THE INFLUENCE OF NOVOCAINE ON PESSIMAL INHIBITION IN VARIOUS LINKS OF THE REFLEX ARC

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Novocaine has in recent years been shown to possess a wide spectrum of action. Besides the generally known properties of anesthesia, novocaine shows the following effects upon resorptive action: depression of transmission of excitation in the central nervous system [2-7], in autonomic ganglia [1, 9, 10, 13] and partially in neuro-muscular synapses [13-16], as well as in the region of m-choline receptors [11].

In the present investigation an attempt was made to discover certain aspects of the mechanism of novocaine action within the framework of studies on its influence on processes of pessimal inhibition in different links of the reflex arc.

The Influence of novocaine on neuro-muscular transmission. Experiments were carried out on decerebrate cats. Records of the contractions of the gastrocnemius muscle were made under semi-isometric conditions. The peripheral segment of the tibial nerve was stimulated by square-pulse stimuli each of 0.5 millisecond duration. The frequency of stimulation was varied from 0.5 up to 300 cps. Stimulation at each frequency was continued for 10 seconds. Novocaine was given intravenously.

Novocaine in doses 2.5-5 mg/kg did not exert any appreciable effect on neuro-muscular transmission. The amplitude of the muscular contractions on stimulation at frequencies of 0.5-10-20 and 50 cps increased slightly or remained unchanged when 10-15 mg/kg novocaine had been administered. At the same time a more rapid decline of the tetanic curve at frequencies of 80-200 cps was observed. Primary twitching at these frequencies was somewhat more pronounced than in the normal. In doses of 25 mg/kg novocaine led to a definite decrease in the amplitude of the myogram at all frequencies of stimulation (Fig. 1). The pessimal reaction began to be apparent at 50 cps and became most definite at 80-200 cps. Restoration began fairly rapidly and after 12-20 minutes was already practically complete. The maximal effect of the substance was attained in the first 5 minutes following its injection.

On repeated injection of novocaine its effect was less marked than that achieved after the first injection.

There are references in the literature to the fact that novocaine can diminish acetylcholine production [13]. With this in mind, experiments were carried out in which the effect of proserine on the activity of novocaine was examined. Proserine was used in doses of 20-40 kg. Under these conditions an increase in the amplitude of single contractions and a considerable shift of the pessimum toward the lower frequencies were observed. The primary twitch of the muscle was somewhat increased with the range of frequencies from 50-200 cps. Administration of novocaine against this background (25 mg/kg) lowered the amplitude of muscular contractions to a considerable extent. Pessimal reaction could already be seen at a frequency of 50 cps.
The action of novocaine passed after 35-40 minutes, whereas changes in neuro-muscular transmission associated with the effect of proserine persisted. This interrelation could also be observed when smaller doses of both the substances were used. Thus, the synergism of proserine and novocaine was observed when proserine was used in such doses (1-5 mg/kg) which by themselves did not alter neuro-muscular transmission appreciably.

**Fig. 1.** The effect of novocaine on neuro-muscular transmission.  

a) Before administration of the substance; b) 2 minutes after injection of 25 mg/kg novocaine; c) after 15 minutes. Frequency of stimulation of the tibial nerve is marked by figures (in cps).

The effect of novocaine on autonomic ganglia.

These experiments were carried out mainly on the superior cervical ganglion of decerebrate cats. Contractions of the nictitating membrane were recorded upon stimulation of the preganglionic trunk by square pulse stimuli at various frequencies. The technique used has been described earlier [12].

The minimal dose of novocaine which exerted an influence on the level of pessimal inhibition in the ganglion was equal to 1-2 mg/kg. The effect was observed particularly clearly when novocaine was used in doses of 5-10 mg/kg (Fig. 2) and higher. In Fig. 2 the initial pessimal frequency was 200 cps; relaxation of the membrane took place gradually. Following administration of novocaine (10 mg/kg) the pessimum occurred at a frequency of 80 cps and the decline of the curve was very steep. Change of the pessimal frequency to the optimal (10 cps) led to restoration of the curve. Such a dependence of the effect on the frequency indicates that the observed inhibition is pessimal. It is characteristic for novocaine that there is usually a change in the reaction to optimal frequency of stimulation too, following its administration. The same figure shows that the height of the mechanogram is decreased at the frequency of 10 cps. This means that the excitability of the ganglion cells is lowered under the influence of novocaine. The possibility is not excluded that a definite role may be played by a reduction of acetylcholine production [13]. Doses of 5-10 mg/kg and higher are associated with a shift of the pessimum toward lower frequencies which occurs parallelly with diminution of the excitability of the ganglion cells. It is possible to observe changes elicited by pessimal inhibition without appreciable lowering of ganglion cell excitability by using novocaine in threshold and near-threshold doses.