to stress may also manifest itself in the inhibition of the antinociceptive system restricting the development of the PAS [2,12].

The data obtained in the present study are consistent with the clinical observations suggesting that adverse emotional experiences aggravate the course of the deafferentation pain syndrome [13]. The fact that the results of this study do not coincide with the experimental data on stress-induced analgesia can be accounted for by the fact that different mechanisms are involved in physiological and pathological pain [2,4,12].

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# Effect of the Somatosensory Cortex on the Development of the Deafferentation Pain Syndrome

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Experimental and clinical data demonstrate that the development of the deafferentation pain syndrome after peripheral nerve injury is caused by morphofunctional changes in the structures of the brain noci- and antinociceptive systems [2,3,7,14]. This is paralleled by increased excitability of peripheral nerve fibers [15], of nociceptive neurons in the spinal cord dorsal horn [13], of the thalamic nuclei [6], and of the cerebral cortex [3,8,10], all this indicating the formation of a pathological algetic system in the structures regulating pain sensitivity [11]. The brain cortex plays an important role in the regulation of pain sensitivity. It participates in the perception and analysis of pain signals [4,5] and has a marked modulating effect on the activity of the antinociceptive structures [4,6].

The study of the role of the somatosensory cortex in the development of the deafferentation pain syndrome appearing in rats after sciatic nerve transection was the aim of this research.

## MATERIALS AND METHODS

Experiments were carried out on 48 male Wistar rats weighing 180-200 g. For stimulation of the deafferen-

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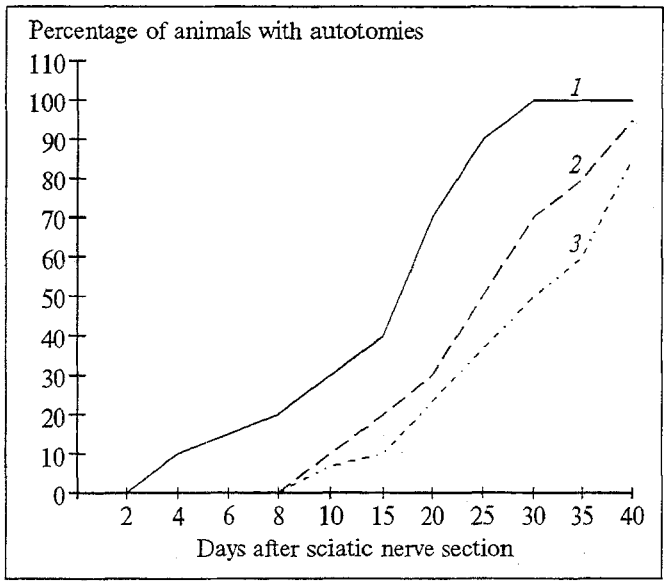


**Fig. 1.** Time course of development of pain syndrome in rats with removed somatosensory cortex after sciatic nerve transection. *1*) development of autotomies in animals with intact cortex; *2*) development of autotomies in animals with cortex destroyed at same time as nerve cut; *3*) development of autotomies in animals with somatosensory cortex destroyed 2 weeks prior to nerve section.

tation pain syndrome in the rats the sciatic nerve was cut under hexenal anesthesia (30 mg/kg intraperitoneally) and its central fragment was placed in a polyethylene capsule. Pain syndrome development was assessed by changed animals behavior, the appearance of signs of autotomy on the operated paws, and the development of hyperalgesia [2]. The intensity of the pain syndrome in rats was assessed using a modified arbitrary rating scale [9]. Injury to one claw corresponded to one point, of two to five claws to two to five points, respectively. Injury to a phalanx on one toe corresponded to six points, on two to five toes to seven to ten points, respectively. The maximal index, eleven points, corresponded to metatarsal bone injury. The pain sensitivity threshold was assessed by the hot-plate test with a plate surface temperature of 55°C. To destroy the somatosensory cortex and implant cortical electrodes trephination holes were bored in the animals above the site of hind paw representation in the somatosensory cortex, the coordinates being as follows: 5 mm in front of lambda and 3 mm to the side of the midline. Cortical sites were destroyed by electrocauterization bilaterally. For electrical stimulation of the cortex bipolar Nichrome electrodes were implanted in the hemisphere contralateral to the paw with the cut nerve. Cortex destruction and electrode implantation were performed simultaneously with sciatic nerve section. Group 1 comprised rats with cut sciatic nerve and removed somatosensory cortex, while group 2 comprised those with cut sciatic nerve and cortex electrostimulation. Group 3 (controls) consisted of rats with cut sciatic nerve and skull trephination without subsequent destruction of the cortex, and in group 4 (controls) the sciatic nerves were cut and electrodes implanted, but no stimulation was carried out. In group 5 rats the somatosensory cortex was destroyed 2 weeks before sciatic nerve section. The cortex was stimulated for 7 days daily, starting from the first day after nerve section, with rectangular current pulses of 0.1 msec duration and 1 Hz frequency for 5 min. The intensity of cortex stimulation was chosen for each animal individually. The increase of current strength was discontinued as the animal showed signs of extraalertness, "standstill", and slight quivering of the whiskers with the frequency of the stimuli applied. The stimulating current strength was 0.2 to 0.9 mA in all the animals. The results were processed by nonparametric statistical methods. After the experiment was over, the brain was removed to verify the sites of electrode implantation and cortex destruction.

## RESULTS

Bilateral destruction of the somatosensory cortex in animals with cut sciatic nerve (group 1) resulted in delayed development of the pain syndrome as against control animals (group 3) in which only the sciatic nerve was damaged (Fig. 1). In group 1 animals signs of autotomies manifested themselves on day 8 after surgery, whereas in the controls such changes were seen on the 2nd day after nerve section. Along with delayed development of the pain syndrome, in the animals with removed somatosensory cortex a reduction of pain in-

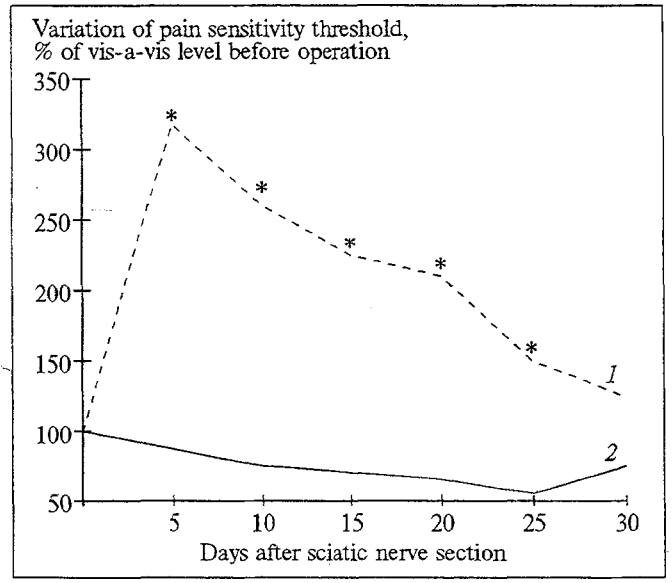


**Fig. 2.** Variation of pain sensitivity threshold in rats after sciatic nerve transection and somatosensory cortex destruction. *1*) animals with cut nerve and destroyed cortex; *2*) animals with cut nerve and intact cortex. Asterisk: $p<0.05$ in comparison with control.

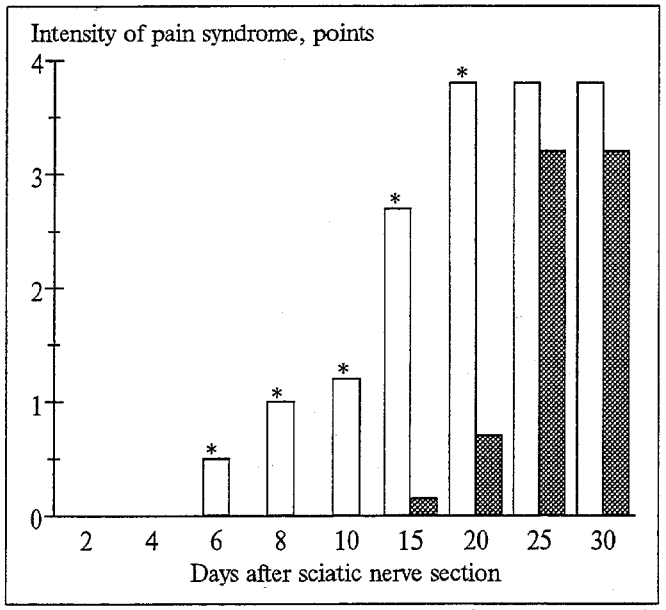


**Fig. 3.** Time course of intensity of pain syndrome in rats with electrical stimulation of the cortex following sciatic nerve section. Open bars: development of pain syndrome in control group of animals with cut nerve without cortex stimulation. Hatched bars: development of pain syndrome in rats after nerve section for electrostimulation of cortex. Other notation as for Fig. 2.

tensity ($p<0.05$) was observed, as assessed by the degree of autotomy manifestation, as well as a marked increase of the pain reaction threshold (Fig. 2). The delayed development of the pain syndrome and the reduction of its intensity in group 1 animals in comparison with the controls may be explained by the functional disengagement of the cortex and not by the injury inflicted, because a similar time course of pain syndrome development was observed in the animals with the somatosensory cortex destroyed 2 weeks before sciatic nerve transection (Fig. 1).

Rats with cut sciatic nerve exposed to electrical stimulation of the somatosensory cortex ceased moving about in their cages, became calm, and closed their eyes as soon as 2-3 min after the onset of stimulation and remained thus until the procedure was over. After the current was switched off the rats resumed movements in the cage. Follow-up of the time course of the pain syndrome in these animals showed its delayed development: it did not develop during seven days of stimulation or during the six days following the cessation of stimulation. By this time autotomies were observed in 90% of the control rats. Somatosensory cortex stimulation reduced the pain syndrome intensity (Fig. 3). The quiet behavior of rats with cut sciatic nerve during a session of cortex stimulation confirmed the absence of deafferentation pain in them during that period.

The uniform changes in the course of deafferentation pain syndrome development after somatosensory cortex destruction and for exposure to electrical stimulation seem to be due to a dual function of the somatosensory cortex in the regulation of pain sensitivity: it is the final component of the system of pain signal perception [4,5,10] and it activates the antinociceptive structures of the brain [4,6]. The delayed development of the pain syndrome after somatosensory cortex destruction may be related to disordered perception of nociceptive signals, as is indicated by the noticeable increase of the threshold of pain reactions. Other scientists report a similar increase of the pain threshold in animals after injury to or functional disengagement of the somatosensory cortex [1,4,5]. These data are in line with the clinical data demonstrating that somatosensory cortex destruction in patients suffering from the deafferentation pain syndrome arrests the pain [12].

The delayed development of deafferentation pain under conditions of electrostimulation of the somatosensory cortex may be caused by increased inhibition of nociceptive neurons at various levels of the central nervous system. Suppression of nociceptive neuron activity during somatosensory cortex stimulation was observed in the spinal cord dorsal horn [7] and in specific and nonspecific thalamic nuclei [4].

Hence, our findings indicate a marked effect of the cerebral cortex on the development of the deafferentation pain syndrome.

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