ACTION OF STRYCHNINE AND ATROPINE ON CORTICAL EVOKED POTENTIALS AND ELECTRICAL RESISTANCE

S. I. Ryabov and N. S. Kositsyn

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The evoked potentials (EP) method has been widely used to analyze the states of different parts of the brain. By means of this method some idea can be obtained of the processes affecting large groups of functionally connected nerve cells in response to the arrival of an afferent signal. One of the main parameters characterizing EP is their amplitude, which varies in different states of the brain [7, 8, 10, 12]. EP are sensitive also to the action of most neurotropic drugs administered to man and animals for therapeutic or diagnostic purposes [1, 2, 5, 6]. In some cases, however, disparity has been found in the change of amplitude of EP accompanying considerable changes in ultrastructure of the cerebral cortex, and also in the behavioral reactions of animals [14]. This suggests the need for a more correct approach to the use of electrical parameters to characterize the state of the brain.

It will be recalled that EP are the result of the passage of an electric current, created by the electrogenic sources of nerve tissue (in this particular case, mainly synaptic sources), along that tissue and, consequently, the amplitude of EP depends both on the density of the generated current and on the electrical resistance of the nerve tissue. Consequently, when changes in the amplitude of EP are assessed, the possibility that both these parameters may change has to be taken into account. Although this is obvious, such an evaluation of the factors causing a change in the amplitude of EP has virtually never been undertaken in different functional states.

The aim of this investigation was to study the relations between changes in amplitude of EP and electrical resistance of the cerebral cortex in response to administration of substances increasing the excitability of the nervous system (strychnine and atropine) to animals. These substances are widely used not only in medicine, but also in experimental neurobiology in order to study conditioned-reflex processes and memory, and they exert their action on the CNS through different mechanisms, both of the synaptic apparatus and of the nonsynaptic zones of the neuron [2, 5].

Conditioned reflex formation is manifested as changed in EP [3, 4]. We also know that the action of atropine (a blocker of muscarinic acetylcholine receptors) on the CNS is associated with slowing of learning and retrograde amnesia [5, 13, 15], whereas that of strychnine (a stimulator of the CNS) is connected with activation of conditioned-reflex activity and acceleration of conditioning [5]. Meanwhile both these substances have an excitatory action on the cerebral cortex, which is manifested electrographically as an increase in amplitude of EP [5, 6, 9]. The use of the EP method to evaluate functional states of the brain and, in particular, excitation, therefore requires additional investigation.

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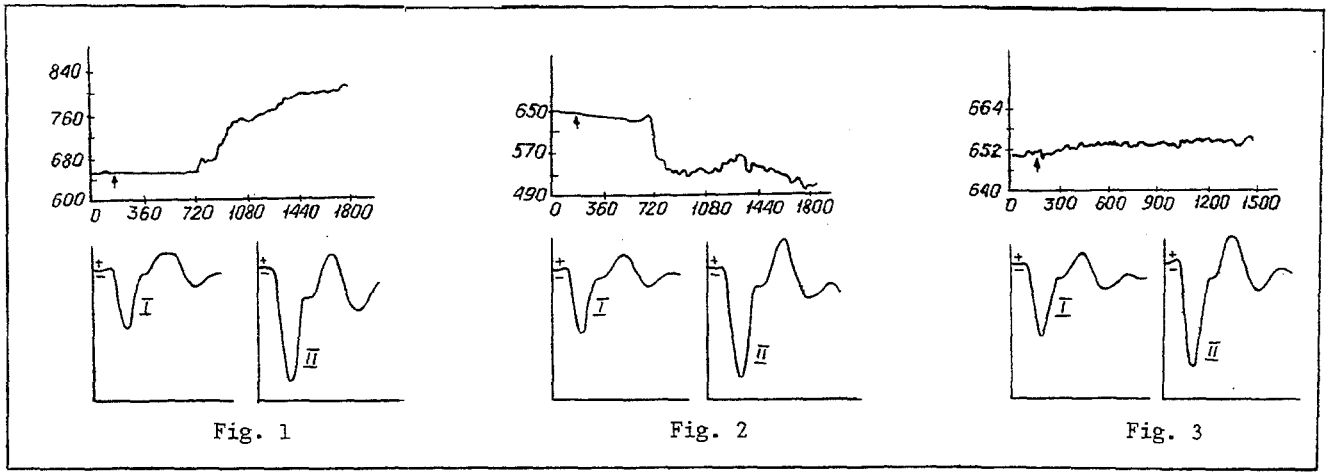

Fig. 1 Fig. 2 Fig. 3

Fig. 1. Increase in electrical resistance and amplitude of EP in response to EDS of limb, arising in sensomotor cortex and after intraperitoneal injection of strychnine. I) EP before, II) after injection of strychnine. Abscissa, time (in sec); ordinate, specific resistance (in $\Omega \cdot$cm). Arrow indicates time of injection of strychnine. (+/−) Polarity of EP recorded. Calibration 200 μV, 10 msec.

Fig. 2. Reduction of electrical resistance and increase in amplitude of EP in response to EDS of limb arising in sensomotor cortex and after intraperitoneal injection of strychnine. Legend as to Fig. 1.

Fig. 3. No change in electrical resistance but increase in amplitude of EP in response to EDS of limb, arising in sensomotor cortex and after intraperitoneal injection of atropine. I) EP before, II) after injection of atropine. Remainder of legend as to Fig. 1.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats, anesthetized with pentobarbital (30-40 mg/kg), and secured in a stereotaxic apparatus. EP, evoked by electrodermal stimulation (EDS) of the hind limb were recorded by a unipolar technique using a glazed tungsten electrode 50 μ in diameter, located in the region of the sensomotor cortex [14]. The potentials were amplified, digitized by ADC, and led into a personal computer. The electrical resistance was measured by the method described previously [11]. Strychnine (0.1% solution) and atropine (1% solution) were injected intraperitoneally in doses [2] not leading to the appearance of seizure activity, or inducing a general toxic effect (strychnine 0.5-1.5, atropine 0.5-10 mg/kg). Altogether 36 animals were used in the experiments.

EXPERIMENTAL RESULTS

After injection of strychnine, in response to electrodermal stimulation an increase in the amplitude of EP by 75-90% was observed in the sensomotor cortex. Evidence of increased excitability during this period is given by lowering of the threshold of the brain response to stimulation of the limb, leading to the appearance of EP. Electrical resistance of the cortical tissue is increased at the same time on average by 19.0 ± 3.2% (scatter from 15 to 42%). An increase in resistance begins to be recorded 10 ± 3 min after intraperitoneal injection of the drug and reaches a maximum after 20-25 min (Fig. 1). In some experiments (up to 30% of the total number), however, besides an increase in amplitude of the EP the cortical resistance was reduced by 10-15% of its initial value (Fig. 2).

Injection of atropine caused no change in cortical resistance (Fig. 3).

Nevertheless, an increase of 17-30% in excitability was observed, and, just as in the case with strychnine, the amplitude of EP also increased significantly (by 50-70%). In this case an increase in amplitude of EP was noted if the dose of atropine was not less than 4-5 mg/kg.

Injection of neurotropic drugs whose action is accompanied by a change in amplitude of cortical EP can thus induce completely different changes in electrical resistance of the region from which they are derived. This makes analysis of the action of these drugs on the cerebral cortex (and, most probably, on any part of the brain) purely on the basis of the character of the changes in amplitude of EP rather incorrect. It will be clear from these experiments that the use of both atropine and strychnine leads to identical electrographic manifestations – to an increase in the amplitude of EP. However, whereas when atropine is used there is a "pure" increase, evidently taking place only through an increase in density of the current creating the EP field, when strychnine is used the situation is not so straightforward. The increase in amplitude of EP in this case is due both to an increase in current density and a change in resistance of the cortical tissue. The opposite nature of these changes may also introduce indeterminacy into the correlation between doses of the drug usually used for experimental purposes and the amplitude of the recorded EP. The varied character of interaction of neurotropic drugs with nerve tissue, leading to a change in its electrogenic properties, and also to a change in electrical resistance, is most probably a characteristic feature of many substances of this type. The difference in the effects in the case of a change in electrical resistance of the nerve tissue must be sought in interaction of these substances with cells (neurons and glia), leading to various structural changes in their membranes and to a change in the ionic balance in the intercellular space. Some such information could be obtained by electron-microscopic study of the state of the nerve tissue during interaction with substances of this kind, but the increase in density of the current creating the EP field can take place both through an increase in strength of the elementary sources of the current and through an increase in their number per unit volume of nerve tissue. Testing these hypotheses requires further physiological experiments both on the whole brain and on a single cortical neuron, as well as comparison of the results of these investigations with the morphometric parameters of nerve and glial cells in the part of the cortex to be studied.

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