

As far as the authors can establish, no report other than that of ALHA<sup>4</sup> has been published on the effect of acute ethanol administration on the calcium level in human serum, but the excretion of calcium in urine has been found to increase<sup>1-3</sup>. According to the latter observations, ethanol produces no major change in the excretion of inorganic phosphorus in urine. In the present study the increase in the excretion of inorganic phosphorus was considerably more marked than that in the excretion of calcium. On the basis of the present observations, it is difficult to explain the mechanism that produces the simultaneous increase in the serum levels of calcium and inorganic phosphorus. The total dose of ethanol given was small, in all cases less than 1 mg/g body weight. The increased activity of alkaline serum-phosphatase, which was noted in some cases, suggests a mobilization of calcium and phosphorus from the bones, although not all test subjects showed increased phosphatase activity.

The increase in calcium and phosphorus content of the serum was particularly marked in two patients: No. 3, a young girl aged 15, who suffered from thyrotoxicosis, and

No. 1, a man aged 40, who suffered from hyperparathyroidism (Tables I and II).

Further studies which may elucidate the mechanism by which ethanol mobilizes calcium and inorganic phosphorus, as well as studies on the kinetics of radioactive calcium and strontium in connection with ethanol administration, are in progress.

*Zusammenfassung.* Äthanol wurde 9 Versuchspersonen i.v. verabreicht (50 ml 94% Äthanol in 500 ml physiologischer Kochsalzlösung). Unter der Infusion stieg der Kalzium- und Phosphorgehalt des Blutes an. Eine gleichzeitige Calciurie und starke Phosphaturie wurde beobachtet. Der Mechanismus dieser Phänomene ist noch ungeklärt.

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### Presynaptic Inhibition of Trigeminal Afferent Fibres during the Rapid Eye Movements of Desynchronized Sleep

It has recently been reported that, synchronously with the rapid eye movements (REM) of desynchronized sleep, the excitability of primary afferents to the spinal cord<sup>1-5</sup> and cuneate nucleus<sup>6</sup> increases, suggesting a presynaptic inhibitory process<sup>7</sup> phasically acting on these terminals during the above-mentioned phase of sleep.

The aim of the present investigation has been to study, by means of WALL's technique<sup>8</sup>, the excitability of primary trigeminal afferents to the brain stem at pontine level during the various phases of sleep and wakefulness, and particularly during the REM episodes of desynchronized sleep<sup>9</sup>.

*Methods.* The experiments were performed on unanaesthetized unrestrained cats with chronic implanted electrodes. The electroencephalogram (EEG), the electromyogram of the cervical muscles (EMG) and the electrooculogram (EOG) were recorded by an ink-writer electroencephalograph. The stimulation of the trigeminal afferents was achieved monopolarly through a stainless steel microelectrode (50,000–100,000  $\Omega$ ) stereotaxically introduced into the rostral part of the spinal tract of the trigeminal nerve at about 6–8 mm rostrally to the obex. The antidromic response evoked by stimulation of the trigeminal fibres was bipolarly recorded, with a type of electrode already described<sup>10</sup>, from the ipsilateral infraorbital nerve after the eye was enucleated. In the same animal, chronic stimulating electrodes were also inserted underneath the skin of the nose in order to stimulate cutaneous afferents of the trigeminal territory able to depolarize the infraorbital nerve afferents<sup>11</sup>. Through this technique the possibility that the trigeminal afferents could be depolarized by conditioning volleys in different experimental conditions was tested.

*Results.* (1) Single shock stimulation (2–3/sec, 0.01–0.05 msec, 30–40 V) of the trigeminal spinal tract 6–8 mm rostrally to the obex evoked in the ipsilateral infraorbital

nerve an antidromic response with 0.6–0.7 msec latency. Conditioning electrical stimuli (4 impulses at 300/sec, 0.1 msec) applied to the nose during wakefulness constantly increased the amplitude of the antidromic test response recorded from the infraorbital nerve. The conditioning curve showed a time course similar to that reported in acute animals<sup>11</sup> with maximal facilitation (up to 30–100% of the control values) at 35–40 msec stimulus interval.

(2) The amplitude of the infraorbital antidromic spike remained stable throughout the entire periods of relaxed wakefulness and synchronous sleep. No tonic modifications of the response were ever observed as the animal passed from synchronized to desynchronized sleep. During the latter phase the amplitude of the antidromic response did not change when the REM were absent (Figure). Synchronously with the most intense periods of REM, a phasic increase of the infraorbital antidromic spike amplitude occurred (Figure). The amplitude variations were

<sup>1</sup> A. R. MORRISON and O. POMPEIANO, *Boll. Soc. ital. Biol. sper.* **41**, 631 (1965).

<sup>2</sup> F. BALDISSERA, M. G. CESA-BIANCHI, and M. MANCIA, *Boll. Soc. ital. Biol. sper.* **41**, 20 (1965).

<sup>3</sup> F. BALDISSERA, M. G. CESA-BIANCHI, and M. MANCIA, *Atti Accad. naz. Lincei, Memorie Cl. Sci. fis. mat., serie VIII*, **39**, 321 (1965).

<sup>4</sup> A. R. MORRISON and O. POMPEIANO, *Archo ital. Biol.* **103**, 517 (1965).

<sup>5</sup> F. BALDISSERA, M. G. CESA-BIANCHI, and M. MANCIA, *J. Neurophysiol.* **29** (1966), in press.

<sup>6</sup> G. CARLI, K. DIETE-SPIFF, and O. POMPEIANO, *Experientia* **22**, 329 (1965).

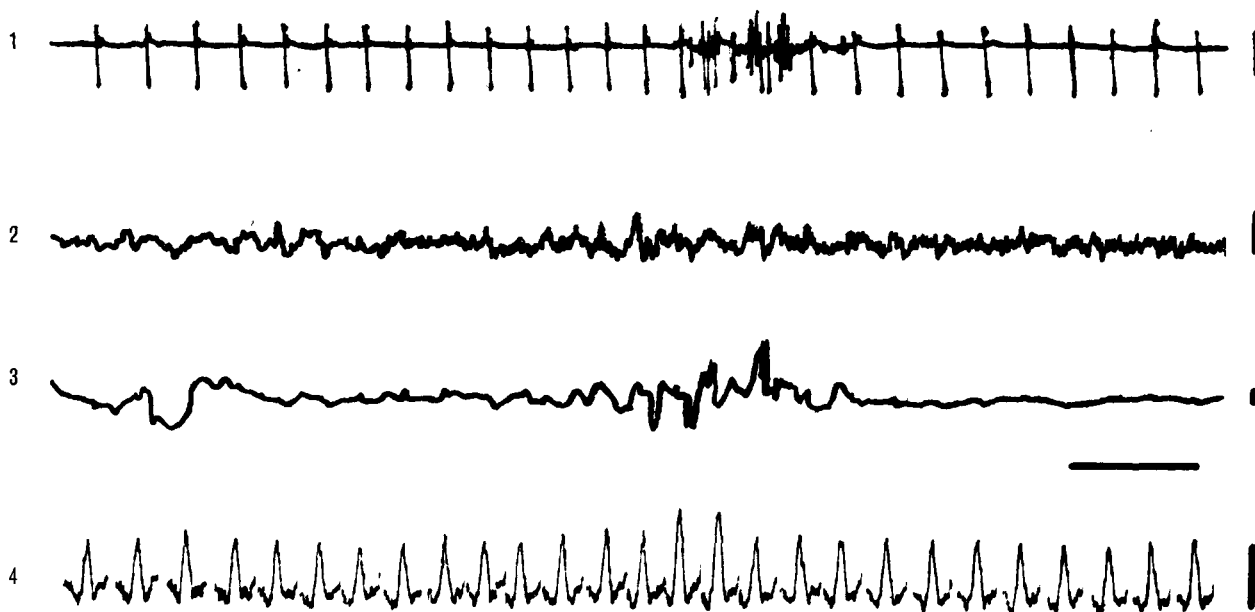
<sup>7</sup> J. C. ECCLES, *The Physiology of Synapses* (Springer Verlag, Berlin 1964), p. 316.

<sup>8</sup> P. D. WALL, *J. Physiol.* **142**, 1 (1958).

<sup>9</sup> M. JOUVET, *Archo ital. Biol.* **100**, 125 (1962).

<sup>10</sup> F. BALDISSERA, G. BROGGI, and M. MANCIA, *Archo ital. Biol.* **104**, 112 (1966).

<sup>11</sup> I. DARIAN-SMITH, *J. Neurophysiol.* **28**, 695 (1965).



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  $\mu$ 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 cord<sup>1-5</sup> and cuneate nucleus<sup>6</sup> 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 rat<sup>1</sup>. Other authors found thyroidectomy to be ineffective in changing the 5-HT content in stomach and intestine<sup>2</sup>. 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 decreased<sup>4</sup>. 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 release<sup>5</sup>, 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

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

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

<sup>3</sup> B. SKANSE and A. HANSON, *Lancet* 282, 1072 (1962).

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

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