EFFECT OF MORPHINE ON SINGLE UNIT ACTIVITY IN THE DORSAL PART OF THE DORSAL HORN OF THE SPINAL CORD

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In doses of 1-2 mg/kg morphine intensified, but in doses of 4-10 mg/kg it depressed, background unit activity. In some cases the action of morphine was exhibited simply as a change in the temporal distribution of discharges. An effect of the depressant action of morphine on activity of some neurons and on the dorsal root potentials was discovered during application of single stimuli to a cutaneous nerve.

It has been suggested [1,2,6,7] that some central effects of morphine, including its analgesic action, are due to changes in activity of neurons of the substantia gelatinosa, which play an important role in controlling the afferent input [13]. However, direct information concerning the effect of analgesics on neurons of the substantia gelatinosa has been obtained only in isolated investigations [8].

The object of the present investigation was to continue the study of the effect of morphine on single unit activity in the substantia gelatinosa.

EXPERIMENTAL METHOD

Experiments were carried out on unanesthetized cats maintained on artificial respiration. Extracellular recordings were made with glass microelectrodes [7]. The microelectrode was inserted by Lebedev's method [9].

Changes in background spike activity (BSA) and in spike activity evoked by single and repetitive (1-5/sec) stimulation of a cutaneous nerve were investigated. Meanwhile the dorsal root potentials (DRPs) were recorded.

The effect of morphine (morphine hydrochloride was injected intravenously in doses of 1-10 mg/kg) was assessed from changes in the mean frequency and type of BSA and in the function of expected density of distribution of discharges after each preceding discharge [12].

EXPERIMENTAL RESULTS AND DISCUSSION

Altogether 16 neurons, of which 14 were in the substantia gelatinosa, were investigated.

Effect of Morphine on Background Spike Activity. Changes in BSA of units in the investigated region were found after the action of morphine in doses of 1-2 mg/kg.

In neurons of the substantia gelatinosa whose BSA consisted of irregular discharges with an independent temporal distribution ("uniform" character of graph of FED), an increase in mean frequency was not accompanied by changes in the type of the BSA and FED (Fig. 1A). Meanwhile, in units with regular and grouped discharges (as a rule, neurons in the lateral parts of the dorsal horn), the distribution of whose

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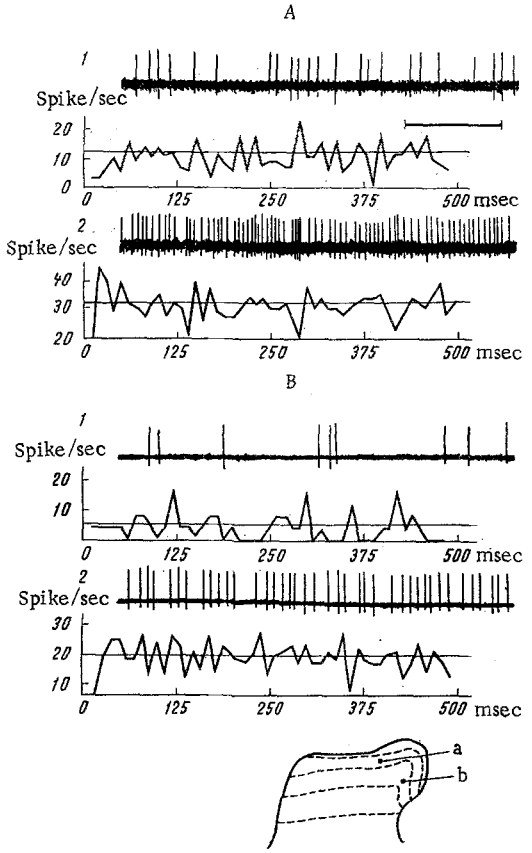

Fig. 1. Effect of morphine on activity of different (A and B) neurons of the substantia gelatinosa: 1) background spike activity; 2) spike activity after injection of morphine in dose of 2 mg/kg. For graphs of function of expected density, given beneath each record, ordinate: frequency (spike/sec); abscissa: time (in msec). Time marker for all records 0.5 sec. On diagram of dorsal horn of spinal cord given below, position of recorded points shown in each case.

discharges were statistically dependent ("uneven" character of FED graph), an increase in the firing rate under the influence of morphine in doses of 1-2 mg/kg occurred with a simultaneous change in the type of the BSA and FED. The latter became "uniform" (Fig. 1B).

In small doses (1-2 mg/kg) morphine had no significant effect on the frequency of BSA of some dorsal horn neurons, and this is usually regarded as indicating the absence of an effect. However, more detailed assessment of the effect of morphine on BSA indicated that this conclusion is not always valid. As is clear from Fig. 2, morphine in a dose of 2 mg/kg had no effect on the firing rate of units located in layers IV and II of the gray matter. However, absence of an effect of morphine in this dose can evidently be described only in the case of the neuron located in layer IV, since the action of morphine on the unit in layer II led to a temporal redistribution of its discharges, as shown by the appearance of two or three waves with a duration of 50-100 msec in the FED graph (Fig. 2B). In this case the effect possibly consists of the appearance of spike activity with a different functional significance.

Morphine in large doses (4, 6, 8, 10 mg/kg) inhibited unit activity. However, total suppression of BSA did not arise. The depriming action of morphine was proportional to its dose and was exhibited even on those cells whose activity was potentiated or remained unchanged under the influence of morphine in small doses (Fig. 2B). Large doses of morphine not only reduced the firing rate, but also changed the character of the temporal distribution of the discharges.

Effect of Morphine on Spike Activity Evoked by Afferent Stimulation. Morphine in doses of 2-10 mg/kg depressed unit responses to stimulation of a cutaneous nerve.

Units whose evoked activity under normal conditions did not correspond in its frequency and temporal parameters to the course of the DRPs, but which consisted of single action potentials (APs) with the latent period of the first AP amounting to 40-60 msec, were the most sensitive to the action of morphine. This depression appeared after a dose of 2 mg/kg and increased progressively with an increase in the dose; it was manifested as a decrease in the number of evoked APs and lengthening of the latent period of the first AP.

The depriming effect of morphine with respect to units responding to single stimulation by a grouped discharge (frequency of APs 100-200/sec with latent period of first AP amounting to 1.5-5 msec) was found after doses of 4-10 mg/kg. Earlier, and under the influence of smaller doses of morphine (4 mg/kg), the APs with longest latencies were suppressed. The amplitude of the DRPs under these circumstances was reduced by 10-20%. Doses of 6-8 mg/kg reduced still further the number of APs; the evoked response consisted of two or three APs. Under the influence of morphine in a dose of 10 mg/kg, in response to stimulation single APs with a latent period of 10-20 msec appeared. In this case the amplitude of the DRP was reduced by 40-50%, in agreement with data in the literature [5, 11].

Parallel character of changes in single unit activity in the substantia gelatinosa and in DRPs under the influence of morphine confirms the suggestion [13] that some neurons in this region participate in the genesis of primary afferent depolarization of cutaneous nerve fibers.

Single unit activity in the substantia gelatinosa during repetitive stimulation of a cutaneous nerve was unchanged by the action of morphine in small doses, and in one case it was actually potentiated. Large

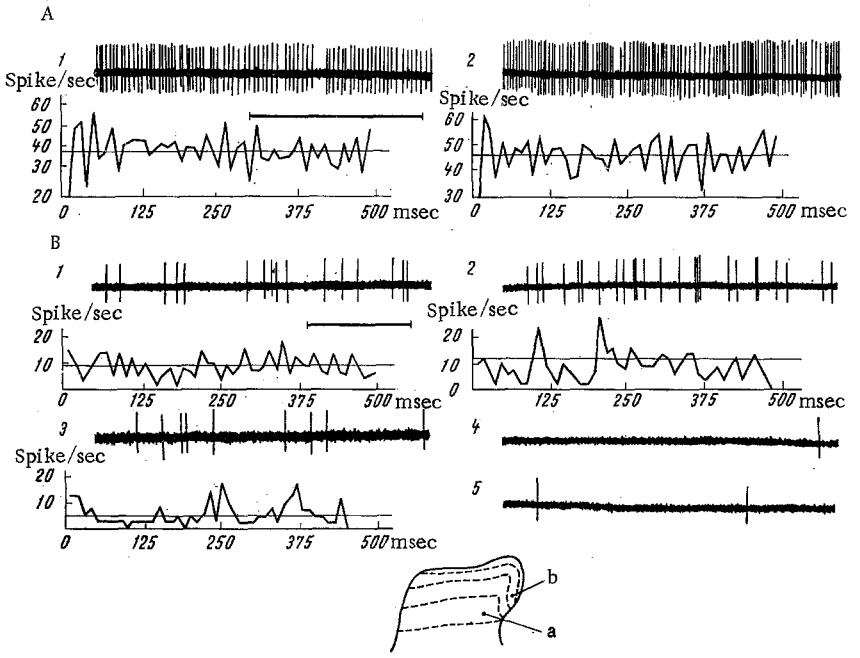

Fig. 2. Effect of morphine on activity of units located in layers IV (a) and II (b) of the gray matter of the dorsal horn: 1) background spike activity; 2) spike activity after injection of morphine in dose of 2 mg/kg; 3, 4, 5) after injection of morphine in doses of 6, 8, and 10 mg/kg respectively. Remainder of legend as in Fig. 1. Time marker for A, 1 sec; for B, 0.5 sec.

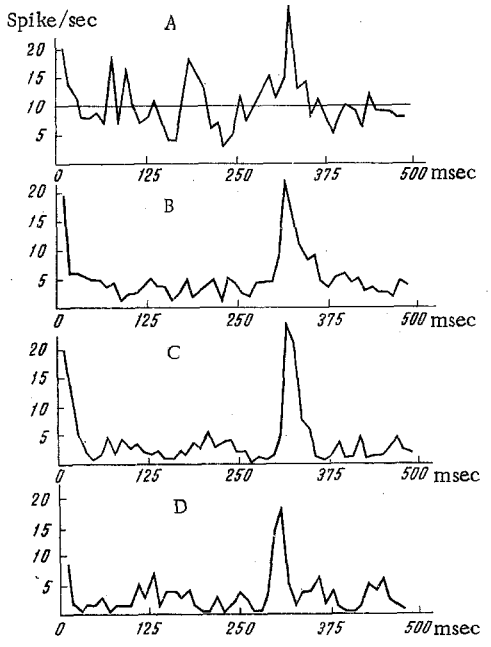

Fig. 3. Effect of morphine on unit activity in substantia gelatinosa during repetitive afferent stimulation: A) graph showing function of expected density under normal conditions; B, C, D) after injection of morphine in doses of 4, 6, and 8 mg/kg, respectively. Ordinate: as in Fig. 1.

doses (4-10 mg/kg) reduced the mean firing rate. A distinctive feature of the depressant effect of morphine was that it acted differently on grouped APs and on discharges not connected with afferent stimulation.

It is clear from Fig. 3A that the FED under normal conditions was an irregular curve with two waves. In accordance with the FED theory [3, 12], these two waves give an idea of the frequency of APs in the grouped discharge and the period with which successive groups of discharges due to intensive synaptic bombardment [4, 10] follow one another; the intermediate part of the graph reflects the mean frequency of discharges arising as a result of asynchronous synaptic bombardment or "autorhythmic" depolarization processes [5]. The functional significance of afferent stimulation in this case is coded in the frequency-temporal distribution of grouped discharges, and APs generated at random have no significant information content. Under the influence of morphine in doses of 4, 6, and 8 mg/kg, no qualitative change in the signal at the output of the rhythmically activated neuron evidently takes place (Fig. 3, B, C, D), and it merely stands out more clearly because of the "filtering off" of information unimportant at that particular time.

It is difficult to decide at present whether inhibition of spike activity under the influence of morphine is the result of depression of asynchronous synaptic bombardment and of "autorhythmic" processes of AP generation, or whether it is due to relative potentiation of other mech-

anisms of discharge generation: rapidly augmenting waves of synaptic depolarization. This problem can only be studied by intracellular recording techniques.

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