DEPRESSION OF PRESYNAPTIC INHIBITION OF SPINAL REFLEXES BY AMMONIUM ACETATE

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In experiments on cats ammonium acetate (AA), injected intravenously (2-4 moles/kg), depresses primary afferent depolarization (PAD), which is associated with presynaptic inhibition of spinal reflexes. Depression of PAD develops parallel with depression of postsynaptic inhibition of monosynaptic reflexes and is reversible in character. Depression of PAD is not connected with blocking of negative postsynaptic dorsal cord potentials or of reflex electrical discharges in ventral roots. It is concluded that one of the mechanisms of the convulsant action of AA is its depression of presynaptic inhibition. It is suggested that depression of PAD by AA may be the result of blocking of the chloride pump which operates in afferent terminals and creates the emf for the outward transmembrane chloride current producing PAD.

KEY WORDS: *spinal cord; ammonium acetate; presynaptic inhibition.*

Ammonium acetate (AA), if injected intravenously in doses of 2-3 mmoles/kg body weight, induces spasms of skeletal muscles that are attributed to depression of postsynaptic inhibition of central neurons [5-7]. The experimental data given below show that AA, if used in doses depressing postsynaptic inhibition of spinal motoneurons, also depresses depolarization of the central endings of primary afferent fibers, with which presynaptic inhibition of spinal reflexes is associated.

EXPERIMENTAL METHOD

Cats were anesthetized with hexobarbital (50 mg/kg intravenously). The spinal cord was divided at the level of segment L1 and the left ventral roots of segments L6-S2 were divided intradurally. Many of the cutaneous and muscular branches of the sciatic nerve were identified in the left lower limb and divided distally. The cats were immobilized with listhenon and artificially ventilated. A cannula was introduced into one carotid artery for continuous measurement of the blood pressure. A bundle of fibers from the caudal part of the left dorsal root of L6 was divided distally and placed on platinum wire electrodes to record electronic potentials. Dorsal cord potentials were derived by a needle electrode from the middle part of segment L6 close to the point of entry of fibers of the left dorsal root into the spinal cord. An aqueous solution of AA (10 or 20%) was injected intravenously at the rate of not more than 0.2 mmole/kg/min to prevent blocking of impulse conduction along the intramedullary regions of the primary afferents [6]. The peripheral nerves were stimulated by square pulses 0.1 msec in duration. The potentials were led to amplifiers with a time constant of 0.3 sec and recorded photographically from a dual-beam oscilloscope.

EXPERIMENTAL RESULTS AND DISCUSSION

The records (Fig. 1, II, III) illustrate the action of AA on inhibition of monosynaptic reflex discharges of motoneurons of the extensor muscles of the ankle (m. gastrocnemius; G) evoked by volleys of afferent impulses in the fibers of the cutaneous nerve of the calf (n. suralis; SUR), a well-known example of postsynaptic inhibition. Before injection of AA volleys of impulses in SUR evoked definite inhibition (a decrease in amplitude) of the test reflexes (Fig. 1, control II, III). Intravenous injection of AA in a dose of 2.8-3.2 mmoles/kg led to the almost complete suppression of this inhibition (Fig. 1, AA, II, III), and it re-

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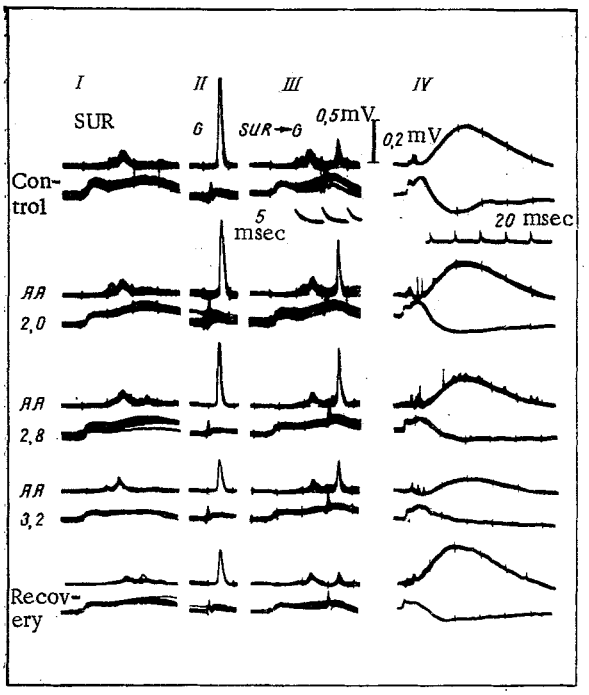

Fig. 1. Action of AA on postsynaptic inhibition of monosynaptic reflexes and of primary afferent fibers. I,II,III) Ventral root L7 potentials (top beam) and dorsal cord potential in segment L6 (bottom beam) evoked by stimulation of SUR (I), G(II), and stimulation of SUR and G successively (III) by single electrical pulses 3 times above threshold strength for the most excitable fibers of SUR and supramaximal for group 1 fibers of G; IV) dorsal root L6 potentials (top beam) and dorsal cord potential in segment L6 (bottom beam), evoked by stimulation of SUR; control) before injection of AA; numbers represent total quantity of AA (in moles/kg) injected up to the time of recording each series of potentials; recovery) 60 min after injection of the complete dose of AA (3.2 mmoles/kg). Calibration: 0.5 mV for ventral, 0.3 mV for dorsal root potentials.

covered again 1 h after the end of AA administration (Fig. 1, recovery II, III). The records in Fig. 1, IV show the action of AA on depolarization of the central endings of the primary afferent fibers which accompanies the arrival of volleys of impulses from SUR into the spinal cord. Clearly AA, in doses depressing postsynaptic inhibition of monosynaptic reflexes considerably reduced both the amplitude of the slow negative electrotonic dorsal root potentials (DRP) and the amplitude of the slow negative wave on the surface of the cord, which reflects the electric field potential arising during depolarization of the intramedullary regions of the primary afferents.

Infusion of AA as a rule was accompanied by a marked decrease in amplitude of the monosynaptic reflexes (Fig. 1, II), and, in some cases, by an appreciable reduction in size (area) of the polysynaptic reflex discharges in the ventral roots of the spinal cord (Fig. 1, I). However, this does not mean that the "ammonium block" of DCP reflects the general "inhibitory action" of AA on spinal neurons. The results of all the experiments show that the ability of volleys of afferent impulses to produce the DCP reappears independently of (as a rule, earlier than) recovery of the amplitude of the reflex electrical discharges in the ventral roots, but always along with recovery of the postsynaptic inhibitory action of afferent volleys on monosynaptic reflexes.

The records (Fig. 2) obtained in an experiment on another cat demonstrate the action of AA on depolarization of the central endings of the primary afferent fibers activated by stimulation of the muscular nerve n. peronaeus profundus (PP) and nn. posterior biceps et semitendinosus (PBST). Clearly AA caused strong reversible depression of the electrotonic DCP and slow positive waves of the dorsal cord potential. It is important to note that the depression of DCP was not connected with any appreciable depression of the postsynaptic negative cord surface potentials (the beginning of these potentials is shown by arrows in Fig. 2, II, III). It is also important to note that ammonium depression of DCP was found when the

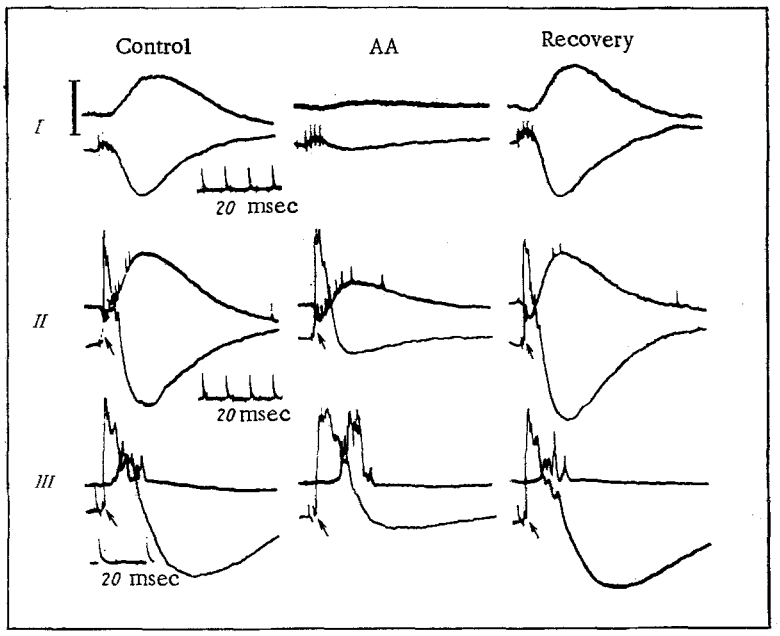

Fig. 2. Action of AA on PAD evoked by stimulation of muscular nerves. Top beam records dorsal (I, II) and ventral (III) root potentials of segment L7; bottom beam in all records shows dorsal cord potentials of segment L6 (potentials in I evoked by stimulation of PBST nerves, potentials in II, III by stimulation of PP nerves by series of 4 pulses at a frequency of 250 Hz) of maximal strength for group 1 fibers of the corresponding nerves; control) before injection of AA; AA) 10 min after injection; recovery) 80 min after injection of complete dose of AA (2.5 mmoles/kg). Calibration: 0.2 mV for dorsal root and dorsal surface potentials, 0.4 mV for ventral root potentials.

magnitude of the polysynaptic reflex discharges in the ventral roots increased appreciably (top beam in Fig. 2, III). Because of both these features, depression of DCP cannot be regarded as the result of blocking of the excitatory synaptic action of impulses in primary afferents on secondary neurons or of depression of interneuron activity.

Infusion of AA in doses of 2-4 mmoles/kg at the rate of 0.2 mmole/kg/min either had no effect, or it increased the blood pressure by 20-30 mm Hg. In neither case could the depression of DCP by AA be connected with changes in the systemic blood pressure.

When injected intravenously in doses of 2-4 mmoles/kg, AA thus depresses depolarization of the central endings of the primary afferent fibers activated by afferent nerve stimulation. Depression of primary afferent depolarization (PAD) was not connected with blocking of the negative postsynaptic dorsal cord potentials or of reflex electrical discharges in the ventral roots of the spinal cord. Depression of PAD developed simultaneously with depression of postsynaptic inhibition of monosynaptic reflexes. Discontinuing the injection of AA was accompanied by parallel recovery of postsynaptic inhibition and of PAD.

It has been claimed that PAD processes facilitate presynaptic inhibition of spinal reflexes and play an important role in the mechanisms of spinal cord function[1, 8]. The convulsant action of substances such as picrotoxin and bicuculline [2, 8] is linked with depression of PAD. If this is so, the convulsant action of AA must be regarded as the result not only of impairment of postsynaptic inhibition of central neurons [5-7], but also of a disturbance of PAD processes.

Depression of PAD by AA is of definite interest also when the physiological mechanisms of PAD are discussed. There is evidence that volleys of afferent impulses producing depolarization increase the conductivity of the membrane of afferent terminals for chlorine ions,

as a result of which those ions begin to move into the fibers from outside, thus creating an electric current which depolarizes the presynaptic membrane [3, 4]. However, this movement of the ions is evidently possible only if a transmembrane gradient of chlorine ions exists from within outward, unbalanced by the membrane potential, in the afferent terminals — a gradient which would have to be maintained by constant activity of the transmembrane chloride pump from without inward. In this connection, the fact that depression of postsynaptic inhibition of central neurons by ammonium salts is due to the blocking of the active transmembrane transport of chlorine ions (admittedly, from within outward), creating an emf for the chloride current producing the IPSP, becomes of special significance [5-7]. The assumption that a chloride pump, similar in its mechanism to the chloride pump in motoneurons but acting in the opposite direction, exists in afferent terminals provides a good explanation for the observed "sensitivity" of PAD to AA and also for the parallel between the disappearance and recovery of postsynaptic inhibition of monosynaptic reflexes and of PAD as a result of injection of AA.

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