EFFECT OF CAFFEINE AND BARBAMYL ON THE SECRETORY CYCLE OF THE THYROID GLAND

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There has been very little study of how substances that influence the central nervous system (CNS) effect the thyroid gland function. Yu. B. Skebel'skaya [6] and E. A. Kolli [3] have shown that Phenamine and caffeine in small doses increase thyroid gland function, but depress it in large doses. Luminal, amytal sodium, Nembutal, and chloral hydrate, according to M. S. Mitskevich [5] and Yu. B. Skebel'skaya [7] considerably inhibit thyroid gland function.

Since the above researchers only investigated the effect of substances influencing the CNS on the hormonogenic function of the thyroid gland, their data can only partially characterize the change in the secretory cycle of the gland. We believe study of the secretory cycle of the thyroid gland under conditions of CNS excitation or inhibition to be important, as it could throw light on the mechanisms of thyroid gland adaptation to environmental factors.

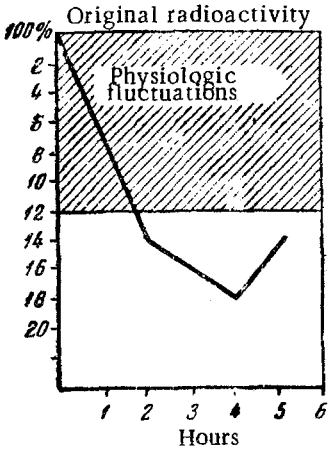

Fig. 1. Effect of caffeine on I^{131} content in thyroid gland.

EXPERIMENTAL METHODS

Dogs were subcutaneously injected with Coffeini puri in a dose of 20-30 mg/kg. The literature data indicate that these doses of caffeine most distinctly enhance conditioned reflexes (higher nervous activity) in dogs. In order to study the effect of caffeine on the hormonogenic function of the thyroid gland, we administered radioactive iodine I^{131} in a dose of 0.5 μC/kg simultaneously or 3 h after the administration of caffeine. The radioactivity of the thyroid gland was counted 1, 3, and 5 h after administration of I^{131}. The secretory function of the gland was determined 48 h and longer after the I^{131} administration. The radioactivity of the thyroid gland was measured at the beginning of the investigation and at various intervals during it.

The effect of Barbamyl on the hormonogenic function was studied by intravenously injecting a 5% solution of this substance in a dose of 1 ml/kg at the same time as the I^{131}. The radioactivity of the thyroid gland was measured for 4 h after this. The first measurement was done after 20 min, when the animal was in a state of light narcotic sleep.

To determine the effect of Barbamyl on the secretory processes of the gland, the radioactivity of the gland was counted every 30 min after the Barbamyl injection for 3 h.

Because of the wide range of fluctuation normally shown by thyroid gland absorption of I^{131}, the experimental and control investigations were carried out on the same animals.

EXPERIMENTAL RESULTS

Normally, thyroid gland absorption of I^{131} gradually increases, the average percent of absorption being 8.4% 3 h after I^{131} administration and 12.4% 5 h after it. After the administration of caffeine, the level of I^{131} absorption was less than the normal level, constituting 4.9 and 5.3%, respectively for these time intervals (Table 1). Therefore, 5 h after the administration of caffeine, I^{131} absorption by the thyroid gland was less than half the normal.

TABLE 1. Effect of Caffeine on Thyroid Gland Absorption of I^{131}

After 1 hour		After 3 hours		After 5 hours	
expt.	control	expt.	control	expt.	control
2.5	3	5.9	10.1	7	14.5
2.8	3.4	3.5	4	3.1	4.6
3.3	3	6.4	7.9	5.4	13.6
2.4	2.9	3.4	6.7	3.8	11
4	3.9	5.3	13.1	5	19.1
3	–	5	–	7.6	–
Mean 3 ±0.2	3.4 ± 0.28	4.9 ± 0.41	8.4 ± 1.15	5.3 ± 0.55	12.4 ± 1.78

TABLE 2. Effect of Barbamyl on Thyroid Gland Absorption of I^{131}

Percent of absorption after Barbamyl injection,					
after 20 min		after 1 h		after 4 h	
expt.	control	expt.	control	expt.	control
4.4	5	4.9	6.8	6.9	14.9
7.8	9.8	8	12.4	8.3	24.2
4.3	6.1	7.2	6.5	7.6	10.3
2.1	4.5	2.1	3.5	1.4	5.4
1.8	4.5	3.7	4.4	1.3	5.1

The data obtained indicate that caffeine inhibits the hormonogenic function of the gland.

The next series of experiments studied the effect of caffeine on the secretion of hormones into the blood. In these experiments, the radioactivity of the gland began to decrease 2 h after the caffeine injection. This reaction developed gradually, becoming maximal after 4 h (Fig. 1). The data obtained indicate that caffeine stimulates the secretory function of the thyroid gland.

Therefore, the effect of caffeine on the secretory cycle of the thyroid gland is characterized by inhibition of the hormonogenic phase and stimulation of the phase in which hormones are secreted into the blood.

Table 2 shows that Barbamyl decreased the level of I^{131} absorption by the gland; the reaction was evident 20 min after the Barbamyl injection, and after 4 h, the level of thyroid gland radioactivity was less than half that of the control.

Study of the hormonal secretion processes showed that the radioactivity of the thyroid gland usually increased under the influence of Barbamyl. This effect of Barbamyl became apparent during the period of deep sleep (Fig. 2, expt. No. 5). If the narcotic sleep was not deep, however, the fluctuations in the radioactivity level were within the physiologic range (see Fig. 2). The data obtained indicate that Barbamyl inhibits thyroid gland secretion of hormonal iodine.

Therefore, this series of investigations showed that Barbamyl affects both the hormonogenic processes and the processes of hormone secretion into the blood, i.e., both stages of a single secretory cycle of the thyroid gland.

This brings us to the question of whether the experimental substances act directly on the thyroid gland tissue or whether their action on the latter is effected through the CNS. Yu. B. Skebel'skaya [6,7] and M. S. Mitskevich [5], who studied the effect of substances that increase the excitation processes in the CNS (caffeine and Phenamine) and of those that increase the inhibition processes (sodium bromide, sodium amytal) have clearly demonstrated that the effect of these substances on the thyroid gland is realized through the CNS.

Clearly, our experimental findings and the literature data give reason to conclude that the experimental substances affect the functional state of the CNS, and this in turn affects the secretory cycle of the thyroid gland.

Our earlier experiments [1] showed that a certain functional state of the CNS causes changes in the secretory cycle of the thyroid gland, consisting in the inhibition of the hormonogenic process and stimulation of hormone secretion into the blood. Analysis of the mechanisms of these changes established the participation of adrenalin in this process [2]. The intravenous injection of adrenalin stimulated thyroid gland secretion of hormones and inhibited the hormonogenic processes.

The changes in the secretory cycle of the thyroid gland observed under the influence of caffeine are similar to the above. One can therefore assume adrenalin plays an important part in the mechanism of change in the thyroid gland secretory cycle attending stimulation of the CNS, no matter which stimuli produce the state of stimulation.

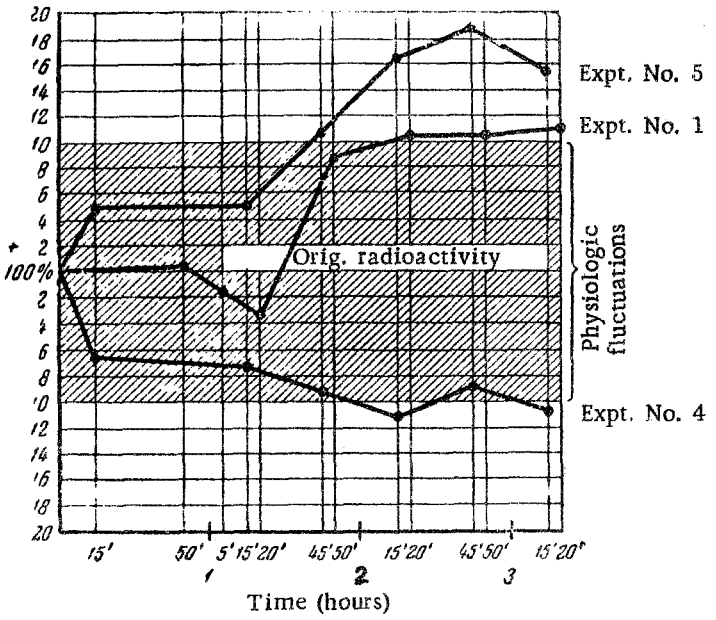

Fig. 2. Effect of Barbamyl on the I^{131} content in the thyroid gland.

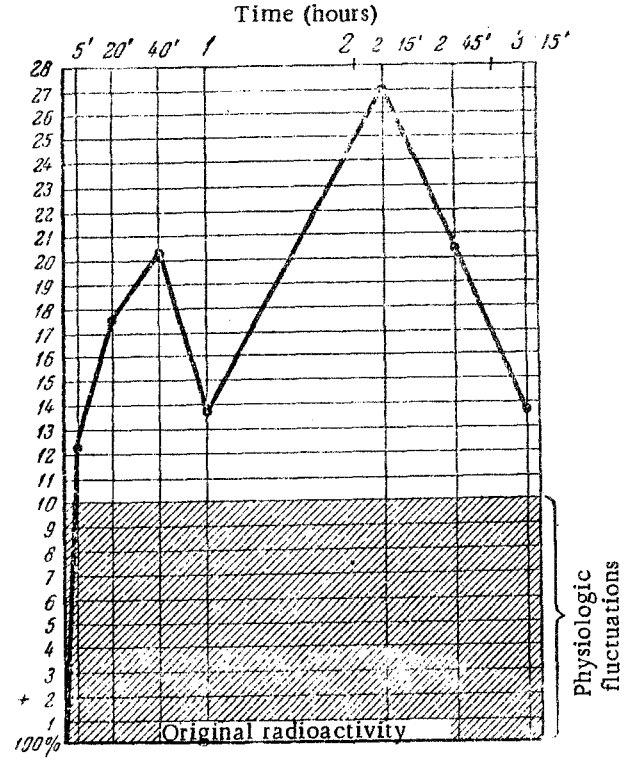

Fig. 3. Effect of noradrenalin on I^{131} content in thyroid gland.

A different picture was observed after the injection of Barbamyl. Barbamyl, which induces diffuse inhibition in the CNS, inhibits both hormonogenesis and the secretion of hormones into the blood. We observed a similar picture in our study of the effect of differentiation and extinction inhibition on the thyroid gland function [1].

In connection with the recently discovered property of noradrenalin, i.e., its selective effect on the vascular tonus [4,9], it is possible that the fall of blood pressure observed during narcotic sleep causes a reflex secretion of noradrenalin. This led us to study the effect of noradrenalin on the secretory cycle of the thyroid gland. If the administration of noradrenalin caused changes in the secretory cycle of the thyroid gland similar to those observed with the administration of Barbamyl, the data obtained could be taken as indirect proof of noradrenalin's participation in the mechanism of Barbamyl inhibition of the thyroid gland function.

There are indications in the literature that noradrenalin inhibits thyroid gland absorption of I^{131} [8]. We could not find information concerning noradrenalin's effect on the secretory function of the thyroid gland. To determine the effect of noradrenalin on the secretion of hormones from the thyroid gland, we intravenously administered noradrenalin in dose of 5 to 10 μg/kg. Two min after the injection, we observed inhibition of I^{131} secretion from the thyroid gland. As Fig. 3 shows, noradrenalin's effect became maximal 2 h and 15 min after its administration, and lasted 3 h after which the I^{131} content in the thyroid gland approximated the physiologic level. It is interesting that the inhibition of the thyroid gland secretory function observed in Barbamyl sleep also usually lasted 3 h.

The literature data and the experiments described indicate that noradrenalin causes inhibition of the secretory cycle of the thyroid gland. This gives us reason to assume that noradrenalin is part of the mechanism of the inhibition of the thyroid gland secretory cycle observed during Barbamyl sleep. In our next report, we shall analyze the changes in the secretory cycle of the thyroid gland as compared with the content of adrenalin and noradrenalin in the blood during different functional states of the CNS.

SUMMARY

A study was made of the effect produced by caffeine and Barbamyl on the secretory cycle of the thyroid gland. Both substances act on the hormone-producing processes, as well as on processes of secreting thyroid hormones into the blood through the central nervous system. Caffeine in a dose of 20-30 mg/kg body weight depressed the hormone production and stimulated the hormone secretion. Barbamyl (1 ml of 5% solution per kg body weight) depressed both the hormone production and the hormone formation and secretion into the blood. A supposition is made that adrenaline takes part in the mechanism of caffeine action, whereas the action of Barbamyl is connected with the secretion of noradrenaline into the blood.

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