# MECHANISM OF MESENCEPHALIC RETICULAR INFLUENCES ON THE HYPOTHALAMIC–PITUITARY–THYROID SYSTEM

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The role of the posterior hypothalamic nucleus in the transmission of mesencephalic reticular influences on thyroid hormone secretion was studied. In response to stimulation of the mesencephalic reticular formation in anesthetized cats the concentration of iodine bound with plasma proteins was increased. After bilateral coagulation of the posterior hypothalamic nucleus this effect disappeared. The results confirm the hypothesis of the leading role of the posterior hypothalamic nucleus in stimulation of thyroid hormone secretion.

KEY WORDS: *Reticular formation; hypothalamus; thyroxine; thyroid function.*

It is well known that reticular neurons, on which efferent influences of all modalities converge, transmit excitation to various brain structures including the hypothlamic-pituitary system. The anatomical basis of these influences is provided by the very numerous axon connections between the mesencephalic reticular formation and the posterior and medial portions of the hypothalamus [6, 15, 16].

It can accordingly be postulated that influences exerted on the mesencephalic reticular system modify the functional state of hypothalamic structures which regulate the secretion of the anterior lobe of the pituitary gland; this, in turn, must modify the secretion of hormones by the peripheral endocrine glands. Information on the role of the mesencephalic reticular formation in thyroid hormone secretion is limited in quantity and contradictory in nature. Some workers [7], after stimulating the mesencephalic reticular formation, observed an increase in the uptake of radioactive iodine by the thyroid gland, whereas destruction of this part of the brain was followed by depression of thyroid function. According to data published by other workers [19], in response to stimulation of the mesencephalic reticular formation the uptake and liberation of radioactive iodine by the thyroid gland were reduced, whereas after coagulation of this region thyroid function was stimulated.

The object of this investigation was to study the character and mechanisms of the influence of the mesencephalic reticular formation on thyroid hormone secretion.

## EXPERIMENTAL METHOD

Experiments were carried out on 25 sexually mature cats weighing 2.5-3 kg, anesthetized with urethane (1.5-2.0 g/kg). Brain electrical activity was recorded on a 17-channel Nihon Kohden (Japan) electroencephalograph. Nichrome wire electrodes 0.3-0.5 mm in diameter and a cannula electrode were inserted into the subcortical structures in accordance with the coordinates of a stereotaxic atlas [18]. The position of the tips of the electrodes and cannula was determined by the projection method [21]. To coagulate the posterior hypothalamic nucleus a direct current of 1.5-2.0 mA was passed for 1-2 min. The experiments were carried out 3 h after coagulation. The EEG was analyzed by means of a two-channel wide-band integrator (Nihon Kohden). Iodine bound with plasma proteins (PBI) was determined in blood from the femoral vein [10, 12]. Blood was taken 30, 60, and 120 min after injection of thyroxine (45 µg), made up in physiological saline at pH 7.4-7.6, into the brain structures.

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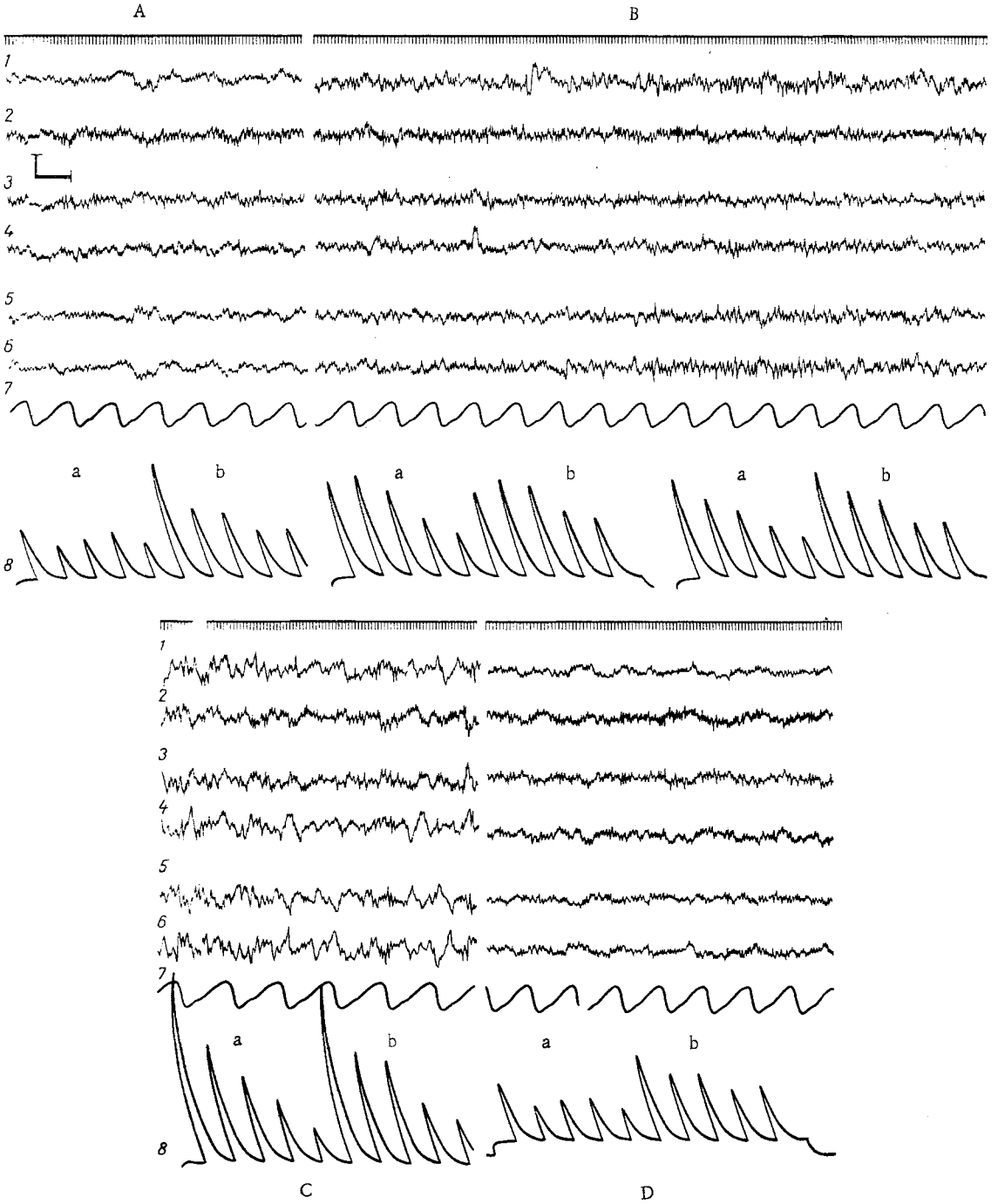


Fig. 1. Effect of thyroxin, injected into mesencephalic reticular formation, on subcortical electrical activity: 1) mesencephalic reticular formation; 2) left posterior hypothalamic nucleus; 3) left hypothalamic arcuate nucleus; 4) right ventromedial hypothalamic nucleus; 5) right posterior hypothalamic nucleus; 6) right lateral hypothalamus; 7) respiration; 8) frequency spectrum of right reticular formation (a) and ventromedial nucleus (b). A) Spontaneous activity; B) immediately after injection of thyroxin; C) 9 min later; 7) 35 min later. Calibration: 50 μV, 1 sec.

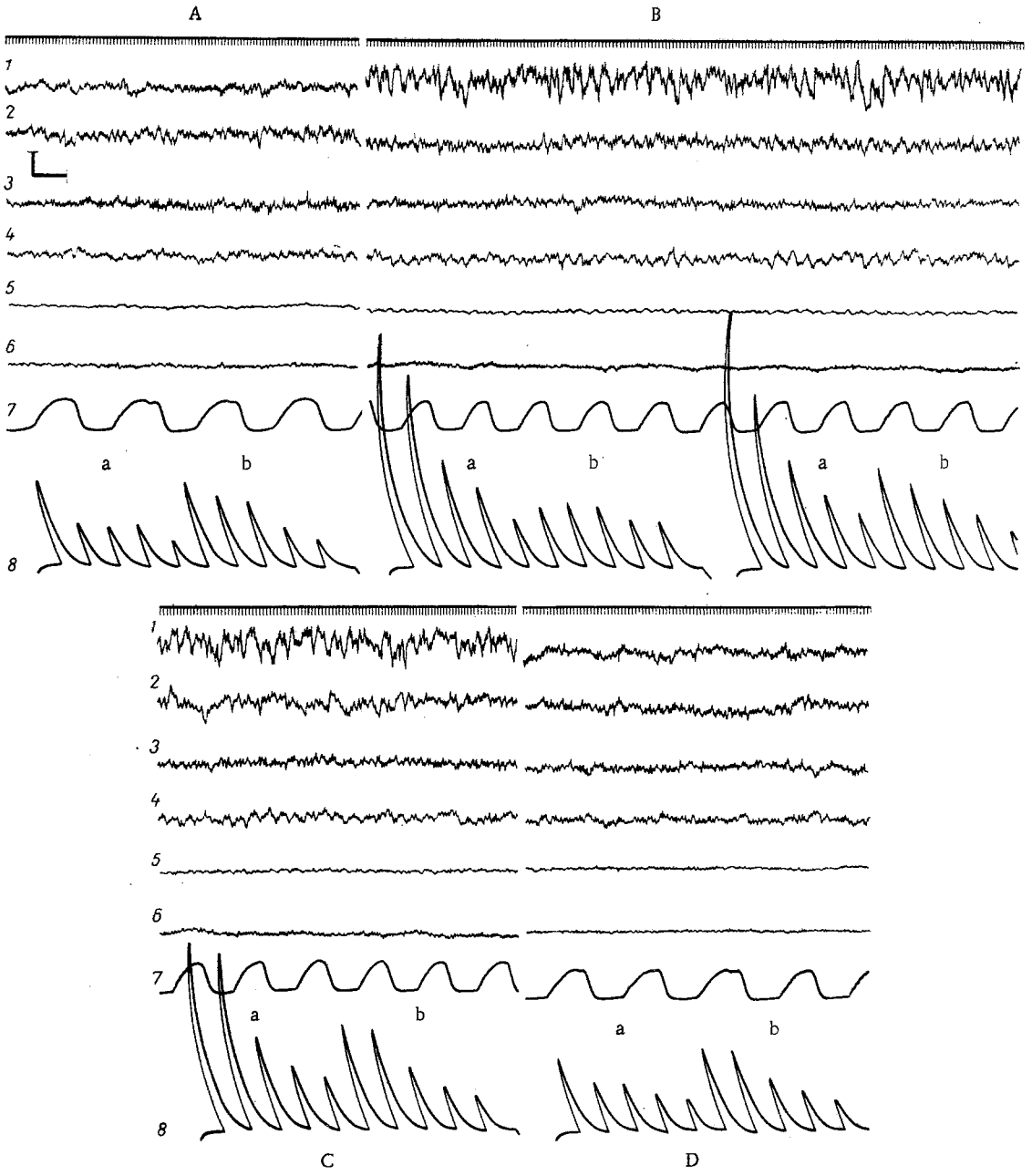


Fig. 2. Effect of thyroxine, injected into mesencephalic reticular formation, on subcortical electrical activity in animals with coagulated posterior hypothalamic nuclei: 1) right mesencephalic reticular formation; 2) right ventromedial hypothalamic nucleus; 3) left hypothalamic arcuate nucleus; 4) right lateral hypothalamus; 5) right posterior hypothalamic nucleus; 6) left posterior hypothalamic nucleus; 7) respiration; 8) frequency spectrum of reticular formation (a) and ventromedial nucleus (b). A) Spontaneous activity; B) 9 min after injection of thyroxine; C) 10 min later; D) 20 min later. Calibration: 50 μV, 1 sec.

## EXPERIMENTAL RESULTS

After injection of thyroxine into the mesencephalic reticular formation, besides local activation of the EEG accompanied by changes in its rhythms, mainly in the slow-wave range, a successive change was observed in the potentials in the posterior hypothalamic nucleus and the ventromedial and lateral hypothalamus; after a short time generalized synchronization developed, when structures situated contralaterally relative to the side of injection of the hormone were activated. The most marked changes were observed in the region of slow rhythms (Fig. 1). Besides the successive involvement of the various hypothalamic structures in the

TABLE 1. Effect of Thyroxine, Injected into Mesencephalic Reticular Formation, on Plasma PBI Level in Cats with Intact and Coagulated Posterior Hypothalamic Nuclei (M±m)

| Group of animals | PBI, μg% | | | |
|---|---|---|---|---|
| | before injection of thyroxine | at various times after injection of thyroxine | | |
| | | 30 min | 60 min | 120 min |
| With intact hypothalamus | 7,60±0,38 (13) | 8,48±0,39 (13) | 9,15±0,66 (8) | 8,63±0,69 (9) |
| *P* | | <0,05 | <0,02 | <0,01 |
| With coagulated posterior hypothalamic nuclei | 5,39±0,23 (8) | 5,46±0,24 (7) | 5,26±0,26 (8) | 4,93±0,34 (6) |
| *P* | | >0,5 | >0,5 | >0,5 |

Legend. Number of animals shown in parentheses.

response, in some experiments activation which spread to all hypothalamic structures at once and which lasted 10 min was observed to develop, after which the response subsided and the EEG returned close to its background level. A fresh response of activation then appeared, in which the posterior hypothalamic nucleus performed the function of triggering mechanism, for its activity increased again before that of the other structures. These cyclic changes in brain electrical activity could be observed for 30 min or more. In some cases there were corresponding changes in the depth and frequency of respiration. The writers previously [3, 4] observed phasic changes in cortical and subcortical brain potentials under the influence of thyroid hormones. Under these circumstances cortical structures were recruited into activation after the subcortical structures, and they also were deactivated later; this fact indicated a role of the cortex in reverberation mechanisms, for it evidently maintained the periodic development of activation in the subcortical structures through the posterior hypothalamus. This conclusion is supported also by results obtained after bilateral coagulation of the posterior hypothalamic nucleus. In such animals both the response of generalized synchronization and the cyclic character of the response disappeared (Fig. 2). The brevity of the response of the ventromedial and arcuate nuclei of the hypothalamus, which are sources of thyrotropin-releasing hormone [8, 9, 11, 13, 14, 17, 20], recruiting them into activation will be particularly noted. Whereas in intact cats this activation was observed periodically throughout the experiment, after the operation its duration did not exceed 2-4 min, after which it disappeared completely. It is this fact (the shortening of the duration of the response) that was discovered to play the decisive role for secretion of thyrotropin-releasing hormone.

When thyroid function was studied during the action of the hormone on the mesencephalic reticular formation in intact animals an increase in the plasma PBI level in the course of 2 h was observed (Table 1). Injection of the hormone in the same way in animals with bilateral coagulation of the posterior hypothalamic nucleus did not affect the blood PBI level. These results indicate that the mesencephalic reticular formation influences thyroid hormone secretion indirectly through the posterior hypothalamic nucleus, and they agree with previous observations [1] demonstrating the leading role of the posterior hypothalamic nucleus in the regulation of thyroid hormone secretion.

The facts described above support the writers' hypothesis of the trigger role of the posterior hypothalamic nucleus in the stimulation of hormonal secretion. It is this structure, which has the highest sensitivity to hormonal influences [2, 5] and which is closely connected with the nuclei of the mediobasal hypothalamus, that is essential for maintaining the nuclei of the hypophysiotropic region of the hypothalamus in a state of prolonged activation. The short-term activation of structures of the mediobasal hypothalamus observed in the animals undergoing the operation was inadequate for producing changes in thyroid hormone secretion.

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