CORTICAL AND SUBCORTICAL ELECTRICAL ACTIVITY DURING THE DEVELOPMENT OF HYPOXIA FROM BLOOD LOSS

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It was shown previously that in some cases during the development of hypoxia polymorphic Δ waves are replaced by synchronous standardized waves, also in the Δ band, which have been called standardized slow complexes (SSC). In the present investigation discharges of the neuron pool were observed during SSC in the caudate nucleus, lateral and medial thalamus, hypothalamus, hippocampus, amygdaloid nucleus, and mesencephalic reticular formation. The highest firing rate of the neurons correlated ($P < 0.01$) with the second half of the negative phase of SSC. Bursts of discharges of the neuron pool during SSC indicate that it reflects physiological processes taking place in these structures.

KEY WORDS: hypoxia; EEG; Δ waves; unit activity.

During the development of hypoxia regular changes take place in the cortical and subcortical EEG, and these have been described by many workers, originally by Pravdich-Neminskii [4]. The earliest effect of hypoxia is manifested as an activation reaction, consisting of a reduction in the amplitude and an increase in the frequency of the waves. During further development of hypoxia the amplitude of the waves increases and their frequency decreases, a stage of Δ waves develops, and the records are dominated by waves of irregular shape with a frequency of 1-4 Hz and an amplitude of up to 100-200 μV. Deepening of the hypoxia leads to complete electrical silence of all brain structures.

Investigation of the connection between the EEG and discharges of single cortical neurons has shown that the neurons increase their discharge frequency during the activation stage, and in the Δ-wave stage the neurons either cease their activity or show a tendency toward the formation of groups of discharges [5-7].

A more detailed investigation of the Δ-wave stage during dying revealed [2] oscillations within the Δ band with a particular shape, consisting of a negative—positive complex, appearing synchronously at all points of the cortex and of the subcortical structures. Oscillations of this type were clearly recorded in monopolar derivations, but less clearly or not at all in bipolar derivations. This form of generalized brain activity during dying as a rule preceded electrical silence, and often the waves themselves were separated by periods with isoelectric brain activity. The constant shape of these waves led to their being named the "standard slow complex" (SSC). Later, SSCs were recorded in man under similar conditions [1].

The possibility of the appearance of SSC in regions known to be destroyed [3] suggested that the spread of these waves over certain brain structures takes place passively. This circumstance, coupled with the fact that no investigations could be found in which the EEG and discharges of cortical and subcortical neuron populations were recorded under hypoxic conditions, served as the grounds for the present investigation.

EXPERIMENTAL METHOD

Experiments were carried out on 15 dogs weighing 9-12 kg. After premedication with pantopon in a dose of 8 mg/kg, under ether or halothane anesthesia tungsten electrodes (electrode tip 5-20 μ in diameter, interelectrode resistance 50 kΩ) were inserted into one of the following brain structures: caudate nucleus, thalamus, hypothalamus, hippocampus, amygdaloid nucleus, mesencephalic reticular formation, and cerebral cortex; their coordinates were determined by reference to the atlas of Lim et al. [8].

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Fig. 1. Relationship between electrocorticogram and activity of neuron population of somatosensory cortex after bleeding. In both figures downward deflection of the pen corresponds to a negative shift of potential; calibration signal here and in Fig. 2 relates to EEG records.

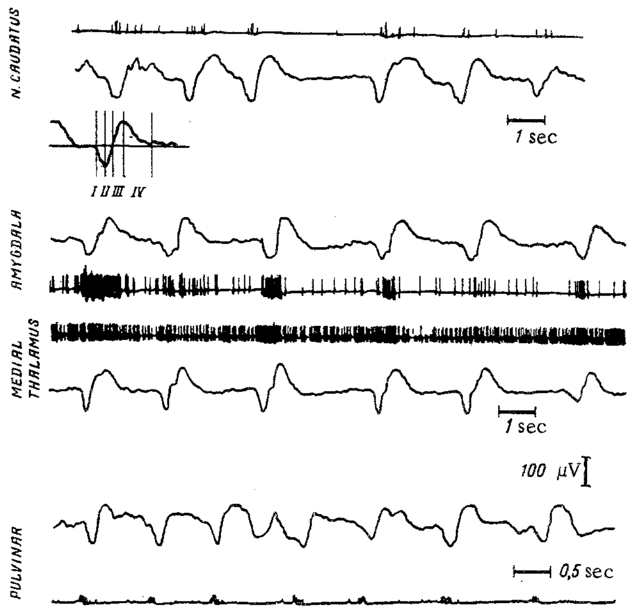

Fig. 2. Relationship between SSC and spike discharge of neuron population in different subcortical formations during bleeding. Formation to which each pair of records of EEG and spike activity belongs is shown on left. For caudate nucleus and medial thalamus, spike activity recorded above EEG; for amygdaloid nucleus and pulvinar, below EEG. SSC and unit activity recorded from amygdaloid nucleus and medial thalamus simultaneously and in same experiment. Scheme in top left corner shows method of dividing SSC into components.

The animals were then immobilized with listhenon or tubocurarine and the lungs artificially ventilated, under the control of a CO_2 analyzer of the GUM-2 type.

Electrical activity of the brain structures was recorded during the development of hypoxia, which was produced by free bleeding from the femoral artery with simultaneous interruption of the artificial ventilation of the lungs. Bleeding was carried out altogether 38 times. For resuscitation, intra-arterial infusion of blood was accompanied by restarting the artificial ventilation of the lungs. In each experiment the EEG and discharges of neuron populations located near the electrode tip were recorded simultaneously from two of the test structures.

To distinguish unit activity, capacitors passing waves with a frequency of 0.3 to 1.2 kHz were mounted in a UBP1-02 biopotentials amplifier. The amplified and filtered signal was led to an amplitude discriminator, incorporating a Schmitt's trigger circuit, with a digital scaler at its output, and which formed a pulse to every 2nd, 4th, 8th, 16th, or 32nd incoming signal above the threshold level (built by K. V. Golubtsov). In the present investigation the threshold was determined from the amplitude of the noise at the moment of contact between the electrode tip and cerebrospinal fluid, and its value was 10 μV. The EEG and pulses from the scaler were recorded on a 16-channel electroencephalograph (Kaiser). The location of the electrode tip was tagged by thermocoagulation and identified histologically.

Correlation between SSC and unit activity was assessed statistically by the difference method. This method was used because the number of neurons whose spike activity was recorded depended on the characteristics of the electrode, its location, the method of fixation, and other factors, so that there was considerable scatter of the variant. By the use of the difference method the effect of scatter on the test index was eliminated. Altogether 190 waves of the SSC type were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The stage of activation of electrical activity, in the form of a reduction in amplitude and duration of the waves of biopotentials, developed 10-15 sec after the beginning of bleeding. Meanwhile the discharge frequency of the neuron pool in the brain structures tested increased on average by $20 \pm 4.1\%$. In the stage of polymorphic Δ waves (PDW), during simultaneous recording of the electrocorticogram from cortical layers IV-VI and from a steel electrode (diameter 1.5 mm) placed epidurally in the same region, the Δ waves were opposite in polarity. With the appearance of PDW, discharges of the nerve cells became grouped. Groups of more frequent spikes coincided mainly (but not always) with the negative phase of the Δ waves recorded from cortical layers IV-VI and disappeared at the end of the PDW period (Fig. 1).

The study of correlation between slow electrical activity of the subcortical formation and unit activity showed that in the brain formations studied, just as in the cerebral cortex, after an increase in the discharge frequency of the neurons during the activation stage a tendency was observed for grouping of the discharges of the nerve cells, which in the PDW stage discharged mainly during the negative phase of the PDW.

Between 2 and 3 min after the beginning of bleeding, when the blood pressure was 10-30 mm Hg, waves of SSC type, accompanied in the subcortical formation by discharges of nerve cells, appeared in the EEG.

For a more detailed determination of relations between discharges of the neurons and the shape of SSC, the negative and positive phases of SSC were divided into two components each, and the firing rate of the neurons was investigated during each component thus distinguished. Component I included part of the wave between the beginning of SSC and the peak of the negative phase, component II part of the wave between the peak of the negative wave and the beginning of the positive phase, component III was located between the beginning and the peak of the positive phase, and component IV between the peak and the end of the positive phase (Fig. 2).

During SSC in all subcortical structures investigated (caudate nucleus, medial and lateral thalamus, hypothalamus, hippocampus, amygdaloid nucleus, mesencephalic reticular formation) discharges of neurons appeared or their frequency increased. Statistical analysis showed that the highest firing rate was associated with component II of SSC, and the lowest was component IV, during which no spike activity whatsoever was recorded in many of the experiments. The firing rate of the neurons determined by the difference method in the second phase differed significantly ($P < 0.01$) from the firing rate during all the other phases. Synchronization of discharges of the nerve cells will be noted within SSC recorded simultaneously from different formations (Fig. 2). In the cortex, discharges of neurons during SSC usually were not observed (Fig. 1), and if they were, it was only when these slow waves were complicated by faster activity.

In some experiments recovery of electrical activity began with waves of SSC type, accompanied by simultaneous bursts of discharges of the neuron pool of the subcortical formations.

The results of the investigation, showing the presence of correlation between PDW in the cortex and bursts of discharges from the neuron pool in cortical layers IV-VI, allowing for the dipole character of the Δ waves, correspond basically to data in [6, 7] which indicate that there is a connection between bursts of discharges of single cortical neurons and the surface-positive phase of the hypoxic Δ waves, but in the present experiments an increase in the discharge frequency of the neuron pool was sometimes observed during the depth-positive phase of the PDW. This can be explained on the grounds that spike activity was recorded, not from single neurons, but from neuron populations.

No reference could be found in the literature to any research which would point to the existence of correlation between unit activity and the shape of the Δ waves in the subcortical formations during hypoxia. The correlation now found between bursts of unit discharges and the shape of the Δ waves in the subcortical formations studied indicates some common mechanism in the origin of the Δ waves in the cortex and lower structures.

Coincidence of bursts of discharges of neurons with the negative phase both of the polymorphic Δ waves and of SSC confirms the previous hypothesis [3] that the SSCs are one type of Δ wave, and that synchronization of SSC in all the subcortical formations of the brain tested means that it is possible to distinguish them among the various types of Δ waves. Synchronization of unit activity recorded from the various brain structures during SSC suggests the existence of a single SSC generator.

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EFFECT OF ELECTRICAL STIMULATION OF THE SUPRAOPTIC REGION OF THE HYPOTHALAMUS ON LIPID METABOLISM AND THE DEVELOPMENT OF ATHEROSCLEROSIS

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Electrical stimulation of the supraoptic region of the hypothalamus for 3 weeks in rabbits kept for 3-8 weeks on an atherogenic diet accelerates and intensifies the development of hypercholesteremia and lipoidosis of the coronary arteries and also the metabolic disturbances in the myocardial tissue. These last disturbances are expressed as a fall in the tissue noradrenalin and creatine phosphate concentration and an increase in the inorganic phosphorus and lactic acid concentration.

KEY WORDS: hypothalamus; coronary arteries; electrical stimulation; lipid metabolism; atherosclerosis.

The role of negative psychogenic factors in the development of hyperlipidemia, atherosclerosis, and ischemic heart disease has been noted by a number of workers [2].

In the present investigation the effect of electrical stimulation of the supraoptic region of the hypothalamus on lipid metabolism and of the development of atherosclerosis of the coronary arteries was studied in rabbits receiving cholesterol.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male rabbits weighing 2.8-3.3 kg. Cholesterol (0.5 g/kg body weight) was administered through a tube for 3-8 weeks before the beginning of electrical stimulation of the hypothalamus and in the period of stimulation. Bipolar nichrome electrodes with a tip 120 μ in diameter and with an

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