THE INFLUENCE OF THE FUNCTIONAL STATE OF THE CEREBRAL CORTEX ON THE SECRETORY CYCLE OF THE THYROID GLAND

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In work of the school of I. P. Pavlov it has already been shown that disturbances of the activity of the endocrine system may cause considerable functional disorders of the central nervous system. Investigations of the state of the higher nervous activity, performed on animals after total or partial removal of the thyroid gland [5, 14, 15, 16], and also after the action of thyroid gland preparations on the animal [12], showed high reactivity of the central nervous system in response to these endocrine changes. At the present time more and more reports of investigations are appearing in which hard and fast relationships are revealed between the nervous system and the endocrine system and the relation between the hormonal function of the glands of internal secretion and the regulating influence of the central nervous system.

However it must be stated that the problem of regulation of the function of the thyroid gland has still not been adequately investigated. Many investigations [1, 3, 6, 13] have been devoted to the study of the state of the thyroid gland in disorders of the brain due to surgical trauma. However the problem of the influence of the cerebral cortex must be solved, in our view, by experiments of long duration in which the central nervous system is not damaged but only affected by functional changes. On this theme only isolated investigations have been made. R. P. Ol'nianskaia [10] demonstrated that the hormone of the thyroid gland took part in the process of basic metabolism in the body under the regulating influence of the cerebral cortex. In work by M. S. Kakhana [7, 8] it was shown that as a result of derangement of the higher nervous activity of rabbits, histological changes took place in the structure of the thyroid gland.

V. I. Arkhipenko [2] studied the function of the thyroid gland in dogs with experimental neurosis. In 4 dogs the author observed diminished function of the thyroid gland and in one the activity of the gland was found to be increased.

The present work is devoted to the study of the influence of the functional state of the cerebral cortex on the separate phases of the secretory cycle of the thyroid gland. This problem is very closely related to the etiology and pathogenesis of thyrotoxicosis and there are few references to it in the literature.

EXPERIMENTAL METHOD

Experiments were performed on dogs in which conditioned electrodermal defensive reflexes had been formed. For a conditioned stimulus was used the sound of a metronome – 120 impulses per minute (M120), which followed 20 seconds behind the unconditioned stimulus. Differentiation was produced to a metronome at 30 impulses per minute. The unconditioned stimulus was an electric current from an induction coil acting for several seconds.

The electrodermal conditioned defensive reflex is known to be formed very rapidly as a rule. The characteristic feature of this conditioned reflex is the fact that if the current is given only in cases where the conditioned reflex is absent, an enduring conditioned connection is forged extremely rapidly. This fact has already drawn the attention of V. P. Petropavlovskii [11], I. I. Laptev [9], A. N. Bregadze [4] and others. Using this feature of the defensive reflex, we set up experiments without using reinforcement over a long period of time; this enabled us to observe the function of the thyroid gland under the influence only of impulses arising from the cerebral cortex.

We determined the functional state of the thyroid gland by the absorption of radioiodine and the excretion of its active products into the blood stream.

The radioactivity of the thyroid gland was measured by means of a γ-ray counter (AMM-4), combined with apparatus B. This counter was firmly attached to the neck over the thyroid gland. To determine the activity of the peripheral tissues the counter was attached to the lower third of the thigh. Radioiodine was administered in doses of from 2 to 5 μC to the dog. Next, after various intervals of time, successive determinations were made of the radioactivity of the thyroid gland and of the peripheral tissues. The absorption of radioiodine was studied during the first 5 hours after its administration. The maximum absorption was detected after 24 hours. The work was done on 6 dogs; in all 270 experiments were performed, in which the activity of the thyroid gland was studied under the influence of the normal and pathological cerebral cortex.

At the beginning of the work we studied variations in the level of radioiodine in the thyroid gland with the dog kept in a chamber and on a machine. It was shown that these variations did not transgress physiological limits, not exceeding ± 10 %.

EXPERIMENTAL RESULTS

The use of an electric current as an unconditioned stimulus stimulates the secretion of radioiodine by the thyroid gland. Even one hour after stimulation of the dog's paw with the electric current the quantity of radioiodine in the gland had sharply diminished, and only 3-4 hours after its action did a tendency appear for it to be restored to its original level.

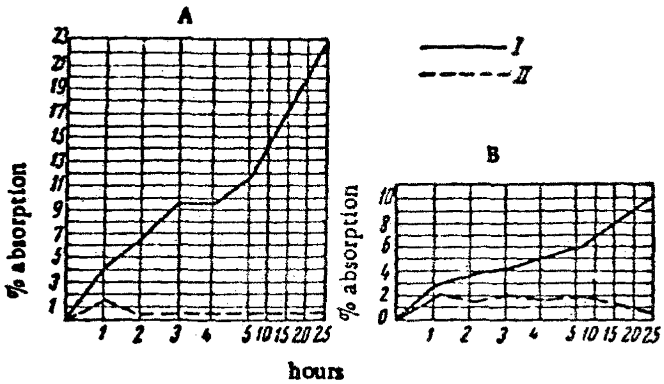

Fig. 1. The influence of defensive conditioned reflexes on the absorption of radioiodine by the thyroid gland.
A) Normal; B) after action; I) thyroid gland; II) blood.

To study the influence of electrodermal defensive conditioned reflexes on the hormone-forming function, the animal was placed in a chamber immediately after the administration of radioactive iodine; during the first hour of the investigation a conditioned stimulus (M_{120}) was given 10 times at 5-minute intervals; next the impulses from the thyroid gland and the thigh were counted after every hour.

As may be seen in Fig. 1, absorption of radioiodine by the thyroid gland in normal, i.e. physiological conditions before the development of conditioned defensive reflexes proceeds more intensively than when superimposed on defensive conditioned reflex activity. A low level of absorption of radioiodine is noted not only during the first 4-5 hours after the injection of I^{131}, i.e. during the time the animal was in the chamber, but also after 24 hours. The percentage absorption was found to be lowered more than twice.

After the development of differentiation in the experiment we applied an alternately postive and inhibitory metronome at intervals of 5 minutes. The inhibitory metronome did not affect the course of absorption at all; it was lowered to the same degree as by the action of the positive metronome alone.

It may be suggested that the lowering of radioiodine absorption during defensive activity was caused by delay in its absorption from the gastro-intestinal tract. In order to verify this hypothesis we measured the radioiodine content in a part of the body remote from the thyroid gland — in the thigh. These measurements made it possible to obtain tentative information on the content of radioiodine in the blood. It was found that the level of radioiodine in the blood of the dogs at the time of the defensive conditioned reflex activity was higher than normal (see Fig. 1).

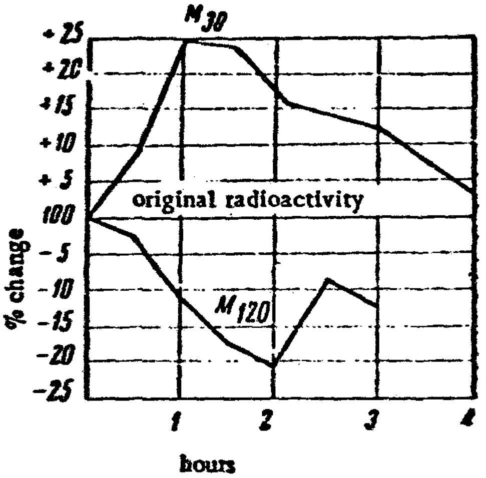

Fig. 2. Excretion of radioiodine by the thyroid gland by the action of a positive (M_{120}) and a negative (M_{30}) stimulus.

It follows from these observations that at the time of defensive conditioned reflex activity the ability of the thyroid gland to assimilate iodine from the environment is depressed. The quantity of iodine contained in the gland is an index of the intensity of hormone formation; it follows from this that the ability of the gland to synthesize organic iodine compounds is also depressed.

Next we studied the influence of defensive conditioned reflexes on the phase of secretion of hormone into the blood. For this the radioactivity of the thyroid gland was measured only 48 hours after the administration of I^{131} to the animal. A conditioned stimulus (M_{120}) was applied 10 times at 5-minute intervals. Calculation of the radioactivity of the thyroid gland was made every 60 minutes for 3-4 hours. The percentage change was calculated in relation to the original value of the radioactivity which was taken to be 100 %.

Under the influence of defensive conditioned reflexes the quantity of radioiodine in the thyroid gland fell. This reaction usually began an hour after placing the animal in the chamber and ended, as a rule, in 3 hours. Thus under these conditions the secretion of the active products of the thyroid gland is stimulated (Fig. 2).

The influence of differential inhibition on the excretion of radioiodine by the thyroid gland was studied in experiments in which the inhibitory stimulus was applied in isolation. It was applied, just like the positive stimulus, 10 times during the first hour at 5-minute intervals. In Fig. 2 it is apparent that even 30 minutes after the application of M_{30} an increase in the radioiodine in the thyroid gland is observed; during the following 2 hours the quantity of radioiodine in the gland rises and only after 3-4 hours does it return to its original level. In cases where differentiation was for some reason disinhibited the radioactivity of the gland fell, i.e. a reaction corresponding to the action of the positive metronome was observed.

Thus a definite relationship is observed between the functional state of the central nervous system and the separate phases of the secretory cycle of the thyroid gland.

In normal physiological conditions, if hormone formation is intensified the secretion of active products of the thyroid gland into the blood is intensified proportionately; on the other hand if hormone formation is slowed up, secretion is also slowed up. Consequently the phases of synthesis and secretion of hormone are interconnected. For this reason the function of the thyroid gland is determined as a rule by study of only one — usually the first — phase of the secretory cycle. Under the influence of defensive conditioned reflexes, in addition to intensification of the second phase of the secretory cycle — the phase of secretion — the first phase, that of hormone formation, is inhibited. For this reason, in such conditions assessment of the thyroid gland function must include consideration of both phases of the secretory cycle.

The next part of the work was devoted to the study of the influence of disturbance of the higher nervous activity on the secretory cycle of the thyroid gland. A change in the state of higher nervous activity was brought about in some experiments by increasing the length of action of the conditioned stimulus (in place of the usual 29 seconds the conditioned stimulus operated for up to 5 minutes) and by increasing the force of the unconditioned stimulus (the induction coil current was given at a distance of 1 cm). As a result of these measures the overstraining of the stimulatory process reached such a severe degree that it brought the animal into a state of prohibitive inhibition. In this state, in addition to a considerable fall in the conditioned reflexes, profound changes arose in the secretory cycle of the thyroid gland. These changes were expressed as an increase in the process of hormone formation and a reduction in the secretion of the active products of the thyroid gland into the blood.

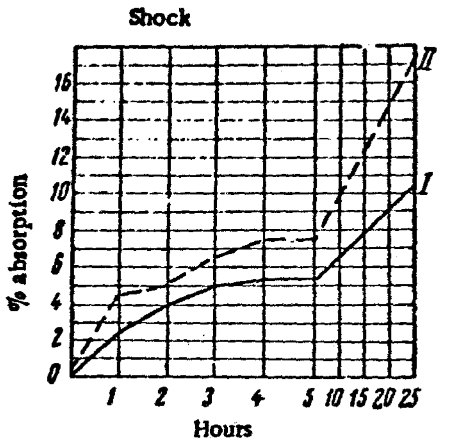

Fig. 3. The influence of derangement of higher nervous activity on absorption of radioiodine by the thyroid gland.
I) Before "shock"; II) after "shock".

Disturbance of the normal activity of the cerebral cortex was also produced by competition between the postive conditioned reflex (M_{120}) and the inhibitory conditioned reflex (M_{30}) for a period of 10 days. Usually the "shock" was applied up to 4 times in the experiment, and even during the first day of the "shock" a sharp falling off in the conditioned reflexes was observed. On subsequent days the conditioned reflexes disappeared completely and then reappeared. On the day when the "shock" was administered,the dog changed its behavior in the chamber, whimpered and would not take its food; towards the end of the experiment it hung on its straps and slept. Thus, inder the influence of the "shock" also, the animal fell into a state of prohibitive inhibition. As with the overstraining of the stimulatory process, changes were observed in the secretory cycle of the thyroid gland, expressed as inhibition of secretion of the active products of the thyroid gland into the blood, and stimulation of hormone formation. Stimulation of the process of hormone formation may be observed both during the first 5 hours after administration of radioiodine to the animal and 24 hours after its administration (Fig. 3). This is evidence of increase of the maximum absorption of radioiodine by the thyroid gland.

With disturbance of cortical function, the second phase of the secretory cycle of the thryoid gland is strongly inhibited. As may be seen in Fig. 4, in the first days of the "shock" a considerable increase in the radioactivity of the thyroid gland is noted, while in the following days the reaction of the thyroid gland to the "shock" has weakened. Subsequent "shocks", administered after various intervals of time (after an interruption of two months or one month), gave nothing new by comparison with previous ones (see Fig. 4)

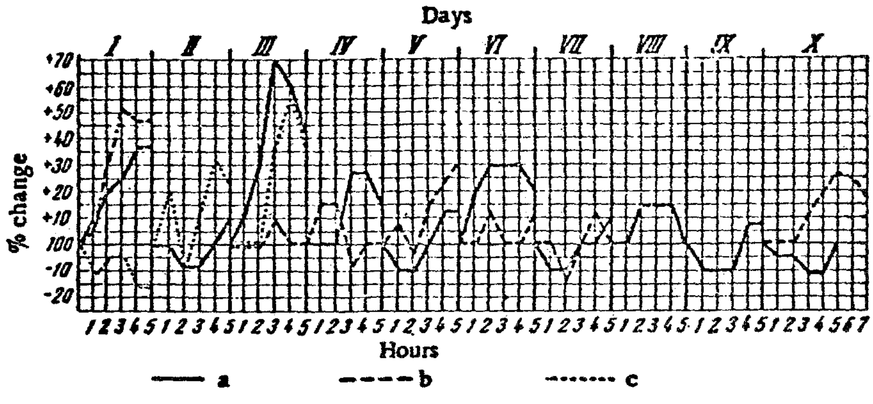

Fig. 4. The influence of derangement of higher nervous activity on the content of radioiodine in the thyroid gland.
a) first "shock" (6–16/II 1956); b) second "shock" (10–20/IV 1956);
c) third "shock" (14–16/V 1956).

It is known that after administration of labelled iodine to an animal, it is found to be deposited in the form of inorganic iodide, diiodotyrosine and thyroxin in the liver, muscles and small intestine [Perlman, Morton and Chaikoff (17)]. It may be supposed that at the time of the "shock" conditions are created for increased assimilation of labelled iodine from these organs. However since the gland at this time is capable of actively taking in iodine, the excreted labelled iodine from these organs may be absorbed into the gland and be stored there. It may be that this is assisted by the retarded process of secretion of radioiodine from the gland. This process demands a special analysis, on which we are engaged at the present time.

As we have shown, a change in the functional state of the cerebral cortex leads to enhanced secretion of the active products of the thyroid gland into the blood; this, we may suppose, is one aspect of a series of events involving high oxidizing processes at the time of the defensive activity. But this high secretion by the gland, because of the compensatory mechanism, is limited by a fall in the level of hormone formation. Thus, under the influence of cortical impulses the activity of the thyroid gland is regulated in accordance with the requirements of the body. At the time of disturbance of the function of the central nervous system of a pathological nature, for example in the "shock", increased hormone formation is combined with accumulation of the hormone in the thyroid gland.

Stimulation of the phase of hormone formation in disorders of cortical function may evidently be regarded as an initial, latent phase of development of thyrotoxicosis. In our investigations the animal fell into a state of prohibitive inhibition as a result of the disturbance of higher nervous activity; for this reason, it appears to us, the second phase of the secretory cycle was found to be inhibited. Derangement of higher nervous activity with overaction of stimulation, most likely leads to stimulation of both the first and second phase of the secretory cycle of the thyroid gland, i.e. to a state similar to that observed in thyrotoxicosis.

SUMMARY

The function of the thyroid gland in dogs was evaluated with the aid of radioactive iodine. The functional condition of the brain cortex was changed by conditioned reflexes. Data were obtained which demonstrate that the function of the thyroid gland is regulated by the brain cortex and depends on its functional condition. The brain cortex influences the process of hormone production and of excretion of metabolic products of the glands into the blood. Thus it coordinates the function of the thyroid gland with the requirements of the whole organism.

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