# THE EFFECT OF GANGLION-BLOCKING AGENTS ON THE GLOSSOMANDIBULAR REFLEX

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Investigations of the effect of gangliolytic drugs on spinal reflexes [3] have demonstrated the facilitating action of mecamylamine hydrochloride and heptamine on the course of the patellar reflex, which may be due to depression by these agents of transmission from the collaterals of the motor neurons to the cells of Renshaw. The depressing action of mecamylamine on the flexor reflex has also been observed. Hexamethonium bromide and azamethonium bromide modified these reflexes to a much lesser degree.

We have studied the effect of gangliolytics on the glossomandibular reflex, the centers of which are situated in the pons and, partly, in the medulla. The desirability of such an investigation is determined by the fact that the synapses at different levels in the central nervous system differ in their sensitivity to the action of drugs [2].

It has been found [7, 9-12] that the glossomandibular reflex is polysynaptic. It has also been shown to be connected with the reticular formation of the brain stem. Stimulation of the rostral end of this formation inhibits the reflex, while stimulation of certain zones in its dorso-medial part facilitates it. The glossomandibular reflex is depressed by myanesin and meprotan (meprobamate), and facilitated by acetylcholine and, in particular, by eserine.

In the present research we investigated the effect of gangliolytics of different chemical structure – hexamethonium, azamethonium, heptamine*, and mecamylamine – on the functional mobility of the centers of the glossomandibular reflex. The ability of the centers of the reflex to reproduce different frequencies of stimulation for a definite period of time was determined. The employment of a time characteristic in this particular case allowed the action of the drugs to be evaluated more accurately [1, 5].

## EXPERIMENTAL METHOD

Experiments were carried out on 32 cats, decerebrated under ether anesthesia at the level of the anterior colliculi. After ligation of the veins in the submandibular region, the masseter muscle was divided and the angle of the mandible freed. The mylohyoid nerve is situated medially to the mandible, on the mylohyoid muscle, and is usually directed, accompanied by a vein, toward the anterior portion of the digastric muscle (the subdivision of this muscle into anterior and posterior bellies is almost absent in cats). The angle of the mandible was removed, after which it became possible to isolate the mylohyoid nerve for an adequate distance. The nerve was divided as near as possible to the digastric muscle. The digastric muscle was divided transversely. After removal of the mylohyoid muscle, the branches of the lingual nerve became visible. The mylohyoid and lingual nerves were carefully separated from their membranes and moistened with vaseline oil warmed to 37°. The lingual nerve, usually its middle branch, was stimulated with rectangular impulses, 0.01-0.1 msec in duration. The reflex potentials were picked up by bipolar electrodes from the mylohyoid nerve and recorded by means of an oscillograph. The experiment began 3-4 h after the final inhalation of ether. During the experiment the body temperature of the animals was kept constant and artificial respiration was performed. The arterial pressure was recorded in most of the experiments. All the drugs were injected intravenously.

## EXPERIMENTAL RESULTS

The effect of the glycolytic drugs on the functional mobility of the centers of the glossomandibular reflex was investigated during stimulation at optimal and subpessimal frequencies (from 10 to 60 stimuli per sec). Mecamylamine,

*2,3,3-trimethyl-2-dimethylaminobutane bromohydrate [6].

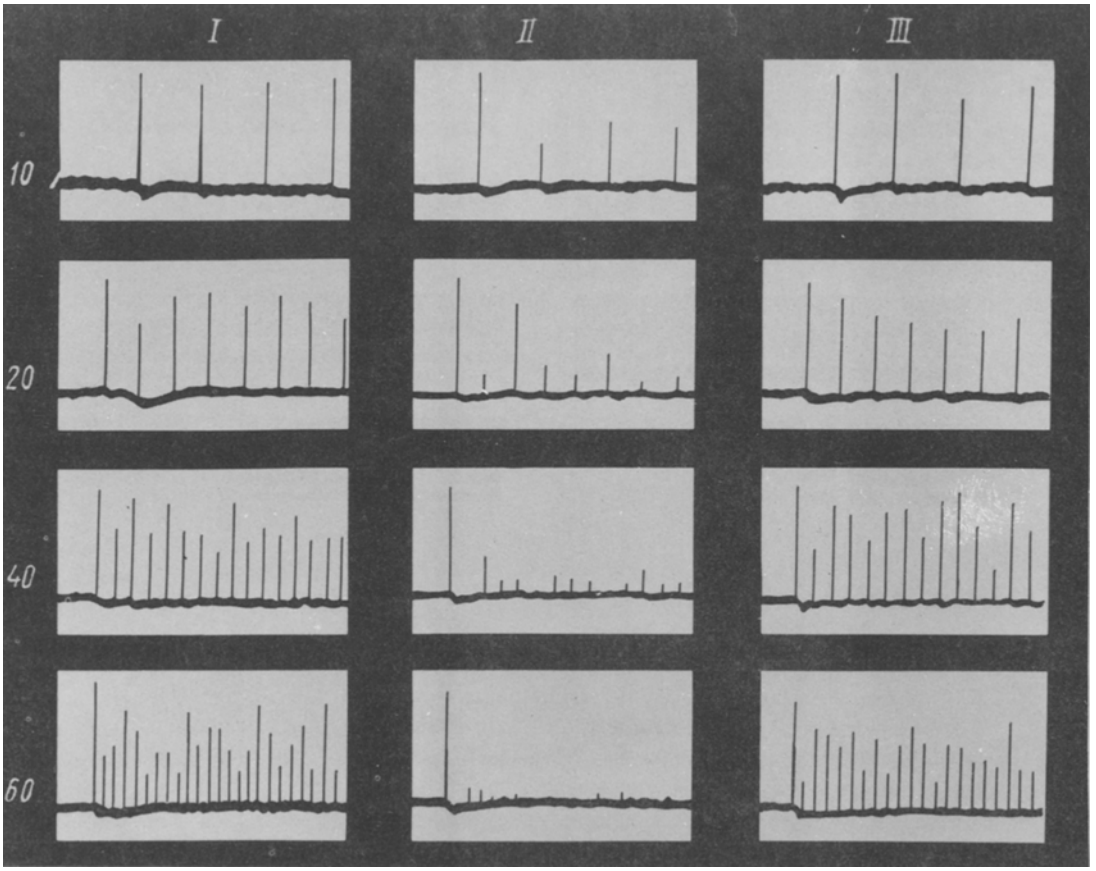


Fig. 1. Effect of mecamylamine on the lability of the centers of the glossomandibular reflex. I) potentials of the mylohyoid nerve during stimulation of the lingual nerve with supramaximal impulses; duration of each stimulus 0.1 msec; II) 5 min after intravenous injection of mecamylamine; III) 30 min after injection of mecamylamine. The numbers on the left denote the frequency of stimulation (per second).

in doses of 2-3 mg/kg, in association with supramaximal stimulation, caused a marked decrease in the lability of the corresponding centers. The oscillograms illustrated in Fig. 1 show that, after the intravenous injection of mecamylamine in a dose of 2.5 mg/kg, in the course of the first second of stimulation a marked decrease in the amplitude of the reflex potentials and the alternation of low- and high-voltage potentials were observed, demonstrating that transformation was taking place. These changes were especially clear at subpessimal frequencies (40-60/sec). With a reduction in the magnitude of the stimuli to submaximal, this effect of mecamylamine became still more marked. At a frequency of 10/sec, for instance, after administration of mecamylamine a reflex response arose only to the first stimulus.

This action of mecamylamine was usually observed for a period of 20-40 min, after which the original level of lability was restored. Meanwhile, the depression of the autonomic ganglia by mecamylamine in a dose of 2.5 mg/kg lasts for longer than 10 h [4].

In a dose of 5 mg/kg, and in association with supramaximal stimulation, heptamine caused an insignificant depression of lability (Fig. 2). In contrast to the action of mecamylamine, the depressing effect of the gangliolytic in this case became apparent only at the 3rd-5th sec after stimulation began.

In similar conditions, hexamethonium and azamethonium, in doses of 5 mg/kg, did not alter the functional mobility of the centers of the glossomandibular reflex. Meanwhile, the arterial pressure fell by 40-60 mm after injection of these drugs.

If the amplitude of the stimuli was reduced to submaximal, the depressant effect of heptamine became more

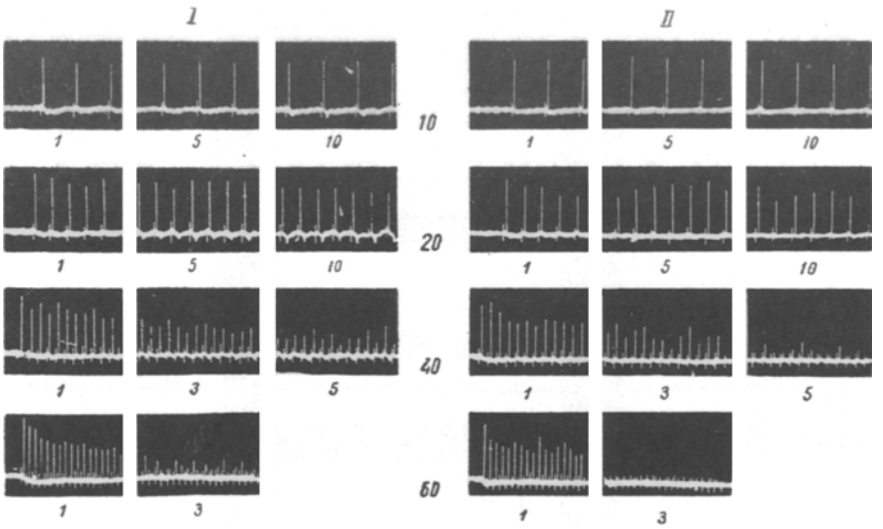


Fig. 2. Effect of heptamine on the lability of the centers of the glossomandibular reflex. I) Potentials of the mylohyoid nerve during stimulation of the lingual nerve with supramaximal rectangular impulses; duration of each stimulus 0.1 msec; II) 5 min after intravenous injection of heptamine in a dose of 5 mg/kg. The numbers below the oscillograms denote the time after the beginning stimulation (in seconds). The numbers in the center give the frequency of stimulation in impulses per second.

obvious. In these conditions, a slight depression of lability was also observed during administration of hexamethonium or azamethonium in a dose of 5 mg/kg. A similar depression of the functional mobility of the centers of the glossomandibular reflex could be seen after the arterial pressure had been lowered by 30-40 mm as a result of bleeding. It is clear that during submaximal stimulation the depression of the glossomandibular reflex was mainly the result of the hypotensive effect of certain gangliolytics (hexamethonium, azamethonium).

However, as we have mentioned above, during supramaximal stimulation a lowering of the arterial pressure by 40-60 mm did not affect the lability of the centers of the glossomandibular reflex. Consequently, in these conditions, the depression of the glossomandibular reflex by mecamylamine (a secondary amine) and heptamine (a tertiary amine) was not due to their hypotensive effect, but probably to their direct action on the centers of the reflex. Bi-quaternary ammonium compounds (hexamethonium and azamethonium) evidently do not possess this property. Meanwhile, the ganglion-blocking and associated hypotensive activity of all the compounds which we tested was approximately equal (although the duration of their action differed).

The difference may be explained by the varied ability of the gangliolytics to penetrate into the central nervous system. The quaternary ammonium compounds are known to pass through the blood-brain barrier with difficulty, and this has been demonstrated to be particularly true of hexamethonium [13]. We also know [8, 14] that the tertiary and secondary amines, for example mecamylamine, when injected intravenously into animals, are found in the brain tissues in comparatively high concentrations.

This suggestion is also confirmed by the unequal effects of gangliolytics of different chemical composition on the spinal reflexes. In this case also, our observations showed that hexamethonium and azamethonium are much less active than mecamylamine and heptamine.

On the other hand, the effect of mecamylamine and heptamine on the polysynaptic reflexes of different levels of the central nervous system also differed in its degree. Mecamylamine, for instance, caused depression of the lability of the centers of the flexor reflex during supramaximal stimulation in a dose of only 5 mg/kg, and this effect became apparent only 3-5 sec after the beginning of stimulation. Heptamine, in a dose of 5 mg/kg, did not affect the functional mobility of the centers of the flexor reflex.

If these findings are compared with the results of the present investigation, it may be concluded that the synapses

of the central part of the glossomandibular reflex are more sensitive to mecamylamine and heptamine than the synaptic structures of the centers of the flexor reflex. In both cases mecamylamine is much more active than heptamine. Meanwhile, the investigation of the effect of these drugs on the (monosynaptic) patellar reflex showed that not only is heptamine not less active than mecamylamine, but is actually more active in its ability to facilitate the course of the patellar reflex. The latter, as we have noted above, has been interpreted as the result of depression of transmission from the collaterals of the motor neurons to the cells of Renshaw.

Hence, when the effect of the gangliolytics on the central nervous system is being evaluated, attention must be directed to their unequal ability to pass through the blood-brain barrier, and also to the differences in the sensitivity of the central structures of the various reflexes to these drugs.


## SUMMARY

In experiments on decerebrated cats a study was made of effects of azamethonium, hexamethonium, heptamine, and mecamylamine on the functional mobility of the glossomandibular reflex centers. Mecamylamine and, to a lesser extent, heptamine, depressed the lability of the corresponding centers in conditions of supramaximal stimulation. Azamethonium and hexamethonium in the same conditions did not change the course of the glossomandibular reflex. It is presumed that this difference is connected with a varying capacity of gangliolytics to penetrate into the central nervous system.


## LITERATURE CITED


1. A. V. Val'dman, Farmakol. i toksikol., 2, 12 (1956).
2. V. V. Zakusov, Pharmacology of the Nervous System [in Russian]. Leningrad, 1953.
3. V. V. Maiskii, Farmakol. i toksikol., 3, 335 (1962).
4. Yu. V. Uranov, Farmakol. i toksikol., 2, 8 (1958).
5. D. A. Kharkevich, Byull. éksper. biol., 10, 34 (1956).
6. D.A. Kharkevich, Farmakol. i toksikol., 2, 156 (1961).
7. M. Bonvallet and B. Minz, C. R. Soc. Biol., 1938, v. 128, p. 158.
8. M. Harrington, P. Kincaid-Smith, and M. D. Milne, Lancet, 1958, v. 2, p. 6.
9. C. D. Hendley, T. E. Lynes, and F. M. Berger, Proc. Soc. exp. Biol. (N. Y.), 1954, v. 87, p. 608.
10. A. Hugelin, C. R. Soc. Biol., 1955, v. 149, p. 1893.
11. E. E. King and K. R. Unna, J. Pharmacol. exp. Ther., 1954, v. III, p. 293.
12. E. E. King, B. Minz, and K. R. Unna, J. comp. Neurol., 1955, v. 102, p. 565.
13. R. R. Levine, J. Pharmacol. exp. Ther., 1960, v. 129, p. 296.
14. M. D. Milne, G. G. Rowe, K. Somers, et al., Clin. Sci., 1957, v. 16, p. 599.


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**All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.**

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