PRIMARY AFFERENT DEPOLARIZATION AND PRESYNAPTIC INHIBITION OF MONOSYNAPTIC REFLEXES

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In experiments on cats the writers showed previously that ammonium ions, injected in convulsive doses intravenously or into the central canal of the spinal cord inhibit long negative electrotonic dorsal root potentials (DRP) of the spinal cord [3-5]. The DRP are considered to be in direct reflection of processes taking place in primary afferent endings responsible for presynaptic inhibition of spinal reflexes [1, 8, 12].

The object of the present investigation was to study whether blocking of DRP by ammonium ions is accompanied by depression of presynaptic inhibition of monosynaptic reflexes.

EXPERIMENTAL METHOD

Experiments were carried out on cats weighing 2.5-4 kg, anesthetized with chloralose (70-80 mg/kg, intravenously). After laminectomy on vertebrae T_{12}-S_2 the spinal cord was divided at the level of segment L_2. The ventral roots of the segments L_6-S_2 and a bundle of fibers (filament) of the dorsal root L_6 were isolated on the left side and divided distally. Many cutaneous and muscular branches of the sciatic nerve in the left hind limb were isolated and divided distally. After secure fixation of the animal, perfusion of the central canal of the lumbosacral portion of the spinal cord with artificial cerebrospinal fluid (CSF) [10] was commenced. In the course of the experiment CSF in which the NaCl was replaced by an equimolar amount of NH_4Cl ("ammonium" CSF) was used. Afferent nerves of the hind limb were stimulated by square pulses 0.1 msec in duration. Reflex electrical responses were recorded from ventral root L_7; electrotonic potentials from a filament of dorsal root L_6; the dorsal cord potential at the level of segment L_6. The potentials were recorded by means of an amplifier with time constant of 0.3 sec and a dual-beam oscilloscope with camera. The method of perfusion of the central canal of the spinal cord and details of the technique used to stimulate the nerves and record potentials were described previously [5].

EXPERIMENTAL RESULTS

The records in Fig. 1A illustrate the action of ammonium ions on DRP (top beam) and the dorsal cord potential (bottom beam) evoked by stimulation of nerves to the flexors of the knee (posterior biceps and semitendinosus, PBST). Perfusion of the central canal with "ammonium" CSF was accompanied by a progressive decrease in the small negative DRP and of the slow positive wave on the dorsal surface of the spinal cord. Toward the end of 1 h of perfusion, DRP disappeared almost completely (trace 4). The records in Fig. 1A indicate partial recovery of DRP and of the positive dorsal cord potential 1 h after the beginning of subsequent rinsing the spinal cord with normal CSF. Records B, C, and D and the corresponding curves b, c, d, e in Fig. 1 illustrate the action of volleys of afferent impulses in the nerves to PBST (in the experiment whose results are given in the record in Fig. 1A) on the amplitude of the monosynaptic reflex discharges of motoneurons for extensors of the ankle (m. gastrocnemius – G). During perfusion of the central canal with normal CSF volleys of impulses in PBST evoked profound and prolonged (over 500 msec) inhibition of the test responses, characteristic of the presynaptic inhibitory action of impulses in the group I afferents of the flexors on monosynaptic reflexes of the extensors [1, 8, 15]. After perfusion of the

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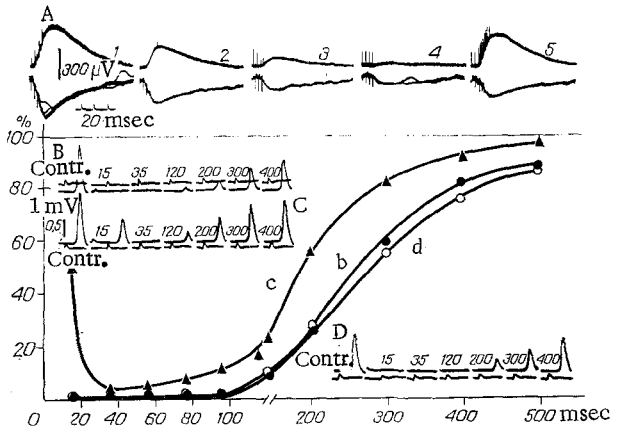

Fig. 1. Action of ammonium ions on presynaptic inhibition of monosynaptic reflexes. A) DRP of segment L_6 (above) and dorsal cord potentials of the same segment (below), evoked by application of four stimuli (220/sec of maximal strength for group I afferent fibers: 1) during perfusion of spinal canal with normal CSF; 2, 3, 4) 23, 35, and 55 min, respectively, after beginning of perfusion of canal with "ammonium" CSF; 5) 1 h after last rinsing of spinal cord with normal CSF; B, (bottom beam), C, and D (top beam) denote maximal monosynaptic reflex discharges in ventral root L_7 evoked by stimulation of G at different time intervals — (in msec for each response) after beginning of stimulation of PBST. Contr. — responses only to one test stimulus. Top beam in B and bottom beam in C and D show dorsal cord potentials of segment L_6; b, c, d) changes in amplitude of test reflexes of G, compiled from records some of which are given in B, C, and D, respectively. Abscissa, time (in msec) between first conditioning stimulation of PBST and test stimulation of G; ordinate, amplitude of test responses (in percent of control, taken as 100%).

central canal for 1 h with "ammonium" CSF this inhibition was somewhat weakened (Fig. 1C, c), although the total duration of inhibition of the test responses was still about 500 msec, but the amplitude of test responses evoked between 25 and 100 msec after the beginning of stimulation of PBST was under 10% of the control value. Complete recovery of the "presynaptic" inhibitory action of volleys of impulses in PBST on monosynaptic discharges of G was observed 1 h after the beginning of rinsing the spinal cord with normal CSF (Fig. 1D, d).

The records shown in Fig. 2, obtained in the same experiment, characterize the effect of perfusion of the central canal with "ammonium" CSF on postsynaptic inhibition of monosynaptic reflexes of G. Inhibition was produced by stimulation of nerves to the extensors of the ankle: mm. flexor digitorum longus and flexor hallucis longus (FDHL) by stimuli of ten times the threshold strength for afferent group I fibers, and above the threshold strength for afferent fibers of groups II and III [9]. Since stimulation of the afferent nerves to FDHL evoked no significant presynaptic inhibition of monosynaptic reflexes [8], depression of the test responses evoked after preliminary stimulation of FDHL was considered to be the result of the postsynaptic inhibitory action of impulses in flexor reflex afferents to motoneurons of extensor muscles [9]. During perfusion of the central canal with normal CSF volleys of

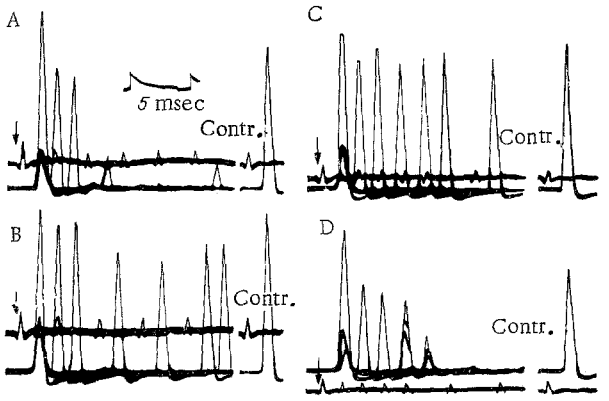

Fig. 2. Action of ammonium ions on postsynaptic inhibition of monosynaptic reflexes. Bottom beam in A, B, and C and top beam in D show superposition of records of maximal monosynaptic discharges in ventral root L_7 evoked by stimulation of G at different time intervals after stimulation of FDHL. Sweep of beam figured synchronously with time of stimulation of FDHL. Top beam in A, B, and C and bottom beam in D show dorsal cord potentials of segment L_7; first triphasic potential, marked by arrow, corresponds to arrival of afferent volleys in FDHL into the spinal cord. Contr.) Responses only to one test stimulation of G. A) During perfusion of spinal canal with normal CSF, B) 30 min and C) 60 min after beginning of perfusion with "ammonium" CSF, D) after rinsing canal with normal CSF for 1 h. Calibration for reflex discharges in A 600 μV, for B, C, and D 1 mV.

afferent impulses in FDHL evoked initially transient facilitation, followed by complete inhibition of the test responses on G (Fig. 2A). The inhibition disappeared during perfusion of the spinal cord with "ammonium" CSF (see Fig. 2B, C) and it was restored after subsequent rinsing of the spinal cord with normal CSF (Fig. 2D).

The data described above are in full agreement with the results of the writers' previous investigations [3, 4, 5] and they show that ammonium ions, injected into the central canal of the spinal cord, depress DRP. Depression of DRP developed parallel with depression of postsynaptic inhibition of monosynaptic reflexes and was not connected with a decrease in amplitude of monosynaptic reflex discharges in the ventral roots of the spinal cord. These results are also evidence of the relative resistance of presynaptic inhibition of monosynaptic flexor reflexes to the action of ammonium. This resistance becomes more evident still if it is recalled that the intensity of depression of monosynaptic reflexes of G evoked by stimulation of PBST is determined under normal conditions by the combined action of pre- and postsynaptic inhibition. For that reason, at least part of the weakening of the inhibitory action of volleys in PBST on monosynaptic reflexes of G as a result of the use of ammonium (Fig. 1C, c) must be attributed to depression of postsynaptic inhibition by ammonium (Fig. 2d). We know that stimuli of maximal strength for group I muscle afferents, namely the stimuli which were used to stimulate PBST, are always above threshold for group II afferent fibers evoking postsynaptic inhibition of extensor motoneurons lasting 20-40 msec [9]. Volleys of impulses in group I afferents of PBST themselves evoke weak IPSPs in motoneurons of G, with a duration of several hundreds of milliseconds [6].

In the modern view presynaptic inhibition of spinal reflexes is due to the action of a chemical transmitter (probably gamma-aminobutyric acid or GABA) on the membrane of primary afferent endings [2, 7, 11]. It is considered that GABA increases the permeability of the presynaptic membrane for chloride ions, which, in accordance with their electrochemical gradient, flow outward from the fibers, creating a current depolarizing the membrane of the terminals. Under these circumstances, the gradient of chloride ions directed from without outward, is maintained by an ionic pump which is responsible for the transmembrane transport of chlorides within the fibers [11]. Previously [5] the writers suggested that blocking of DRP by ammonium ions is due to depression of the chloride pump and, consequently, to dis-

appearance of the emf for the chloride current producing the DRP. If this is true, the resistance of the presynaptic inhibition of monosynaptic reflexes to the action of ammonium can logically be explained on the grounds that during blocking of the chloride current evoked by GABA the increase in conductance of the presynaptic membrane may itself weaken the excitatory synaptic action of impulses in Ia afferents to motoneurons.

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EFFECT OF BLOCKING PROJECTION (SOMATOSENSORY AND VISUAL) AREAS OF THE BRAIN ON EVOKED POTENTIALS IN PARIETAL ASSOCIATION AREAS OF THE OPPOSITE HEMISPHERE

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Compensatory-repair processes are the basis of the restoration of health, and their study is therefore of great practical clinical experience as well as of theoretical interest. Recent investigations have shown several possible mechanisms for these processes. First, there is hyperfunction of structures remaining intact or only partially injured, interhemispheric (bilateral) interaction, definite duplication of certain brain systems, and so on [1-3, 5, 6]. Meanwhile an important pathway for the restoration of function is the intensive activation of polymodal (nonspecific) neurons and their constellations, which because of their polysensory nature, may to some degree perform certain simple functions of specific systems. This hypothesis may apply above all to the association structures (cortical and subcortical) and to the reticular formation.

The object of this investigation was to study the character of changes in bioelectrical reactions on the parietal association areas of one hemisphere after reversible blocking by cold of the cortical projection structures of the opposite hemisphere.

EXPERIMENTAL METHOD

Acute experiments were performed on 40 cats anesthetized with chloralose (60-70 mg/kg) with the addition of pentobarbital (20-30 mg/kg). Evoked potentials (EP) were recorded by a monopolar technique; the reference electrode was fixed to the bones of the frontal sinus and recording electrodes were located in the parietal region of both hemispheres.

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