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Spontaneous Activity and Evoked Potentials in the Caudal Trigeminal Nucleus, Ventrobasal Thalamus, and Cerebral Cortex of Rats with Neuropathic Trigeminal Neuralgia

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Incomplete compression of the infraorbital nerve in rats leads to spontaneous neuronal activity in the form of bursts in the caudal trigeminal nucleus and to epileptiform activity in the ventrobasal thalamus and cerebral cortex. From the latter, afterdischarges are also recorded.

Key Words: *evoked potentials; caudal trigeminal nucleus; ventrobasal thalamus; cerebral cortex, rats; neuropathic trigeminal neuralgia*

The experimental pain syndrome elicited by incomplete compression of the sciatic nerve has been found to be accompanied by a pathologically augmented activity in peripheral nerve fibers [8], dorsal horns of the spinal cord [12,13], and the ventrobasal thalamus [7]. These findings are consistent with the view [2] that at the basis of pain syndromes lies a pathological system composed of various structures pertaining to various levels of

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conduction and integration of nociceptive signals. In our previous studies on rats with the neuropathic trigeminal pain syndrome caused by incomplete compression of the trigeminal nerve, epileptiform activity was recorded from the somatosensory area of the cerebral cortex [1,3]. The magnitude of this activity correlated with behavioral manifestations of the pain syndrome and with microcirculatory disturbances characteristic of pathological pain [4]. The present study is concerned with electrical activity in the major relays of the trigeminal system for pain sensitivity, namely the caudal trigeminal nucleus (CTN), the ventrobasal thalamus (VBT), and the somatosensory cortex of the brain (SSC,) which may be involved in the formation of a pathological system in this particular trigeminal pain syndrome.

MATERIALS AND METHODS

For the study, 20 male Wistar rats with an incompletely compressed infraorbital nerve and 5 sham-operated controls were used. Incomplete compression was produced by application of two loose ligatures to the nerve. Three to seven weeks after the operation, when marked changes in behavior (increased scratching of the face causing damage to the skin) and microcirculation were in evidence to indicate that a pain syndrome had developed, the animals were tested for changes in spontaneous electrical activity and evoked potentials (EP) which were recorded simultaneously from the CTN, VBT, and SSC. The operations for nerve compression and trephining of the skull were performed under ether anesthesia. Before the recording of electrical activity was started, a muscle relaxant (Myo-Relaxin) was administered to the rats and artificial pulmonary ventilation was instituted.

The infraorbital nerve was stimulated with rectangular pulses of 0.1 msec duration at current strengths of 0.1-10 mA via needle electrodes inserted into symmetrical points on the face in the area of the infraorbital foramen proximal to the compression site. EP were recorded from symmetrical points of the right and left CTN, VBT, and SSC in the foci of maximal activity during infraorbital nerve stimulation. Electrical activity in the SSC was recorded via spherical silver electrodes with a tip diameter of 1 mm, while that in the CTN and VBT was recorded via insulated steel electrodes having a tip diameter of 10-20 μ that enable both the total EP and the extracellular neuronal activity to be recorded using various pass bands for the amplifier signal. EP in the structures on both sides of the brain were recorded for

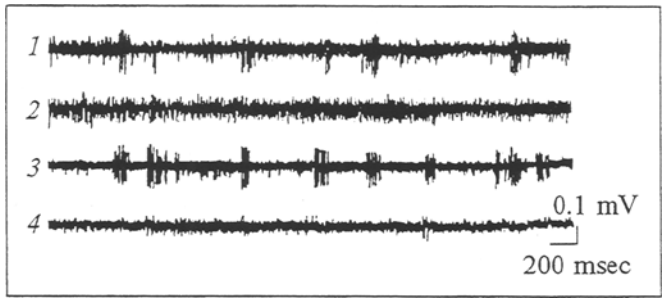

Fig. 1. Spontaneous neuronal activity in the contralateral (*1*) and ipsilateral (*2*) VBT and the ipsilateral (*3*) and contralateral (*4*) CTN relative to the damaged nerve in rats with the trigeminal pain syndrome elicited by infraorbital nerve compression.

stimulation of the intact and damaged nerve at current strengths that exceeded 2 and 8 times their threshold values for eliciting EP in the contralateral SSC with stimulation of the intact nerve.

RESULTS

In 5 of the 16 rats in which electrical activity was recorded in the CTN, increased spontaneous neuronal activity on the side of nerve compression was observed in the form of bursts (Fig. 1) that were manifested as peaks of negative polarity when focal potentials were led off (Fig. 2). In 3 of those 5 rats, epileptiform activity occurred in both CTN, although the discharges on the side contralateral to the compressed nerve were less marked. In all rats, changes in evoked activity of the CTN on the compressed nerve side were significant (Fig. 3). These changes included primarily a well-defined negative component of presynaptic nature with a peak latency of 3.0±0.1 msec. The postsynaptic EP component in the CTN on the compressed nerve side showed an increased threshold for its

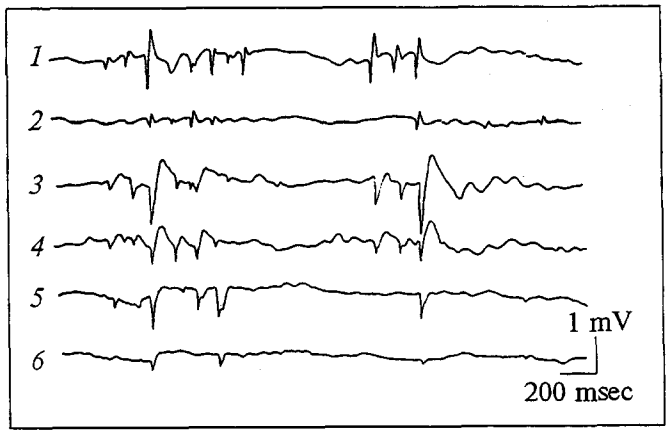

Fig. 2. Spontaneous epileptiform activity in the contralateral (*1*) and ipsilateral (*2*) SSC, the contralateral (*3*) and ipsilateral (*4*) VBT, and the ipsilateral (*5*) and contralateral (*6*) CTN relative to the damaged nerve in rats with the trigeminal pain syndrome elicited by infraorbital nerve compression.

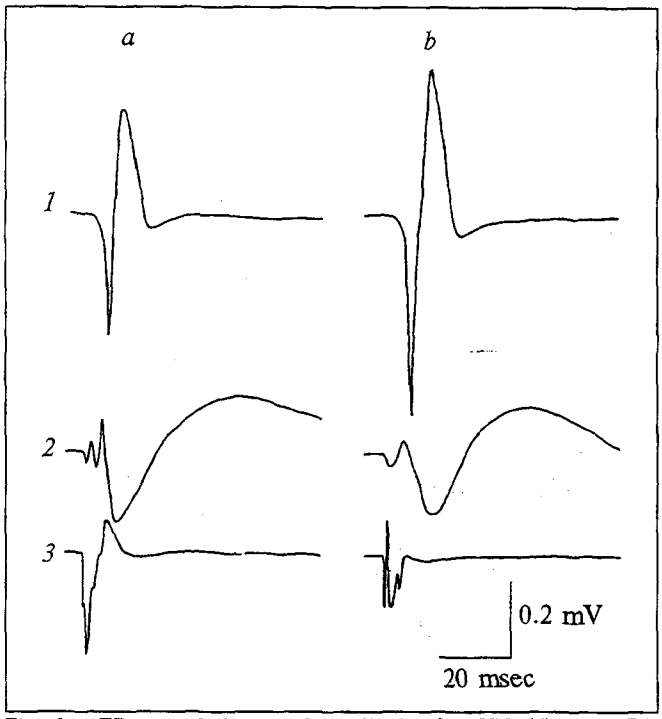

Fig. 3. EP recorded contralaterally in the SSC (*1*) and VBT (*2*) and ipsilaterally in the CTN (*3*) for stimulation of the intact (*a*) and damaged (*b*) nerve in rats with compressed infraorbital nerve.

occurrence and a smaller amplitude when stimuli of different intensities were applied (Table 1). In contrast to the well-defined positive postsynaptic EP component with a peak latency of 3.4±0.1 msec in the intact CTN, postsynaptic activity in the CTN on the compression side was represented by two late positive-negative complexes with peak latencies of 5.6±0.1 and 9.3±0.3 msec, respectively.

Spontaneous activity from the VBT was recorded in 15 rats, and bursts of epileptiform discharges were observed in 6 of them (Figs. 1 and 2). Spontaneous epileptiform activity was recorded from both the contralateral and the ipsilateral thalamus. Evoked activity of short latency in the VBT contralateral to the damaged nerve, was inhibited in all 15 rats (Fig. 3). When stimuli of different intensities were applied to the damaged nerve the amplitudes of the EP component with an 8 to 10 msec latency were significantly reduced ($p<0.05$) as compared to those of the EP arising in response to stimulation of the intact nerve (Table 1), and a tendency was also noted toward a reduction in the amplitudes of the late EP component with a latency of >25 sec. When the intact nerve was stimulated, the contralateral EP contained, as a rule, three early peaks with latencies of 3, 6, and 8 msec, respectively, whereas only one early peak with a latency of 4.5 msec invariably appeared upon stimulation of the damaged nerve.

In the SSC, epileptiform activity in the form of spontaneous peak-wave discharges and sharply-pointed waves (Fig. 2) were more often recorded (in 40% of the 20 rats) only from the hemisphere contralateral to the nerve compression side, but in 25% of the rats epileptiform activity also occurred in the other hemisphere. The EP arising in the contralateral hemisphere when stimuli of different intensities were applied to the damaged nerve had significantly greater amplitudes in 90% of the rats than did the EP recorded from the contralateral hemisphere in response to intact nerve stimulation. Afterdischarges, too, were recorded more often from the hemisphere contralateral to the compressed nerve. Upon stimulation of this nerve afterdischarges occurred in 60% of the rats, and in 25% of these bilaterally. Finally, afterdischarges in the hemisphere contralateral to the compressed nerve were also elicited in 45% of rats by stimulation of the intact nerve, and in 30% of them they were bilateral.

A synchronization of spontaneous epileptiform discharges was observed among the CTN, VBT, and SSC on the respective projection side (Fig. 2).

Thus, as shown in this study, incomplete compression of the infraorbital nerve considerably altered the electrical activity in the tested structures of the trigeminal system. First, a pathological spontaneous activity developed - high-frequency bursts in the CTN and peak-wave epileptiform activity in the SSC, which were very rarely recorded in the intact or sham-operated animals. Second, the EP arising in the contralateral SSC upon stimulation of the compressed nerve had increased amplitudes, indicating an enhanced neuronal response to both weak and strong peripheral excitation. Third, there appeared a prolonged afterdischarge, which is not usually observed in intact animals and which reflects a long-continued reverberation of excitation in the nerve structures. Lastly, spontaneous and evoked activities were altered at different levels of the nociceptive projection system (in the trigeminal complex, thalamus, and cerebral cortex). Apart from the structures to which afferent signals were projected directly from the damaged nerve, pathological activity was in many cases also displayed by homologous structures of various levels on the opposite side of the brain. In the SSC, afterdischarges also appeared in response to stimulation of the intact nerve. These findings all point to a generalization of the pathological process.

On the whole, the results of this study permit the conclusion that compression of the infraorbital nerve results in changes of a systemic nature and in the formation within the trigeminal

TABLE 1. Characteristics of the Primary EP Components in the Caudal Trigeminal Nucleus (CTN), Ventrobasal Thalamus (VBT), and Somatosensory Cortex (SSC) of Rats with Neuropathic Trigeminal Neuralgia. The Values are Means±SEM

Structure and stimulation	Threshold for EP occurrence upon nerve stimulation, mA		EP amplitude with weak (2 thresholds) nerve stimulation, mV		EP amplitude with strong (8 thresholds) nerve stimulation, mV	
	intact nerve	damaged nerve	intact nerve	damaged nerve	intact nerve	damaged nerve
CTN, ipsilateral	0.55±0.07	0.88±0.14*	0.43±0.11	0.11±0.02*	0.75±0.14	0.37±0.03*
VBT, contralateral	0.73±0.10	0.90±0.14	0.20±0.06	0.08±0.03*	0.36±0.08	0.23±0.03*
SSC, contralateral	0.81±0.09	0.86±0.09	1.10±0.33	2.10±0.48*	2.36±0.36	4.13±0.42*

Note. The asterisk indicates a significant difference ($p<0.05$).

nerve system of a pathological algetic system which constitutes the pathogenetic basis of the resulting pain syndrome. The observation that spontaneous epileptiform discharges arose synchronously at the different tested levels of the nociceptive trigeminal projection system suggests the existence in this system of a generator of pathologically enhanced excitation which is, in the final analysis, responsible for the pain syndrome.

The sequential appearance of pathological activity in relay structures of different levels (dorsal horns of the spinal cord and their nuclei [5,6,11]; thalamus and cerebral cortex [6,9,10]) has been demonstrated in earlier studies using a rat model of the deafferentation pain syndrome caused by extensive interruption of the dorsal roots of the brachial plexus. In that model of the pain syndrome, however, a pathological neuronal activity in the thalamus and cerebral cortex was only observed six months after the rhizotomy, when the hyperactivity at the primary relay level had become much weaker. In contrast, our previous study in rats with the trigeminal pain syndrome produced by incomplete compression of the infraorbital nerve showed that the somatosensory cortex exhibited pathological activity during the first few weeks following the compression [3]. Early changes were also recorded for the ventrobasal thalamus both in the present study and in an animal model of peripheral neuropathy of the sciatic nerve [7]. Differences between the time courses and sequences with which different projection structures are induced to develop pathological activity are important for understanding how a pathological algetic system is formed and merit further investigation.

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