CHANGES IN SENSOMOTOR CORTICAL EVOKED POTENTIALS DURING ELECTRIC ACUPUNCTURE IN RABBITS

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Electrical acupuncture stimulation of tsu-san-li points in rabbits caused gradual disappearance of the second positive wave of the EP and the EEG desynchronization reaction in the sensomotor cortex, and also disappearance of the response of tachycardia to electrodermal stimulation, indicating the development of a state of analgesia in the animals. Discontinuation of the electric acupuncture led to gradual recovery of the indices mentioned above.

KEY WORDS: electric acupuncture; cortical evoked potentials; analgesia; electrodermal stimulation.

The analgesic effect of acupuncture is well known from clinical observations [3], but the mechanisms of its analgesic effect are still debated. Behavioral tests [5] and changes in the EEG and autonomic responses [2] can be used to evaluate the effect of acupuncture in animals objectively. However, the effect of acupuncture on changes in the EEG and evoked potential (EP) has not yet been studied [4].

EXPERIMENTAL METHODS

Fifteen experiments were carried out on 10 rabbits. In five experiments the effect of electric acupuncture stimulation (EAS) on changes in the EEG and EP in the sensomotor cortex in response to electrodermal stimulation (EDS) was investigated in animals anesthetized with urethane (1 g/kg). In 10 experiments on waking animals changes in EP were studied, and in five experiments ECG was recorded to determine the heart rate. EDS consisted of application of a single square pulse 1 msec in duration and with a strength of 3-9 mA to the animal's hind limb, either alone or between series of pulses of EAS. Before the experiments, the threshold of the behavioral flight response was determined in the unrestrained animal. EAS was applied to both limbs (tsu-san-li points [2]), with the following parameters: bipolar square pulses, 60 Hz, 70-90 pulses per series, with an interval of 1-2 sec between series, and with a current of 200-400 μA.

The EEG of the sensomotor cortex was recorded by bipolar leads from the calvaria on a Galileo 8-channel electroencephalograph. Mean values of 10 EPs were recorded on an NTA-1024 amplitude-phase analyzer (Orion, Hungary). The duration of the R–R interval was recorded on the ECG in groups of five values following immediately after application of EDS, every 5 min in response to 10 EDS, or to each EDS for 5 min.

EXPERIMENTAL RESULTS AND DISCUSSION

In certain doses urethane [1] can block ascending activation of wakefulness, but under these circumstances activating nociceptive influences can pass freely to the cortex without awakening the animal. In the present experiments, 15-20 min after injection of urethane into the animals, the sensomotor cortical EEG of the rabbits was dominated by slow waves with a frequency of 1-3 Hz and an amplitude of 100-200 μV. During application of a series of 10 EDS and 10-15 sec later a desynchronization reaction appeared on the EEG (Fig. 1, 1). The sensomotor cortical EP in response to EDS consisted of a primary response (PR) with a latent period of 10-13 msec and an amplitude of 25-30 μV and a clearly defined secondary positive wave with a latent period of 20-40 msec and an amplitude of 200-250 μV (Fig. 1, 1).

During the first 5-10 min after the beginning of EAS no appreciable changes were observed in the sensomotor cortical EEG and EP indices in response to EDS, although in some experiments there was a small increase in amplitude of the secondary response of EP during the first minute of EAS.

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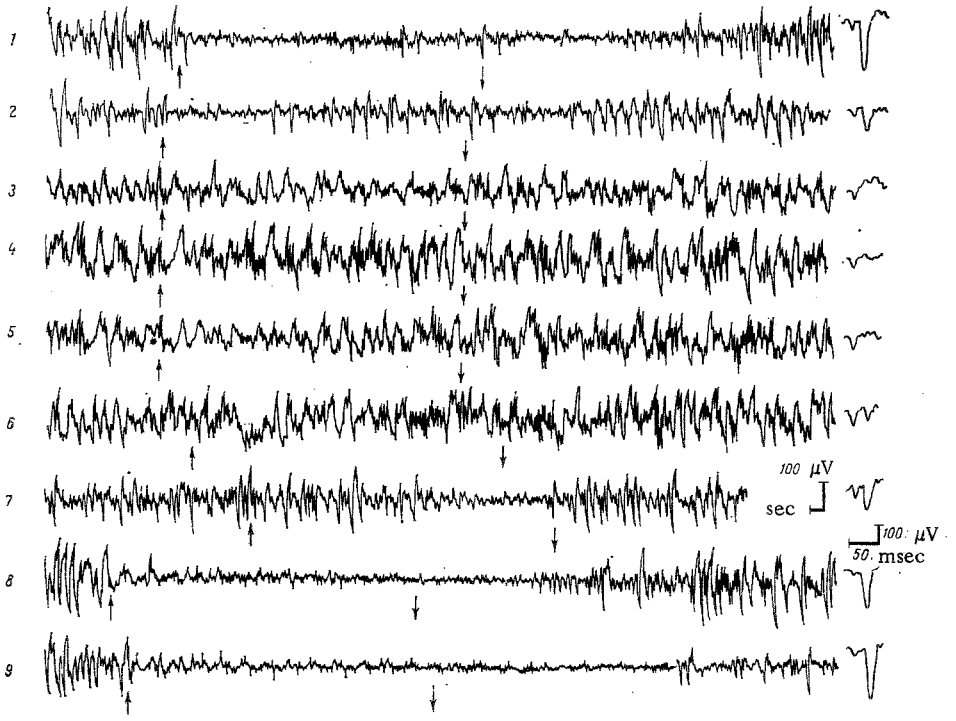

Fig. 1. Dynamics of changes in EEG and EP (results of averaging of EP by analyzer) of sensomotor cortex of rabbit anesthetized with urethane in response to EDS before (1) and 10-15 min (2), 20 (3), and 30 min (4) after beginning of EAS and 5-10 (5), 10-15 (6), 15-20 (7), 25 (8), and 30 min (9) after its termination. Arrows indicate times of starting and stopping series of EDS.

After 10-15 min of EAS the EEG-desynchronization reaction in response to a series of single EDS was exhibited as a rule to the first stimuli, but to the 5th-7th EDS and after the termination of EDS it disappeared (Fig. 1, 2). At the same time there was a marked decrease in the amplitude of the secondary positive wave of EP, which was only half its initial amplitude (Fig. 1, 2).

At the 15th-20th minute of EAS, a further gradual although fluctuating decrease in amplitude of the secondary positive wave of the sensomotor cortical EP was observed in response to a series of single EDS. As a rule, by the 20th minute of EAS the secondary positive wave of EP and the EEG-desynchronization reaction of the sensomotor cortex no longer appeared in response to EDS (Fig. 1, 3). This pattern of changes in EEG and in the configuration of EP in the sensomotor cortex in response to EDS persisted later, while EAS continued (Fig. 1, 4).

In some experiments a small increase in the primary response of EP was observed at this time, its amplitude reaching 30-50 μV (see Fig. 1, 4).

After the ending of EAS, the changes described above on the EEG and EP of the sensomotor cortex in response to EDS continued for the first 5-10 min: no EEG-desynchronization reaction was present, and the EP consisted of the primary response only (Fig. 1, 5).

At about 10-15 min after the termination of EAS the secondary positive wave of EP began to appear (Fig. 1, 6) and subsequently it gradually increased in amplitude; an EEG-desynchronization reaction appeared at the same time in the sensomotor cortex in response to a series of single EDS (Fig. 1, 7). As a rule the EEG-desynchronization reaction was exhibited only at the end of the series of EDS (Fig. 1, 7).

Finally, by the 20th-25th minute after the ending of EAS the original pattern of changes in the EEG and EP of the sensomotor cortex in response to EDS was restored: The EEG-desynchronization reaction was clearly exhibited and it persisted for a short time also after the end of a series of single EDS, whereas EP consisted of a primary response with an amplitude of 25-30 μV and a well-marked secondary positive wave with an amplitude of 200-250 μV (Fig. 1,8); in two experiments, moreover, the amplitude of the secondary response of EP was higher than initially and reached 300-350 μV (Fig. 1, 9).

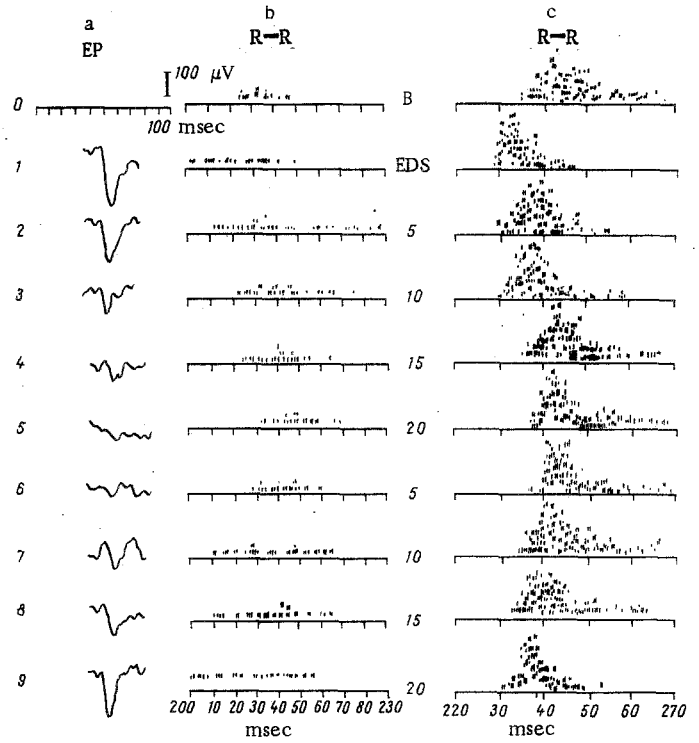

Fig. 2. Changes in sensomotor cortical EP (a) and R–R interval of ECG [five averaged values in response to application of 10 EDS every 5 min (b) and in the course of 5 min (c)] in response to EDS in unanesthetized rabbits during and after the end of EAS. Legend (from top to bottom): B) background values of R–R interval without application of EDS; EDS) before application of EAS (1), and 5 (2), 10 (3), 15 (4), and 20 min (5) after beginning of EAS; 5 (6), 10 (7), 15 (8), and 20 (9) min after end of EAS.

Consequently, in rabbits anesthetized with urethane, EAS induced a gradual inhibition of the EEG-desynchronization reaction and of the secondary positive wave of the EP in the sensomotor cortex in response to EDS over a period of 20-25 min. This effect continued for 5-10 min, and the responses returned to their initial values 20-25 min after the end of EAS.

Experiments on unanesthetized rabbits showed similar dynamics of changes in the sensomotor cortical EP in response to EDS during application of EAS: a gradual decrease in amplitude of the secondary positive wave of EP (Fig. 2a, 1-4) progressing to its complete disappearance after 20 min of EAS (Fig. 2a, 5), and maintenance of these changes for 5-10 min after the end of EAS (Fig. 2a, 6, 7). Restoration of the secondary positive wave of EP to its initial amplitude was observed on average by 20-25 min after the end of EAS (Fig. 2a, 7, 9].

The study of the heart rate also revealed a definite pattern of changes in the response of the unanesthetized animals to EDS during application of EAS (Fig. 2b, c). Before EDS the mean duration of the R–R interval on the ECG of different rabbits was 230-250 msec (Fig. 2b, c, 0), i.e., 260-240 heartbeats per minute. During EDS the R–R interval of different animals was from 200-230 to 230-240 msec (Fig. 2b, c, 1), i.e., 300-250 heartbeats per minute.

During the first 5-10 min after the end of EAS no statistically significant changes were observed in the duration of the R–R interval (Fig. 2b, c, 2-3).

By the 15th-20th minute of EAS a marked increase in the duration of the R–R interval was observed in response to EDS; it differed significantly from its initial duration and its mean value was 240-245 msec (Fig. 2b, c, 4-5), i.e., 250-245 heartbeats per minute. The duration of the R–R interval was almost the same on the EEG of rabbits in the initial state – before application of EDS. Consequently, by the 15th-25th minute of EAS the heart rate was virtually identical before and after application of EDS.

During the first 5-10 min after the end of EAS the duration of the R–R interval of the ECG in response to testing EDS remained the same as at the 20th minute of application of EAS (Fig. 2b, c, 6-7). By the 10th-15th minute after the end of EAS, shortening of the R–R interval of the ECG on average to 230-240 msec began to appear in response to EDS (Fig. 2b, c, 7-8). By about the 20th-25th minute after the end of EAS the R–R interval of the ECG returned more or less to its initial value in response to EDS (Fig. 2b, c, 9).

Electrical stimulation of other nonacupuncture points of the animal's hind limbs, incidentally, did not give rise to the changes in the EEG and EP of the sensomotor cortex described above in response to EDS, and as a rule under these circumstances tachycardia was observed.

Consequently, during EAS gradual disappearance of the response to tachycardia to EDS is observed and after the end of EAS the response is gradually restored.

The results of these experiments thus showed that EAS cause disappearance of the secondary positive wave of the sensomotor cortical EP in rabbits, inhibits the response of tachycardia, and under superficial urethane anesthesia, causes disappearance of the EEG-desynchronization reaction in response to EDS. These observations point to the development of a state of analgesia in the animals. Characteristically the changes in these functions gradually increase during the course of EAS, but after its end gradual recovery takes place, in agreement with the results of clinical observations and of experiments on animals [2, 5]. The study of changes in indices of CNS function such as EP and the EEG in animals can evidently be used for the evaluation of acupuncture analgesia and for the study of its neurophysiological mechanisms.

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THE USE OF HETEROGRAFTS IN DIFFUSION CHAMBERS TO STUDY INDIVIDUAL DRUG SENSITIVITY OF HUMAN OVARIAN CARCINOMA TO CHEMOTHERAPEUTIC AGENTS

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Experiments with heterografts of human ovarian carcinoma (10 patients) in diffusion chambers revealed considerable individual differences in their sensitivity to chemotherapeutic agents. In four of five cases in which it was possible to compare the experimental results with the results of treatment of the patients with the same agents, correlation was found between the experimental and clinical findings.

KEY WORDS: heterotransplantation; ovarian carcinoma; chemotherapy.

Among the many experimental models which can be used to study the treatment of malignant tumors, the use of heterografts of human tumors in diffusion chambers is particularly interesting. By contrast with the method of culture of human tumors in vitro, in this method various forms of interaction are maintained between the tumor under investigation and the living organism, and the action of therapeutic substances on the tumor can be tested indirectly through the host animal. The use of heterografts in diffusion chambers for the study of individual sensitivity of tumors in particular patients to therapeutic agents is of special interest.

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