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DYNAMICS OF TRANSCALLOSAL POTENTIALS DURING LOCAL ACTION OF A HIGH TEMPERATURE ON THE CEREBRAL CORTEX

E. D. Bulochnik and M. G. Kurbatov

UDC 612.826.22.014.423-06:612.825.014.43

The effect of local heating of an area of the sensomotor cortex on transcallosal responses was studied in acute experiments on cats anesthetized with pentobarbital. Short and prolonged heating of localized areas of the cortex of both hemispheres, starting from temperatures above 44°C, was found to cause initial depression of the negative component of the transcallosal response, followed by irreversible blocking of both phases of the response within the range 47-49°C. It is concluded that the direct inhibitory effect of high temperatures on cortical neurons is manifested only within the range of extremal temperatures, incompatible with vital activity of the whole animal. Experiments with heat blocking of an area of the cortex of one hemisphere provide evidence that transcallosal responses may arise chiefly through direct stimulation of callosal fibers beneath the stimulating electrodes and may entirely reflect postsynaptic potentials.

KEY WORDS: *high temperature; cerebral cortex; evoked potentials.*

Previous investigations showed that the effect of a high degree of hyperthermia on the intact organism is to inhibit dendritic and transcallosal potentials [3]. However, the role of the temperature factor itself in the mechanism of the change in excitability of the cortical neurons remained obscure, for the changes recorded could have been caused by changes in the functional state of other systems of the body in general hyperthermia. To investigate this problem, local heating of a localized area of the brain surface, whereby the direct effect of the high temperature on cortical function can be assessed under normothermic conditions of the rest of the body, can be used as an adequate model. Meanwhile this technique has certain possibilities also for the study of the genesis of cortical potentials [2, 8, 11].

The object of this investigation was to analyze changes in the transcallosal response (TCR) during a local increase in temperature of the cerebral cortex and after restoration of temperature homeostasis.

EXPERIMENTAL METHOD

Acute experiments were carried out on 15 cats anesthetized with pentobarbital (40 mg/kg). Burr-holes 10 mm in diameter were drilled above the sensomotor cortical areas, the dura was removed, and a transparent plastic plate of corresponding diameter, into which stimulating

Central Research Laboratory, Rostov Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR P. N. Veselkin.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 84, No. 10, pp. 408-411, October, 1977. Original article submitted December 8, 1976.

 0007-4888/77/8410-1400$07.50 © 1978 Plenum Publishing Corporation

TABLE 1. Dynamics of Amplitude Parameters of TCR in Sensomotor Area of Cortex during Local Action of High Temperatures (in % of spontaneous level, M ± m)

Temperature of cortex, °C	TCR	
	positive phase	negative phase
38—40	106,3±8,5	106,4±6,7
40—42	110,7±7,1	96,2±6,3
42—44	107,0±6,2	90,0±8,4
44—46	116,8±10,8	67,8±5,8*
46—47	70,1±5,7*	32,5±5,7*

* $P < 0{,}001$.

and recording electrodes made of silver wire 0.2 mm in diameter, with an interelectrode distance of 1-2 mm, were mounted, was firmly fixed into the burr-hole until it touched the brain surface. The plate with the electrodes was then fixed to the cranial bones with the aid of plastic. The cortex was stimulated through bipolar electrodes by single square pulses 0.01-0.1 msec in duration from an ESU-1 electronic stimulator with radiofrequency outputs. Activity was recorded by a monopolar method, the reference electrode being inserted into bone above the frontal sinus. Electrical responses were recorded from the screen of a type S1-18 cathode-ray oscilloscope by superposition during cortical stimulation at a frequency of one pulse every 5 sec. Upward deflection of the beam corresponded to negativity under the active electrode.

For local heating of areas of the cortex a special thermode was fixed in the region of the plate with the electrodes, and through it mineral oil warmed to a temperature of 65-70°C was passed continuously. The temperature of the heated area of cortex was verified by needle thermoelectric transducers at a depth of 0.5 mm from the brain surface. The rectal temperature, measured by an electrothermometer at a depth of 5 cm, was maintained throughout the experiment at 37-38°C by means of an electric heater.

Transcallosal potentials were recorded during stepwise elevation of the cortical temperature every 1-2°C at a mean rate of 1°C/min over the range from 37 to 49°C. The rate of recovery of the indices of the cortical responses within the above range of temperatures was studied during the hour after the heating stopped. The results were subjected to statistical analysis on the Odra computer.

EXPERIMENTAL RESULTS

The TCR in the sensomotor cortex is a positive-negative complex with a latent period of 3-4 msec, an amplitude of the positive wave of 100-200 μV, and a duration of not more than 15 msec; the parameters of the negative wave were 200-200 μV and 15-25 msec respectively. The main characteristics of the TCR in these experiments were similar to those described elsewhere [5, 7, 11, 13-15].

A successive increase in the temperture of symmetrical areas of the cortex of both hemispheres to 38-40, 40-42, and 42-44°C was accompanied by dissimilar changes in the amplitude of TCR, for in different experiments an increase, a decrease, or no change in the amplitudes of the two waves of the response were recorded. Changes in the amplitude-temporal parameters of TCR within the above-mentioned temperature ranges, as statistical analysis of the data showed, were not significant (Table 1). However, when the brain surface was heated to 44-46°C, weakening of the negative component of TCR on average by 30-40% ($P < 0{,}001$) and some increase in the amplitude and duration of the positive wave were recorded (Fig. 1). It can accordingly be postulated that the initial depression of the negative wave during the direct action of a high temperature on the cortex "unmasks" preexisting positivity, by increasing the amplitude and duration [2, 11]. Further heating of the cortex led with regular constancy to progressive depression of TCR or even its total blockade between temperatures of 47 and 49°C. Under these circumstances, after disappearance of the response to testing stimulation, as a rule it did not appear when the strength of the stimulus was increased, nor did it recover in the course of time after restoration of the normal temperature (Fig. 2). Complete disappearance of the dendritic potential during a local increase in the cortical temperature

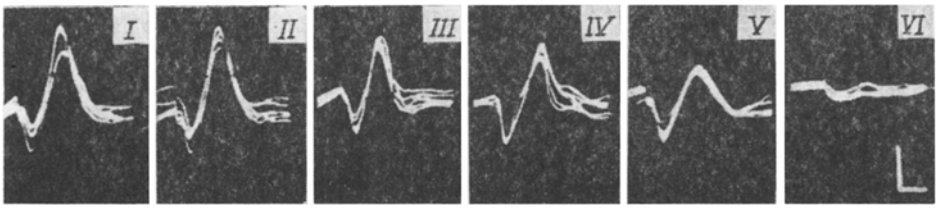

Fig. 1. Changes in parameters of TCR during local heating of symmetrical areas of cortex of both hemispheres: I) 38°C; II) 40°C; III) 42°C; IV) 44°C; V) 46°C; VI) 48°C. Here and in Figs. 2 and 3, amplitude calibration 100 μV; time marker 10 msec.

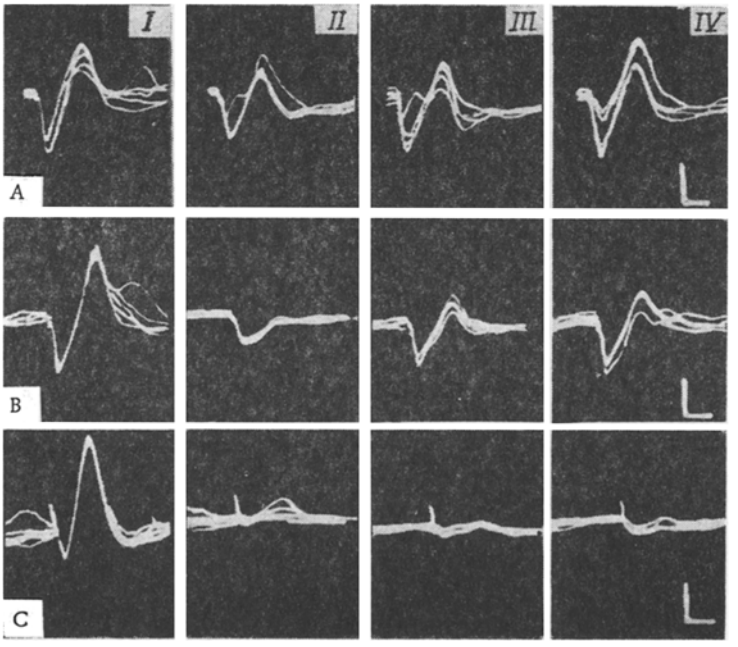

Fig. 2. Restoration of parameters of TCR depending on degree of previous local heating of symmetrical areas of cortex of both hemispheres. A, B, C) Separate experiments on different cats. I) 37°C; II: A, B, and C) 45, 47, and 49°C, respectively; III) 37°C; IV) 1 h after stopping heating.

in the 50°C range was described by Chang [12]. Within these temperature limits cortical neurons are evidently injured, as a result of which an irreversible temperature block to transcallosal transmission of excitation is produced. Comparison of the rate of extinction of the two phases of the TCR during the action of extremal temperatures of the brain surface showed that the initial positive wave of the response is most resistant.

The higher sensitivity of the negative component of the TCR than of its positive component, revealed by these experiments, was evidently due to the fact that during heating of the cortex the surface layer, which participates in the mechanism of formation of the negative wave of the response, is primarily and differentially inactivated.

Similar results were obtained during prolonged heating of the cortical surface. Maintenance of the cortical temperature between 42 and 44°C for 15 min had no significant effect on the amplitude and temporal parameters of TCR. However, prolonged heating of the brain surface above this level was accompanied by a steady reduction of the negative component of the TCR and by a less marked decrease in amplitude of the positive wave.

Regular changes in the parameters of TCR arising under the influence of the local action of high temperature thus depend on the amount of the increase in the cortical temperature and

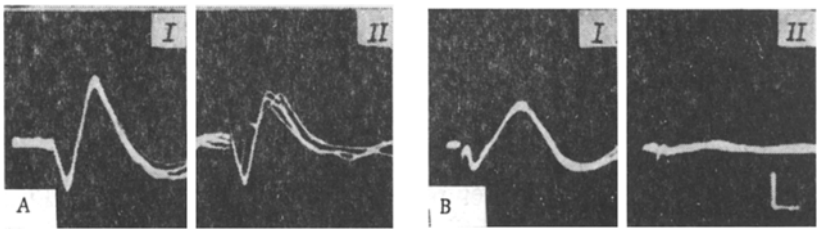

Fig. 3. Changes in parameters of TCR after local heating of an area of cortex of one hemisphere to 50°C. A, B) Separate experiments on different cats. I) Before heating. II: A) response in intact left hemisphere after heating and stimulation of symmetrical area of right hemisphere; B) response in left hemisphere after heating of that hemisphere and stimulation of symmetrical area of intact right hemisphere.

on the duration of action of the temperature factor.

Restoration of the original cortical temperature after previous short- and long-term heating to temperatures of 46°C or more was characterized by a very slight tendency toward normalization of the parameters of TCR, reflecting slow recovery of functional activity of the pyramidal neurons (Fig. 2).

Experiments with local heating of an area of the cortex of one hemisphere to 50°C are of definite theoretical interest. Stimulation of a cortical point under these conditions evoked hardly altered TCR in the opposite, intact hemisphere (Fig. 3A). This fact is evidence that TCR arise in the intact cortex chiefly as a result of direct stimulation of callosal fibers, for within this range of temperatures trans-synaptic excitation of neurons under the stimulating electrodes is blocked. At the same time, unilateral local heating of the cortex led to complete disappearance of the response in the same hemisphere during stimulation of the opposite hemisphere (Fig. 3B). The possibility of complete temperature blocking of TCR during stimulation of the symmetrical point of the opposite intact hemisphere confirms the view that this response entirely reflects postsynaptic potentials [6, 13].

When the results are analyzed, the considerable resistance of cortical neurons to the local action of high temperatures must first be noted. This is shown by the long preservation of the parameters of TCR and the appearance of the first significant changes in the range of extremal temperatures absolutely incompatible with the viability of the intact organism. The high resistance of the cortical potentials to local heating of the brain surface which was found may be due to the relative resistance of the mechanism of synaptic transmission of excitation in the cortex to the direct action of the temperature factor. Meanwhile, temperature blocking of TCR when the cortical temperature is raised to 47-49°C is probably connected with the beginning of profound injury to the nerve cells at this temperature, as a result of which total depolarization of the neuron membrane takes place. However, the intimate mechanism of the direct harmful action of high temperatures on cells of different tissues of the body, including those of the nervous system, has not yet been finally elucidated [1, 4, 9, 10].

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EFFECT OF CHLORPROMAZINE ON CHANGES IN CORTICAL ELECTRICAL ACTIVITY CAUSED BY *Clostridium perfringens* TYPE A TOXIN

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UDC 612.822.3.014.46:[576.851.555.097.29]-06:615.214.22

Experiments on cats showed that injection of chlorpromazine (3 mg/kg, intramuscularly) 1 h before injection of *Clostridium perfringens* type A toxin prevents the desynchronization of cortical electrical activity which usually arises in the first phase of poisoning, delays the phase of depression of electrical activity in the second phase, and increases by 50-100% the duration of survival of the animals. The effect of chlorpromazine is evidently connected with blocking of adrenergic structures of the reticular formation of the brain stem.

KEY WORDS: *electrocorticogram; toxin of* Clostridium perfringens; *chlorpromazine; reticular formation.*

Previous work showed that phasic changes in cortical electrical activity arise in poisoning caused by the toxin of *Clostridium perfringens* type A [16]. In the first phase desynchronization of electrical activity takes place, in the second it is deeply depressed. Desynchronization of cortical electrical activity was not observed after division of the midbrain (mesencephalic preparation), evidence of the role of the reticular formation (RF) in this effect. In the present investigation it was decided to study the effect of pharmacological "blocking" of the brain-stem RF on the dynamics of the EEG in this form of poisoning. A drug with such an action is chlorpromazine [2, 4, 5, 17, 20, 21].

EXPERIMENTAL METHOD

Experiments were carried out on 26 cats. Preliminary operations (tracheotomy, trephining of the skull, implantation of electrodes) were performed under local procaine anesthesia, after which pentobarbital (15-20 mg/kg) was injected intraperitoneally. The spontaneous electrocorticogram (ECoG), evoked potentials (EP) to single flashes (energy 0.3 J, distance of source of light from the cornea 40 cm), and the rhythm binding response (RBR) were recorded after 1 h. The electrocardiogram (ECG) and electromyogram (EMG) of the antigravity muscles of the neck were recorded with needle electrodes. Toxin of *Cl. perfringens* type A (100 MLD/kg body weight) and chlorpromazine (3 mg/kg body weight) were injected intramuscularly. The toxin was injected into 18 animals after EEG rhythm modification by chlorpromazine; the above indices were recorded after 6, 12, 24, 30, and 40 h.

EXPERIMENTAL RESULTS AND DISCUSSION

In cats anesthetized with pentobarbital, before injection of the toxin waves in the α and θ bands were predominant in occipital and frontal derivations; extensor tone of the anti-

Department of Microbiology and Department of Pathological Physiology, N. I. Pirogov Odessa Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 84, No. 10, pp. 412-416, October, 1977. Original article submitted March 23, 1977.

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