Bioelectrical Activity in the Sensorimotor Cortex in the Rats with the Spinal Pain Syndrome

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Formation of allodynia and the spinal pain syndrome of different intensity by application of penicillin to the dorsal surface of lumbar segments of the spinal cord are accompanied by dose-dependent changes in spontaneous and evoked bioelectric activity in the sensorimotor cortex.

Key Words: *spinal pain syndrome; allodynia; sensorimotor cortex; electrocorticogram; evoked potentials*

Behavioral and electrophysiological studies showed that unilateral application of penicillin to the dorsal surface of lumbar segments of the spinal cord (L_{IV}-L_{VI}) provokes the spinal pain syndrome in a dose-dependent manner [1-3]. Application of a 6×1.5×2 mm agar plate containing 50,000 U penicillin per 1 ml agar induced strong pain syndrome with frequent spontaneous pain seizures. In a dose of 25,000 U the syndrome was weaker, and 12,500 U penicillin produced only allodynia. Recording of evoked potentials (EP) in the neurons of the L_V lamina in the spinal cord dorsal horns showed that all three doses of penicillin increased EP amplitude, decreased EP threshold, and induced long-term high-amplitude secondary depolarization waves in response to stimulation of the sciatic nerve. These waves attest to generation of self-sustained excitation in the population of these neurons that work as a pathologically hyperactive generator. Activation of this generator sends intense flow of nerve impulses to the supraspinal subdivisions of nociceptive system, and recruit them to the pathological algetic system [5].

Our aim was to study the changes in electrical activity in a supraspinal part of the pathological algetic system, the sensorimotor cortex (SMC) during application of penicillin to the dorsal surface of lumbar segments of the spinal cord. Penicillin was used as a tool that provokes a dose-dependent spinal pain syndrome of various intensities.

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MATERIALS AND METHODS

Experiments were performed on 40 male Wistar rats (270-320 g) in strict adherence to the ethic requirements for neurophysiological studies of pain in animals [7,8]. The rats were maintained under standard vivarium conditions with a natural day-night cycle and food and water ad libitum.

The rats were anesthetized by intraperitoneal urethane (1400 mg/kg) and placed in a stereotaxic apparatus. The lumbar region of the spine was additionally fixed; the left-hand laminectomy was performed in the lumbar segments region preceded by opening of dura matter. Trepanation was done to the right from SMC. The rats were immobilized with a muscle relaxant (Myo-Relaxin, 50 mg/kg intramuscularly) and artificially ventilated. To simulate the pain syndrome of various intensities, generators of different activity were formed in the dorsal horns of the spinal cord lumbar segments with the help of penicillin known to disturb the GABAergic inhibition [4]. Penicillin (sodium chloride salt) was applied to the dorsal surface L_{IV}-L_{VI} of the left lumbar segments in a 6×1.5×2 mm

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agar plate that contained 50,000, 25,000, or 12,500 U per 1 ml agar.

The ongoing electric activity and EP in SMC were recorded with a monopolar silver-surface electrode. The reference electrode was attached to the skull. The signals were fed to a VC-9 broad band amplifier (Nihon Kohden). Evoked potentials were recorded in the maximum activity focus (MAF) of the sciatic nerve in the projection area of the left hind limb [6] in response to 0.1-msec current pulses applied to the left sciatic nerve isolated at the level of popliteal fossa. In addition, EP in the sciatic nerve MFA in SMC were studied in response to stimulation of forelimb with subcutaneous needle electrodes. The control records were made in each rat before application of penicillin plate and in a special series with application of penicillin-free agar plate.

Analysis of averaged EP (n=10-15) was performed with the help of a Microlink data acquisition system (Biodata Limited). The results were statistically analyzed using Wilcoxon's nonparametric *U* test and Student's t test (p=0.01).

RESULTS

Application of penicillin in any of the three doses to the dorsal surface of lumbar segments of spinal cord produced changes in the SMC electrical activity. The thresholds of EP in SMC elicited in response to the sciatic nerve stimulation were decreased in comparison with control values (Table 1). When stimulating current (0.15 mA) was set equal to the control threshold value, EP increased for all tested doses of penicillin. They consisted of a positive-negative complex with afterdischarges either in the form of a peak-wave complex (50,000 U) or a group of sharp waves (25,000 and 12,500 U, Fig. 1). There was a tendency of threshold decrease and amplitude increase of EP with penicillin dose, but the significant differences between the groups with all three various doses of the drug were not revealed (Table 1).

TABLE 1. Threshold and Amplitude of the Primary Complex of EP in SMC of Rats After Application of Different Doses of Penicillin to Spinal Cord Dorsal Surface (*M*±*m*)

Penicillin dose (U/1 ml agar)	Threshold current, mA	Amplitude, mV
Control	0.15±0.01	0.10±0.02
50 000	0.05±0.02*	0.24±0.03*
25 000	0.06±0.02*	0.18±0.03*
12 500	0.08±0.02*	0.15±0.02*

Note. *p<0.01 compared with the control. The amplitudes of EP in response to the control threshold current of 0.15 mA were averaged.

The ongoing electrical activity registered in SMC after application of a large dose of penicillin (50,000 U) to the dorsal surface of the spinal cord lumbar segments L_{IV}-L_{VI}, which provokes a pronounced pain syndrome in unrestrained rats [1], demonstrated spontaneous peak-wave complexes in the sciatic nerve MAF (Fig. 2). These complexes were absent before penicillin application or after a penicillin-free agar plate had been applied (the control record in Fig. 2). Application of penicillin in a dose of 25,000 U, which provoked a relatively weak pain syndrome with spontaneous seizures in unrestrained rats [2], also modified the electrocorticogram, where spontaneous groups of sharp waves appeared (Fig. 2). Application of penicillin in a dose of 12,500 U, which induced only allo-

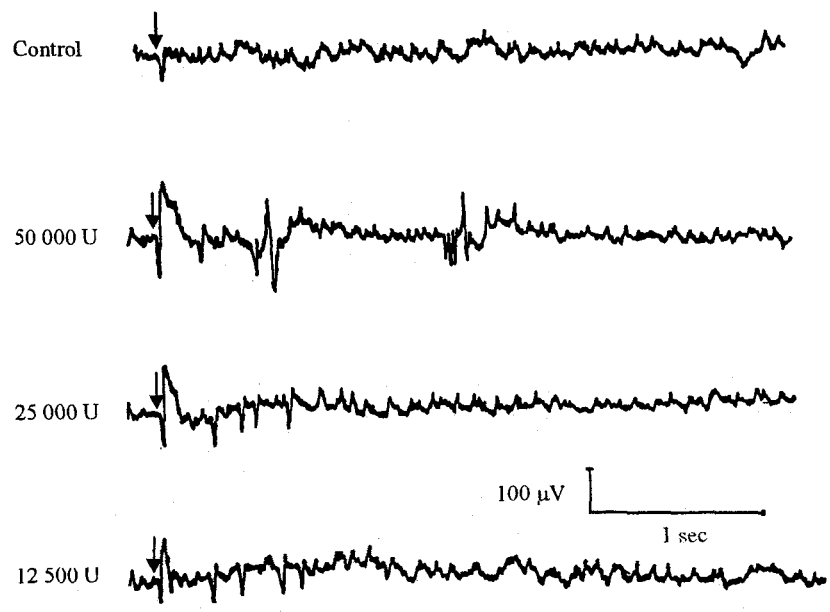

Fig. 1. Evoked potentials (single runs) in sensorimotor cortex in response to stimulation (arrows) of sciatic nerve ipsilateral to the side of penicillin application before and 40 min after application of the drug to the dorsal surface of the spinal cord lumbar segments L_{IV}-L_{VI}. Stimulating current was equal to the EP threshold in the control (0.15 mA).

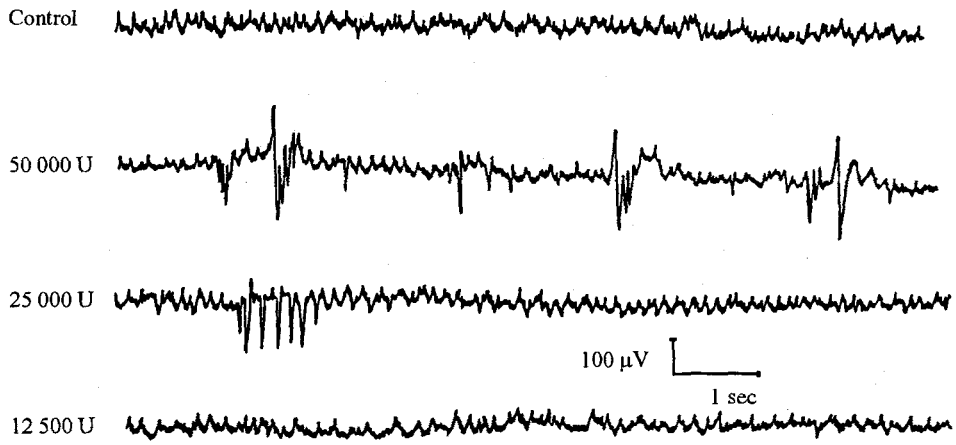

Fig. 2. Ongoing electrical activity (single runs) in sensorimotor cortex in control and 30 min after application of penicillin to the dorsal surface of the spinal cord lumbar segments L_{IV}-L_{VI}.

dynia of the hind limb area somatotopically related to the penicillin-treated spinal cord area in unrestrained rats [3], did not produce any changes in electrocorticogram in comparison with control (Fig. 2).

In control rats, rhythmic stimulation of the forelimb ipsilateral to the side of penicillin application did not evoke responses in the sciatic nerve MAF in SMC (Fig. 3). However, the stimulation induced characteristic afterdischarges after application of penicillin (50,000 and 25,000 U) to the dorsal surface of the spinal cord lumbar segments L_{IV}-L_{VI} (Fig. 3). The responses were provoked by the first stimulus when penicillin was applied in a dose of 50,000 U and by the 3rd-5th impulse when it was applied in a dose of 25,000 U. Application of penicillin in a dose of 12,500 U did not induce evoked activity in the sciatic nerve MAF in response to stimulation of the forelimb (Fig. 3).

Penicillin in all tested doses increased EP in SMC and decreased their thresholds. This led to afterdischarges consisting of peak-wave complexes and groups of sharp waves provoked by stimulation of the sciatic nerve with an electric current whose value was just a threshold for EP under the control conditions. These are manifestations of enhanced excitability and reactivity of the cortical neurons. Hyperactivity of the spinal cord generator leads to formation of pathological activity in response to the threshold (subnociceptive) stimulation. These changes of evoked activity in SMC correlate with behavioral feature in unrestrained rats in which pain seizures were provoked by tactile stimulation [1-3].

The large doses of penicillin (50,000 and 25,000) applied to the spinal cord dorsal surface produce a generator with sufficiently high power to send intensive flow of nerve impulses that provoke the pain syndrome with spontaneous seizures. In this case the electrocorticogram demonstrates spontaneous peak-wave complexes or groups of sharp waves which are not a mere reverberation of the cortical neurons to hyperactive spinal generator. This activity testifies to

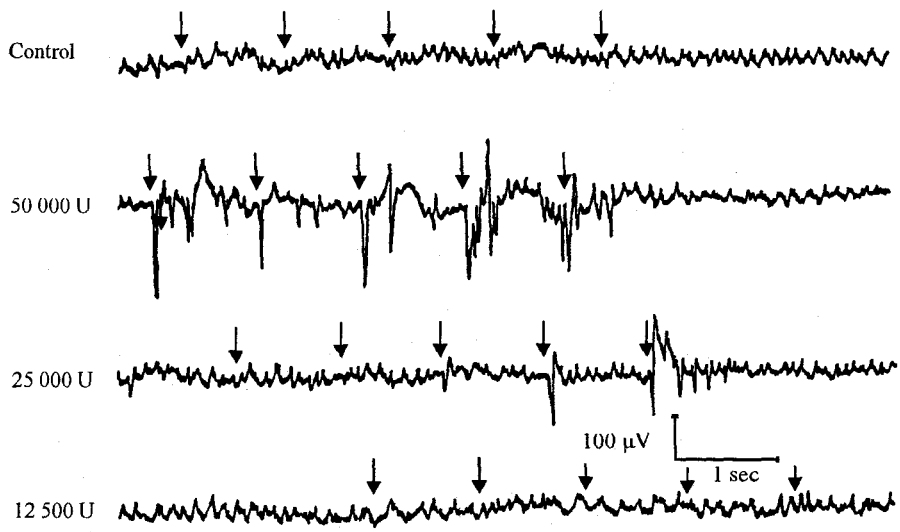

Fig. 3. Evoked potentials (single runs) in sensorimotor cortex recorded in the maximum activity focus of sciatic nerve in response to stimulation (arrows) of the forelimb ipsilateral to the side of penicillin application. The records were made before and 50 min after application of the drug to the dorsal surface of the spinal cord lumbar segments L_{IV}-L_{VI}. Stimulating current: 10 mA, 0.1 msec, repetition rate 1 Hz.

essential plastic rearrangements in the thalamocortical system. This inference agrees with the appearance of EP with afterdischarges recorded in the sciatic nerve MAF in response to stimulation of the forelimb.

When applied in a small dose of 12,500 U, penicillin induced only allodynia. In this case the power of the primary spinal generator was not sufficient to induce plastic rearrangements that underlie pathological spontaneous activity of cortical neurons. Therefore, the corresponding electrocorticogram was not different from the control, and additional peripheral stimulation is needed to provoke the pain syndrome.

The changes observed in bioelectric activity of SMC depend on the dose of penicillin applied to dorsal surface of the spinal cord. These changes indicate that the degree of involvement of SMC in the formation of pathoalgetic system is different in rats with spinal pain syndrome of various severity and in rats with allodynia.

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