

A STUDY OF NEW METHODS OF EXPERIMENTAL THERAPY BASED ON "DESTRUCTION" OF PATHOLOGIC CONDITIONED REFLEXES

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Soviet clinicians and physiologists recently received new convincing experimental data pointing to the possible decisive significance between pathologic conditioned reflexes and the development of a number of illnesses [1-6, 11]. In particular, the works of A. L. Myasnikov [7, 8] show that pathologic conditioned reflexes play a significant role in the development of hypertension. This conclusion was confirmed in the experiments of Kh. S. Koshtoyants and A. V. Napalkov [9, 10].

The above-mentioned investigations permit new concepts on the development of several illnesses and open new possibilities for a therapeutic approach [2, 3, 5].

Persistence is one of the most characteristic properties of conditioned reflexes. These reactions are not extinguished by repeated applications of isolated conditioned stimuli [3, 4, 6, 9, 10, 11]. In this connection the physiologist is faced with the problem of finding methods for "destroying" the conditioned reflexes that are harmful to the organism.

The aim of this study was further clarification of the above questions. In experiments on dogs with acute hypertension an attempt was made to work out new methods for the "destruction" of pathologic conditioned reflexes and to determine whether such destruction would lead to normalization of blood pressure levels. This study was carried out during 1949-1952 at the suggestion and under the leadership of Prof. Kh. S. Koshtoyantz.*

EXPERIMENTAL METHODS

The experiments were carried out on four dogs in a non-soundproofed chamber. The investigation included blood pressure level determinations and registration of the animals' activity and breathing. The blood pressure levels were determined in the usual way by a tonometer which in turn was checked against a mercury manometer.

The complex of conditioned motor reflexes responding to food was worked out in every animal at the beginning of the investigation (in answer to the conditioned reflex stimulus the dogs lifted the cover of the feeding-trough with their snout). Then a steady elevation of blood pressure was obtained in these animals in connection with the development of a neurosis. A detailed description of the method for producing hypertension was given in a special communication [9, 10]. As a result of the development of a neurosis in the dog all previously obtainable conditioned reflexes connected with food disappeared; the animals did not take meat, and vomiting, copious salivation and shortness of breath occurred. The blood pressure levels were 220/140 mm Hg.

*The following students took part in carrying out the experiments: Z. I. Maksimova, D. A. Sakharov and V. A. Shaternikov.

for one dog, Belka (normal 110/70); and 250/160 for the other, Djan (normal 135/90). The tension remained at the high level under the experimental setup, whether in or out of the chamber. There was no decrease 5 months after the dogs were excluded from the experiments. It became clear that pathologic conditioned reflexes were the deciding factors in the rise and maintenance of the hypertensive state. The pathologic stimuli for Djan were the following: a knock, the sound of the interrupter of the induction coil, a whistle, etc., while those for Belka were the beat of a metronome set at 120/min, the ringing of a bell, the sound of a horn, etc. A rise in blood pressure (50-80 mm Hg) and an intensification of the other signs of a neurosis followed the application of these stimuli. In some dogs vomiting occurred in response to the conditioning stimulus. Conditioned reflexes causing the development of hypertension were found to be extremely stable. Thus for instance the conditioned response to the sound of the metronome remained after 900 applications over 1½ months without reinforcement, by an unconditioned stimulus.

EXPERIMENTAL RESULTS

The possibility of abolishing pathologic conditioned reflexes by creating foci of severe excitation in other areas of the cerebral hemispheres was investigated in the first series of experiments.

The possibility of abolishing pathologic conditioned reflexes at a time of acute hunger was investigated in particular. This was carried out by means of repeated application of isolated conditioning stimuli linked with food (a detailed description of this method is given in the previous communication [9]). During periods of severe hunger pathologic conditioning stimuli were applied repeatedly (the metronome in experiments on Belka, for instance). Against this background the conditioned reflex became extinct after 70 applications of the metronome for a period of 4 days. It is worthy of note that this inhibition of the conditioned reflex remained. In the absence of the stimulus of hunger pathologic stimuli did not cause any reflex activity in the course of several days. The results of the cited experiments show that when the cortex of the cerebral hemispheres were sufficiently stimulated it was possible to abolish pathologic conditioned reflexes.

Simultaneously with the study of conditions leading to extinction of pathologic reflexes an investigation with a view to converting the above mentioned pathologic stimuli into unconditioned alimentary reinforcements was carried out (second series of experiments). An attempt was made to convert pathologic stimuli (knock and sound of the metronome) into unconditioned alimentary stimuli by reinforcing them directly with meat. These experiments were carried out on animals that for the preceding ten days were kept on marginal rations. These experiments did not lead to any positive findings.

Record of One of the Experiments on Belka

Time of experiment	Stimulus	Duration of action of the stimulus (in seconds)	Latent period (in seconds)	Reaction and condition of animal	Blood pressure level (mm/Hg)
14 hrs 10 min	—	—	—	dyspnea, salivation, pathologic motor activity	200/130
14 hrs 15 min	white lamp (alimentary conditioned stimulus)	35	4	stands still, wags tail, no dyspnea	—
14 hrs 15 min 20 sec	Bell (pathologic stimulus)	10	—	dyspnea, slight pathologic activity	—
14 hrs 15 min 30 sec	Meat	10	3	eats meat	210/130

In this connection an investigation for the purpose of working out special methods for switching reflexes was undertaken. Positive results were obtained in the combined application of conditioned and unconditioned stimuli. The sequence of application of stimuli to Belka is shown in the records of the experiment.

Positive results were also obtained in establishing secondary conditioned reflexes. In this instance the animal was shown meat followed by the sound of a pathologic conditioned stimulus (in experiments on Djan the sound of the interrupter of the induction coil). A conditioned stimulus of the second order was obtained in the animal. The sight of meat called forth a pathologic reaction, specifically, an increase in blood pressure. However, after 2-3 days the situation was reversed. At the sight of meat the animal no longer responded with the pathologic reaction, and the pathologic stimulus (sound of the interrupter) now called forth an alimentary reaction. It is important to note that the thus transformed pathologic stimulus acquired therapeutic significance. Its inclusion brought about an attenuation of the experimental neurosis and a lowering of blood pressure of 20-30 mm.

Thus it was proven that by the method of switching it was possible to convert a pathologic stimulus into one that decreases the intensity of the pathologic state.

A special method, "insinuation," was worked out for the "destruction" of pathologic conditioned reflex pathways (Experiments of A. Ya. Karas).

The pathologic conditioned reflex responses causing the development of a neurosis and a stable hypertension were usually generalized. Still, in every case it was possible to find a stimulus which due to its physical properties did not call forth a response. For instance, if the pathologic conditioned stimulus was a metronome with a rate of 210 beats per minute, the experiments were started with a metronome beating 10 times per minute and diminished intensity of sound. When it became evident that this stimulus did not call forth a response from the animal, the rate of the metronome and intensity of sound were gradually increased until the level of the pathologic conditioned reflex was reached.

Continuing this "insinuation" several days in succession it was possible to inhibit the very stable pathologic conditioned reflex reaction. The sound of the metronome did not cause a rise in blood pressure of the animal after application of this method of experimental therapy. It was also possible by this means to destroy other conditioned reflexes.

The condition of the experimental animals gradually returned to normal following "destruction" (inhibition) of pathologic conditioned reflexes by any of the methods described above. The previously inhibited alimentary conditioned reflexes reappeared: dyspnea, vomiting, salivation disappeared; the blood pressure usually returned to normal within 3-4 days.

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