EFFECT OF HYPERTHERMIA INDUCED BY A HIGH AMBIENT TEMPERATURE ON THE DIRECT CORTICAL RESPONSE

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The direct cortical response in the supresylvian gyrus during hyperthermia and after restoration of temperature homeostasis was investigated in acute experiments on anesthetized cats kept in a hot chamber in which the air temperature was 45°C. As soon as the body temperature reached 40°C hyperthermia began to cause initial inhibition, followed by total disappearance, of the slow negative potential, and only when the temperature exceeded 43°C was gradual depression of the dendritic potential found. Restoration of normothermia after preceding hyperthermia was accompanied by a slight tendency for the parameters of the slow negative potential to return to normal. Analysis of changes in the dendritic potential to paired stimuli showed that a high temperature affects chiefly the presynaptic components of axodendritic cortical synapses. On the basis of the differential action of heat on the various components of the direct cortical response it is concluded that functionally different cortical cells differ in their sensitivity to hyperthermia.

KEY WORDS: hyperthermia; cerebral cortex; evoked potentials

Electrophysiological analysis of the action of a high temperature directly on the excitability of single units in the projection cortex to stimulation of receptors or of peripheral nerves is difficult because hyperthermia may have a marked effect on the mechanisms of impulse conduction in the nuclei of the corresponding sensory pathways [1-3, 8]. To characterize the cortical mechanisms proper, when the heat balance is disturbed, it is therefore necessary to study those bioelectrical responses whose mechanism is confined to the cortical level. An adequate method for such investigations is to use the direct cortical response (DCR) to stimulation of the cortical surface, which reflects activity not only of apical dendrites, but also of glial cells [5, 6, 10, 13, 14]. The effect of hyperthermia on pre- or postsynaptic transmission of excitation in cortical axodendritic synapses can be assessed by studying the relationship between dendritic potentials to paired stimuli [7].

The object of this investigation was to study the various components of the DCR and the character of interaction of the dendritic potentials during hyperthermia.

EXPERIMENTAL METHOD

In acute experiments on 12 cats the cerebral cortex was exposed under deep pentobarbital (60-70 mg/kg) anesthesia. The cortical surface was stimulated by square pulses (0.05-0.1 msec, 5-30 V, 0.2 Hz) through silver bipolar electrodes (interpolar distance 0.5 mm) from an ÉSU-1 stimulator. In most experiments the intensity of stimulation was 3-10 V for evoking paired dendritic potentials with an interval of 50 msec and 20-30 V for reproducing the slow negative potential. The DCR was recorded by a monopolar technique using silver electrodes (diameter of tip 0.3 mm), located 1-2 mm away from the stimulating electrode. The steel needle reference electrode was inserted into bone above the frontal sinus. After amplification of the potentials by means of an ac amplifier with time constants of 0.7 sec the DCR was recorded from the screen of a C_1-18 cathode-ray oscilloscope.

Hyperthermia was induced by placing the animal in a hot chamber in which the air temperature was automatically maintained at 45°C. The degree of hyperthermia was recorded by an electrothermometer inserted into the rectum for a distance of 5 cm. The DCR was investigated as the temperature was raised degree by degree, and in the terminal phase of hyperthermia when the body temperature was 44-45°C. The results were subjected to statistical analysis by the "Odra" computer.

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TABLE 1. Changes in Amplitude Parameters of Direct Cortical Response during Hyperthermia (in % of initial level); M ± m

Rectal temperature, °C	DP	SNP
38	94,5±3,5	96,1±3,7
39	88,5±5,5	86,5±4,8
40	96,4±9,9	78,9±6,6*
41	99,7±10,9	77,5±10,4*
42	107,3±9,4	65,5±9,0*
43	89,0±7,7	67,8±8,9*
44	72,2±2,9*	32,0±2,9*
45	61,2±8,1*	8,8±3,2*

*Values differing statistically significantly from initial values.

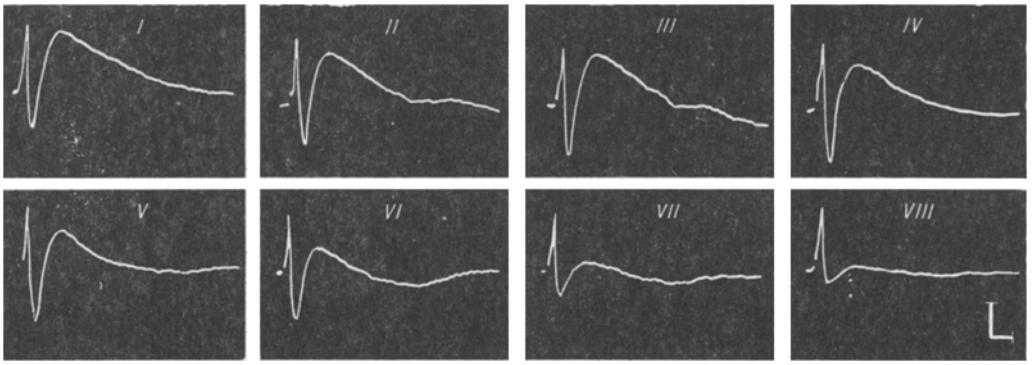

Fig. 1. Changes in DCR during hyperthermia: I) 37°C; II) 38°C; III) 39°C; IV) 40°C; V) 41°C; VI) 42°C; VII) 43°C; VIII) 44°C. Calibration: amplitude 500 μV, time 20 msec.

EXPERIMENTAL RESULTS AND DISCUSSION

The DCR in the suprasylvian gyrus in response to stimulation of about threshold strength consisted of a true dendritic potential (DP), formed by a negative wave with a latent period of 0.5-1.5 msec and an amplitude of 715.4 ± 137.5 μV and a duration of not more than 20 msec. With an increase in the strength of stimulation, the initial negative wave and after-positivity were followed by a slow negative potential (SNP), with an amplitude of 594.9 ± 102.2 μV and a duration of not more than 200 msec.

Exposure to a high temperature was accompanied by regular changes in the cortical potentials (Table 1).

Elevation of the body temperature from 37 to 39°C caused various changes in DP and SNP, which weakened or increased in intensity in different experiments on the average by 15-25% (Fig. 1). Sometimes a definite dissociation of the various components of DCR was observed, as reflected in an increase in voltage of DP with simultaneous depression of the amplitude of SNP. However, changes in the amplitude and temporal parameters of the electrocortical responses within the temperature range were not statistically significant. Raising the temperature from 40 to 43°C caused a marked decrease in the duration and intensity of SNP on the average by 24-35% and an increase in amplitude of the positive potential by 20-40%, whereas the magnitude of DP was not appreciably changed. A further increase in hypothermia as a rule was accompanied by progressive depression of SNP, the successive degrees of which were reached considerably in advance of those of DP. The differential effect of hyperthermia on the components of DCR was particularly clearly manifested within the temperature range of 43-44°C, when slight depression of the initial DP could sometimes be combined with a complete block of SNP.

Comparison of the rates of extinction of DP and SNP in the final stages of the process showed that the former was much more resistant to the action of hyperthermia. The late positive wave of the response, connected with secondary excitation of the deep layers of the cortex, also was depressed sooner than DP.

The higher sensitivity of SNP than of the other components of DCR was confirmed by the change in their amplitudes during spontaneous restoration of normal body temperature after hyperthermia to 42°C. After the

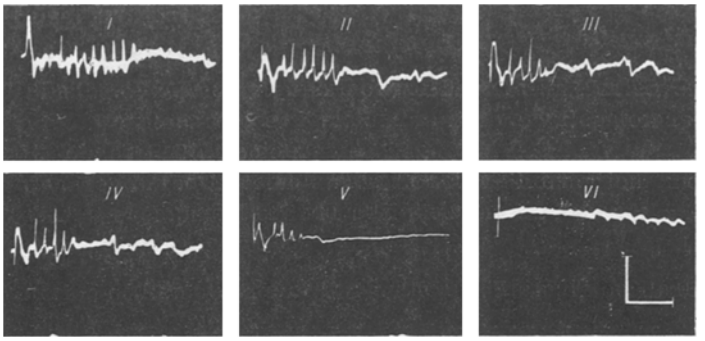

Fig. 2. Changes in after-discharges during hyperthermia. I) 37°C; II) 39°C; III) 41°C; IV) 42°C; V) 43°C; VI) 44°C. Calibration: amplification 500 μV, time 250 msec.

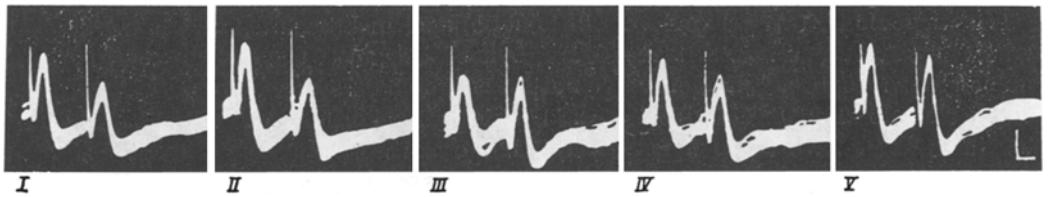

Fig. 3. Changes in dendritic potentials to paired stimuli during hyperthermia. Interval between stimuli 60 msec. I) 37°C; II) 39°C; III) 40°C; IV) 41°C; V) 42°C. Calibration: amplification 500 μV, time 20 msec.

initial temperature had been reached the characteristics of DP differed only a little from their initial values, whereas SNP was only 70-80% of its initial value, indicating slow recovery of the functional activity of the cortical cells responsible for the mechanisms of generation of the long electrical potentials.

In some cases single stimulation of the cortical surface caused an after-discharge consisting of a series of negative waves (Fig. 2). With a high degree of hyperthermia a decrease in the amplitude and duration of the after-discharges was observed, or they disappeared completely in the terminal stage of the process. Changes in the after-discharge discovered in the final stages of hyperthermia were probably due to a disturbance of the reverberation of excitation under these conditions between the cortex and the nonspecific thalamic nuclei [5].

When changes in DP to paired stimuli were studied the weakening of the second response in the interval up to 60 msec was evidently due to exhaustion of the mediator at the time of arrival of the second stimulus [7]. When the body temperature was raised to 40°C the amplitude of the first DP remained stable as the potential increased in response to the second stimulus, so that the difference in magnitude of the two responses disappeared (Fig. 3). With a further increase in hyperthermia this tendency continued. Considering that the presynaptic impulse causes the synchronous development not only of an increase in liberation of the mediator, but also its mobilization, the character of interaction of DP to paired stimuli observed in these experiments may be evidence that hyperthermia influences mainly the presynaptic components of the cortical axodendritic synapses.

During analysis of these results the first point to note is the high resistance of the cortical neurons when temperature homeostasis is disturbed. On the basis of Roitbak's hypothesis [6, 7] on the glial origin of long electrical potentials it can tentatively be suggested that the initial depression and even the complete block of SNP recorded in the present experiments are evidence of a direct inhibitory effect of hyperthermia on cortical glial cells. The development of hyperthermia evidently primarily depresses the mechanisms of glial depolarization without any significant initial effect on postsynaptic activity of the apical dendrites of pyramidal neurons.

The data of Svaetichin et al. [15] are evidence of the higher sensitivity of the glia than of the neurons to changes in temperature homeostasis. In this connection it can be suggested that even within the cortex itself there are marked differences in the sensitivity of functionally different types of cells to hyperthermia. The dissociation in the character of response of elements of the neuroglial complex, responsible for the interdependent influences of neurons and glial cells [4, 6, 9, 11, 12] could be one of the mechanisms leading to a disturbance of cortical integrative activity in the hyperthermic organism.

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LIBERATION OF HISTAMINE AND SEROTONIN AND VASCULAR PERMEABILITY IN AN ACUTE ASEPTIC INFLAMMATORY FOCUS

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Degranulation of mast cells of a peritoneal suspension and of the mesentery of the small intestine and liberation of histamine and serotonin in albino rats with acute aseptic peritonitis were shown to begin during the first minute after injury and to reach a maximum at the fifth minute. By the 15th minute the concentrations of the free amines had fallen sharply and did not differ significantly from the initial levels. The dynamics of the immediate phase of increased vascular permeability corresponded to the dynamics of the free amines. The most marked increase in vascular permeability was observed at the 10th-15th minutes. By the 20th minute it was appreciably lower. Preliminary exhaustion of histamine and serotonin reserves reduced the degree of disturbance of vascular permeability only during the first 15 min after application of the inflammatory agent. It is concluded that histamine and serotonin cause disturbance of vascular permeability in acute aseptic peritonitis chiefly during the first 15 min after injury.

KEY WORDS: acute aseptic inflammation; mast cells; histamine; serotonin; vascular permeability

The principal mediators of the microcirculatory changes that characterize the initial phase of inflammation are histamine and serotonin. However, the duration of the period within which the action of these amines is the determining factor in the increased vascular permeability in a focus of acute inflammation has not yet been established.

Most of the data on the role of histamine and serotonin in the immediate phase of increased vascular permeability are based on their pharmacodynamic action. The dynamics of the mediators in the focus of inflammation directly after application of the inflammatory agent has not been studied.

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