EFFECT OF SEROTONIN (5-HYDROXYTRYPTAMINE) ON EVOKED POTENTIALS OF THE OPTIC CORTEX IN UNANESTHETIZED RABBITS

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In the light of views concerning the mediator function of serotonin, extensive studies have been made of its effect on neurophysiological processes. Several authors have described the depressant action of serotonin on the synaptic transmission of nervous excitation in the cerebral cortex and in certain subcortical structures [4-6,9,11].

At the same time, serotonin is known to cause phasic changes in the spontaneous electrical activity of the cerebral cortex, marked by alternation of its desynchronization with the appearance of slow waves on the electroencephalogram (EEG).

It therefore appeared interesting to study the effect of serotonin on the evoked potentials (EP) of the cerebral cortex in comparison with its background electrical activity during various phases of the action of serotonin, and the present investigation was carried out for this purpose.

EXPERIMENTAL METHOD

The investigation was carried out on 15 rabbits with electrodes implanted in the brain. To avoid a potentiating effect of serotonin in relation to anesthetics, the changes in the EP under the influence of serotonin were studied in chronic experiments on unanesthetized animals. The electrodes were implanted 5-7 days before the experiment. Cortical electrodes, 0.5 mm in diameter, were implanted in the bone of the skull epidurally above the optic and motor areas of the cortex. The electrodes above the optic cortex were placed within the limits of projection of the focus of maximal activity on the skull [3,14]. The subcortical electrodes, 0.15 mm in diameter, were introduced into the region of the hypothalamus by means of a stereotaxic apparatus in accordance with the coordinates of Sawyer and co-workers [13].

Photic stimulation was applied in the form of single flashes of light at intervals of 2.5-5 sec from a "Kaiser" photostimulator. The source of light was placed at a distance of 15-20 cm in front of the animal's head. The animal's eyes were atropinized.

The EP were recorded by a monopolar technique on an ink-writing "Kaiser" encephalograph, giving simultaneous recordings of the EEG, electrocardiograph (ECG), and respiration, so that the relationship between the EP and the background electrical activity of the cerebral cortex and the autonomic reaction could be analyzed.

To produce stabilization of the EP in response to photic stimulation in the unanesthetized animal and to increase the reliability of the experimental data, additional measures were used. Before the injection of serotonin, flashes of light were applied for 20 min without recording, after which the background EEG and the EP were recorded. To prevent the phenomenon of habituation to photic stimulation, the flashes of light were applied in series of 20 pulses and the intervals between the series were varied. After the injection of serotonin, all the indices were recorded for a period of 3 h.

The results of each experiment were analyzed statistically: all the impulses in each series were counted, and the character of the background electrical activity coinciding with each evoked response was simultaneously determined. To describe the background electrical activity, a conventional numerical classification was used, reflecting the mean amplitude of the oscillations in each cut. During the analysis of the results, only the positive deflections of the primary response (PR) were taken into consideration.

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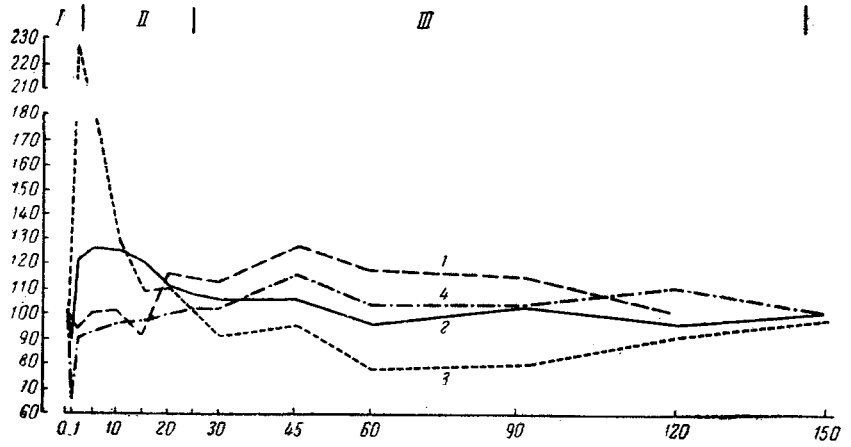

Fig. 1. Changes in primary responses of the optic cortex to photic stimulation (1), in the background electrical activity (2), the respiration rate (3), and the heart rate (4) in unanesthetized animals under the influence of the intravenous injection of serotonin in a dose of 2 mg/kg. Along the axis of ordinates – changes in the above-mentioned indices (in %) in relation to their value before injection of serotonin, taken as 100; along the axis of abscissas – time (in minutes); I, II, and III – phases of the action of serotonin.

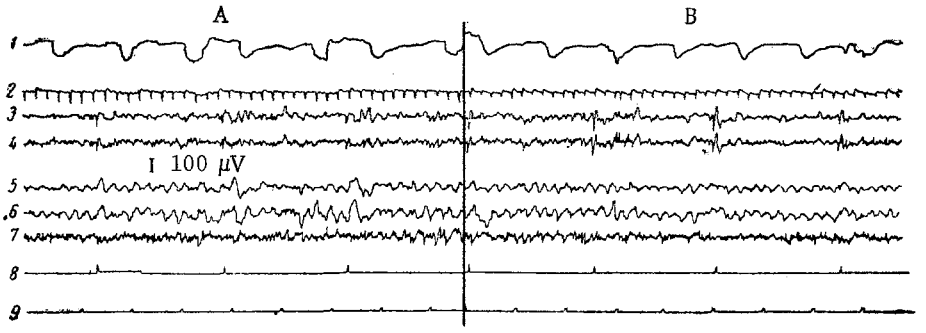

Fig. 2. Increase in the amplitude of the primary response to photic stimulation in the optic cortex of a rabbit under the action of serotonin: A) before injection; B) 45 min after injection of serotonin in a dose of 2 mg/kg. 1) Restoration; 2) ECG; 3) optic cortex on the left side (monopolar recording); 4) optic cortex on the right side (monopolar); 5) optic cortex on the left side (bipolar recording); 6) optic cortex on the right side (bipolar); 7) motor cortex on the right side (bipolar); 8) marker of stimulation; 9) time marker (in minutes).

Serotonin was injected intravenously in a dose of 1-2 mg/kg. For control purposes, in a series of experiments the animals received an injection of physiological saline.

EXPERIMENTAL RESULTS

The injection of serotonin into unanesthetized rabbits produced changes in electrical activity which occurred in three phases.

Initially a brief "activation reaction" appeared in the cortical EEG, in the form of the development of a more regular, synchronized rhythm in the optic cortex and desynchronization of the electrical activity in the motor cortex. This phase of the action of serotonin was accompanied by a marked slowing of the heart rate and an increase in the respiration rate.

Next followed a phase of an increase in the amplitude of the background electrical activity. Slow waves with a high amplitude, reaching 100 μV, and a frequency of 2-3 CPS appeared in the optic cortex, and against this background a faster rhythm of low amplitude could be distinguished. In the motor cortex in this phase of the action of

serotonin, spindle-shaped bursts of electrical activity were observed. The phase of high-amplitude, slow activity described above lasted in most experiments for 25-30 min. By this time the initial heart and respiration rates had usually been restored in the animals.

In the 3rd phase of the action of serotonin, the amplitude of the background electrical activity fell and came close to the electrographic equivalent of the "activation reaction" of the cerebral cortex, interrupted by periods of slower rhythms. This phase of the action of serotonin lasted 2.0-2.5 h, in the course of which stabilization of the autonomic indices was observed at a somewhat modified level, characterized by a slower respiration rate and a faster heart rate than were observed initially.

Restoration of the initial background of cortical electrical activity was observed 2.5-3 h after the injection of serotonin.

The changes in the EP also were phasic in character. In the first phase of the action of serotonin, the amplitude of the positive deflection of the PR in the optic cortex underwent a very slight change, falling by only 10%. The oscillations of the EP were also ill defined in the second phase of the action of serotonin, characterized by slow high-amplitude electrical activity. The most marked changes in the amplitude of the PR were observed in the third phase of the action of serotonin, characterized by stabilization of the autonomic indices. In this period of its action an increase in the positive component of the primary responses was observed, amounting to 27% of its initial value.

The changes described in the primary responses, compared with the changes in the background EEG and the autonomic indices in different phases of the action of serotonin are shown in Fig. 1, reflecting the mean results of all the experiments.

It is clear from Fig. 1 that, despite the very marked changes in the autonomic reactions observed in the first stage of the action of serotonin, the changes in the amplitude of the positive deflection of the PR were very small. These changes were equally small in the second phase of the action of serotonin, characterized by a shift of the cortical electrical activity towards the side of slow waves. The greatest change in the amplitude of the positive deflection of the PR was observed in the period of the prolonged activation reaction of the cortex characterizing the third phase of the action of serotonin.

The character of the changes in the PR at this period of the action of serotonin is illustrated in Fig. 2, which shows that serotonin had a facilitating action on the PR of the optic cortex.

Hence, the results of these investigations, in agreement with those obtained by other authors [2,10,12], demonstrate that the action of serotonin on the cortical electrical activity takes place in several phases.

The character of the effect of serotonin on the PR of the optic cortex was found to differ in different phases of the action of serotonin. Judging by the changes in the positive deflection of the PR, the facilitating effect of the drug was most marked.

Arising from the view that the positive deflection of the PR reflects excitation of a group of cortical neurons in response to a flow of afferent impulses, it may be supposed that serotonin facilitates the temporal and spatial summation of this excitation, thus bringing about an increase in the amplitude of this potential.

It may seem that this conclusion with respect to the character of the action of serotonin contradicts the results obtained by other investigators who observed depression of the evoked potentials under the influence of serotonin [4-6,9,11,etc.]. However, this is not so. The conclusions reached by these investigators, that the action of serotonin on the EP is inhibitory, were drawn only in relation to the initial phase of the action of serotonin. In this phase, a very slight decrease in the EP was also observed in the present experiments. Since this initial phase of the action of serotonin was accompanied by sharp changes in respiration and in the activity of the heart, it may be assumed that the decrease in the amplitude of the EP at this period was due to its reflex action on the vascular receptors and respiration. Other authors have also described the participation of these factors in the mechanism of the influence of serotonin on the EP [6,7,11].

From our point of view, it is the last phase of the action of serotonin which is most interesting. As shown above above, in this phase of its action, serotonin caused facilitation of the PR of the optic cortex, coinciding in time with the encephalographic activation reaction of the cerebral cortex. The absence of marked autonomic changes at this period suggests that it is this phase of the action of serotonin which reflects its central effect. The late appearance of this effect may be due to the slow penetration of serotonin through the blood-brain barrier.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.
