THE SECRETORY CYCLE OF THE THYROID GLAND IN EXPERIMENTAL NEUROSIS

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It is now established beyond doubt that disorganization of the work of the cerebral cortex leads to disturbance of various vegetative functions (cardiovascular, gastro-intestinal, excretory, and so on). Numerous clinical observations confirm the exceptional importance of the central nervous system in the pathogenesis of the endocrine diseases and, in particular, of the thyrotoxicoses. However, the state of the thyroid gland in experimental neuroses has received inadequate study.

Only a few scattered papers may be found on this subject. M. S. Kakhana [2] and V. I. Arkhipenko [1] studied the structural changes in the thyroid gland in neuroses and found that the function of the gland is increased in these circumstances. In the researches of E. A. Loskutova and N. F. Nikolaenko [4] and of V. I. Arkhipenko [1], using radioactive iodine (I^{131}) as an indicator of thyroid function, a lowered absorption of I^{131} by the thyroid gland was discovered.

We undertook the task of studying the function of the thyroid gland in experimental neurosis as revealed by the indices of hormone formation and secretion into the blood stream. These two indices are known to characterize the principal phases of the secretory cycle of the thyroid gland, and to give a reasonably complete picture of its functional state.

EXPERIMENTAL METHOD

The investigation was carried out on four dogs. The functional state of the cerebral cortex was altered by means of conditioned defensive reflexes, formed in response to the sound of a metronome giving 120 beats per minute (M_{120}); differentiation was produced to a metronome giving 30 beats per minute (M_{30}). The unconditioned stimulus was a subthreshold induction current. The conditioned stimulus followed 20 seconds after the unconditioned. In order to disturb the dynamics of the fundamental nervous processes, the duration of action of the conditioned stimulus was lengthened to 4 minutes. A disturbance of the normal activity of the cerebral cortex was also produced by causing the positive conditioned stimulus (M_{120}) and the inhibitory conditioned stimulus (M_{30}) to clash for a period of 10 days. Usually this clash was applied up to 4 times in the course of the experiment. Under these circumstances, within the course of the first day of the clash a marked decrease in the magnitude of the conditioned reflexes was observed. During subsequent days the conditioned reflexes sometimes disappeared, sometimes reappeared. The changes in the behavior of the dogs under these conditions were very marked both in the experimental room and in the vivarium. In the experimental room the dogs whimpered and refused to eat, and at the end of the experiment they hung in their straps and dozed. In the vivarium the dogs resisted being taken from their cages, growled, and displayed aggressiveness. Some dogs showed nutritional disturbances, and developed areas of loss of fur or suppuration of the skin, with loss of weight although they remained on a steady diet.

The thyroid gland function was determined by the absorption of I^{131} and the excretion of hormonal iodine from the gland. The absorption of iodine by the thyroid glands of the dogs was measured for a period of 5 hours and 24 hours after its administration. The phase of excretion of hormonal iodine from the thyroid gland was investigated after 48 hours and later, i.e., at a time when the process of absorption of the administered iodine had practically ceased. I^{131} was given in milk in a dose of 0.5 μC/kg body weight.

EXPERIMENTAL RESULTS

The effect of neurosis on I^{131} absorption by the thyroid gland

It will be seen from Table 1 that when the fundamental nervous processes were disturbed a lowering of the I^{131} absorption by the thyroid gland was observed in 3 of the 4 dogs. A low level of iodine absorption was found not only

TABLE 1. The Effect of Neurosis on the Absorption of I^{131} by the Thyroid Gland

Dog	Date	Before exposure					
		Time (in hours)					
		1	2	3	4	5	24
		Absorption (in %)					
Seryi	12/12/1954	4.7	6.2	9.1	9.7	11.5	23.2
Seryi	5/20/1955	2.9	4.4	9.0	10.3	13.6	21.1
Seryi	12/28/1955	4.2	6.3	9.3	9.3	11.5	22.4
Tuzik	11/15/1954	3.8	5.8	7.0	11.0	12.6	28.0
Zheltok	4/19/1954	4.2	6.3	9.3	11.5	13.0	26.7
Druzhok	11/2/1955	2.6	3.9	4.4	5.0	5.0	10.6

Dog	Date	After exposure						Remarks
		Time (in hours)						
		1	2	3	4	5	24	
		Absorption (in %)						
Seryi	4/25/1956	3.6	5.5	6.1	6.7	8.1	16.2	
Seryi	5/17/1956	4.4	5.1	6.5	7.4	7.4	17.3	
Seryi	2/10/1955	1.2	1.1	1.6	1.7	–	15.9	
Tuzik	3/10/1955	2.1	4.6	4.5	5.1	5.2	16.0	Outside experimental room One month after neurosis
Zheltok	1/4/1955	1.9	3.9	4.4	5.0	5.4	16.0	
Zheltok	2/4/1955	1.1	1.9	2.4	2.6	2.8	9.4	
Druzhok	12/20/1955	4.4	5.1	6.5	7.4	7.4	17.3	
Druzhok	1/20/1955	3.8	4.0	4.0	4.5	5.3	11.1	Outside experimental room One month after neurosis

while the animals remained in the experimental room, but also 24 hours later. The fall in the value of maximal I^{131} absorption was evidence of a low level of hormone formation.

It is interesting to observe that the repeated production of a neurosis in the dog Zheltok during a considerable overstraining of the process of stimulation (the conditioned stimulus acted for 270 seconds) led to an even greater fall in the absorption by the thyroid gland. After the first neurosis in Zheltok the maximal absorption was 16%, and after the second, only 9.4%, compared with a normal maximal absorption of 26.7% for this dog. An investigation carried out outside the conditioned reflex room one month after the production of a neurosis in the dog Tuzik showed the same low level of absorption as when undertaken inside the conditioned reflex room during the neurosis.

The results obtained with the dog Druzhok were different. The absorption of I^{131} by the thyroid gland was stimulated in this dog by neurosis. The absorption was increased after the first hour of the investigation, and after 24 hours it amounted to 17.3% compared with the normal value of 10.6%. When the investigation was repeated one month later outside the room, in contrast to the other dogs the normal function of the thyroid gland was restored; at this time both the absorption during the first 5 hours after administration of iodine and the maximal absorption approximated to the initial figures obtained before production of the neurosis.

These distinctive features of the reaction of the thyroid gland in the dog Druzhok may be related to the type of the dog's higher nervous activity.

The effect of neurosis on excretion of hormonal iodine by the thyroid gland

The production of a neurosis by means of overstraining the process of stimulation by prolonging the isolated action of the conditioned stimulus to 4 minutes inhibited the excretion of hormonal iodine from the thyroid gland. This could be estimated by the increased radioactivity of the thyroid gland. This reaction developed 30 minutes

TABLE 2. The Effect of Neurosis on the Excretion of I^{131} by the Thyroid Gland

Date	Time after exposure in minutes								Delay before switching on metronone (in seconds)
	30	60	90	120	150	180	210	240	
1954									
20/XII	+9	+19	+19	+19	—	+2	—	—	100
21/XII	+12	+20	+14	+14	—	+12	—	—	100
22/XII	+21	+21	+21	+9	—	—	—	—	100
23/XII	+10	+29	—	+22	—	+16	—	—	120
24/XII	+21	+18	—	+18	—	+7	—	—	120
25/XII	+7	+18	+25	+22	—	+22	—	—	120
1955									
6/I	—	+12	—	+17	—	+22	—	+17	270
7/I	—	+13	—	+37	—	+22	—	+15	270
15/I	—	+14	—	+19	—	+19	—	+16	120
17/I	—	+18	—	+18	—	+7	—	—	120
18/I	+34	+34	+31	+23	+13	—	—	—	120
19/I	—6	+29	+31	+26	—	+24	—	+13	120
20/I	+14	+28	+34	+28	—	+20	—	+14	120
24/I	+11	+29	+25	+25	—	+21	—	+14	120
25/I	+11	+18	+34	+45	+48	+26	+15		150
26/I	+28	+32	+48	+48	—	+32	—	+24	150
27/I	+25	+46	+42	+33	+21	+8	—	—	150
28/I	+24	+34	+43	+48	+38	+24	+9	—	180
29/I	+21	+37	+48	+43	+32	+11	—	—	180
31/I	+5	+41	+41	—	+40	—	+28	+17	180

Note. The figures denote the percentage of changes. The initial radioactivity of the thyroid gland is taken as 100%.

after placing the animal in the conditioned reflex room and lasted 4 hours. The highest radioactivity of the thyroid gland was observed between 90 and 120 minutes after exposure, after which it fell gradually and approximated to its normal level after 4 hours (Table 2).

The disturbance of the higher nervous activity caused by the "clash" also led to inhibition of the excretory function of the thyroid gland, but in this case the excretion of hormonal iodine was inhibited to a greater degree and for a longer time. In Druzhok the excretory function of the thyroid gland was inhibited to the same degree by the neurosis as in the remaining animals. Thus, in Druzhok, which showed a different reaction from the other animals when the hormone-forming function of the thyroid gland was investigated, no distinctive feature was observed when the excretory function of the thyroid gland was investigated.

These results indicate a close relationship between the function of the thyroid gland and the state of the higher divisions of the nervous system.

It is clear from the results described above, and also from the observations of several workers [3, 6, 7, 8, 9], that stimuli causing extreme excitation of the nervous system produce limiting inhibition of the cerebral cortex and depress the thyroid gland function.

I. P. Pavlov [5] considered that "...exhaustion is one of the more important physiological impulses promoting the appearance of inhibition as a protective process ..... This state is, on the one hand, pathological for it deprives the patient of the possibility of normal activity, and on the other hand, from the nature of its mechanism it is physiological, because it protects the cortical cells against threatened destruction from work beyond their capacity."

In the course of the investigation it was noted that the more severe the trauma to the nervous system, the more marked the depression of the thyroid function. We gained the impression that this depression is a physiological manifestation. Apparently in conditions of neurosis the normal functioning of the thyroid gland overloads the affected cortical cells. However, besides the depression of the function of the thyroid gland during neurosis, in one dog

(Druzhok) we observed a very curious and transient change in the secretory cycle of the thyroid gland in which the hormone forming function was stimulated and the excretory function depressed. This disturbance of the secretory cycle of the thyroid gland is of particular interest and evidently indicates the beginning of a breakdown of the compensatory mechanisms.

It follows from this investigation that the disorganization of the working of the cerebral cortex affects both stages of the secretory cycle of the thyroid gland, both the process of hormone formation and that of excretion of hormones into the blood stream. We regard these changes in the secretory cycle of the thyroid gland as an initial, latent stage of thyroid gland malfunction.

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