PHYSIOLOGY

ANALYSIS OF CUTANEOUS RECEPTION OF PRESSURE IN MAN USING THE METHOD OF CONDITIONED VASCULAR REFLEXES

COMMUNICATION IV. THE EFFECT OF VARIOUS PHARMACOLOGIC SUBSTANCES ON THE CHARACTER OF CONDITIONED VASCULAR REACTIONS DEVELOPED TO BAROSTIMULATION OF THE SKIN

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It was shown in the preceding communication [10] that the cerebral cortex played a definite role in the regulation of cutaneous reception of pressure in man. The level of excitatory and inhibitory processes in the cerebral cortex and their interaction at every given moment determine both the character of the unconditioned and conditioned vascular reaction to barostimulation of the skin and the intensity of perception of the sensation caused by the stimulation. These features are very clearly brought out in the process of elaborating conditioned vascular reflexes to loads of 1 g and 500 mg, as well as in experiments with anesthesia [10].

The present work is concerned with the study of the influence of pharmacologic substances which have a selective action on the excitatory and inhibitory processes in the cortex on conditioned vascular reflexes to pressure and on the intensity of sensation produced by barostimulation.

It is known from literature that one of the most active substances with respect to inhibitory processes is bromine [4, 5, 6]. In small doses it improves conditioned reflex activity by balancing excitatory and inhibitory processes in the cerebral cortex, while in large doses it promotes spread of inhibition over the whole cortex which leads to deterioration of conditioned reflex activity [3].

We used bromine with the latter aim in view.

Phenamine (benzedrine) enhances the excitability of the cerebral cortex and improves conditioned reflex activity [2, 7]. Its effect on cutaneous baroreception was investigated.

In the first series of experiments a study was made of the effect of bromine on conditioned vascular reflexes elaborated in two subjects (T. and D.) to loads of 1 g and 500 mg, placed on the dorsal aspect of the right hand, the conditioned stimuli used being bells of different tone. The effect on conditioned vascular reflexes elaborated in subject V. to stimulation by touch of the inferior-lateral aspect of the right shoulder, the conditioned stimulus in the latter case – a load of 1 g placed on the dorsal aspect of the right hand – was also studied. The effect of bromine on the intensity of sensation produced by the barostimuli used was also determined.

The experimental method has been described in detail in Communications I and II [9, 10].

The stimuli mentioned above always produced a vasoconstrictor reaction in all the subjects investigated; this reaction began from the moment at which the conditioned stimulation was applied; a sensation of weight or touch was also constantly present during all experimental combinations. The subjects were given a 4% solution of sodium bromide 3 times a day, one tablespoonful of which corresponded to about 1.5 g pure sodium bromide per day. Bromide was administered for 6 days, i.e., each subject received a total of up to 8 g bromine.

Impairment of conditioned reflex activity was noted in the subject T. the next day after she had taken the first 1.5 g bromine; this included disappearance of the conditioned phase of the vascular reaction and considerable lengthening of the latent period of the reflex in seven out of eight combinations. The normal conditioned vasoconstrictor reaction, commencing with the sound of the bell, only appeared on the eighth combination. Sensation of weight proved to be somewhat diminished and on one occasion the subject failed to feel the load altogether.

By the 5th day, when the subject had received 6 g sodium bromide, even greater impairment of conditioned reflex activity and of sensation could be demonstrated. A load of 1 g, used without the corresponding conditioned stimulus, produced delayed and slight vasoconstriction and failed to produce a sensation of pressure (weight). On repeating the experiment (also without the bell) no vascular reaction occurred, but the sensation of weight was perceived. Of nine combinations of loads of 1 g and 500 mg with corresponding conditioned stimuli almost no vascular reaction was noted in the first 2-3 combinations (Fig. 1, a), in some combinations vasoconstriction only appeared as an after effect and only in the ninth combination, which concluded the experiment, (Fig. 1, b) did a slowly developing, slight conditioned vasoconstrictor reaction appear and increas as an after-effect. In a number of combination the perception of load was diminished.

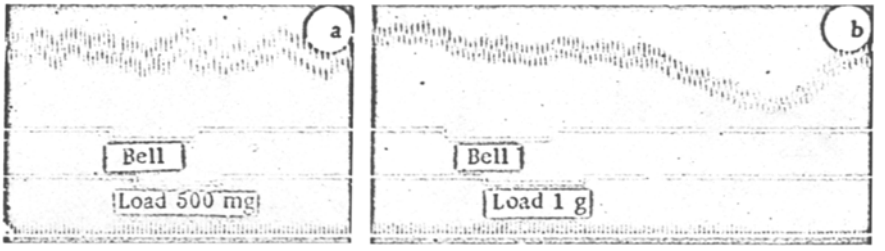

Fig. 1. Impairment of conditioned vascular reflexes in the subject T. to the combination: bell + load 500 mg (a), and bell + load 1 g (b), after administration of 6 g bromide (5th day of administration). Records from above down: plethysmogram; marker denoting conditioned stimulus; marker denoting unconditioned stimulus; time marker (2 seconds).

The same results were observed in this subject on the 6th day of bromide administration.

Similar impairment of conditioned reflexes was caused by bromide in the other subjects investigated. In the case of subject V., for whom a load of 1 g served as the conditioned stimulus and stimulation by touch as the unconditioned one, no vascular reaction occurred during the first two of six combinations (load of 1 g and touch) on the 2nd day of bromide administration, and only after the last two combinations was some slight vasoconstriction observed from the moment of application of the load. Perception of weight and touch was considerably diminished in all the combinations. During subsequent days marked inhibition of conditioned vascular reflexes was also noted; these were only restored by the last combination in the experiment; diminution of the intensity of sensation produced by the stimuli used was also observed.

On cessation of bromide administration the conditioned vascular reflexes were gradually restored, apparently running parallel with elimination of bromide from the organism. Thus, in the case of subject T., persistent impairment of conditioned vascular reflexes to load was observed on the 2nd day following cessation of bromide intake. Thrice-repeated application of the load without combination with the conditioned stimuli failed to produce a vascular reaction; perception of weight was faint. There was almost no reaction in six out of eight combinations of loads with corresponding bells. Only during the eighth combination a slight conditioned vasoconstriction reaction appeared; perception of weight was diminished. On the 3rd day the conditioned vasoconstrictor reaction became already apparent by the fourth combination. From the 4th day the conditioned vasoconstrictor reaction appeared from the first combination in all experiments. The intensity of sensation produced by the loads also underwent gradual restoration.

An approximately similar picture of restoration was noted in the case of subjects V. and D.

Restoration of conditioned vasoconstrictor reflexes towards the end of each experiment during administration of bromide suggests that the cerebral cortex can restore temporarily disrupted interrelations and coordinations even in the presence in the body of considerable amounts of a pharmacologic agent which lowers cortical excitability. Owing to the dynamic nature of cortical processes, a temporarily disrupted conditioned reflex pathway undergoes restoration on repeated application of appropriate combinations.

The second series of experiments was devoted to the study of the influence of a single dose of phenamine (0.02 g, therapeutic dose) administered 40 min prior to the beginning of experiment, on the conditioned vascular reflexes evolved to loads of 1 g and 500 mg in the subjects T. and D. and to touch in the subject V.; its influence on perception of weight was also studied.

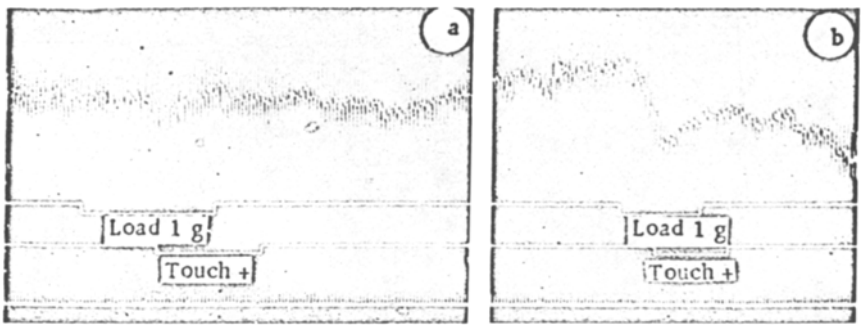

Fig. 2. Impairment of conditioned vascular reflexes in subject T. to combination "load 1 g + touch" before administration of phenamine (a) and after administration of 0.02 g phenamine (b). Records the same as in Fig. 1.

Phenamine caused a state of slight "drunkenness," vertigo, tearfulness in subject T. Forty minutes after taking the preparation, she was subjected to examination. Thrice-repeated application of 1 g and 500 mg weights without combination with conditioned stimuli produced no vascular reaction, while in the course of eight combinations with corresponding bells conditioned vasoconstrictor reactions appeared only from the fifth combination onwards. Perception of weight was present inconstantly.

Phenamine produced a similar effect on the subject V. Of nine combinations (load of 1 g and touch) vasoconstriction was associated with only the last two, beginning at the moment of application of the load (Fig. 2, b); during the seventh combination vasoconstriction started from the application of touch; in the six initial combinations there was practically no vascular reaction (Fig. 2, a).

It can thus be said that phenamine in the dose of 0.02 g exerts considerable inhibition on conditioned vascular reflexes to load and touch and also diminishes the intensity of sensation of weight. Such action of phenamine can evidently be explained by the fact that the given dose, which is generally recommended for stimulation of cerebral cortical activity, proved to be somewhat high for the subjects and produced a state of overstimulation and supra-threshold inhibition of the cortex. This would account for the absence of the expected increase in conditioned vascular reflexes and increased intensity of weight perception. But here, too, restoration of vasoconstrictor conditioned reactions was observed during the last combination in the experiment. Smaller doses of phenamine led to increased conditioned vascular reactions in the same subjects without unpleasant side-effects ("drunkenness," confusion etc.).

The same dose of phenamine had an opposite effect on the subject D. First, it produced neither vertigo nor a state of "drunkenness" in D. Secondly, the conditioned vascular reflexes to loads, which were not particularly strong in this subject prior to administration of phenamine (Fig. 3, a), were markedly enhanced after taking phenamine (Fig. 3, b). Phenamine was without effect on the intensity of weight perception by D.

The different results obtained in this investigation are being provisionally explained by individual "type features" of the subjects examined. A phenamine dose of 0.02 g proved to be too high for subjects with a more excitable nervous system (T. and V.) and gave rise to a state of supra-threshold inhibition. In the case of subject D. who showed weaker excitatory processes, phenamine only enhanced the excitatory process with consequent increase of conditioned vascular reflexes to loads..

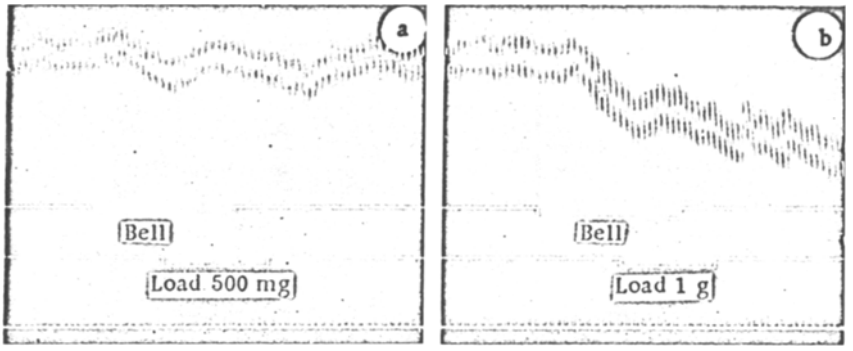

Fig. 3. Effect of phenamine (0.02 g) on magnitude of conditioned vascular reflexes to combination "bell + load of 1 g" and "bell + load of 500 mg" in subject D.
a) Before administration of phenamine; b) after administration of phenamine.
Records the same as in Fig. 1.

The importance of variations in "type features" with respect to reaction to phenamine has been pointed out by L. I. Kotliarovskii [1].

The investigation has shown that pharmacologic substances which alter the functional state of the cerebral cortex in the direction of excitation or of inhibition cause corresponding changes in conditioned reflex activity associated with barostimulation of the skin as well as the intensity of sensation produced by such stimuli.

SUMMARY

The author studied the effect of bromide and phenamine (benzedrine), which act selectively on the processes of inhibition and excitation in the cortex, on conditioned vascular reflexes to loads and to the intensity of perception of the barostimuli. Bromine caused inhibition of conditioned and unconditioned vascular reflexes to loads and decreased the intensity of perception of weights. Phenamine in the dose of 0.02 g also caused inhibition of unconditioned and conditioned vascular reflexes to weights in 2 cases and weakened the intensity of sensation. In lower doses, phenamine increased the vascular conditioned reflexes. In one case with a weaker excitability, phenamine in the dose of 0.02 g considerably increased the vascular conditioned reflexes to weights. Vascular conditioned reflexes to weight which were disturbed by bromide and phenamine returned to normal at the end of each experiment. This took place in all cases, although the pharmacological agent decreasing the excitation of the cerebral cortex was till present in the organism.

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