THE EFFECT OF OVERSTRAINING THE DIFFERENTIATING INHIBITION PROCESS ON THE MICROSTRUCTURE OF THE THYROID GLAND IN RATS

N. E. Kovaleva

From the Department of General Biology (Head – Prof. G. M. Litver)
of the I. P. Pavlov 1st Leningrad Medical Institute
(Presented by Academician V. N. Chernigovskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 53, No. 2,
pp. 67-71, February, 1962
Original article submitted March 23, 1961

Under normal and pathological conditions, change in reactivity of the thyroid gland parenchyma is connected with the condition of the fundamental nervous processes, i.e., with excitation and inhibition in the cerebral cortex. When the equilibrium between the latter is disturbed, pathological changes in the function of the gland ensue. In experimental neurosis, bromine treatment restores disturbed thyroid gland activity [4]. When inhibition in the cerebral cortex is intensified by Barbamyl (amytal sodium), the reaction to the thyroid gland to thioureate is sharply diminished [6]. When protective inhibition develops because of overstrain of the stimulating process, hormonopoiesis increases and the excretion of hormones is inhibited [3]. Extraordinary stimuli (stress) change the level of hormonopoiesis in the thyroid gland, and this change is reflected in the microstructure of the gland [13].

Despite the quantity of experimental material conclusively demonstrating the effect of the cerebral cortex on the activity of the thyroid gland, the questions of whether this activity changes under conditions of chronically disturbed equilibrium between the fundamental nervous processes and of how important are the typological properties of the nervous system to the reaction of the thyroid gland need further investigation.

The purpose of this work was to study the changes in the histological picture of the thyroid gland under conditions of a chronically overstrained process of differentiating inhibition.

EXPERIMENTAL METHODS

The experiments were performed on 25 white rats – young males, five of which served as the control. Attention was given to the typological properties of the rats' nervous system as well as to the sex and age of the animals. The animals used in the experiment were of two basic types: 1) with a predominant stimulating process (excitable type); 2) with a predominant inhibitory process (inhibited type).

First, positive motor-food conditioned reflexes to an average-strength electric bell and the lighting of a 10-watt electric bulb were developed in the rats. When the conditioned reflexes had become fixed, differentiation stimuli were introduced: a flashing light from another 10-watt bulb and a buzzer.

An overstrained inhibitory process was obtained by daily use of the differentiation stimuli 5-7 times in one experiment and by increasing the time of their action from 20 seconds to 1, 2, and 3 minutes.

The microstructure of the thyroid gland in the experimental rats was investigated at different phases in the development of overstrain of the inhibitory process. The functional condition was evaluated from the following indices: the diameter of the follicles (DF), the height of the thyroid epithelium (HTE), the character of the colloid in the follicles and the vacuolation and vascularization of the gland.

Zenker-formol was used to fix both lobes of the thyroid gland, after which paraffin sections were cut 6 microns thick and stained with hematoxylin-eosin. An ocular micrometer was used to measure DF and HTE on the glandular sections (MBI-4 microscope, magnification: objective 40 ×, ocular 7×). The data obtained were processed by the method of statistical variation. The measurement data are given in ocular micrometer divisions.

EXPERIMENTAL RESULTS

In the rats of the excitable type, the first use of the differentiation stimulus caused intensified motor food excitation due to the irradiation of new excitation in the food center – an indication of the stable generalization of the

food excitation process in animals of this group. It took two weeks to develop the first differentiation in these animals; the second developed more rapidly and was much better defined. The rats became calmer, but the differentiations often became disinhibited. Considerable intensification of the food motor reaction and general excitation of the animals were observed from the very first day of the experiments producing overstrain of the inhibitory process.

TABLE 1. Diameter of Follicles (DF) and Height (in Ocular Micrometer Divisions) of Thyroid Epithelium (HTE) in Control Group of Rats

Rat No.	DF	HTE
1	6,49±0,21	3,04±0,03
2	6,52±0,15	3,07±0,04
3	6,43±0,31	3,13±0,02
4	5,97±0,27	3,00±0,03
5	7,32±0,41	2,97±0,02

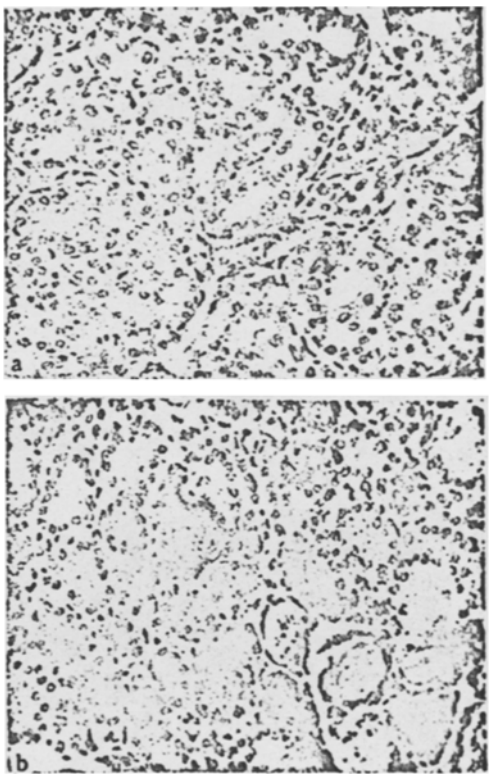

Fig. 1. Thyroid gland of white rats. a) Of control rat; b) of rat of inhibited type with-overstrained differentiating inhibition-phase of sharply increased motor food excitation: intensive vacuolation of colloid, follicular lumen enlarged. Stained with hematoxylin-eosin. Magnification: objective 40 X, ocular 5 X.

This condition lasted ten days and was succeeded by a period of four or five days in which the excitation and inhibition processes were relatively well defined. Then the inhibitory process gradually grew weaker. The activity of the food-derived reaction increased from experiment to experiment. The rats gnawed the edges of the plate with the food troughs, the floor and the walls of the chamber. During the pauses, the animals ran around in circles, shook themselves and scratched frantically. All these signs pointed to the development of "nervous difficulty" in the rats. The ensuing period was characterized by over-increasing inhibition in the cerebral cortex. Cases in which the conditioned reflex act was disturbed were often observed, followed by almost total loss of the developed food activity in most of the animals. The subcortical reactions (washing, cleaning their fur) declined considerably.

In the inhibited type of rat, overstrain of the differentiating inhibition led to depression of their general motor activity and the development of a somnolent condition. After two weeks of continuous experiments, there was a period of three or four days in which food excitation gradually increased and the differentiations became stronger and better defined. Food excitation increased from experiment to experiment, and the food-derived reflex became as forceful as in the rats of the first group. Subsequently, the excitation process grew weaker, and a gradual intensification of passive diffuse inhibition in the cerebral cortex was observed. After one or two uses of a differentiation stimulus, the rats usually curled up in a corner of the chamber and went to sleep.

The experiments with overstrain of the inhibitory process proved the reaction of the cerebral cortex to be similar in the two types of rat (excitable and inhibited). There were two main phases in the reaction – strong motor food excitation and the inhibition of the latter [8].

In the rats with an undisturbed central nervous system, the cells of the thyroid epithelium were cuboidal on the whole, with an average height of 2.97-3.13; the average follicular diameter was 5.97-7.32, with the largest follicles equal to 15 divisions in diameter. Colloid occupied the whole volume of the follicle and stained weakly with hematoxylin-eosin. Most of the follicles contained vacuoles. Vascularization of the gland was moderate (Table 1, Fig. 1a).

In the excitable type of rat under conditions of overstrained differentiating inhibition, during the phase when the excitation and inhibition processes were relatively well defined and at a high level, the histological structure of the thyroid gland changed as follows: vacuolation of the colloid increased, DF decreased, HTE increased and the lumen of the blood vessels dilated; all of which indicated the glandular function to be enhanced (Table 2). In these rats, the follicles increased considerably in volume during the phase characterized by sharp intensification of the excitation process and decline of active (internal) inhibition, some becoming as much as 25-30 divisions in diameter. Intense marginal vacuolation was observed, the thyroid epithelium became high and distended and vascularization increased. The balance between the formation and discharge of colloid was evidently disturbed in this case (latter process retarded), as the increased diameter of the follicles indicates (Table 2, Fig. 2a).

TABLE 2. Diameter of Follicles (DF) and Height (in Ocular Micrometer Divisions) of Thyroid Epithelium (HTE) in Excitable Type Rats with Overstrain of Differentiating Inhibition

State of nervous processes	Rat No.	DF	HTE
Equilibration of nervous processes at a high level	1	5,34±0,22	3,11±0,02
	2	5,82±0,21	3,21±0,02
	3	6,04±0,30	3,11±0,01
Sharp intensification of excitation process	4	8,96±0,64	3,26±0,03
	5	9,94±0,57	3,32±0,02
	6	10,24±0,63	3,31±0,01
	7	10,31±0,42	3,11±0,01
Stimulating process weakened, inhibitory intensified	8	13,31±0,41	2,56±0,03
	9	14,67±0,57	2,42±0,01
	10	16,28±0,51	2,58±0,02

During the nervous difficulty phase, when the excitation process was considerably weakened and limiting inhibition had developed, the histological structure of the thyroid gland showed its function to be inhibited. There was a great increase in the diameter of the follicles; they were acutely distended with a dense, fissured and deeply-staining colloid. There were no vacuoles in most of the follicles. The gland was mildly vascularized. To judge from the condition of the thyroid epithelial cells, it would seem that the process of colloid discharge was more inhibited in this case than that of its formation (Table 2, Fig. 2b).

In the rats of the inhibited type, the histological structure of the thyroid gland indicated its reduced functional activity during the phase in which acute passive inhibition developed in the animals as the acting time and number of uses of the differentiation stimuli were increased. The follicles were enlarged, and the thyroid epithelium was flattened; the colloid was dense, vacuolation sharply reduced (Table 3).

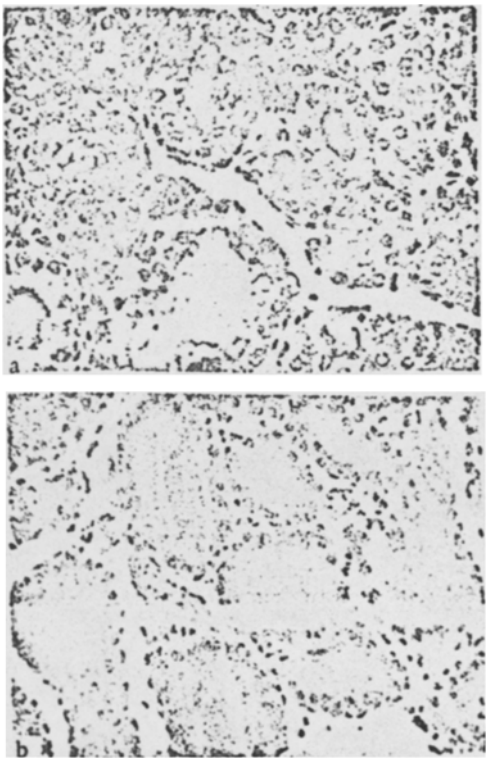

Fig. 2. Thyroid gland of excitable type of white rat under conditions of overstrained differentiating inhibition. a) During phase of acute motor food excitation; intense marginal vacuolation, enlarged follicular lumen, high thyroid epithelium. Stained with hematoxylin-eosin. Magnification: objective 40 ×, ocular 10 ×; b) during phase in which inhibited condition developed in cerebral cortex; follicular lumen acutely dilated, colloid dense and fissured, very little vacuolation. Stained with hematoxylin-eosin. Magnification: objective 40 ×, ocular 7 ×.

The activity of the thyroid gland increased during the short period of relative equilibrium of the excitation and inhibition processes. Vacuolation increased, the diameter of the follicles decreased and the height of the thyroid epithelium cells increased (see Table 3).

During the phase of intense motor food excitation in the rats, the thyroid gland follicles contained a great number of vacuoles; the colloid in some follicles, however, was very dense and contained no vacuoles. The height of

the thyroid epithelium cells approximated that observed in the control animals. In this case, the colloid formation process was evidently enhanced, while excretion of the colloid was retarded (see Table 3, Fig. 1b). In the phase near the end of the experiment, when profound diffuse inhibition and sleep developed, functional inhibition of the thyroid gland was again indicated by its histological structure, but to a lesser degree than in the first phase. It is possible that protective inhibition developed in the rats of this group, giving some stability to the activity of the thyroid gland. In two rats (No. 19 and 20) in which the passive-defense reflex was very marked and the excitation process weak, a picture of profound inhibition of general thyroid gland activity was observed during this phase. The follicular lumen was constricted, containing little colloid, and vacuoles were only observed in single follicles; the epithelium was flattened (see Table 3).

TABLE 3. Diameter of Follicles (DF) and Height (in Ocular Micrometer Divisions) of Thyroid Epithelium (HTE) in Inhibited Type Rats with Overstrained Differentiating Inhibition

Condition of nervous processes	Rat No.	DF	HTE
Development of passive inhibition	11	14.32 ± 0.61	2.11 ± 0.01
	12	12.82 ± 0.54	2.23 ± 0.02
Equilibration of nervous processes	13	7.39 ± 0.47	2.89 ± 0.01
	14	7.72 ± 0.47	2.74 ± 0.03
Acute intensification of excitation process	15	9.36 ± 0.37	2.96 ± 0.03
	16	9.69 ± 0.42	2.91 ± 0.03
Development of inhibited state and decline of excitation process	17	11.42 ± 0.61	2.58 ± 0.01
	18	12.29 ± 0.46	2.63 ± 0.02
	19	6.02 ± 0.09	2.0
	20	6.41 ± 0.18	1.83

The histological picture of the thyroid gland in the experimental rats shows the functional condition of the thyroid gland to be solely dependent on the condition of the cortical nervous processes.

The activity of the thyroid gland is enhanced when the excitation and inhibition processes in the cerebral cortex are equalized at a high level. I. P. Pavlov's school has established that a condition of increased tonus in the cerebral cortex is attended by increased activity of the internal organs [14].

When the cortical excitation process is pathologically intensified, colloid formation is enhanced, its excretion retarded.

In a pathologically inhibited state, excretion of the colloid is depressed to a greater degree than its formation, so that colloid accumulates in the follicles.

When the normal cortical activity of rats is disturbed, it is evidently the function providing for the excretion of the products of thyroid gland activity which is primarily affected.

The data obtained emphasize the importance of nervous factors to the activity, and therefore to the structure, of the thyroid gland [1, 2, 3, 12]. These data also testify to the surprisingly explicit reaction of the thyroid gland to changes in the condition of higher nervous activity, which is in accord with the theory that the gland is a highly reactive organ constantly influenced by the cerebral cortex and having, in turn, a great deal of influence on the latter [5, 10, 11, 13].

The significance of the typological properties of the rats in the function of the thyroid gland was clear from the moment the first inhibitory stimuli were used in the experiment. Thyroid gland activity was enhanced in the rats of the excitable type, while the opposite occurred in the rats of the inhibited type, i.e. depression of the thyroid gland activity was observed. Later, in the experiments producing overstrain of differentiating inhibition, both types of rat were affected in the same way by the condition of the nervous processes. This indicates that the nervous processes in the rats of the two groups were similar in strength. In two of the rats (inhibited type) in which the nervous system was weak (No. 19 and 20), overstrain of the differentiating inhibition caused acute depression of thyroid gland activity.

SUMMARY

In two groups of male albino rats – excitable and inhibited according to the type of their nervous system – the author studied the microstructure of the thyroid gland during chronic overstraining of differentiated inhibition.

In pathological intensification of the cortical process of excitation there is an increase of the intensity of colloid formation in the follicles, while its discharge is delayed. In pathological inhibition the function of the colloid excretion is depressed more than its formation. The significance of the typological peculiarities of rats for the thyroid gland function was demonstrated during the first introduction of differential stimuli into the experiment. The thyroid gland activity was augmented in the excitable rats, whereas in the inhibited animals – it decreased.

In the course of experiments the same state of the nervous processes had a similar effect on the activity of thyroid glands of both the excitable and inhibited rats.

LITERATURE CITED

1. B. V. Aleshin, N. S. Demidenko, R. V. Vyazovskaya, et al., in: Contemporary Questions of the Physiology and Pathology of the Endocrine Glands [in Russian]. Khar'kov, p. 6 (1959).
2. M. G. Amiragova, Fiziol. zhurn. SSSR, No. 1, p. 65 (1957).
3. M. G. Amiragova, Byull. éksper. biol. i med., No. 2, p. 7 (1958).
4. V. I. Arkhipenko, Probl. endokrinol. i gormonoter., No. 1, p. 42 (1956).
5. K. M. Bykov, The Cerebral Cortex and the Internal Organs [in Russian]. Moscow-Leningrad (1947).
6. A. A. Voitkevich and S. N. Gordina, Zhurn. vyssh. nervn. deyat., No. 3, p. 439 (1954).
7. M. S. Kakhana, Probl. endokrinol. i gormonoter., No. 2, p. 63 (1956).
8. N. E. Kovaleva, Byull. éksper. biol. i med., No. 2, p. 103 (1961).
9. Z. V. Novokhatskaya and I. N. Sharkevich, in: Contemporary Questions of the Physiology and Pathology of the Endocrine Glands [in Russian]. Khar'kov, p. 116 (1959).
10. R. P. Ol'nyanskaya, Abstracts of the Proceedings at the Convention on Problems of Cortical Regulation of the Endocrine Glands [in Russian]. Leningrad, p. 52 (1953).
11. M. K. Petrova, Transactions of the I. P. Pavlov Laboratories of Physiology [in Russian]. Moscow-Leningrad, Vol. 12, No. 1, p. 5 (1945).
12. A. G. Pugachev, Byull. éksper. biol. i med., No. 1 (7), p. 1 (1953).
13. E. I. Tarakanov, in: Contemporary Questions of Endocrinology [in Russian]. Moscow, No. 1, p. 245 (1960).
14. M. A. Usievich, Zhurn. vyssh. nervn. deyat., No. 1, p. 19 (1951).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical litereture may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
