THE MECHANISM OF CORTICAL CONTROL OVER THE THYROID

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We have shown previously [1] that in conditioned reflex defensive activity, cortical influences reach the thyroid by the humoral path.

We here report a study of the problem of whether the humoral connection between the cortex and the thyroid is universal, or whether the transmission may change according to the influence of the surrounding medium on the central nervous system.

METHOD

The experiments were carried out on nine dogs. The functional condition of the central nervous system was altered by means of feeding conditioned reflexes. Conditioned reflexes were established in response to the sound of a metronome at 120 beats per second, and to intermittent light from a 50 w electric lamp. Inhibitory conditioned reflexes were developed to a metronome operating at 30 beats per minute, and by intermittently extinguishing positive conditioned reflexes. The activity of the thyroid gland was estimated from its content of radio iodine. Radio iodine was given orally, as was the sodium salt, the dose being 0.7 μC per kg. The experiments were carried out 48 hours or more after injecting I^{131}. The radioactivity of the thyroid was determined immediately after presenting the conditioned stimuli, after 15 minutes, subsequently at 30 minute intervals for 3-4 hours. The change was expressed as a percentage of the original value of the radioactivity which was assumed to be 100%.

RESULTS

At the outset, a careful study was made of the variation of the radio iodine content of the thyroid while the dogs were kept in the room and in the conditioned-reflex test compartment. It was found that in neither place did the level vary by more than ±10%, a result which showed that the conditions of the experiment themselves did not cause appreciable changes in thyroid activity. In this way we determined the normal level during the period of the experiments. The animal was then given a meat powder while it was in the conditioned-reflex test compartment, the portions consisting of 25 g which were given at 5 minute intervals 5-6 times during one experiment. It was found that here too the thyroid gland activity did not vary by more than ±10%. It was therefore, established that the food stimulus is without effect on thyroid activity.

The next stage was to determine the effect of the conditioned food stimuli on the thyroid activity.

Even the first experiments in elaborating feeding conditioned reflexes showed that a considerable change in the level of thyroid radio iodine occurred.

It can be seen from Fig. 1 that when conditioned reflexes are developed to M_{120}, the amount of radio iodine in the thyroid gland is reduced and that the low level is maintained for 2-3 hours, after which it returns to its

TABLE 1

Effect of the Development of Conditioned Feeding Reflexes on the I^{131} Content of the Thyroid in Hypophysectomized Animals

Date of experiment	Original radioactivity (in imp/min)	Change in the I^{131} content during time: 30 min		1 hr 5 min–1hr 20 min		2 hr 5 min – 2 hr 20 min		3 hr 5 min–3 hr 20 min		4 hr 5 min–4 hr 20 min	
		imp/min	% change	imp/min	% change	imp/min	% change	imp/min	% change	imp/min	% change
1958 г.											
1/VII	1 184	1 180	—0,3	1 120	—5,4	920	—22,3	928	—21,6	992	—16,2
3/VII	799	799	0	863	+8,0	799	0	799	0	863	+8,2
12/VII	384	336	—12,5	272	—29,2	224	—41,7	240	—37,5	341	—11,2
14/VII	288	224	—22,3	176	—38,9	208	—27,8	240	—16,7	320	+11,1
21/VII	153	99	—35,4	71	—53,7	82	—46,5	102	—33,4	108	—29,5
1959 г.											
26/I	2 832	2 152	—24,1	1 824	—35,6	1 872	—33,9	1 936	—31,7	1 936	—31,7
27/I	2 000	1 744	—12,8	1 744	—12,8	1 808	— 9,6	1 872	— 6,4	1 936	— 3,2
30/I	1 376	1 108	—19,5	1 044	—24,2	1 140	—17,2	1 220	—11,4	—	—
2/II	1 040	770	—26,0	720	—30,8	752	—27,7	810	—22,2	878	—15,6
3/II	1 040	844	—18,9	878	—15,6	944	— 9,3	966	— 7,2	990	— 4,8

original value. With training, the response of the thyroid to the conditioned stimulus is reduced, and disappears when well reinforced conditioned reflexes are established (See Fig. 1). The development and reinforcement in a single animal of a conditioned reflex to a second new stimulus, for example, to intermittent light, produces a change in thyroid gland activity similar to that which has just been described.

The effect of inhibition (extinction) on the secretion of the labelled hormone is increased in some animals and in others it is depressed (see Fig. 1). M. A. Usievich [2] observed a rather similar effect when studying the influence of the cerebral cortex on visceral function. He was able to show that the greatest change in the activity of the stomach, pancreas, liver, and other organs occurred during the period when either positive or inhibitory conditioned reflexes were being elaborated.

I. N. Knipst, T. A. Korol'kov, and M. N. Livanov [3] also showed that the synchronization of cortical activity was best shown during the development of a conditioned reflex and was maintained for a short while after it had been elaborated, i.e., when it was most completely generalized. The increased synchronization of cortical electrical activity was also observed when the conditioned reflexes were being extinguished.

The results reported show that in contrast to unconditioned reflexes, for conditioned reflexes the whole set-up of the experiment and the application of conditioned stimuli to dogs is a very delicate task. Conditioned reflex activity requires a considerable potential in the cerebral cortex, particularly when the animal is first confronted with a new stimulus which induces widespread excitation of the central nervous system. This result is reflected in some way in the operation of the viscera, and, as our experiments have shown, on the work of the thyroid. As conditioned reflex training continues, the excitation becomes concentrated, and a well-developed conditioned reflex has no appreciable effect on visceral function, or, in particular, on the operation of the thyroid.

Thus, the results obtained for the thyroid indicate the immensely important part played by the functional condition of the central nervous system, or, more accurately stated, by the condition of the cells of the cerebral cortex in controlling endocrine activity.

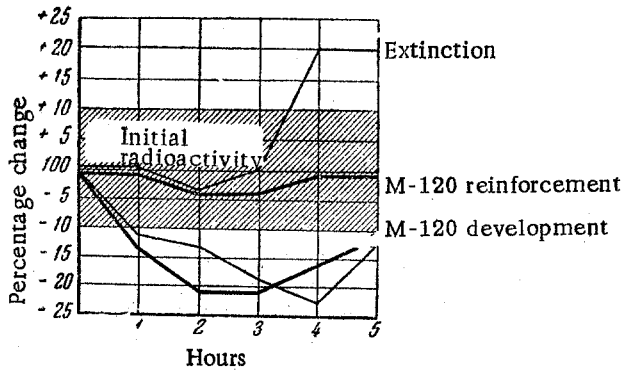

Fig. 1. The effect of conditioned food stimuli on the I^{131} thyroid gland content.

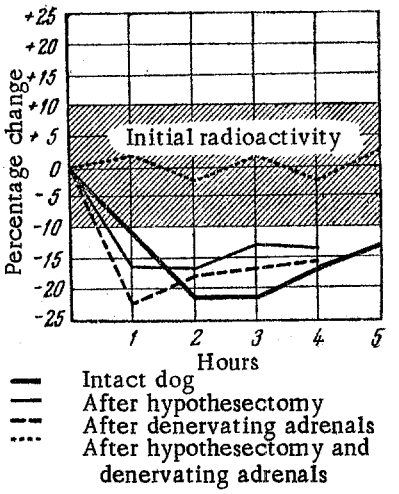

Fig. 2. Change in the amount of I^{131} in the thyroid gland of a dog during feeding conditioned reflex activity. Experiment conducted after breaking the connection between the central nervous system and the adrenals.

It was extremely important to determine in what way the influence of the central nervous system on the thyroid is conveyed. Using the method described previously [1], we have studied the transmission path from cortex to thyroid in three sets of experiments. It was first required to determine whether the cortical influence travels along the same pathway as it does during defensive conditioned reflex activity.

The first experiments were carried out on hypophysectomized animals in order to determine whether the hypophysis is an essential link in the transmission between cortex and thyroid. The animals were used for the experiment three weeks or more after removing the anterior lobe of the hypophysis. In the operated animals, it was difficult to develop conditioned reflexes; thus, in one operated dog, the first conditioned reflex appeared on the 17th combined application of the conditioned and unconditioned stimuli. As a rule, the latent period varied between 3 and 5 seconds, and sometimes was as long as 7 seconds. The reflexes were difficult to reinforce, and frequently even after reinforcement, it was difficult to obtain a prompt response to the initial stimulus. Hypophysectomy therefore produced a definitely deleterious influence on higher nervous function.

As can be seen from Table 1, the effect of the formation of conditioned feeding reflexes in the hypophysectomized animals was to increase the secretion of radio iodine from the thyroid. In most cases this response appears immediately at the end of stimulation; during the next 2-3 hours the reaction increases further, and then gradually declines. The same result was obtained in almost all the experiments of this series. The results shown in Table 1 indicate that the cortical effect on thyroid gland function can take place without the involvement of the hypophysis, a conclusion which is in line with the results which we obtained on defensive conditioned reflex activity.

In the next set of experiments we studied the part played by the adrenal glands in the transmission of the cortical influence on thyroid function. The animals were used for the experiment after removing the anterior pituitary lobe, and after separating the adrenals from the central nervous system by dividing the left-splanchnic nerve and removing the right adrenal gland. In these animals, conditioned reflex activity was approximately the same as in the hypophysectomized dogs.

It can be seen from Table 2 that food conditioned stimuli had no effect on thyroid function. Variations in the level of radio iodine in the gland did not exceed ±10 %. As was pointed out previously, such variations are within normal limits. Consequently, no change in thyroid function is caused by the elaboration of conditioned reflexes. Therefore, in this case cortical influence does not extend to the thyroid gland. In these animals, under the influence of internal inhibition the amount of radio iodine in the thyroid gland again does not exceed the normal limits of variation. Thus, after removal of the hypophysis and destroying the connection between the

TABLE 2

The Effect of the Development of Positive and Inhibitory Feeding Conditioned Reflexes on the I^{131} Thyroid Gland Content after Hypophysectomy and the Disassociation of the Adrenals from the Central Nerous System

Date of experiment	Initial radio-activity (in imp/min)	Change in the I^{131} content during time:										Remarks
		30 min		1 hr 5 min - 1 hr 20 min		2 hrs 5 min. - 2 hrs 20 min		3 hrs 5 min - 3 hrs 20 min.		4 hrs 5 min.- 4 hrs 10 min.		
		imp/ /min	% change	imp/ /min	% change	imp/ /min	% change	imp/ /min	% change	imp/ /min	% change	
1958 r.												
1/IV	440	440	0	440	0	440	0	440	0	440	0	
3/IV	362	362	0	362	0	362	0	362	0	362	0	
5/IV	238	238	0	238	0	238	0	238	0	238	0	
7/IV	240	240	0	240	0	240	0	240	0	240	0	
24/IV	17 114	18 394	+7,4	16 538	—3,4	19 226	+12,3	16 538	—3,4	—	—	
28/IV	13 904	13 200	—4,9	13 392	+3,8	13 712	—1,3	13 520	—2,8	14 032	+0,9	
29/IV	12 880	12 304	—4,6	12 816	—0,5	12 672	—1,7	12 816	—0,5	12 176	—5,5	
4/V	7 834	7 898	+1,0	8 154	+4,0	8 090	+3,2	8 026	+2,4	7 962	+1,6	After injecting thyrotropic hormone
7/V	6 409	6 537	+1,9	6 281	—2,0	6 153	—4,0	6 089	—5,0	6 163	—4,0	
8/V	5 836	6 156	+5,4	5 644	—3,7	5 900	+1,0	5 836	0	5 836	0	
16/V	3 982	4 110	+3,2	4 110	+3,2	4 174	+4,9	4 110	+3,2	4 046	+1,6	
22/V	1 557	1 493	—4,1	1 557	0	1 429	—8,3	1 493	—4,1	1 493	—4,1	
23/V	1 316	1 380	+4,8	1 380	+4,8	1 380	+4,8	1 380	+4,8	1 380	+4,8	Extinction
24/V	1 120	1 184	+5,7	1 184	+5,7	1 120	0	1 120	0	1 184	+5,7	»
26/V	989	989	0	989	0	989	0	989	0	989	0	»
8/XII	943	922	—2,3	937	—0,7	928	—1,6	928	—1,6	928	—1,6	
10/XII	825	883	+7,0	843	+2,2	873	+5,8	857	+3,9	873	+5,8	
12/XII	666	650	—2,5	666	0	666	0	660	0	666	0	Differentiation
13/XII	374	366	—2,2	382	+2,1	382	+2,1	382	+2,1	—	—	
15/XII	407	444	+9,0	407	0	453	+11,3	425	+4,4	417	+2,4	

adrenals and the central nervous system, neither the development of positive conditioned reflexes nor the establishment of internal inhibition exerts any influence on the secretion of labelled thyroid hormone.

Because it is known that thyroid function is reduced by hypophysectomy, it would be expected that the failure of the thyroid to respond to cortical impulses would occur as a result of its reduced level of activity. In order to discount this explanation, it was required to stimulate thyroid function in these animals, which was done by repeatedly injecting thyrotropic hormone. Thus, in the dog Lorta, 7 months after operation the maximal absorption of radio iodine was reduced from the normal value of 22.4% to 4.8%. After subcutaneous injections of 0.5-1 ml of the thyrotropic hormone "Ambinon", the maximum absorption of radio iodine by the thyroid had increased to 45%. The results of experiments carried out on animals in whom the thyroid gland had been stimulated in this way were no different from those described above (see Table 2).

The results of this set of experiments completely agree with those obtained in the study of defensive conditioned reflexes. After hypophysectomy and the interruption of the nerve supply to the adrenals, all possibility of the transmission of cortical influence to the thyroid gland had been excluded.

The problem then arose as to whether the adrenals are normally involved in the transmission of cortical influence to the thyroid, when the hypophysis is still present.

After severing the nerve supply from the central nervous system to the adrenals as described above, the development of conditioned relfexes was associated with a greater excretion of labelled hormone into the blood stream (Fig. 2). This result shows that in this case the link between the central nervous system and the thyroid includes the hypophysis. For the sake of clarity, in Fig. 2 the results for all three sets of experiments are shown.

The following conclusions may be made from the results obtained: the effect of the cerebral cortex on the liberation of thyroid hormone can occur only when either the hypophysial or the adrenal hormonal link is present.

Because the existence of this hormonal link is essential for the transmission of both defensive and feeding conditioned reflexes, i.e., for the realization of different influence from the surrounding medium, it may be taken as established that humoral transmission is a quite general means of association between the central nervous system and the thyroid gland.

SUMMARY

The action of the cerebral cortex upon the thyroid gland is effected humorally during both feeding and defensive reflex activity.

In both instances either the hypophysis or the adrenal glands are involved. It is concluded that humoral transmission is quite a general form of connection between the cerebral cortex and the thyroid.

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*Original Russian pagination. See C. B. translation.