VERY SLOW RHYTHMIC VARIATIONS IN THE POTENTIAL OF THE NUCLEI OF THE HYPOTHALAMUS AND THE THALAMUS

N. A. Aladzhalova and A. V. Kol'tsova

From the Institute of Biological Physics (Director – Corresponding Member of the AMN SSSR G. M. Frank) of the Academy of Sciences of the USSR, Moscow

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It has been established [1, 2] that besides the electrical activity which is usually revealed by the electrocorticogram, in various areas of the brain it is possible to register very slow periodic variations in potential, with a frequency of 5-8 per minute and an amplitude of 0.3-0.8 mv. We have called these "hyperslow" or "infraslow" [3]. Investigations [1-7] have shown that in a number of cases there is a definite connection between the phase of the very slow wave and the pattern of the electrocorticogram: for example periodic outbursts of rapid activity are observed at one of the extremes of the very slow variation [3]; in other cases intensification of the very slow rhythms accompanies synchronization of the activity of the neurones [4, 7].

The very slow variations in the intact animal are asynchronous in different areas of the hemispheres and they may have different parameters in the upper and lower layers of the cerebral cortex [5]. In a state of general anesthesia (with ether and barbiturates) they undergo depression, whereas by action on certain links in metabolism, for instance by cholinesterase inhibitors or by oxygen lack, intensification of the very slow rhythms ensues [4, 7]. Increase in the regularity and amplitude of the very slow variations is also found during prolonged stimulation of the receptors of the visual and taste analyzer [6].

Influences affecting the region of the hypothalamus as a rule stimulate the very slow variations in potential in the cerebral cortex [3, 4, 6], for instance a local injection of acetylcholine into the region of the hypothalamus leads to an increase in the regularity and amplitude (three-fold) of the very slow waves in the cerebral cortex [7]. In order to understand the mechanism of this stimulation we considered it desirable to investigate the presence of very slow variations in the structures of the hypothalamus and the thalamus.

EXPERIMENTAL METHOD

Twenty-four experiments were performed on 13 waking rabbits with impressed electrodes. To the surface of the sensomotor zone of the cerebral cortex of one or both hemispheres in each rabbit were applied plated silver electrodes for bipolar leads, 4 mm in diameter and at a distance of 6 mm between their centers. In addition two or three bipolar electrodes were impressed into the nuclei of the thalamus and hypothalamus of each rabbit. In all 20 experiments to record the potential in the nuclei of the thalamus were performed and 10 in the hypothalamus. As leads from the subcortical nuclei nichrome electrodes were used, 50-100 μ in diameter. In the case of a bipolar lead two such electrodes were fixed together with a bakelite varnish in such a way that the distance between the tips of the leads was 150 μ. In these conditions both points of the leads could be in the same nucleus of the thalamus or hypothalamus. The same electrodes were used for stimulation of the subcortical nuclei. In the case of a unipolar lead from the subcortical structures, an indifferent plated electrode was applied to the surface of the cerebral cortex in an area from which very slow variations in potential were absent. As a control of the state of the nucleus the electrothalamograms and hypothalamograms were recorded. The position of the electrode was determined by a control histological examination of the brain (thickness of section 10 μ). Electrical stimulation was carried out by rectangular impulses with a frequency of 50 cps and

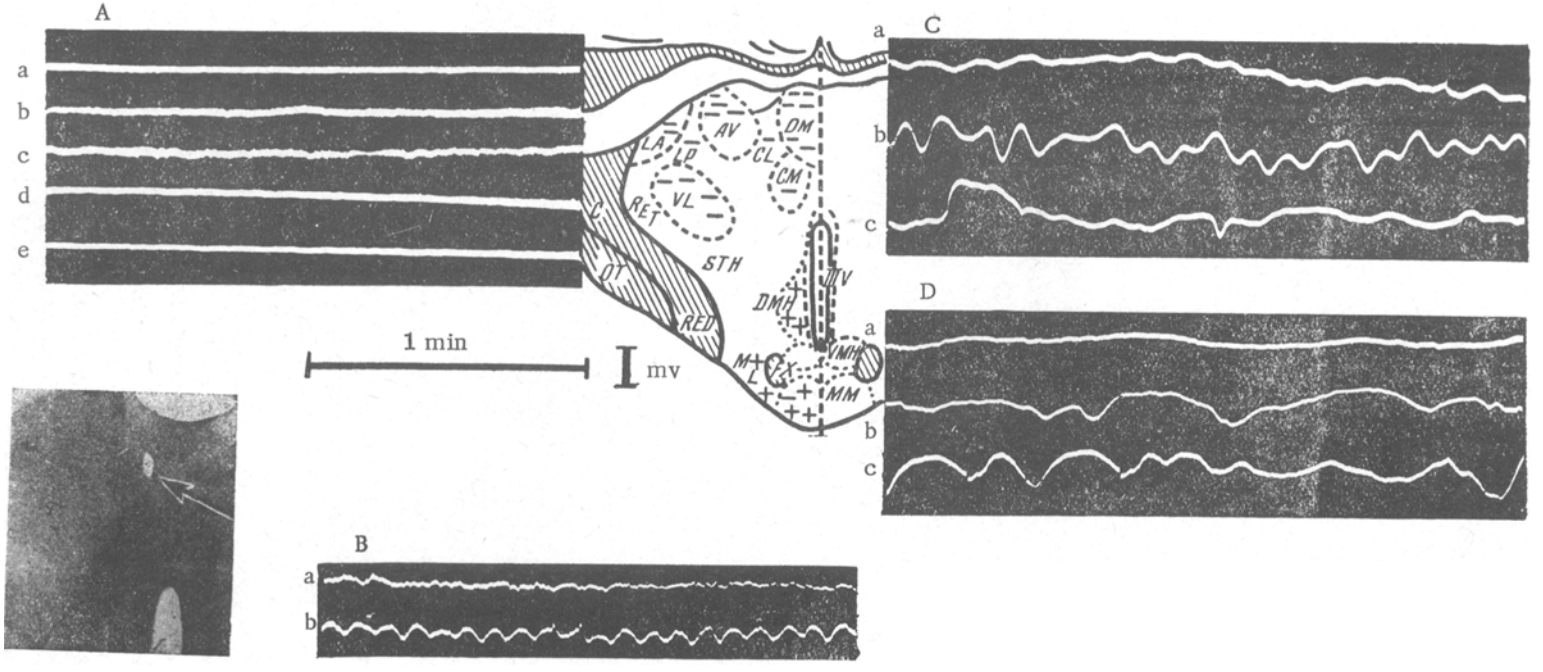

Fig. 1. Very slow variations in potential in the nuclei of the hypothalamus (+) and their absence from the nuclei of the thalamus (−). A) Lead from the thalamus: a) nucleus lateralis posterior (LP); b) nucleus medialis dorsalis (DM); c) nucleus lateralis anterior (LA); d) nucleus ventralis lateralis (VL). B) Very slow variations in potential in the DM of the thalamus before (a) and 95 minutes after (b) injection of atropine intravenously (10 mg/kg) — see section of the brain. C and D) Examples of very slow variations in the sensomotor cerebral cortex and in the premamillary region of the hypothalamus (two different rabbits): a) cortex of the right hemisphere; b) cortex of the left hemisphere; c) premamillary region of the left side of the hypothalamus (irregular very slow variations).

amplitude of 2 v, which did not cause any motor reaction. The duration of one stimulus varied from 20 seconds to 3 minutes. Electrical stimulation of the region of the hypothalamus was carried out in 12 experiments and stimulation of the lateral and medial thalamic nuclei in 10 experiments, and in 5 experiments intravenous and subcutaneous injections of strychnine were given. The potentials were recorded by means of a direct current amplifier [1] with a symmetrical input and a 5 T loop output.

EXPERIMENTAL RESULTS

In Fig. 1 are indicated in conventional form in one plane the outlines of the nuclei of the thalamus and hypothalamus in which the electrodes were impressed. The – sign indicates points in which very slow potentials were not found, while the + sign indicates where these very slow rhythms were present. In waking rabbits, subjected to no form of activity apart from the operation of insertion of the electrodes, no very slow rhythms were present in any of the 20 cases in the thalamic nuclei. In Fig. 1, A are given tracings from both the lateral and medial nuclei of the thalamus; the character of the electrograms recorded from these nuclei was proof of their preservation of function. Very slow rhythms could not be detected in the nuclei of the thalamus with either bipolar or unipolar leads. However, in the region of the premamillary hypothalamus, in the dorsal medial and ventral medial nuclei, in 9 cases out of 10 irregular very slow variations with a frequency of 5-7 oscillations per minute and an amplitude of 0.3 mv were recorded. In tracings from the sensomotor zone of the cerebral cortex, very slow rhythms were also present in 10 of 13 rabbits. In Fig. 1, C and D are shown the very slow variations in potential in the premamillary region of the hypothalamus and in symmetrical zones of the cortex of both hemispheres. In these experiments the very slow variations in the cerebral cortex were more clearly shown on the side in which the hypothalamic electrodes were impressed. This may be the result of the stimulating effect of the electrodes [3].

Ether anesthesia leads to complete depression of the very slow variations in both the hypothalamus and the cerebral cortex.

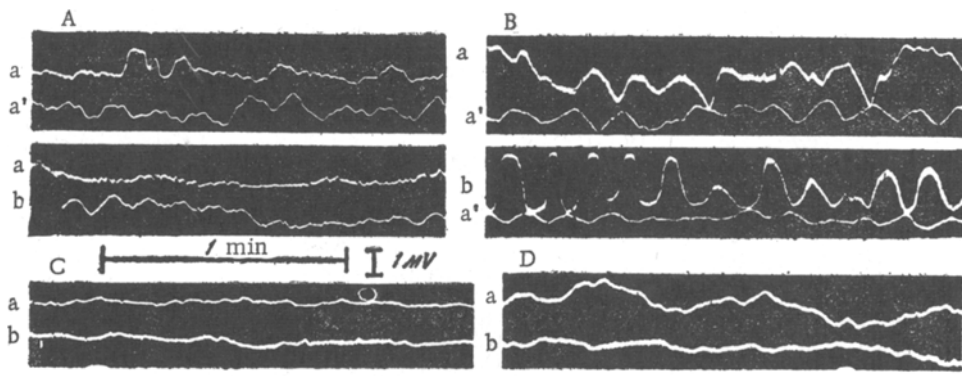

Fig. 2. The influence of electrical stimulation of the hypothalamic and thalamic nuclei on the very slow variations in the potential in the cerebral cortex and the hypothalamus. A) Two-channel tracing before stimulation of the doral medial nucleus of the hypothalamus (DMH); B) the same afrer prolonged stimulation of the DMH; a) DMH on the rightside; a') sensomotor zone of the left hemisphere; b) sensomotor zone of the right hemisphere; C and D) examples of absence of intensifying effect from the thalamus on the very slow variations in the potential of the cerebral cortex. C) Sensomotor cortex before (a) and after (b) stimulation of the thalamus – nucleus centralis pars lateralis (CL) on the ipsilateral side; D) before (a) and after (b) stimulation of the DM of the thalamus.

The irregular variations in potential in the hypothalamus may, as a result of certain influences, become more regular in amplitude and frequency. A stimulating factor of this sort is electrical stimulation. Stimulation of the dorsal medial nucleus of the hypothalamus (DMH) lasting for 2-3 minutes may cause excitation of this region, as judged by the increase in the rapid activity on the hypothalamogram (to 12 cps), although in

some cases there were no visible changes in the rapid activity. At the same time only 2 minutes after stimulation it was possible to observe clear intensification of the very slow variations at first in the hypothalamus itself and later (after 20 minutes) in the ipsilateral cerebral cortex, and still later (after 120 minutes) in the contralateral cortex.

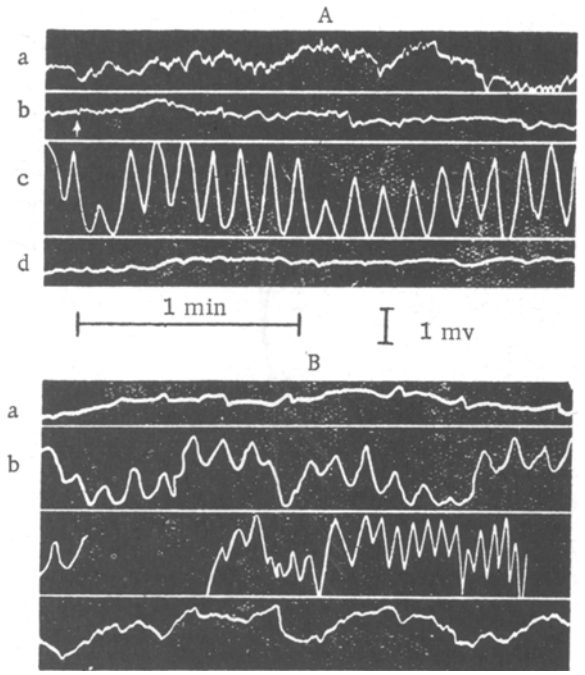

Fig. 3. The effect of strychnine on the very slow potential in different structures. A) Premammilary region of the hypothalamus; a) before injection; b) 17 minutes after injection of strychnine in a dose of 0.5 mg/kg intravenously (– convulsion); c) 25 minutes afterwards (regular rhythm of 8 cycles per minute); d) after 80 minutes (depression of the rhythm). B)The cerebral cortex in the same experiment; a) before injection of strychnine; b) 40 minutes after injection (rhythm of 8 cycles per minute); c) after 47 minutes (rhythm of 16 cycles per minute); d) after 60 minutes.

However, in order to obtain clearly the effect of intensification of the very slow variations in the hypothalamus and cerebral cortex, it was sometimes necessary to use stimuli to the hypothalamus which were repeated several times, as a result of which synchronous very slow rhythms arose in symmetrical areas of the hemispheres and in the hypothalamus. In Fig. 2 A and B are given two-channel records from the dorsal medial nucleus of the hypothalamus and the cerebral cortex of both hemispheres before stimulation (A) and after stimulation three times of the DMH (B) lasting for up to 30 seconds. As a result, synchronous oscillations appeared in all three regions in a frequency of 5 per minute and an amplitude of 1 and 1.5 mv.

Electrical stimulation of the thalamic nuclei: central lateral (CL), dorsal medial (DM), lateral anterior (LA) and lateral ventral (LV) did not produce this effect and could even cause depression of the very slow oscillations in the cerebral cortex (Fig. 2 C and D).

Injection of strychnine increased the frequency and amplitude of the very slow variations in the hypothalamus and the sensomotor zone of the cerebral cortex.

In Fig. 3, A it is seen that after intravenous injection of strychnine (0.5 mg/kg) a phase of depression of the very slow variations appears after 15 minutes in the premamillary region of the hypothalamus, associated with which are observed convulsions, temporary respiratory paralysis and, in consequence of this, asphyxia. After recovery from this state, 25 minutes after the injection, a very regular slow rhythm arises in the region of the hypothalamus, with a frequency of 8-9 cycles per minute and an amplitude rising to 2.5 mv. Forty minutes later this same rhythm was recorded in the cerebral cortex (Fig. 3, B), and after 7 minutes the frequency of the rhythm increased to 16 cycles per minute. After an hour the very slow variations in both the hypothalamus and the cerebral cortex became weaker.

In another experiment in which strychnine was injected subcutaneously in a dose of 0.6 mg/kg, without complication by asphyxia after brief convulsions associated with depression of the very slow variations, after 40 minutes there appeared in the hypothalamus a rhythm with a frequency of 6 per minute and an amplitude of 2 mv; after 75 minutes there were recorded in the cerebral cortex variations at the rate of 9 per minute with an amplitude of 1 mv; there was no effect in the anterior lateral nucleus of the thalamus (LA).

The absence of very slow variations in the potential of the thalamus in the intact animal and their presence in the hypothalamus, and also the possibility of their appearance in the thalamus after action on the metabolism of the brain, evidently indicate the existence of an intimate connection between the phenomenon of very slow variations and peculiarities of the metabolic processes.

A specific property of the hypothalamus is its regulating action on the very slow potential of the cerebral

cortex. This is clearly observed during electrical stimulation of the dorsal medial and ventral medial nuclei of the hypothalamus.

During the action of strychnine the change in the parameters of the very slow rhythms in the hypothalamic region outstrips the changes in the cerebral cortex by 10-30 minutes. This time sequence admits the possibility of a nervous mechanism of regulation of the very slow rhythms in the cerebral cortex by the hypothalamus, since it is at roughly this same interval of time after injection of strychnine into the nucleus of the hypothalamus that discharges appear in the cerebral cortex [8]. It may be supposed that the mechanism of regulation consits of changes in the local chemical gradients in the structures of the cerebral cortex.

The appearance of synchronous pulsation of the very slow variations in different areas of the hemispheres and in the hypothalamus itself after stimulation indicates the onset of a generalized effect, during which the separate regions of the cerebral cortex may take part in synchronized activity.

Equality of the functional potentials in the different zones is organized in this case through a neuroendocrine mechanism.

Synchronization of the very slow variations evidently reflects the tuning of different areas of the hemispheres to a single metabolic level. At the same time the electrical field created in the cortex by the intensified very slow variations of potential extended to cover a considerable mass of dendrites, and by affecting the electrotonic potentials of the dendrites, it was able to alter periodically the excitation of the system of cortical neurones [4, 9]. Evidently the very slow potential is one of the links in the mechanism linking the neuroendocrine function of the brain and its electrical activity, thereby taking part in the integrative action of the brain.

SUMMARY

Infraslow oscillations (8 cycles per minute, 0.5 – 1 mv) formerly revealed in the rabbit's brain cortex, were also registered in the premammillary hypothalamus. This infraslow rhythm was absent in the thalamic nuclei of intact animal, but could be revealed after acting upon the brain metabolism by strichnine or atropine.

Electric stimulation of hypothalamic dorsal-medial and ventral-medial nuclei increases the amplitude and the regularity of the infraslow rhythm in the sensomotor brain cortex and the hypothalamus proper.

After strychnine injection the intensification of the infraslow fluctuations appears in the hypothalamus 10-30 minutes earlier than in the brain cortex.

Prolonged stimulation of hypothalamus may cause generalized infraslow oscillations synchronic in different portions of the brain. Creating a definite gradient of electric field in the brain cortex the infraslow potential affects the excitability of neurons, reflecting the association between the neuroendocrine function and the electric activity of the brain. Infraslow oscillations are one of the links in the integrative brain activity.

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