

Amplitude variations of antidromic spike evoked in the infraorbital nerve by microelectrode ipsilateral stimulation of the rostra part of the trigeminal spinal tract during REM sleep. Chronic cat. (1) Cervical EMG; (2) bifrontal EEG; (3) eye movements; (4) antidromic response. Calibration 100 μ V and 1 sec.

up to 80% of the values recorded during the other phases of sleep in the absence of REM.

Spontaneous or naturally induced arousal was also generally accompanied by a phasic increase of the antidromic spike amplitude. These phasic augmentations during the sleep-wakefulness cycle were quite comparable to those induced by conditioning electrical stimulations of the skin of the nose at the best interval.

Conclusions. The results show that the trigeminal primary afferents undergo a phasic process of depolarization during desynchronized sleep and arousal. It is concluded that in analogy to what has been reported for primary afferents to the spinal cord¹⁻⁵ and cuneate nucleus⁶ trigeminal fibres are presynaptically inhibited during the REM of desynchronized sleep and at the moment of arousal.

Riassunto. Durante i movimenti oculari rapidi nel sonno desincronizzato ed al momento del risveglio si assiste ad un aumento in ampiezza della risposta antidromica evocata nel nervo infraorbitario dalla stimolazione microelettroica del tratto spinale del trigemino a livello pontino. Tali variazioni suggeriscono un processo di inibizione presinaptica che agisce fascicamente sulle terminazioni afferenti primarie del trigemino.

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The Effect of Thyroid Gland on 5-Hydroxytryptamine (5-HT) Level of Brain Stem and Blood in Rabbits

The relationships between thyroid function and tryptophan metabolism are not well elucidated. Thyroxine, or the extract of thyroid gland, produced a transient increase in the 5-HT content of abdominal skin and ileum of the rat¹. Other authors found thyroidectomy to be ineffective in changing the 5-HT content in stomach and intestine². It has also been noted that in the urine of patients with thyrotoxicosis there was an increased excretion of 5-hydroxyindoleacetic acid (5-HIAA), while in some hypothyroid patients the excretions of 5-HIAA were decreased⁴. Hyperthyroid patients treated with

reserpine showed a carcinoid syndrome from 3-6 h after the first dose of reserpine which may have been due to 5-HT release⁵, as the patients with hyperthyroidism had a significant increase in urinary 5-HIAA in the first 6 h after reserpine. It is also known that the daily injection

¹ P. S. J. SPENCER and G. B. WEST, *Int. Archs Allergy appl. Immun.* 20, 321 (1962).

² R. H. RESNICK, G. T. SMITH, and S. J. GRAY, *Am. J. Physiol.* 207, 571 (1961).

³ B. SKANSE and A. HANSON, *Lancet* 282, 1072 (1962).

⁴ B. J. HAVERBACK, A. SJOERDSMA, and L. L. TERRY, *New Engl. J. Med.* 255, 270 (1956).

⁵ M. BLUMENTHAL, R. DAVIS, and R. P. DOE, *Arch. int. Méd.* 116, 819 (1965).

of thyroxine decreased significantly the monoamine oxidase (MAO) activity in the rat liver but not in the brain⁶.

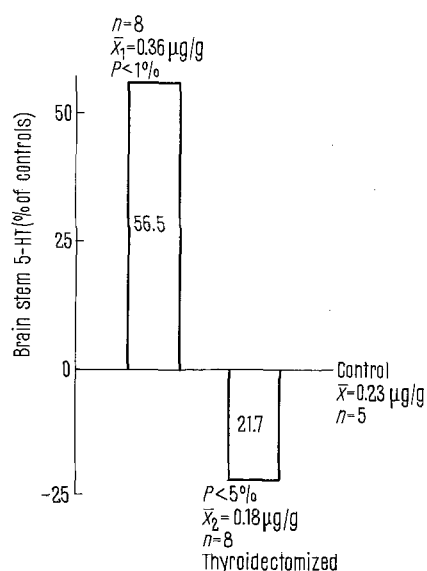
In our experiments we have attempted to answer the following questions: (1) How does the 5-HT level of brain stem change after feeding the animals with desiccated thyroid gland, or after thyroidectomy? This is a particularly interesting problem because an increase in the 5-HT level of the brain generally causes an increased activity of the central nervous system⁷, and a decrease in the 5-HT content produces sedation. (2) How does the 5-HT content of blood change under the influence of thyroid? It is well known that the 5-HT content of blood in rabbits is so high that a marked quantity of it might remain in the brain stem after bleeding the animals.

Male and female rabbits weighing 2–3.5 kg were used. At the beginning of the experiments, the 5-HT content of whole blood was determined by the fluorometric method of UDENFRIEND et al.⁸, taking 0.5 ml of blood samples from the ear vein (using Zeiss PM QII. spectrophotofluorometer). On one group of animals a total thyroidectomy was performed under Intranasal anaesthesia. The other group of rabbits was fed on a daily dose of 50 mg/kg body weight desiccated thyroid (Richter) for 14 days. On the 14th day the 5-HT level of the whole blood was determined in both groups. After bleeding, 1 g of brain stem was excised and the 5-HT content extracted, using borate buffer according to the method of UDENFRIEND et al.⁸. Oxyhemoglobin determinations were made in half of the homogenized brain-stem samples⁹ in order to subtract the blood 5-HT content.

We have found that rabbits fed with thyroid lost from 400–600 g body weight, showed hypermotility, and on an average their temperatures increased 0.3°C. The body weight of the thyroidectomized group increased more than 300–400 g, and in the meantime the motility and rectal temperature decreased 0.2°C on the average.

The 5-HT content of brain stem in fed animals increased 56.5% ($p < 1\%$), while in thyroidectomized animals it showed a 21.7% decrease ($p < 5\%$).

The increase of 5-HT content of whole blood was the same as that seen in the brain, though the decrease in blood 5-HT level in the thyroidectomized group was more marked.



The influence of thyroid gland on the alteration of 5-HT level in the rabbit brain stem. Fed with desiccated thyroid gland.

These observations are of interest in connection with the supposed physiological significance of the 5-HT function in the brain. It might be supposed that the peripheral symptoms of hyperthyroidism and hypothyroidism are mediated not exclusively by the effect of the thyroid gland on the peripheral tissues but through the tryptophan metabolism, which influences the activity of the central nervous system. On the basis of our results such symptoms as hyper- and hypomotility, nervousness, etc. in thyroid disorders may be explained by the alterations in the 5-HT levels in the brain stem.

The effect of thyroid gland on 5-HT level of whole blood in rabbits

Group fed with desiccated thyroid gland			
	Before treatment μg/ml	After treatment μg/ml	Increase in %
1.	1.2	1.5	25.0
2.	1.55	1.65	6.4
3.	3.6	4.8	33.3
4.	2.2	2.55	15.9
5.	1.7	1.95	14.7
6.	3.6	4.1	13.8
7.	1.8	1.95	8.8
8.	2.05	2.35	15.0

$S = 0.28; p < 1\%$.

Mean 19.1%

Thyroidectomized group			
	Before treatment μg/ml	After treatment μg/ml	Decrease in %
9.	5.4	1.0	28.5
10.	5.3	3.1	41.5
11.	1.45	1.0	31.0
12.	4.1	2.1	48.7
13.	2.7	1.7	37.0
14.	2.7	1.45	46.2
15.	1.6	0.9	43.7
16.	1.6	1.2	25.0
17.	2.2	1.25	43.3

$S = 0.57; p < 0.1\%$.

Mean 38.3%

Zusammenfassung. An Kaninchen wurde die Wirkung von Schilddrüsenfütterung und Thyreoidektomie auf das 5-HT-Niveau im Hirnstamm und Blut untersucht. In hyperthyreotischem Zustand ist der 5-HT-Spiegel im Blut und im Hirnstamm erhöht, bei Athyreose ist er verringert. Der Schilddrüseneffekt wird in der Veränderung des Tryptophan-Stoffwechsels über das zentrale Nervensystem gesehen.

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⁶ M. H. ZILE, *Endocrinology* 66, 311 (1960).

⁷ J. H. QUASTEL, *Br. med. Bull.* 21, 49 (1965).

⁸ S. UDENFRIEND, H. WEISSBACH, and B. B. BRODIE, *Methods of Biochemical Analysis* (Interscience Publ., New York 1958), vol. VI, p. 95. Ed. D. GLICK.

⁹ S. TÓTH and I. JÓKAY, *Kisérlet. Orvostud.* 17, 666 (1965).