THE EFFECT OF STRYCHNINE ON THE ACTIVITY OF INDIVIDUAL INTERCALARY NEURONS OF THE SPINAL CORD

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The ability of strychnine to strengthen the polysynaptic reflex responses of the spinal cord is well established [1, 6, 16, 17]. On this basis it is usually accepted that strychnine possesses the property of causing intensive excitation of the intercalary neurons. We have investigated the effect of strychnine on the activity of individual intercalary neurons by means of the direct registration of their volleys with a capillary microelectrode.

EXPERIMENTAL METHOD

Experiments were carried out on 30 decerebrate cats, immobilized by firm fixation and curarization with diplacin (5 mg/kg intravenously). Artificial respiration was used in all the experiments.

The electrical potentials were recorded extracellularly by means of glass capillary microelectrodes, the tip of which had a diameter of 1-3 μ, and filled with a 2.5 M solution of potassium chloride with the addition of red blood salt, having a resistance of about 5 M. The microelectrodes were inserted by means of a micromanipulator into an area on the posterior surface of the caudal segments of the spinal cord at the level of the 6th-7th lumbar segment, from which the meninges had been removed. The potentials were amplified by means of an alternating current amplifier of type UBP 1-01, the input cascade of which acted as cathode repeater. The potentials obtained were photographed in a moving film from the screen of an electronic oscillograph, and also by means of a permanent magnet moving coil oscillograph. In the course of the experiment the registered reactions were kept under constant viscual and acoustic control. Stimulation with rectangular electrical impulses was applied to the 7th posterior lumbar root or to the ipsilateral peripheral nerves—the tibial, peroneal, and lateral nerve to the gastrocnemius muscle.

The localization of the recording was ascertained by the method which we described previously [2]. Strychnine was injected intravenously as a 0.1 or 0.01% solution of the nitrate.

EXPERIMENTAL RESULTS

In the present research we investigated the effect of strychnine on the spontaneous activity of the intercalatary neurons and on their activity caused by afferent stimulation, the potentials being recorded mainly from the posterior horns of the spinal cord. The character of the spontaneous activity was very varied. In most cases single volleys were registered, some of which were regular in rhythm (the intervals between the peaks did not vary by more than 5-10%). The rhythm of the volleys from other elements was less regular (the intervals between the peaks varied by as much as 100%). Finally, in a third series of elements, no regular rhythm could be detected. Grouped volleys were found in a few elements.

The precise localization of several points from which potentials were recorded was marked on a diagram of a transverse section through the 6th lumbar segment of the spinal cord (Fig. 1A). This diagram shows that there was an obvious relationship between the character of the spontaneous activity and the localization of the recording. For instance, rhythmic volleys were most frequently recorded from the dorsal divisions of the posterior horn formed by the substantia gelatinosa Rolandi. Volleys of a very regular rhythm were found here, especially in the dorsomedial part of the posterior horn. Single volleys with no definite rhythm were found equally often in all divisions of the posterior horn. Grouped volleys were recorded most frequently when the electrode penetrated into the very nucleus of the posterior horn.

The different types of spontaneous activity of the intercalary neurons were altered in different ways after administration of strychnine. Those units from which the volleys were strictly regular in rhythm usually did not change their activity after injection of strychnine in doses up to 0.05 mg/kg. If the dose of strychnine was increased to 0.1-0.2 mg/kg, depression of the volleys was observed, as shown by a decrease in their amplitude and a slowing of their rhythm (Fig. 1B). As the diagram (Fig. 1A) shows, this effect of strychnine was manifested in respect of units situated not only in the dorsal part of the posterior horns, but also at the base of the anterior horn, i.e., it did not depend on the localization of the particular element but on the character of its spontaneous activity. It could occasionally be observed that strychnine either caused only a slowing of the rhythm (Fig. 2) or only an appreciable reduction of the amplitude (Fig. 3) of the spontaneous rhythmic peak potentials.

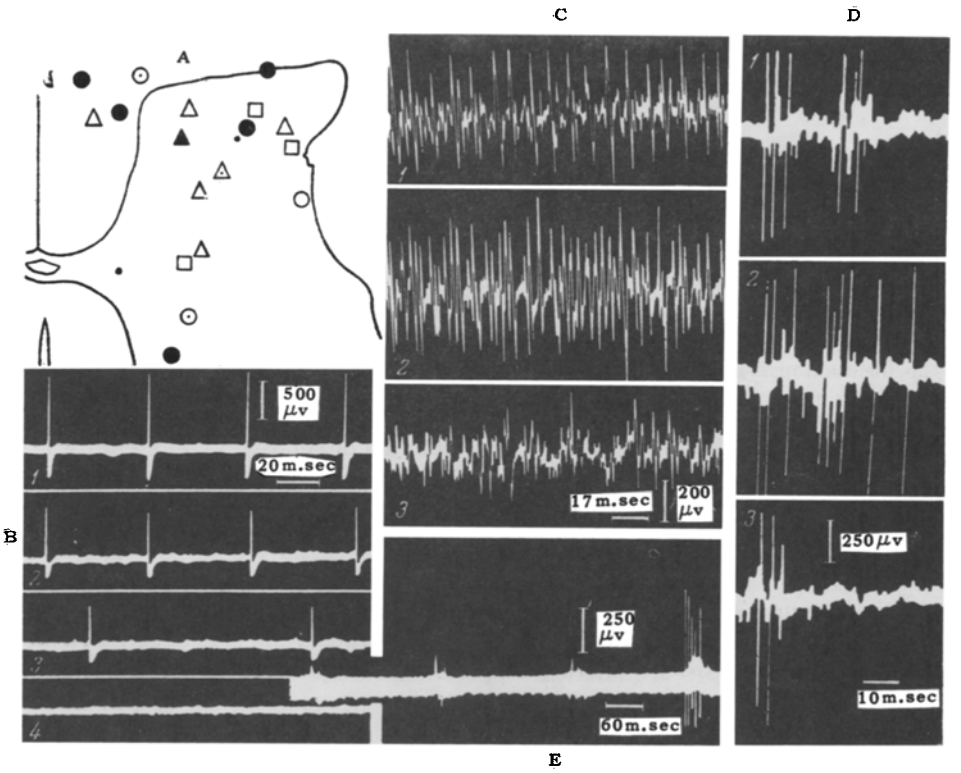

Fig. 1. The effect of strychnine on the activity of individual units of the spinal cord in relation to their localization. A) Diagram of a transverse section through the 6th lumbar segment; the points from which spontaneous, single volleys of a regular rhythm were recorded are denoted by circles; volleys with no definite rhythm are denoted by squares; groups of volleys by triangles; effects of strychnine: shaded figures—depression; figures containing a dot—no change; unshaded figures —increased strength of spontaneous volleys; B) single spontaneous volleys of strictly regular rhythm before (1) and after (2, 3, 4) injection of strychnine in a dose of 0.1 mg/kg, after intervals of 30 seconds, 3 and 5 minutes respectively; C) single spontaneous discharges of a less regular rhythm before (1) and after injection of strychnine in a dose of 0.05 mg/kg (2) and 0.2 mg/kg (3); D) groups of spontaneous volleys arising against the background of the synaptic potential before (1) and after injection of strychnine in a dose of 0.1 mg/kg (2) and of nembutal in a dose of 20 mg/kg (3); E) the appearance of a grouped volley at the height of the synaptic potential caused by stimulation of the posterior root (supramaximal stimulation with a rhythm of 6 impulses per second, against the background of the action of strychnine in a dose of 0.1 mg/kg.

It is important to point out that, against the background of a decrease in the frequency of the volleys, they displayed a clear tendency to form groups (see Fig. 2), and the rhythm of succession of the peak potentials was slower than the rhythm of the initial background activity. It may be deduced from this fact that this grouping of the rhythmic potentials may be of great significance in the mechanism of development of the rhythmic colvulsive volleys, so characteristic of strychnine tetany [5].

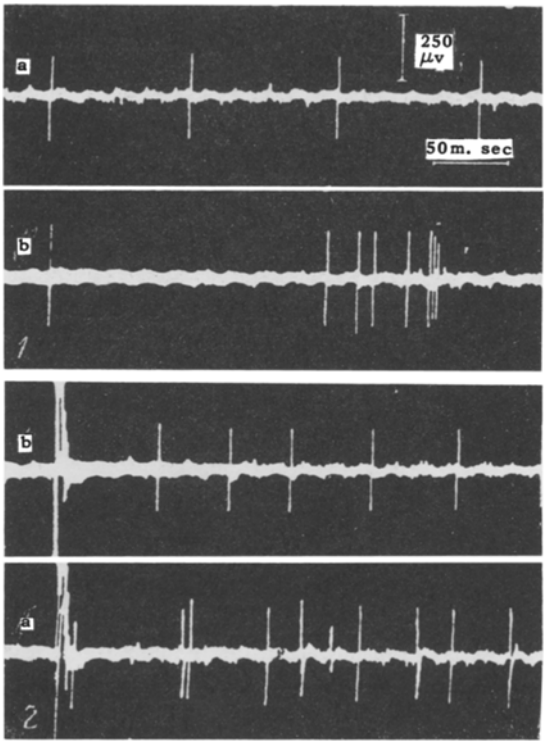

Fig. 2. Spontaneous rhythmic activity (1a) and response to a single supramaximal stimulation of the posterior root (b) of an individual element of the posterior horns; 2a and 2b) the corresponding activity after injection of strychnine in a dose of 0.1 mg/kg.

The activity of the units generating a less regular rhythm was sometimes intensified by strychnine in doses of 0.03-0.05 mg/kg. This was shown by a quickening of the rhythm, whereas the amplitude of the peaks was unchanged or only slightly increased. A subsequent additional injection of strychnine (up to 0.2 mg/kg) could cause depression of this type of activity (Fig. 1C). As a rule the spontaneous volleys following without any definite rhythm were quickened by the action of strychnine in doses of up to 0.3 mg/kg.

The responses of the rhythmically discharging neurons to single and tetanic stimulation of the posterior roots or peripheral nerves were considerably strengthened under the influence of strychnine. Facilitation of the response was shown by a slight shortening of its latent period and by an increase in the number of peak potentials arising immediately after afferent stimulation. This was apparent even against the background of the reduction of rate or amplitude of the spontaneous volleys (see Figs. 2, 3). The after effect of the impulse was also considerably increased, which, if we accept Lorente de No's hypothesis [14], may be evidence of facilitation of the circulation of excitation around the closed, self-exciting chains of intercalary neurons.

Strychnine caused a considerable increase in the strength of the grouped volleys. The rhythm of succession of the groups became faster and the volleys themselves were more numerous. The grouped volleys recorded from the region of the nucleus of the posterior horns of the spinal cord usually arose against the background of slower waves (Fig. 1D), which may be interpreted as synaptic potentials [3, 7, 10]. The grouped volleys caused by afferent stimulation were also generated against the background of these potentials.

During the action of strychnine the synaptic potentials were considerably increased, and a larger number of peaks appeared on their apex (see Fig. 1D). Whereas before injection of strychnine, only synaptic potentials appeared in response to rhythmic afferent stimulation, under the influence of strychnine they sometimes increased to such a degree that a grouped peak volley appeared for a time against their background (Fig. 1E). Since, according to Hunt and Kuno [13], spontaneous grouped volleys may result from afferent impulses not taken into consideration in the experiment, in the same way the effect of strychnine in relation to spontaneous and induced grouped discharges may indicate a considerable facilitation of synaptic transmission.

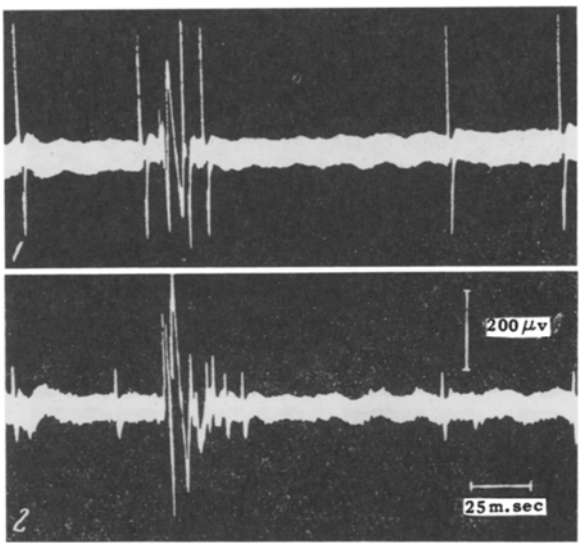

Fig. 3. Response of an intercalary neuron giving regular rhythmic volleys to single stimulation of the posterior root and successive inhibition before (1) and (2) injection of strychnine in a dose of 0.1 mg/kg.

The mechanism of the facilitating action of strychnine on synaptic conduction has not yet been precisely explained, and different interpretations have been suggested. According to McCulloch [15], for instance, it may be explained by the influence of the drug on presynaptic structures, but the findings of Brooks and Fuortes [6] and Frank and Fuortes [12] favor depolarization of the dendrites. More recently, Eccles and his co-workers [4, 9] have attributed this effect of strychnine not with its direct exciting action, but with its ability to abolish inhibition. However, according to the observations of P. G. Kostyuk [1], strychnine does not block the development of primary inhibition of the motor neurons when the strength of the inhibiting stimulus is slightly increased. Moreover, strychnine does not abolish completely the descending segmental inhibition of the spinal reflexes [5], although it considerably diminishes the postsynaptic inhibition potentials arising in these circumstances in the motor neurons [8].

Our findings show that strychnine did not change the inhibition of the spontaneous activity of the intercalary neurons during afferent stimulation. The successive inhibition also remained unchanged (see Fig. 3).

It may thus be suggested that strychnine has a direct facilitating effect on the process of synaptic transmission of excitation in the region of the intercalary neurons, although in these circumstances the ability of these neurons to generate spontaneous rhythmic activity may be depressed.

As a strychnine antagonist we investigated nembutal which, in doses of 10-20 mg/kg, constantly abolished all the exciting effects of strychnine (see Fig. 1D) but did not affect its depressant effect. The effects of nembutal could not be abolished, however, by strychnine.

To summarize the results discussed in this article, it may be concluded that strychnine has various effects on different intercalary neurons. It depresses the spontaneous rhythmic volleys from individual units, brings about the grouping of single volleys, and at the same time facilitates synaptic conduction, the development of grouped volleys, and the after-effect of the impulse. The inhibition of the intercalary neurons is not altered by the action of

strychnine. The results indicate that strychnine tetanus, with its characteristic autorhythmicity, is brought about by strengthening of existing sources and the creation of new sources of grouped volleys, which in time undergo synchronization as a result of the facilitation of synaptic conduction.

SUMMARY

Experiments were conducted on decerebrated curarized cats. With the aid of capillary microelectrodes discharges of individual units of the posterior horns of the VI-VII lumbar spinal cord segments were led off. Strychnine (0.1-0.2 mg/kg) depressed spontaneous rhythmic discharges slowing their rhythm and reducing their amplitude. It increased the frequency of group discharges, facilitated the appearance of responses to the afferent stimuli and intensified the impulse after effect. No change was seen in the inhibition of the interneurones against the background of strychnine action. A suggestion is made that strychnine tetanus caused by intensified group discharges and the appearance of new sources of group discharges, which become synchronized as a facilitated synaptic conductivity.

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