SUPRASPINAL EFFECTS ON MOTONEURONS IN LOCAL TETANUS

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Experiments on cats with local tetanus showed that during stimulation of brain-stem structures excitatory postsynaptic potentials (EPSPs) are recorded in motoneurons of the poisoned lumbosacral segments of the spinal cord and inhibitory postsynaptic potentials are absent. Even if single stimuli are applied, potentiated polysynaptic EPSPs are recorded in the motoneurons, often culminating in action potentials. These effects are explained by disturbance of inhibitory mechanisms at the segmental level under the influence of the tetanus toxin. Short-latency monosynaptic descending responses remain unchanged. The excitability of the motoneuron membrane, measured by direct stimulation, is unchanged.

In local tetanus, in which various types of segmental postsynaptic inhibition are disturbed [12], changes also take place in the effects of stimulation of medullary structures giving descending facilitatory and inhibitory effects [3, 4, 10, 11].

The object of the present investigation was to study these effects by recording the intracellular potentials of motoneurons in the lumbosacral segments affected by local tetanus.

EXPERIMENTAL METHOD

Cats weighing 2-4 kg were anesthetized with pentobarbital (35-45 mg/kg). The animals were immobilized with Flaxedil and maintained on artificial respiration. All operative procedures (laminectomy, opening of the dura mater, division of the roots, dissection of muscular nerves) were carried out a few hours before the experiment. Potentials of motoneurons of the lumbosacral region were recorded intracellularly by glass microelectrodes with a tip less than 1 μ in diameter, filled with 3 M potassium chloride solution and 0.6 M potassium sulfate solution. The motoneurons were identified by stimulating the nerves supplying the gastrocnemius, peroneus profundus, quadriceps, posterior biceps + semitendinosus (PBST), and plantaris muscles and also the corresponding ventral roots. Simultaneously, during stimulation of the suprasegmental structures, the dorsal surface potential of the spinal cord was recorded, so that the interval between the wave of excitation arriving along the descending tracts and the beginning of the intracellular responses could be determined. A silver ball electrode placed on the dorsal surface of the spinal cord close to the point of insertion of the intracellular microelectrode was used for this purpose. To investigate the excitability of the motoneuron membrane, square pulses of depolarizing current (0.1-0.5 msec, 0.1-1 mA) were passed through the intracellular microelectrode [8].

The suprasegmental structures were stimulated through bipolar electrodes with a tip 20-40 μ in thickness and interelectrode distance 0.1-0.2 mm. The electrodes were inserted stereotaxically through the cerebellum using the coordinates from Szentagothai's atlas. The following brain structures were stimulated:

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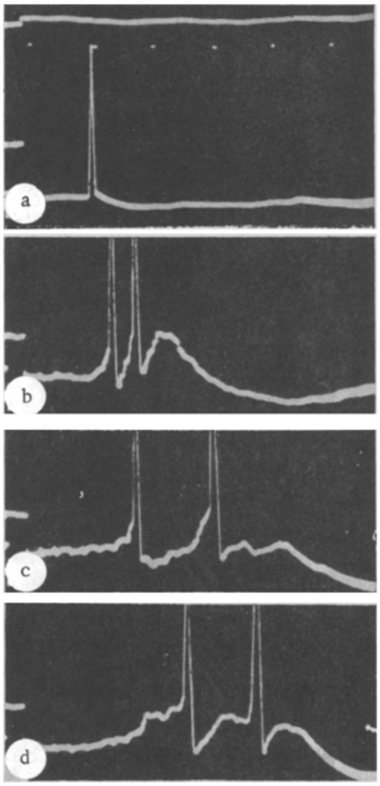

Fig. 1

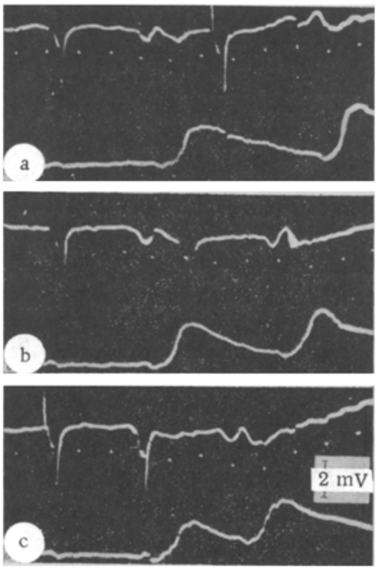

Fig. 2

Fig. 1. Responses of flexor motoneuron to stimulation of various nuclei in the medulla and pons. Response to antidromic stimulation of nerve to PBST (A). Effects during application of a short series of stimuli to the caudal nucleus of the pons (B), the nucleus of Deiters (C), and nucleus of the raphe (D). Time marker 10 msec, calibration pulse in A 20 mV, in B-D 5 mV.

Fig. 2. Responses of extensor motoneuron to paired stimuli applied to lateral vestibular nucleus with intervals of 6 (A), 4 (B), and 3 (C) msec between pairs. Top beam records dorsal surface potential of spinal cord. Bottom beam records monosynaptic vestibular EPSPs. Time marker 1 msec.

the caudal nucleus of the pons, the nucleus of Deiters, the gigantocellular nucleus, the reticular ventricular nucleus, and the nucleus of the raphe [20]. The position of the electrode tip in the brain structures was verified histologically in each experiment (sections were stained by Nissl's method). The systemic arterial pressure was recorded in the carotid artery.

Local tetanus was produced by injection of tetanus toxin in a dose of 0.005-0.02 MLD for cats at several points into the left gastrocnemius and quadriceps muscles. When injected by this method the toxin reached the lumbosacral segments of the spinal cord comparatively uniformly along the corresponding muscular nerves, and to begin with attacked the structures of the ventral horn [1]. The experiments were carried out on the 3rd-6th day after injection of the toxin.

EXPERIMENTAL RESULTS

Of the 100 motoneurons belonging to flexors and extensors studied, stimulation of the medulla (gigantocellular nucleus, ventral reticular nucleus, and nucleus of the raphe) during tetanus poisoning caused the appearance of an inhibitory postsynaptic potential (IPSP) in only one. In all the rest there was no IPSP, and instead, especially in the late periods of poisoning, excitatory postsynaptic potentials (EPSPs) appeared, frequently culminating in an action potential (Fig. 1).

During stimulation of Deiters' nucleus, extensor motoneurons are mainly facilitated and flexor inhibited, whereas during stimulation of the caudal nucleus of the pons the opposite relations are observed [7,

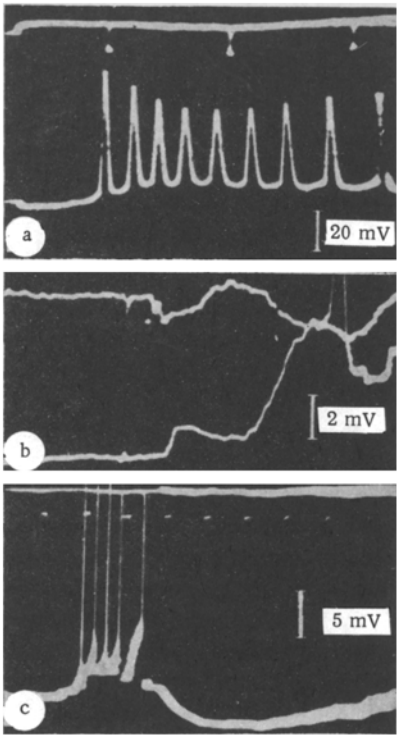

Fig. 3. Responses of 3 different motoneurons to repetitive (A) and single (B) stimulation of Deiters' nucleus and to single stimulation of gigantocellular nucleus (C). Time marker 10 msec.

15, 18]. In tetanus, however, as the investigations showed, only excitatory synaptic effects are recorded in the same motoneuron during stimulation both of the caudal nucleus of the pons (Fig. 1B) and Deiters' nucleus (Fig. 1C). A similar effect – the appearance of EPSPs and generation of an action potential in the same motoneuron – also was observed in response to stimulation of the nuclei of the raphe (Fig. 1D).

It is an interesting fact that monosynaptic excitatory descending influences undergo no significant change (Fig. 2). They maintained their usual amplitude (on the average about 2 mV), latency (less than 4 msec), and segmental delay (0.3-1 msec). Polysynaptic responses of the motoneuron were considerably increased in tetanus. This was shown by a sharp increase in the polysynaptic components of the EPSP and also in the fact that responses of motoneurons were generated with a high frequency of up to 500/sec (Fig. 3A). Even in response to a single stimulus a powerful polysynaptic EPSP was generated in the cell, culminating in an action potential (Fig. 3B). Frequently in response to the application of a single stimulus to the bulbar structures a slow depolarization wave and multiple discharge could be observed in the motoneuron (Fig. 3C), just as during the action of strychnine [6].

The effects of tetanus toxin examined above could not be connected with increased excitability of the motoneuron membrane. Investigations with direct stimulation of motoneurons by passage of pulses of depolarizing current through the intracellular microelectrode showed that under these conditions there was no decrease in the threshold of excitability of the motoneuron membrane. This agrees with observations showing that in tetanus, at least in the early stages of the disease, the amplitude of the monosynaptic reflexes is unchanged [12]. The results suggest that the changes observed are largely connected with an increase in the activity of the system of interneurons, just as is observed in strychnine poisoning. Attention must also be directed to a further characteristic feature of the intracentral relations in tetanus poisoning of the spinal cord: under these conditions the normally latent or not universally detectable convergence of excitatory volleys from different sources on the same motoneuron was clearly manifested (Fig. 3). A similar phenomenon has also been observed in strychnine poisoning [6, 9].

The results are in agreement with observations [13] indicating weakening of inhibitory postsynaptic potentials during stimulation of the anterior lobe of the cerebellum in tetanus poisoning.

Special attention must be drawn to the fact that in local tetanus not only are the inhibitory descending influences lost, but they are replaced by facilitatory effects. Similar relations are observed when segmental responses are tested in tetanus [2]. This general principle can be explained on the assumption that during stimulation of structures whose stimulation gives rise to inhibition the motoneurons experience mixed effects: both inhibitory and excitatory [2, 5, 6, 14, 16, 17, 19]. Under normal conditions the inhibitory component is stronger than the excitatory, but if the inhibitory component is removed, the excitatory becomes manifest; in addition it is intensified through the increasing polysynaptic activity [2, 3, 4].

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