EFFECT OF EXPERIMENTALLY INDUCED HEART DISEASE ON CONDITIONED REFLEXES INHIBITING RESPIRATION AND THE ACTIVITY OF THE HEART

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The view that the nervous system plays an important part in the mechanism of the compensatory process developing in heart disease was first advanced by S. P. Botkin [2], on the basis of his extensive clinical material, and has been studied experimentally by Timofeev [7], working with I. P. Pavlov [6], Ballint [8], Hulmangyi et al. [10], L. Ya. Balonov [1], and others.

Insufficient attention has, however, been paid to the actual mechanisms whereby continuous compensatory hyperfunction of the heart, and the timely deployment of extracardiac compensatory factors, are assured in heart disease.

We have shown in our previous communications [4, 5] that in the stage of stabilized compensation of heart defects experimentally induced in rabbits there was a pronounced weakening of the unconditioned reflex reaction to stimulation of the upper respiratory passages with ammonia vapor, and consisting of respiratory arrest and bradycardia. The duration of the unconditioned reflex apnea and the degree of bradycardia are 3-5 times smaller in rabbits with heart defects than in controls. This change is associated with strengthening of sympathetic nerve reflexes augmenting the activity of the heart. Thus a specific readjustment of nervous centers takes place, ensuring uninterruptible hyperfunctioning of the defective heart, and excluding the possibility of reflex inhibition of respiration and cardiac activity.

The present paper describes the results of a study of the effects of cardiac defects on conditioned reflexes formed on the basis of unconditioned reaction to exposure of the upper respiratory passages to ammonia.

EXPERIMENTAL METHODS

The animal material consisted of 16 male rabbits, weighing 2-2.5 kg.

Experimental aortic stenosis was produced by the method described in a previous paper. The aortic cross section was reduced to a quarter to one sixth by the application of a silk ligature. Stenosis was associated with the characteristic x-ray and morphological changes in the heart. In the first group of experiments, on 6 rabbits, we formed a stereotype of conditioned reflexes, and aortic stenosis was then induced in 4 of them; a ligature was applied to the aorta of the remaining 2, but was not tightened. The conditioned reflexes of all 6 animals were then followed during the 10 days after the operation, i. e., up to the stage of stable compensation of the defect, and after the effects of operational trauma and of the initial severe reactions to the stenosis had passed off. In the second group of experiments we formed conditioned reflexes in 4 rabbits which had been subjected to experimental aortic stenosis a month earlier, and in 6 control rabbits, which had not been operated on at all, with the object of ascertaining the effect of a pre-existing heart defect on the process of formation of conditioned reflexes.

All the experiments were conducted with the animals in the prone position. Respiration was recorded on an electrokymograph, and cardiac activity by means of an electrocardiograph (EKP-4M), with a fitted electrical recorder of stimulations.

Unconditioned reflex apnea and bradycardia were caused by irritating the upper respiratory passages with ammonia. In the unoperated rabbits the duration of reflex apnea was 15-20 seconds, and bradycardia was manifested by an abrupt fall in the heart rate from 250 to 30-50 beats per minute, returning to normal within 20-30 seconds.

The conditioned reflexes were formed on the basis of the given unconditioned reflex. The conditioning stimuli were a metronome, frequency 300 beats per minute, and a green light. The differentiating stimulus was a metronome of frequency 30 beats per minute. The duration of exposure to the conditioning stimuli was 10 seconds. Delaying was not at first practiced; the conditioned stimulus was applied immediately after exposure to ammonia. A delay of 1 second was then instituted, and this delay was gradually increased, up to 6 seconds. The conditioned reflexes appeared after 4-8 combinations, and a constant delay of 6 seconds was reached after 15-20 combinations.

Until the reflex was formed neither M-300 nor green light had any perceptible effect on the respiratory and ECG tracings. After its formation the isolated sounding of M-300 caused apnea lasting as long as it was sounded, with pronounced bradycardia, involving retardation of heat rate from 240-260 to 60-80. The light stimulus caused equally pronounced reactions. Differentiation (M-30) was formed after 6-10 associations, and was incomplete in about a third of the animals, i. e., some retardation of respiration and heart rate was observed. The conditioned reflexes were of great stability, and could only be extinguished after 25-30 unreinforced stimulations.

The respiratory and cardiac components of the conditioned reflexes were of parallel intensity, and for convenience we usually assessed the strength of the reflexes from the respiratory component only. The strength of the reflexes was calculated by determining a mean normal value for respirations per minute for each animal, and then finding the number during a period of 6 seconds.

If, for example, the respiratory rate was 75 per minute, then there would be $7\frac{1}{2}$ respirations in 6 seconds. We then counted the number of breaths shown on the pneumograms during a 6 second period of action of the conditioned stimulus. If the number of breaths was the same as before stimulation, e.g., $7\frac{1}{2}$, it followed that the conditioned stimulus had no effect on the respiratory rhythm, and the strength of the conditioned reflex was 0. If, on the other hand, respiration was arrested with the moment of application of the conditioned stimulus, and was absent during the whole of the 6-second period of stimulation, the strength of the reflex was at a maximum, and amounted to 100%.

If the respiratory rate was half the normal value during stimulation, the strength of the reflex was 50%.

The strength of the conditioned reflex was found to vary from 60 to 100% during a given experiment, in a group of 6 control rabbits.

The strength of the reactions to the auditory and visual stimuli bore a constant relationship. The magnitude of the reflex to M-300 was 70-100%, and of the reflex to green light 27-50%.

EXPERIMENTAL RESULTS

The previously described weakening of unconditioned reflexes was observed 10 days after constriction of the aorta of all 4 rabbits of the first group, in which conditioned reflexes had been formed before the operation; the duration of unconditioned reflex apnea was reduced from 15-20 to $7\frac{1}{2}$-$12\frac{1}{2}$ seconds, and the degree of bradycardia from 30-50 to 100-120 beats per minute. The strength of the conditioned reflexes fell correspondingly. The strength of the auditory conditioned reflexes to M-300 fell from 100-60 to 40-27%, and of the conditioned reflex to light to 0. The corresponding conditioned reflex bradycardia fell from 30-50 beats per minute to 120-200 beats per minute, and was altogether absent in some experiments (Figs. 1 and 2). There was no change in the reaction to the discriminating stimulus. The extent of weakening of conditioned reflexes varied for different animals, parallel to the weakening of unconditioned reflexes in the given rabbit.

Application of a ligature to the aorta, without causing stenosis, caused a certain retardation of heart rate, and led to prolongation of unconditioned reflex apnea. No significant changes were observed in the strength of conditioned reflexes in these two animals.

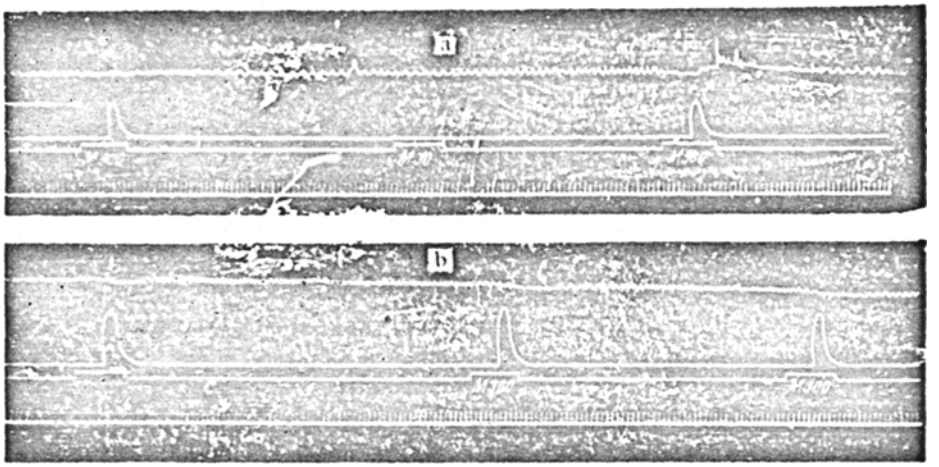

Fig. 1. Conditioned reflexes in a normal rabbit (a), and in the same animal a month after constriction of the aorta (b).
Explanation of curves (from above down): respiration, unconditioned stimulus, conditioned stimulus, time marker.

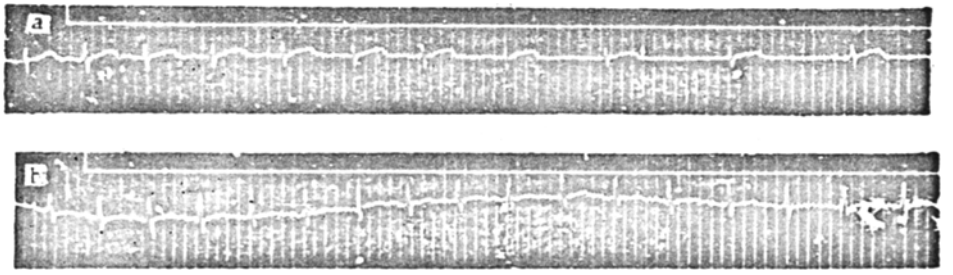

Fig. 2. Conditioned reflex bradycardia in a normal rabbit (a); in a rabbit which had been subjected to aortic stenosis a month earlier (b) – bradycardia is absent.
The upper tracing shows time and duration of the auditory stimulus.

In the second group of experiments the formation of conditioned reflexes in response to the M-300 auditory stimulus in animals with pre-existing aortic stenosis was, naturally, more difficult, in view of the weakening of the unconditioned reflex. The first appearance of the conditioned reflex was observed after 3-7 associations, in both groups of animals, with or without aortic stenosis. The two groups diverged widely thereafter, however. Whereas the strength of the conditioned reflex varied in the control group from 60 to 100% after 15 associations, it rarely exceeded 35-40% in the group with aortic stenosis, even after 35 associations. Apart from this, the operated group differed from the control in that stabilization of the reflexes did not occur – failure to respond occurred periodically.

The weakness and the instability of the conditioned reflexes in rabbits suffering from heart defects was a hindrance to formation of delayed reflexes. Whereas a delay of 6 seconds was achieved in the control group after 13-15 associations, this was not possible in the operated group even after 35 associations.

SUMMARY

A reduction of the unconditioned reflex, which caused apnea and bradycardia was noted in animals with compensated experimental aortic stenosis. The sound and light conditioned reflexes which were formed on its base were, likewise, reduced. The process of formation of the new conditioned reflexes on the base of the above unconditioned reflex became more difficult. These experimental data were evaluated in view of I. P. Pavlov's conception of the closure of the conditioned association between the cortical representation of unconditioned reflex and the cortical representation of the corresponding conditioned stimulant. It may be suggested that the reduction of the above unconditioned reflex in heart defect causes decreased excitability of its cortical representation. As a result of this the power of the process of excitation is decreased, the existing temporary associations are disturbed to a certain degree and the formation of new temporary associations becomes more difficult. The adaptive significance of reduction of unconditioned and conditioned reflexes, which inhibit the heart activity consists (in condition of heart defect) in the fact that it more or less guarantees the vitally important continuity of the compensatory hyperfunction of the heart.

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