NEUROPHYSIOLOGICAL AND HORMONAL CORRELATES OF CHRONIC IMMOBILIZATION STRESS

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Adaptation of the organism to repeated stressors is characterized by a gradual fall in secretion of corticosteroids [4, 6, 8, 9]. However, the role of the CNS in these processes has received very little study. Accordingly, in the investigation described below, a comparative study was made of the dynamics of hormonal secretion and cortical and subcortical electrical activity during the development of emotional stress caused by chronic immobilization of animals.

EXPERIMENTAL METHOD

Chronic experiments were carried out on five cats weighing 3.5-4 kg exposed to immobilization stress. The animals were placed in a restraining chamber, through a narrow hole in the front panel of which the head protruded, and was outside the chamber. One hind limb was brought out through a hole in the back panel of the chamber and also was fixed outside it. The animals were immobilized four times, for 4 h each time. Blood for determination of hormones was taken through a catheter previously implanted into the jugular vein. Blood was taken before the experiment, 1 h and 4 h after its beginning, and 1 h after the end of the experiment, outside the experimental chamber. To exclude the effect of the circadian rhythm on the blood hormone levels, blood samples were taken from the control animals at the same time intervals. The total thyroxine and corticosteroid concentrations in the blood serum were determined by radioimmunologic assay using special kits. Thyroxine was determined by the T_4 Res-O-Mat kit (Byk-Mallinckrodt). Cortisol was determined by a competitive binding method using Cortipac kits (from Amersham Corporation, England), according to instructions given by the firm. Electrodes were implanted by means of a stereotaxic apparatus into the lateral, ventromedial, and posterior hypothalamic nuclei, dorsal hippocampus, medial amygdaloid nucleus, mesencephalic reticular formation, and sensomotor and frontal regions of the cerebral cortex. Deep electrodes were inserted in accordance with an atlas of the cat's brain [4]. The location of the electrodes was verified histologically [9] and their positions in the brain structures were identified from maps in the same atlas of the cat's brain [4]. Potentials were derived by a monopolar method. The reference electrode was located above the frontal sinus. The experiments were conducted in a screened chamber. The animals were kept on a constant diet and blood was taken on an empty stomach, 18 h after eating. Brain electrical activity was recorded on a 17-channel polygraph (Nihon Kohden, Japan). Frequency analysis of the EEG was carried out by means of a two-channel wide-band integrator, made by the same firm.

EXPERIMENTAL RESULTS

It will be clear from Fig. 1a that values of all rhythms in the background electrical activity recorded from cortical and subcortical structures of unrestrained cats were relatively uniformly distributed. The posterior hypothalamic nucleus in which, judging from frequency analysis, values of theta-rhythms and high-frequency beta-rhythms predominated, was to some extent an exception in this respect.

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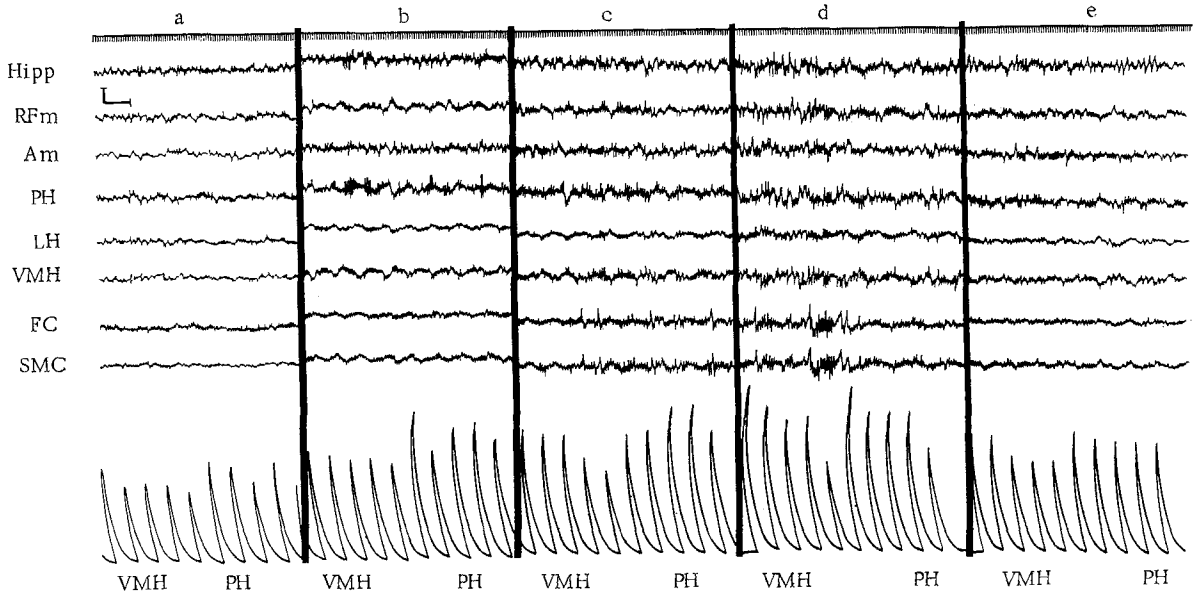

Fig. 1. Time course of EEG changes during first section of immobilization. Hipp) Dorsal hippocampus, RFm) mesencephalic reticular formation, Am) amygdala, PH) posterior hypothalamic nucleus, LH) lateral hypothalamic nucleus, VMH) ventromedial hypothalamic nucleus, FC) frontal region of cerebral cortex, SMC) sensomotor cortex. Spectral analysis of EEG rhythms illustrated below. a) Background recording, b) 10 min, c) 1 h, d) 4 h after beginning of immobilization, e) 1 h after end of immobilization.

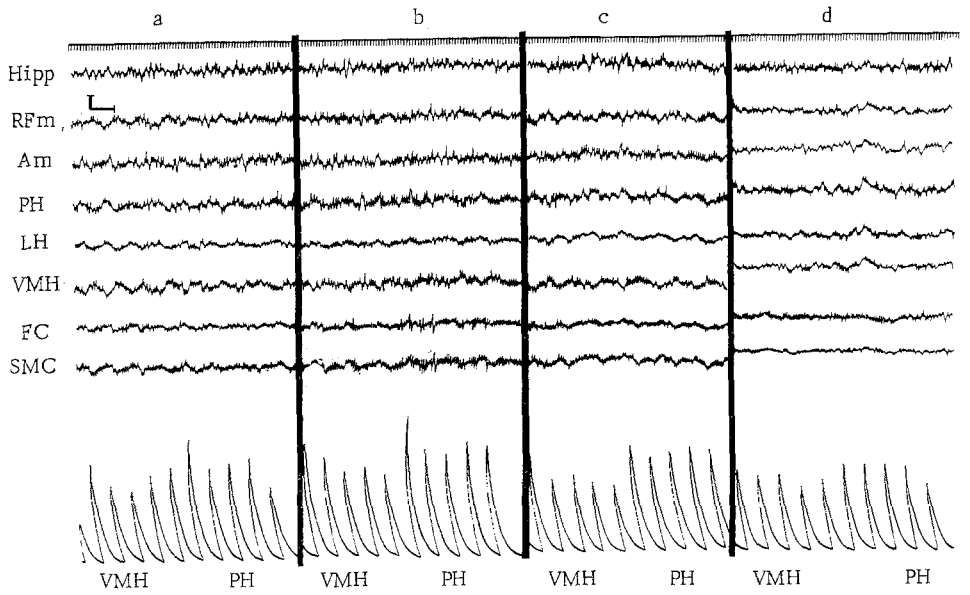

Fig. 2. Time course of EEG changes during 4th session of immobilization. a) Background recording, b) 1 h, c) 4 h after immobilization, d) 1 h after end of immobilization. Remainder of legend as to Fig. 1.

After the animal had been placed in the restraining chamber, the electrical activity of the brain structures showed characteristic changes. At first this was most clearly apparent in the posterior hypothalamic nucleus, where the power of all the rhythms were grouped into distinctive volleys. These also were recorded in the hippocampus. In the course of 1 h the activity of other brain formations, including the cerebral cortex, gradually increased. During the 4th hour cycles of "bursting" activity of slow waves appeared, and at the same time the power of the high-frequency rhythms increased. The "bursting" synchronized activity disappeared 1 h after the end of immobilization, in the unrestrained animals, but in deep brain structures and, in particular, in the posterior and ventromedial hypothalamic nuclei, epileptiform slow-wave discharges were recorded, evidence of the high functional state of the deep brain structures. During the second immobilization changes in brain electrical activity described above increased in intensity, the cycles of "bursting" activity, once having begun, became dominant in character and were recorded throughout the experiment. During the after-period the electroencephalographic activity of the brain formations was similar to that described after the first immobilization. During the first two sessions of immobilization changes in electroencephalographic activity thus reflected in high level of negative emotional strain.

A fundamentally different picture was found during the third and fourth immobilizations. At this time single volleys of high-amplitude epileptiform slow-wave activity were recorded on the EEG of the cortex and deep brain structures, especially during the first hour. "Bursting" activity as a rule did not appear. During the after-period the changes described above disappeared and the electrical activity of the brain reverted closely to the background values (Fig. 2a). This analysis thus revealed how the electrographic reflection of the functional state of the cortex and deep brain structures depended on the dynamics of development of the emotional reaction during immobilization stress. In the course of the first two sessions of immobilization, when the predominant response was one of fear (vocal responses, piloerection, dilatation of the pupils, micturition, attempts to run away), "bursting" activity appeared on the EEG. During the next sessions of immobilization the animals no longer exhibited external features of negative behavior, and the electrical activity of their brain structures as a rule consisted of irregular, sporadic and brief increases in the values of individual rhythms in various brain structures, arising sporadically at certain times. As the results showed, signs of adaptation developed in structures of the CNS forming negative emotional stress at this stage.

The results of analysis of the electrographic responses during the development of immobilization stress are particularly important when compared with the dynamics of accompanying hormonal secretion. To investigate hormonal responses, the background serum levels of

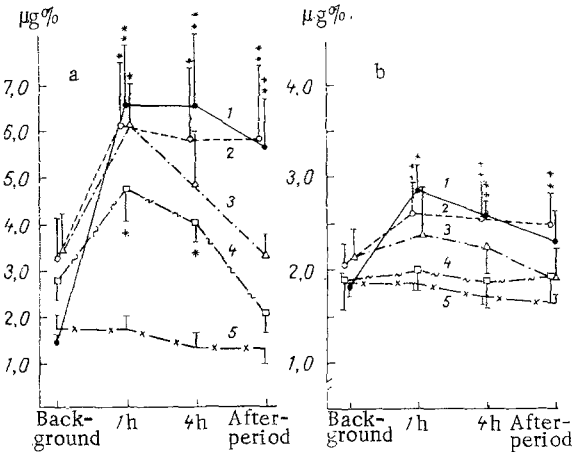

Fig. 3. Changes in blood cortisol (a) and thyroxine (b) levels during immobilization stress. 1) 1st session, 2) 2nd session, 3) 3rd session, 4) 4th session of immobilization; 5) dynamics of background blood hormone levels. *P < 0.05-0.01 compared with background level of hormone on corresponding day, ** P < 0.05-0.01 for differences between 1st and 4th sessions of immobilization.

corticosteroids and thyroxine were determined from several days at the same time intervals as on days of the experiment. In addition, before the beginning of each experiment blood was taken from animals in the animal house daily and changes in the levels of the above-mentioned hormones in response to immobilization were determined. The reason why daily determinations of the hormone level were necessary was that after the first session of immobilization their concentrations did not return in the after-period to the initial level. This was seen particularly clearly with respect to corticosteroids, although appreciable changes also were found in the thyroxine concentration (Fig. 3). During the first two sessions of immobilization maximal secretion of both corticosteroids and thyroxine was found during the first hour of immobilization, but later the hormone levels gradually fell although they still remained high, above their initial values (Fig. 3), even 1 h after the end of immobilization (under unrestrained conditions). A different picture was observed during the 3rd and 4th immobilizations, At that time corticosteroid secretion remained significantly increased only during immobilization, and in the after-period the hormone levels fell, almost to their initial level on the 3rd day and below it on the 4th day. On these days the dynamics of thyroid secretion was rather different. During the 3rd immobilization the blood thyroxine level, although showing a tendency to rise, did not undergo statistically significant changes, and 1 h after immobilization the thyroxine concentration was back at its initial level. During the 4th immobilization there was virtually no response of the thyroid gland. Comparison of the response of the adrenal cortex in volume and time course with the corresponding response of the thyroid gland during immobilization for four days showed that secretion of corticosteroids was much greater in volume than secretion of thyroxine, whereas adaptation of the latter developed earlier and was more complete. So far as the adrenal cortex is concerned, although it responded significantly to immobilization throughout the period of four days, evidence of the higher reactivity of the pituitary-adrenal system, the volume of corticosteroid secretion fell regularly (Fig. 3), another sign of the development of adaptation. It is rightly stated in the literature [10] that adaptation is not always the synonym of complete normalization of function. Comparison of electrographic responses of the CNS with hormonal responses gave the following result: During the first two immobilization sessions a high degree of negative emotional stress developed in the CNS, and this state of the CNS was matched by an accompanying high level of hormonal secretion of both the adrenal cortex and the thyroid gland. On subsequent days of immobilization, during the development of adaptive changes in the CNS, the hormonal responses were correspondingly depressed. Under these circumstances the pituitary-adrenal system, as the most reactive system [2, 6], continued to respond with significant changes in corticoid levels, although their volume was reduced compared with the first days, and the response of the thyroid gland at this time was negligible. Similar changes in thyroid activity were observed previously during a behavioral avoidance reaction [1].

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MODULATING EFFECT OF THE SECOND SOMATOSENSORY AREA OF THE CORTEX ON UNIT ACTIVITY IN SPECIFIC AND NONSPECIFIC THALAMIC NUCLEI DURING ELECTROACUPUNCTURE

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Much attention has recently been paid to the study of the neurophysiological mechanisms of pain and the search for the most effective methods of its relief [1-3, 5, 6, 10].

The second somatosensory area of the cortex (SII) is not only one of the cortical areas containing the mechanism of primary analysis and screening of incoming information into the CNS, but it also participates in the evaluation of extremal, including nociceptive, stimuli [3]. On the basis of the fact that both the facilitatory and inhibitory influences of the cerebral cortex play an important role in determination of the functional state of deep brain structures [4], it has been suggested that blocking the conduction of nociceptive impulses by electroacupuncture (EAP) stimulation may be largely determined by a change in the character of cortico-subcortical interaction [8, 9], in particular in the specific and nonspecific thalamic nuclei [7].

In connection with this problem the aim of the present investigation was to study the modulating influence of area SII on the character of electrical responses of single neurons in the specific and nonspecific thalamic nuclei evoked by nociceptive and nonnociceptive stimulation against the background of EAP stimulation.

EXPERIMENTAL METHOD

Acute experiments were carried out on 16 cats anesthetized with thiopental sodium (25 mg/kg, intraperitoneally), immobilized with suxamethonium, and artificially ventilated. After fixation of the animal in a stereotaxic apparatus all regions of operations were infiltrated with 0.5% procaine solution and the skull was trephined. Unit activity in the posterior ventromedial nucleus (VPM) and parafascicular complex (PFC) of the thalamus was recorded

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