# THE LOCAL ACTION OF SODIUM BROMIDE ON THE TISSUES OF THE LIMBS

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In numerous investigations by I. P. Pavlov's co-workers [3-8, 10], it was shown that sodium bromide, when administered to an animal, has the power of intensifying and concentrating the process of inhibition, and by contrast, of enhancing the process of excitation of the cerebral cortex. It was also shown that for a correct balance between the excitatory and inhibitory processes the size of the dose of bromide was important; other factors of importance were the type of nervous system, the age and condition of the animal and so on.

In view of these properties, sodium bromide has held a prominent position among drugs used to aid the recovery of disorders of the higher nervous activity of man and animals.

Reports have recently appeared in the literature [1] of a local action of bromide on the activity of the gastric glands, but we have not seen any reference to the local action of bromide on skeletal muscle tissue. In 1952, we established experimentally that changes in the consitutional chronaxie of the denervated muscles of autotransplanted dogs' limbs took place in response to the action of a 5% solution of sodium bromide administered to the animals in a dose of 10 mg / kg body weight. In these cases, the action of sodium bromide on the tissues of the grafted limb was effected 15-20 minutes after its administration to the animal. Under these circumstances, the chronaxie of the muscles of the grafted limb was changed more than that of normal limbs. From this we assumed that denervated tissues have increased sensitivity towards bromide, especially since with restoration of the innervational connections of the limbs with the rest of the body, the reaction of their tissues to bromide decreased.

The facts obtained require explanation. We carried out experiments which in principle, would either exclude or confirm the local action of sodium bromide on the limb tissues.

## EXPERIMENTAL METHOD

We used the method of vascular isolation of the limb described by V. N. Chernigovskii and A. Ya. Yaroshevskii [9] for studying the chemoreception of the bone marrow. Keeping to the method described, we left one of the hind- or forelimbs of the dog connected to the body of the animal by its main nerve trunks. All the soft tissues of the limb were divided and the bone was sawn through. The operation was carried out under morphine-sodium amytal anesthesia.

After such an operation, the limb vessels were perfused for 15-30 minutes with about 0.5 l of Tyrode solution, and then, for the same time, with the same volume of 1% sodium bromide solution. The action of sodium bromide on the tissues was abolished by repeated and sometimes prolonged perfusion with Tyrode solution, necessary to restore the initial indices of the tissues. The complete experiment lasted $1\frac{1}{2}$ to 2 hours.

The tests employed to study the local action of bromide were the skin temperature and the muscle chronaxie of the extensors of the foot of the perfused limb. These measurements were made at the same time on the opposite limb.

The reflex action of bromide could be judged both by examination of the opposite limb and by the pneumographic and electrocariographic findings.

The experiments were performed on 11 dogs.

## EXPERIMENTAL RESULTS

In 3 control experiments carried out on the dogs Buket, Fingal and Mal'va, Tyrode solution was perfused through the limb vessels for a period of $1\frac{1}{2}$ hours, and every 5-10 minutes the values of the skin temperature and the subordinational chronaxie of the muscles of the perfused and opposite limbs were recorded. As may be seen from Fig. 1, the values of the subordinational chronaxie of the muscles of the perfused limb hardly varied in 2 control experiments and in the third did not exceed 0.6 μf at the end of an experiment lasting $1\frac{1}{2}$ hours.

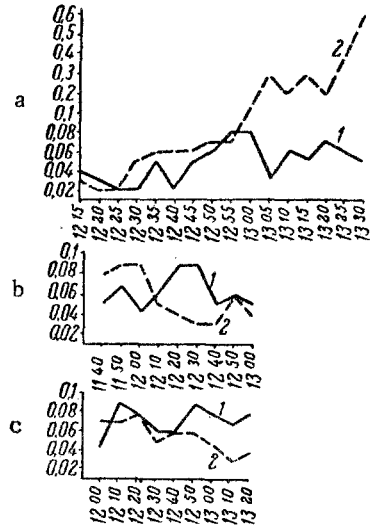


Fig. 1. Chronaxie of the extensor muscles of the foot of the perfused and opposite limbs, in control experiments. a) Experiment on September 21, 1954, dog Buket; b) experiment on October 8, 1954, dog Fingal; c) experiment on October 9, 1954, dog Mal'va. 1) values of the chronaxie of the opposite limb; 2) chronaxie of the perfused limb.

The temperature of the skin of the soles of both limbs fell equally by 2-5° or remained unchanged. No edema of the tissues was observed.

Different results were obtained in the next 6 experiments, in which a marked change was observed in the rheobase and the chronaxie of the muscles of the perfused limb, together with edema of the tissues of the limb under the influence of bromide.

In every case, perfusion with sodium bromide solution caused a significant increase of the threshold of excitation of the muscles (to 80-100 v), which was reversed by subsequent perfusion with Tyrode solution; but the changes in muscle excitation caused by the repeated action of bromide acquired an irreversible character.

The value of the muscle chronaxie rose during perfusion with sodium bromide solution to 8-40σ and over (from 0.02-0.2 to 2-10 μf). Subsequent perfusion of the muscle with Tyrode solution restored the original values of the chronaxie, but when the action of bromide was repeated, irreversible changes ensued. This is clearly illustrated in Fig. 2 for one (the dog Barbos) and two (the dog Bul'ka) applications of bromide.

The results of the whole series of experiments were evidence of a local action of sodium bromide on the tissues of the perfused limb, as demonstrated by a sharp rise in the values of the rheobase and chronaxie of its muscles.

We were unable to observe any regular changes in the skin temperature of the perfused limb. No reflex action of bromide was revealed by the indices of the opposite limb, by the rhythm of respiration and the pulse, or by the character of the electrocardiogram. Only a local action of bromide was found on the state of excitation of the skeletal musculature. Proof that these changes in excitation of the muscles were due to the action of bromide ions required exclusion of any action on the part of the hypertonic Tyrode solution in which the 1% sodium bromide solution was made up. For this purpose, we carried out a further 3 control experiments on dogs. Sodium bromide was dissolved in Tyrode solution from which an equimolecular quantity of sodium chloride had been deducted (8 g sodium chloride in 1 l pure Tyrode solution and 2.32 g sodium chloride in 1 l Tyrode solution with the addition of 10 g sodium bromide). These control experiments confirmed the previous results.

First experiment. Duration of the experiment 1 hour 25 minutes. The vessels of the left forelimb were perfused. The chronaxie of the muscles of the opposite limb varied, during the experiment, within normal limits (0.02-0.05 μf); the chronaxie of the muscles of the perfused limb before the action of bromide was 0.06-0.07 μf, and, after perfusion for 15 minutes with 1 % sodium bromide solution, it rose to 0.1 μf. Washing out the vessels

with Tyrode solution reduced the muscle chronaxie to normal (0.04-0.05 μf). A second perfusion with sodium bromide increased the muscle chronaxie still more (0.3 μf), and subsequent washing with Tyrode solution could not restore the previous excitation of the muscle.

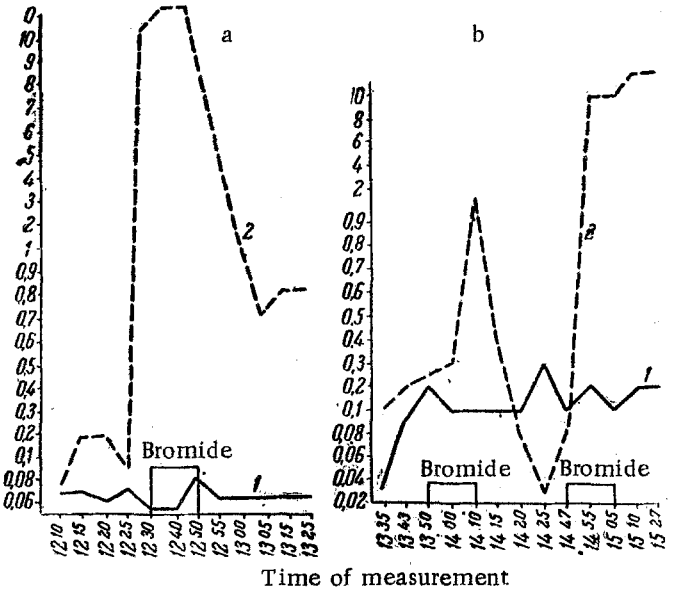


Fig. 2. Changes in the chronaxie of the perfused limb by the action of bromide. a) Experiment on September 18, 1954, dog Barbos, perfusion of the right forelimb; b) experiment on September 3, 1954, dog Bul'ka, perfusion of the left forelimb.

Second experiment. Duration of the experiment 1 hour 35 minutes. The left hindlimb of the dog was perfused. Before the action of sodium bromide, the chronaxie of the muscles of the perfused limb varied between normal limits (0.06-0.07 μf). By the subsequent action of a 1% solution of sodium bromide for 15 minutes, the muscle chronaxie was increased to 0.2 μf. Rinsing the vessels with Tyrode solution lowered the muscle chronaxie to 0.07-0.09 μf. A second perfusion with sodium bromide caused a sharp increase in the muscle chronaxie (4-6 μf, or 16-24σ). Even in this case, however, subsequent rinsing of the vessels with Tyrode solution for 15 minutes lowered the muscle chronaxie to 0.1 μf, or 0.4σ.

Third experiment. Duration of the experiment 2 hours. Perfusion of the left forelimb was performed. The chronaxie of the muscles of the opposite limb remained normal all the time, and that of the perfused limb, before the action of bromide, was 0.04-0.08 μf; the subsequent action of a 1% solution of sodium bromide for 15 minutes caused a sharp rise in the muscle chronaxie to 1.0 μf or 4.0σ. Rinsing the vessels with Tyrode solution lowered the chronaxie to normal (0.09 μf). On repeating the action of sodium bromide, the muscle chronaxie of the perfused limb again rose sharply (3.0 μf, or 12.0 σ), but in this case too, it was possible to restore the normal chronaxie of the muscle (0.06 μf) by further rinsing of the vessels with Tyrode solution.

Our previous findings [2] on the action of sodium bromide on the tissues of the autotransplanted limb were thereby explained, since the local action of bromide on the tissues of a perfused limb was discovered. Sodium bromide, injected into the blood stream, changed the functional state of the denervated muscles of the grafted limb, thanks to its local action on the tissues.

## SUMMARY

11 experiments of alternating perfusion with Tyrode's solution and 1% sodium bromide have been conducted through the blood vessels of an extremity which retained the nervous connection with the dog's body. The tissues excitability of the extremity has been judged by comparing the rheobases and chronaxia indices of the muscles of the perfused and the contralateral extremities. As demonstrated, under the local effect of sodium bromide in the perfused extremity, the indices of muscle excitability are lower.

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