading to the onset of an inhibitory state of the central nervous system.

As is clear from Fig. 2, the reaction of the thyroid to a differential stimulus (M_{60}) differed radically in the dogs undergoing the operation from the reaction in the intact animals. The secretion of the gland stimulated by the experimental environment, which acts as part of the system of defensive stimuli and behaves as a conditioned stimulus, could not be arrested by the action of a well consolidated inhibitory conditioned stimulus. A high rate of secretion continued throughout the experiment, and showed no significant fluctuation over a period of 3 h (see Fig. 2). The development of an inhibitory state in the cerebral cortex during an overstress of stimulation, like the action of the inhibitory reflex, proved powerless to prevent the increased secretion of hormones into the blood, stimulated initially by the defensive external situation.

The results of one such experiment are given in Fig. 3. In this experiment the action of the positive conditioned stimulus (M_{120}) lasted for 3 min instead of the usual 20 sec. The latent period of the conditioned reflex was considerably increased and sometimes reached 40 sec, indicating the development of inhibition in the cerebral cortex. In these circumstances too, however, the secretion of the thyroid gland did not cease but remained at a high level throughout the experiment.

The secretion of the denervated thyroid was next investigated in the conditions of a conflict between excitation and inhibition. A state of conflict was applied up to four times in the course of 9 days. After an interval of 1 week the experiments were resumed. As a result the conditioned-reflex activity was disturbed; the dog now did not raise its paw in response to the positive conditioned stimulus, but reacted to the inhibitory stimulus; at the end of the experiment it hung in its straps and dozed.

Under the influence of conflict the content of radioiodine in the denervated thyroid fell to 30-40% of the initial level. Similar results were obtained in both the first and second periods of the experiments in which a conflict was used (Fig. 3,B). The accumulation of radioiodine in the thyroid was never observed, as is usually the case in analogous conditions in intact dogs.

Hence, the experiments showed that the denervated thyroid is no longer capable of reacting adequately to impulses arising in the cerebral cortex. Unlike the intact gland, which ceases to secrete hormones into the blood under the influence of inhibitory reflexes, the denervated gland in the same conditions cannot inhibit its secretion and, as a result, the liberation of its hormones into the blood stream continues.

The differences observed in the secretion pattern of the denervated gland, namely its high intensity and prolonged course, may be attributed to the fact that the gland, on account of its denervation, ceases to experience regulatory influences from the central nervous system. This suggests that the autonomic nerve supply plays a part in the adaptive reaction of the thyroid gland, ensuring the delicate and precise functioning of the gland in the course of constantly changing external environmental conditions.

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