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HORMONE SUPPLY OF THE ORGANISM IN PROLONGED EMOTIONAL STRESS

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16. Abstract

A study was made of the effect of prolonged emotional stress of varying genesis on the hormonal function of the pancreas, thyroid gland adrenal cortex. The dynamics are revealed of the hormonal secretion depending on the type of adaptation activity and its duration. High secretion of the hormones observed outside the adaptation activity is examined as an index of the phase transition of defense reactions to the phase of overstress.

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HORMONAL SUPPLY OF THE ORGANISM IN PROLONGED EMOTIONAL STRESS

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A study was made of the effect of prolonged emotional stress of varying genesis on the hormonal function of the pancreas, thyroid gland adrenal cortex. The dynamics are revealed of the [hormonal] secretion depending on the type of adaptation activity and its duration. High secretion of the hormones observed outside the adaptation activity is examined as an index of the phase transition of defense reactions to the phase of overstress.

In the opinion of P. K. Anokhin [9], "the most pathogenic feature of /945 * negative emotions is their continuity." Currently it is known that the constantly increasing information and requirements for mankind in all fields of its activity often result in prolonged emotional overstress that is accompanied by a vast complex of neurovegetative and neurohumoral changes. Precisely the duration and recurrence of negative emotions play an important role in the transition of the defense reaction phase to the phase of overstress that is the beginning of the formation of pathological syndromes. Thus, prolonged emotional overstress becomes the background that facilitates the development of a number of neurogenic diseases such as hypertonia, myocardial infarct and others.

In numerous studies conducted since the time of G. Sel'ye the important role has been shown of the hormonal link in the organization of the general

*Numbers in margin indicate pagination in original foreign text.

adaptation syndrome to the stress effects. However, they were mainly carried out under conditions of an acute experiment, and therefore the question as to the nature of the hormonal supply of the organism in prolonged emotional stress even today remains open in the same way as the question of the role in these processes of emotional stresses that differ in genesis.

Clarification of the tasks set was carried out under conditions of the chronic effect on animals of stress factors that induce different types of adaptation activity.

For this purpose the animals were systematically exposed to emotionally adverse effects; here in one case a situation was created that completely excluded the possibility of avoiding a painful stimulation, and in another--this possibility depended on the rapidity of mastering the instrument behavior of avoiding the painful stimulation. In the first case the prolonged immobilization of the animal was combined with electrical skin stimulation by a superthreshold force. This combined stress simulated the situation of helplessness since the animals were completely deprived of the possibility of avoiding the painful stimulation. In his time G. F. Lang [10] viewed this type of situation as non-reacted emotions, believing /946
that they create an especially dangerous situation for the organism since the entire charge of excitation falls on the autonomic centers. In the second--the stress model was an instrument reaction of avoiding the painful stimulation which in contrast to the aforementioned model made it possible for the animal with training to avoid the painful stimulation, and therefore under these conditions the situation of helplessness was excluded.

By using the described stress models we studied the dynamics of secretion of insulin, thyroid hormones and corticosteroids.

Technique

The work was conducted under conditions of a chronic experiment on 6 cats weighing 3.5-4.0 kg and 6 mongrel dogs weighing 15.0-20.0 kg on the model of active avoidance of an electrical skin stimulation (ESS) (cats)

and on the model of combined emotional stress (dogs and cats).

The animals were trained to avoid the ESS by pressing a pedal. Each session of training consisted of presenting 20 combinations of conditioned signal: simultaneous presentation of continuous light (electrical lamp--40 w) and sound (electrical ring--60 db) for 30 s, and unconditioned signal (passage of electrical current with voltage 40-45 v through a metal floor for 10-15 s). The sources of light and sound were 30-70 cm from the animal. The unconditioned stimulus was separated from the conditioned signal by 15-20 s. In this interval of time joint use of the conditioned and unconditioned stimuli occurred. At any moment of pressing the pedal the conditioned and unconditioned stimuli were disengaged. The signals were presented aperiodically for 60 min. In the stage of reinforcement of the reaction the correct responses were reached in limits of 75-80% of the cases. The criterion for the secured reaction was the pressing on the pedal in 100% of the cases. The sampling of "background" blood was taken in the cats through a catheter previously implanted in the jugular vein outside the experimental chamber for several minutes before the start of the "session." The next two blood samples were taken in the experimental chamber: one in 60 min., the other in 120 min. after the start of the "session." The last blood sample was taken in 180 min. after the start of the experiment(60 min. after removal of the animals from the experimental chamber).

For the cats immobilization was achieved by placing the animals in a close chamber; here the head was pushed out through a narrow opening on the front panel of the chamber and thus was outside it. One of the hind extremities was pushed out through the opening in the rear panel of the chamber and was also fixed outside it. Immobilization lasted for 5 h. During immobilization ESS of the crus was carried out by single aperiodically applied square impulses with the following parameters: voltage 40-50 v, length of impulse 1 s, with mean frequency of application 1 impulse in 1 min. for 10 min. in 3 h after the start of immobilization. Taking of blood for study of the content of hormones and sugar was done through a catheter previously implanted into the jugular vein, before the beginning of the

experiment, in 3 h, 5 h after its start, and in 1 h after the end of the experiment.

Experiments were set up on models of combined emotional stress. The negative emotional stress was induced by means of rigid immobilization of the animal for 4-5 h, during which electrical skin stimulation of the crus was presented in single impulses of superthreshold strength. The parameters of stimulation: voltage 30-50 v, duration of square impulse 1 s. Ten electrical impulses were applied aperiodically for 10 min. each hour. The series of experiments consisted of 4-5 experiments conducted daily for a week and it ended with the taking of blood from the femoral vein outside the experimental situation for the next 3-5 days. Besides this, the blood was taken before the start of the experiments for a week 3-4 times, then directly before the start of each experiment and immediately after the end.

The following were analyzed in the taken blood: content of insulin and thyroxin by the radio-immunochemical method by using special sets "KIT" of the firm "Corning" with the instructions of this firm; insulin activity of the blood on the fatty tissue of rats of the "Wistar" strain [17]; blood sugar content according to the toluidene method [12]; iodine (SBI) bonded to plasma proteins [13] and the content of 11-oxycorticosteroids by the fluorometric method [11].

Results of the Study and Their Discussion

In the stage of generating the instrument reaction of avoiding the painful stimulation when the number of erroneous responses is great, and as a rule reaches 60-70%, the insulin content in the blood during the experiment is considerably reduced. The low hormone level is defined even an hour after the end of the experiment when the animal is outside the experimental chamber. However, with a further reinforcement of the behavior when the number of erroneous reactions is reduced and does not exceed 10-25%, the hormonal reaction acquires a phase nature. Here the low level of insulin established during the conducted session of training by the second hour of the experiment was replaced by its increase and /947

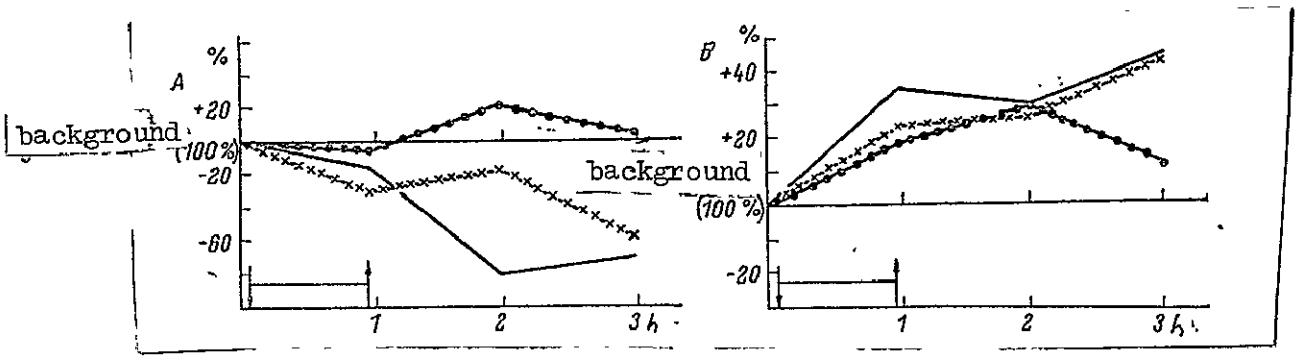

Figure 1. Effect of Instrument Reaction of Avoiding on the Dynamics of Insulin (A) and Thyroxin (B) Content in Blood of Cats.
On x-axis--time, in h; on y-axis--% of change in hormone content in blood. solid line--stage of generation; crosses--reinforcement; black circles--secured instrument reaction of avoiding. arrows--beginning and end of training session.

reached the background value, and at the end of the experiment when the animal was outside the experimental room for an hour, the hormone level again dropped. In the stage of secured instrument behavior, when the reactions were errorless, the insulin content in the blood was practically not altered, its oscillations were in limits of the background values and did not exceed +20% (fig. 1,A).

Analysis of thyroxin made in the same blood samples demonstrated that the thyroid gland activates its activity at all stages of the instrument behavior. However, as is apparent in fig. 1, B the highest level of thyroxin was observed at the stage of generation and reinforcement of this reaction, and it is characteristic that here the content of the hormone continued to increase even after the end of the experiment when the animal was outside the experimental chamber for an hour. The other dynamics of change in the thyroxin content was revealed in the stage of secured behavior, although in the beginning this state was accompanied by an increase in the hormone level in the blood, however this reaction lasted only 2 h. After the end of the experiment the hormone level acquired the background value already after an hour.

In comparing the findings attention is drawn to that fact that in the stage of secured instrument behavior when the response reactions to the

conditioned stimuli are automated and errorless the content of insulin in the blood is not altered, while the level of thyroxin, although briefly is still increased. The noted difference in the hormonal reactions is apparently governed by that motor agitation that is created in the process of implementing the reaction of avoidance, when the animal after the presentation of the conditioned signal, as a rule, threw itself rapidly towards the wall where the pedal was mounted in order, by pressing it to prevent the engagement of the pain stimulus. It is known from the literature that the motor activity of the organism increases the secretion of the thyroid gland, and vice versa, physiological immobilization reduces its activity [20].

Other hormonal reactions are established during training in the generation and reinforcement of the instrument behavior. Under these conditions prolonged retardation of insulin secretion not only during the experiment, but also an hour after its end indicates the high emotional stress of the animal, which, as was shown by a number of researchers [16, 19, 21], as well as in our works [7,8] is always accompanied by a drop in the level of this hormone in the blood. Simultaneously, the function of the thyroid gland was increased for just as long a time, which, as is known [2,3,5,15] also is an indicator of the emotional stress of the animal. As is apprent from the cited data the dynamics of the content of studied hormones in the blood clearly reflects the changing needs of the organism for hormonal supply at different stages of the given behavioral reaction. /948

Further, a study was made of the insulin, thyroid hormones and corticosteroid content under conditions of combined emotional stress. As is apparent from fig. 2 for 5 h of the experiment a low level of insulin was defined in the blood with simultaneous hyperglycemia. Insulin remained on a low level even an hour after the experiment ended under conditions of free behavior of the animal. At the same time determination of the level of thyroid hormones showed a reliable increase in them in the peripheral blood. For example, in one of the studied animals the value of the level

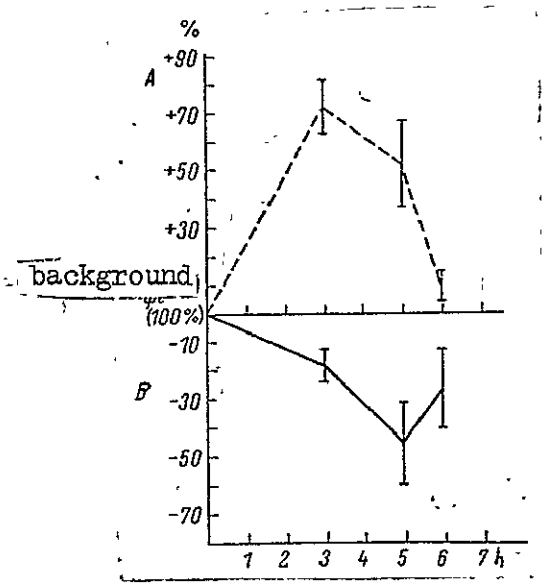

Figure 2. Effect of Combined Emotional Stress on Dynamics of Content of Sugar (A) and Insulin (B) in Blood of Cat.
On x-axis--time, in h; on y-axis--% change in sugar content and insulin content in blood with root-mean-square error. Dotted line--%change in sugar in blood; solid line --% change in insulin in blood.

of thyroid hormones according to the iodine bonded with plasma proteins before the experiment was 5.50±0.17 (γ%), after the end of the experiment it reached 9.27±0.29 (γ %) ($d < 0.001$).

In order to clarify the role of the recurrence or continuity in the emotional loads on the nature of the hormonal secretion we attempted to conduct experiments daily for 5 days. The data obtained in this series (fig. 3,B) demonstrate that with such an experimental set-up one can observe the gradual, from day to day, increase in the background level of thyroid hormones, as well as the clearly pronounced direct reaction of the thyroid gland to the presented factor. It is remarkable that the background content of these hormones is normalized only 3-4 days after the end of the experiments. The level of corticosteroids in these same blood samples (fig. 3,A) is altered in the same direction, however, one should stress that the reaction of the adrenal cortex under these conditions is pronounced more strongly than the reaction of the thyroid gland. The content of both thyroid hormones and corticosteroids in acute stress, as was shown by many researchers including our data [6-8] arrives at the initial value soon after the end of the experiment.

The data we obtained demonstrated very clearly the peculiarities of hormonal secretion in emotional stresses. Here it is appropriate to note that one could not observe the hormonal reactions described in this work in all the animals. In some of them we observed the interesting fact

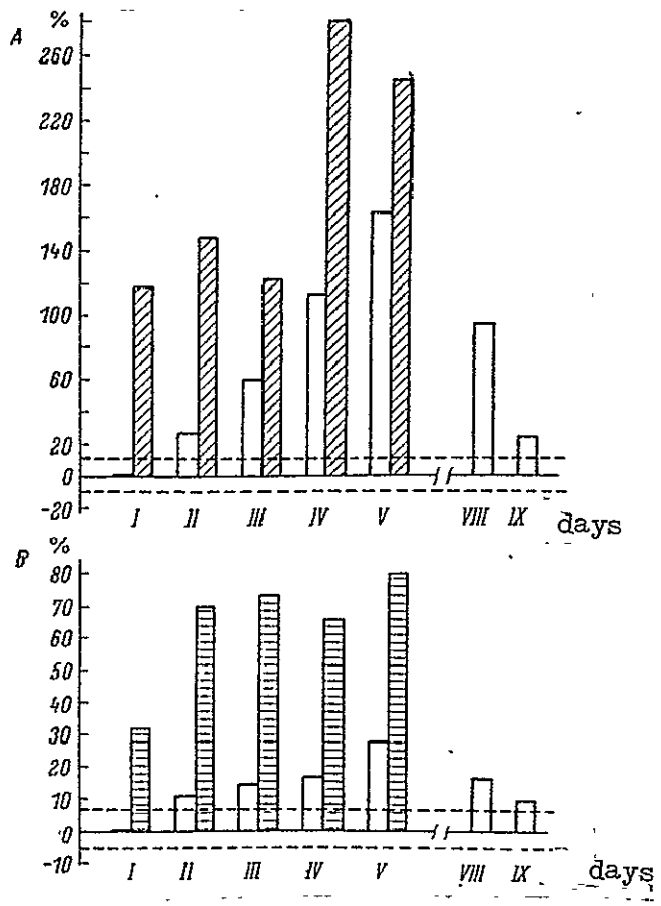

Figure 3. Effect of Chronic Combined Emotional Stress on Dynamics of Content of Corticosteroids (A) and SBI (B) in Blood of Dog.
On x-axis--days of emotional stress (I-V) and after-effect (VIII-IX); on y-axis--% change in hormone content in blood. Dotted line--% change in hormone content in blood in intact dogs normally. empty columns--%change in corticosteroid and SBI content before experiment; oblique-hatched columns--% change of corticosteroid content immediately after end of experiment; horizontally-hatched columns--% change of SBI content immediately after end of experiment.

when in the generation of the instrument reaction of avoidance in the presence of a reaction of the insular apparatus of the pancreas that is characteristic for this stress model the hormonal reaction of the thyroid gland is completely lacking (fig. 4). It is difficult now to explain this phenomenon but we recall it, considering it important for an understanding of the individual differences in the hormonal components of the emotional stress.

Thus, in combined emotional stress we observed prolonged changes in hormonal secretion. It is especially important to focus attention on the increase in background level of hormones both between the experimental days, and after the cessation of the experiments. Similar changes in the intensity of the hormonal secretion, as it seems to us, can indicate the transition /949 of the phase of defense reactions to the phase of overstress. In contrast to this under conditions of instrument reaction of avoidance one can note a clearly pronounced adaptation reaction of the insular apparatus of the pancreas and thyroid gland at different stages of training..

Comparison of these two, completely dissimilar in essence, models of stress makes it possible to further postulate the fact that different forms of interaction of the organism with the environment is accompanied by a very differentiated hormonal supply of the organism. As we saw, the difference in hormonal reactions is revealed not only between individual types of adaptation activity, but also in the limits of one adaptive reaction, which with a certain percentage of probability can be linked with the participation, differing in nature, of individual hormones in the metabolic processes that occur on the periphery.

At the same time, our studies demonstrated that the most pathogenic (of the studied models) for the organism, judging from the hormonal secretion, was the combined stress. In the latter case in contrast to stress that emerges under conditions of instrument reaction of avoidance, as the studies of the reaction are repeated, especially of the thyroid and adrenal glands, the function of these glands was intensified, and what is very important, was increased even outside experimental conditions. Under conditions of instrument behavior, when the animal had already been /950 trained to avoid the painful stimulus, confidently fulfilling the behavioral reaction it ceases to obtain the painful reinforcement it loses the foundation for the stimulation and the hormonal secretion is normalized.

Another situation is created in combined stress when the animal constantly from day to day is under continuous emotionally negative influence of the environment. Under these conditions the stimulation of the

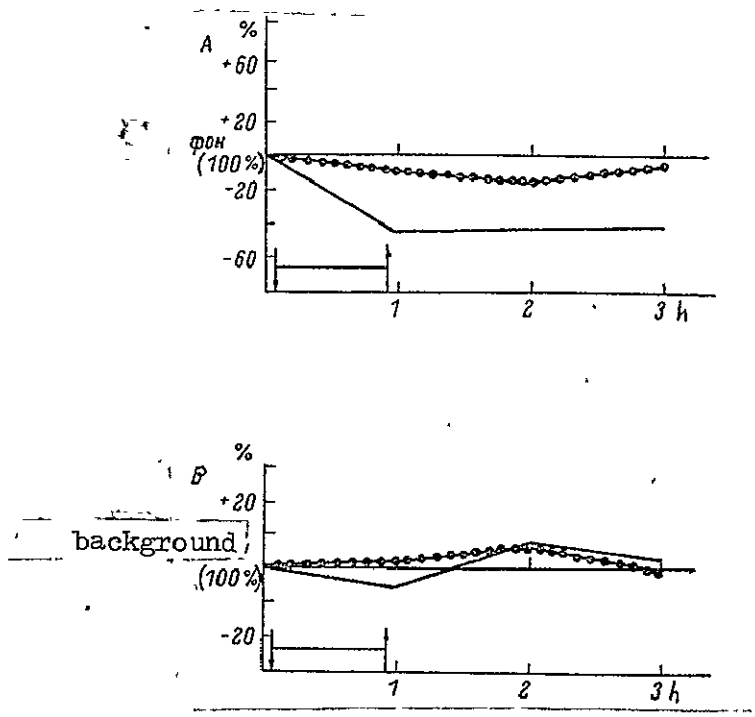

Figure 4. Effect of Instrument Reaction of Avoidance on Dynamics of Content of Insulin (A) and Thyroxin (B) in Blood of Cat. Designations the same as in figure 1.

hypothalamus and reticular formation is maintained by the high secretion of noradrenaline from the adrenals as an unchanged satellite of negative emotions, which in turn facilitates the secretion of corticotropin- and thyrotropin-releasing factors, and thus, the high secretion of the adrenal cortex and the thyroid gland is maintained.

In relation to the aforementioned we turn to an examination of the possible mechanisms for the increase in background level of thyroid hormones and corticosteroids under conditions of combined emotional stress, and it is appropriate here to recall that previously we observed this phenomenon in the study on the effect of the defense conditioned reflex activity on the secretion of thyroid hormones [5]. Then we attempted to explain it by the mechanisms lying outside the hypophysis-thyroid relationships. It seems to us that among the factors determining the functional activity of the glands that depend on the tropic functions of the anterior

hypophysis, in relatively normal conditions of vital activity the feedback relationship dominates. However, with a change in the state of the organism, especially the functions of the central nervous system, lengthy activation of the secretion of both the thyroid hormones and the corticosteroids can be maintained by the extra-hypophyseal mechanisms.

It is known that thyrotoxicosis in the majority of cases is accompanied not by an intensification of the production of the thyrotropic hormone, but on the contrary, often its attenuation. In hypoxia or under conditions of an increase or decrease in the environmental temperature with an extrathyroid rise in the main metabolism the secretion of the hypophysis and /951
the thyroid gland is altered in one direction [1, 18], which clearly contradicts the principles of negative feedback. Therefore it is most likely that under our experimental conditions the high secretion of thyroid hormones and corticosteroids is maintained by extrahypophyseal mechanisms, among which a significant role can be played by the cyclically occurring excitation described in the literature [4, 14] between the hypothalamus and the cerebral cortex, in which the trigger role belongs to the posterior hypothalamus.

The obtained facts provide the foundation to consider that precisely on this path one should search for the possibility of expanding further research to simulate continuous emotional stress and its effect on the hormonal secretion. This will make it possible to differentiate the phase of defense stress from the phase of overstress, and to reveal the peculiarities of the hormonal reactions in the transition from adaptation to "breakdown."

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