EFFECT OF TRIMEPERIDINE, SODIUM HYDROXYBUTYRATE, AND CHLORALOSE ON POSTTETANIC POTENTIATION OF DORSAL ROOT POTENTIALS EVOKED BY STIMULATION OF CUTANEOUS AND MUSCULAR NERVES

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Experiments on unanesthetized cats showed that trimeperidine in doses of 2-4 mg/kg and sodium hydroxybutyrate in doses of 25-50 mg/kg inhibit posttetanic potentiation of dorsal root potentials. After administration of trimeperidine in doses greater than 4 mg/kg and of sodium hydroxybutyrate in doses greater than 50-75 mg/kg there was a progressive depression of posttetanic potentiation. Chloralose had no significant effect on posttetanic potentiation in doses of 20-40 mg/kg but an inhibitory action in doses of 100-120 mg/kg. The inhibition of posttetanic potentiation of the dorsal root potentials is considered to be due to abolition of segmental hyperpolarization effects and to be one cause of the strengthening of presynaptic inhibition under the influence of these drugs in small doses.

Besides mechanisms of presynaptic inhibition, an important role in the control system of the afferent input is also ascribed to presynaptic facilitation [6, 7], based on hyperpolarization of afferent terminals. However, the effects of drugs on segmental hyperpolarization are virtually unstudied. Posttetanic potentiation of dorsal root potentials (DRPs) has been shown to be one manifestation of this hyperpolarization of the afferent terminals.

The effect of trimeperidine, sodium hydroxybutyrate, and chloralose on posttetanic potentiation of DRPs evoked by stimulation of cutaneous and muscular nerves was studied on account of its interest in connection with the discovery of the mechanisms of action of these substances on segmental afferent input processes for afferents of different modalities.

EXPERIMENTAL METHOD

Experiments were carried out on 38 unanesthetized, curarized cats. The preliminary operation was carried out under deep ether anesthesia. DRPs were recorded from single filaments of dorsal roots L_7-S_1 with silver electrodes. After appropriate amplification (UBP-02 amplifier, time constant 0.5 sec) the potentials were recorded on moving film from the screen of a double-beam oscilloscope. A single stimulation of cutaneous (sural, superficial peroneal nerves) and muscular (nerve to the gastrocnemius) nerves was applied as square pulses (5-15 V, 0.1-0.5 msec). Tetanization of the nerves was carried out for 10-15 sec at a frequency of 300-500/sec.

The drugs were injected intravenously: trimeperidine in doses of 1, 4, 8, and 10 mg/kg, sodium hydroybutyrate in doses of 25, 50, 200, and 600 mg/kg, and chloralose in doses of 20, 60, 100, and 120 mg/kg.

EXPERIMENTAL RESULTS AND DISCUSSION

Under normal conditions posttetanic potentiation of the DRPs was clearly revealed 5-30 msec afer high-frequency tetanization and was exhibited as an increase in the amplitude of the DRPs on the average

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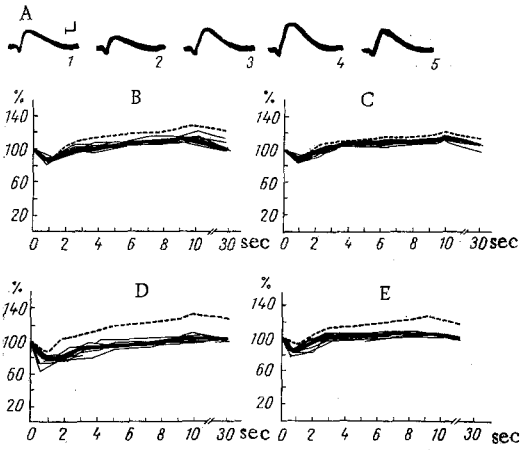

Fig. 1. Effect of trimeperidine and sodium hydroxybutyrate on posttetanic potentiation of DRPs. A) Posttetanic potentiation of DRPs under normal conditions: 1) original DRP; 2,3,4,5) DRPs 1,4,6, and 10 sec, respectively, after tetanization. Records obtained by superposition of 4-6 sweeps of the beam. Calibration: amplitude 250 μV, time 20 msec. B,C) Changes in posttetanic potentiation of DRPs of cutaneous (B) and muscular (C) nerves produced by trimeperidine in a dose of 2 mg/kg. D,E) Changes in posttetanic potentiation of DRPs of cutaneous (D) and muscular (E) nerves under the influence of sodium hydroxybutyrate in a dose of 25 mg/kg. Abscissa, time after tetanization (in sec); ordinate, amplitude of DRPs (in %). Broken line represents posttetanic potentiation under normal conditions (mean data); thin lines show posttetanic potentiation in individual experiments during the action of drugs; thick line gives combined data.

by 20-30%. In some cases the duration of potentiation reached 2 min, with an even greater increase (by 40-50%) in amplitude of the DRPs 5-10 sec after tetanization (Fig. 1A). Posttetanic potentiation of the DRPs was preceded as a rule by a short (1-2 sec) phase of depression [3]. The posttetanic potentiation was always more marked for DRPs evoked by stimulation of the cutaneous nerve (Fig. 1). Potentiation of DRPs of the muscular nerve was always extremely slight, in agreement with data in the literature [2, 4].

Trimeperidine inhibited the posttetanic potentiation of the DRPs. Results showing the effect of trimeperidine in a dose of 2 mg/kg on posttetanic potentiation are illustrated in Fig. 1. Under the influence of trimeperidine in "analgesic doses" (2-4 mg/kg), although the initial DRPs were increased [1], the increase in their amplitude was reduced 5, 10, and 30 sec after tetanization. The decrease in posttetanic potentiation by trimeperidine was more marked for DRPs of the cutaneous nerve (Fig. 1B, C). An increase in the dose of trimeperidine to 8-10 mg/kg was followed by progressive inhibition of the posttetanic potentiation of the DRPs and a simultaneous decrease in the absolute magnitude of the potentials.

Like trimeperidine, sodium hydroxybutyrate also inhibited posttetanic potentiation, although by a greater degree (Fig. 1C, D). The decrease in posttetanic potentiation was clearly revealed by the action of sodium hydroxybutyrate in doses of 25-50 mg/kg and it was stronger for DRPs evoked by stimulation of the cutaneous nerve. In large doses (over 100 mg/kg), sodium hydroxybutyrate completely suppressed posttetanic potentiation and, at the same time, it reduced the amplitude of the original DRPs.

Chloralose had a less marked action than trimeperidine and sodium hydroxybutyrate on posttetanic potentiation. Under the influence of chloralose in doses of 20-40 mg/kg there was a very small (by 5-10%) and inconstant reduction in the increase in amplitude of the DRPs after tetanization with no significant change in its duration. Complete suppression of the posttetanic potentiation of the DRPs was observed by the action of chloralose in doses of 100-120 mg/kg.

The experiments thus showed that trimeperidine and sodium hydroxybutyrate and, to a lesser degree, chloralose in small doses increased the amplitude of the DRPs and, at the same time, inhibit the posttetanic potentiation of these potentials. The potentiations of the DRPs was more marked through the action of sodium hydroxybutyrate. Posttetanic potentiation is known to be based on hyperpolarization of the terminals, whereas the DRPs reflect their depolarization and both processes are connected with changes in the membrane potential level of the afferent fibers [5, 6]. It can accordingly be assumed that the increase in presynaptic inhibition observed under the influence of trimeperidine and sodium hydroxybutyrate in small doses is due (more so for sodium hydroxybutyrate) to the removal of segmental hyperpolarization effects.

Very probably the inhibition of presynaptic facilitation and the increased presynaptic inhibition brought about by these drugs in small doses lie at the basis of their primary analgesic action at the spinal level, manifested as elevation of the pain threshold.

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