

THE EFFECT ON CARDIAC REFLEXES OF REMOVAL OF THE CHROMAFFIN TISSUE

Z. V. Urazaeva

Department of Normal Physiology (Head, Docent Z. V. Urazaeva)

Altai Medical Institute, Barnaul

(Presented by Active Member AMN SSSR V. V. Parin)

Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 52, No. 7,

pp. 9-14, July, 1961

Original article submitted July 5, 1960

Adrenalin is the precursor for the synthesis of the sympathetic nervous mediator sympathin. From experiments on various animals, removal of large amounts of chromaffin tissue reduces the amount of adrenalin in the blood, and so impairs sympathetic function in different organs [3]. This method of interfering with the synthesis of sympathin in order to assess its physiological role may also be used to determine its effect on the cardiosympathetic nerves, and to study the trophic effect of such nerves, which exert a stimulating effect on the heart [4-7,9]. In experiments in which large amounts of chromaffin tissue were removed from the adrenal glands [2,3] it was found that there were also certain changes in higher nervous activity: there was a reduced internal inhibition and an overt or concealed weakening of the process of stimulation; the same operative measure reduced the frequency of occurrence of the cardiac component of the conditioned defensive reaction [10].

The aim of the present work has been to study the part played by the chemical mediator sympathin in conditioned reflex effects affecting the heart, and in particular to find its effect on the rate and strength of the cardiac contractions.

METHOD

The experiments were carried out on five dogs over a period of 5-6 months. Cardiac contractions were recorded by means of a balloon; the thin-walled rubber balloon was introduced through a fistula into the pericardial cavity, and connection to a Marie's capsule was made by means of an air and water system. First a pericardial fistula was established using a modified version of N. P. Sinitsyn's method [8]. It was then possible to record not only the rate, but also the amplitude of the cardiac contractions. The amplitude can not be recorded by most of the methods applicable to chronic preparations, such as electrocardiography, or recording the blood pressure. The method is therefore important not only for the purpose of the present study, but also as enabling changes in frequency and amplitude of the heart beat to be recorded in chronic preparations. After the animals had become used to the experimental set-up, conditioned reflexes to a sound stimulus, consisting of a moderately large electric bell, were established. A special square-wave generator in which the frequency and voltages of the pulses could be controlled was used to supply the unconditioned reinforcement. The stimulating current was supplied to the shaved surface of the upper third of the left forelimb. At first, the experiments were performed on unoperated dogs, and subsequently were continued for long periods after the operation. In four animals, in order to cause a temporary impairment of the synthesis of sympathin, the right adrenal was removed, and the medulla of the left adrenal was cauterized. Two dogs served as controls: in one, to compensate for the removal of the adrenal medulla, injections of 1 ml of 1:1,000 adrenalin were given daily, and in the other a mock operation was made in which the abdominal cavity was opened without the adrenal glands being touched, and the wound in the anterior wall was sewn up in layers.

RESULTS

In response to the signal alone, which accompanied the unconditioned pain stimulus, in all the dogs, usually after 10-14 combined applications (and in one after the third combined application) both the amplitude and frequency of the heart beat increased. The increase in amplitude was made greater by the application of the unconditioned stimulus (Fig. 1).

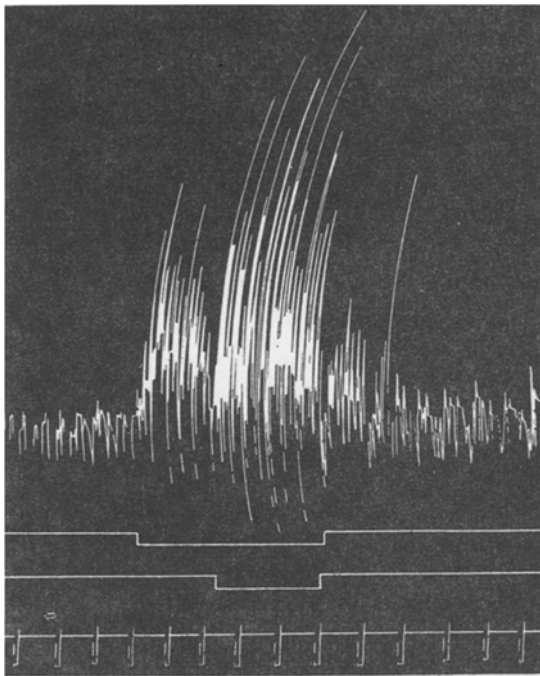


Fig. 1. Change in cardiac activity due to conditioned and unconditioned stimuli. Curves, from above downwards: cardiac contractions; conditioned stimulus marker; unconditioned stimulus marker; time marker (3 seconds).

tion or complete absence of cardiac conditioned reflexes was simply due to the trauma caused by the operation. The disturbance in the reflexes concerned only the response of the heart to the conditioned signal; the response to the unconditioned stimulus was normal: there was a regular increase in strength and frequency of the heart beat in response to a painful stimulus. Evidently the operative trauma does not noticeably affect the heart's response to unconditioned stimuli.

Later, after the removal of the adrenal medulla (from the 5-6th day onwards) there was a disturbance of the conditioned and unconditioned cardiac regulation. There was now a difference between the experimental and control groups in the responses to both conditioned and unconditioned stimuli; the rate and rhythm of the cardiac contractions were affected differently. The first effect was on the strength of the contractions. The changes were phasic: the first phase lasted 8-15 days, and the second for 10-11 days, while the third commenced 20-28 days after the operation. In the first phase, the reflex effect on the strength of the contractions was weaker than it had been before. During the next phase it was stronger: 20-28 days after the operation the strength of the response had returned to normal and was maintained at this level for the whole of the period for which observations were made.

The effect on the strength of the contractions in response to the unconditioned stimulus, which began on the 5-6th day, became reduced, and remained so for a long time. Recovery to the preoperational level in response to the unconditioned stimulus was not observed until the 52-62nd postoperational day.

In comparing the effects of the conditioned and unconditioned stimuli on the strength of the cardiac contractions, the extent and the duration of the reduction of the effect were most clearly shown in the case of the unconditioned stimulus. The graph shown in Fig. 2 illustrates this point; it shows the change in the strength of the contractions in dog No. 1, while Fig. 3 shows the results for dog No. 2.

No differences between the experimental and control groups were found in the change in the amplitude of the cardiac contractions. The only effect observed was that already described, and which occurred in the first few days after the operation. It should also be noted that the increased frequency of the contractions which occurred in animals from which the adrenal medulla had been removed showed some changes: the marked increase which occurred on certain days after the operation was followed by a period when no appreciable changes in rate occurred.

After the conditioned reflexes had been well established, the greater part of the chromaffin tissue was removed, and three days after the operation systematic studies were resumed. In spite of individual differences, it was nevertheless possible to make out the general direction of the changes in the regulation of cardiac activity.

In all the operated dogs, including the controls, 3-5 days after the operation there was a disturbance of the conditioned reflex cardiac regulation. The cardiac response to the conditioned signal was either weak, or did not occur at all; in some cases it could be elicited only by two or three repetitions of the stimulus. Because there could be no profound impairment of the formation of sympathin soon after the operation [3], we attributed these changes not to the specific operation, but to the general postoperative effects due to anesthesia and trauma.

This explanation was confirmed by experiments on the control dog; after laparotomy performed without removing any adrenal medulla, the cardiac conditioned reflexes were absent for 2-3 days (from 3 to 5 days after the operation), but subsequently returned. Similar results were noted in experiments on the second control dog, in which the chromaffin tissue of the adrenals was removed, but which received compensatory injections of adrenalin. The similarity of the results obtained on the two dogs during the first few days after the operation suggested that the reduc-

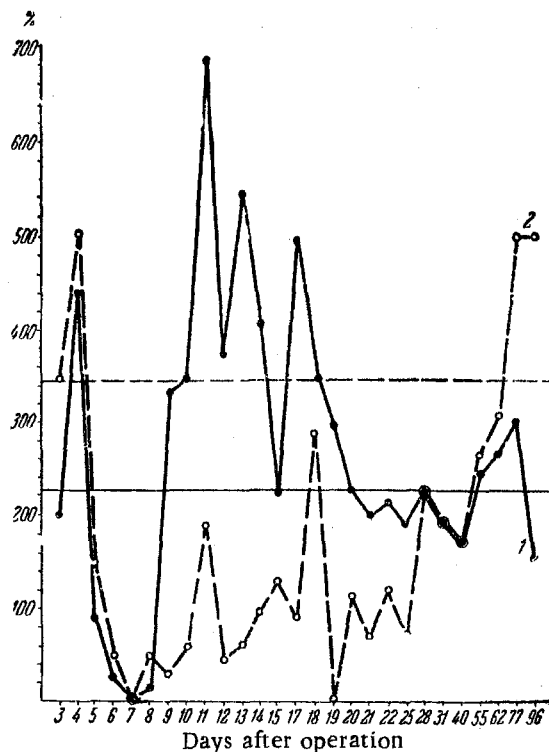


Fig. 2. Changes in the extent to which the strength of the cardiac contractions alters in response to conditioned and unconditioned stimuli, at different times after removal of the adrenal medulla.
 1) Change in the amplitude of the cardiac contractions in response to the conditioned stimulus;
 2) same in response to the unconditioned stimulus;
 abscissa—days after the operation; ordinate—change in the amplitude of the cardiac contraction expressed as a percentage of the amplitude before stimulation.

Thus, removal of the adrenal medulla causes a considerable effect on the nervous regulation of the amplitude of the heart beat, but has little effect on the regulation of the frequency. The continuation of the normal effect on heart rate in response to the conditioned stimulus could be found even when the adrenergic mechanisms were blocked by aminasin [1].

Elimination of most of the chromaffin tissue reduces the amount of adrenalin in the blood stream, and appears to prevent the synthesis of sympathin; the effect is shown in the reflex regulation of cardiac activity. The chief effect is on the control of the amplitude of the cardiac contractions. This effect was shown by the dog which received adrenalin after removal of the adrenal medulla. Here, there was no reduction in the control over the amplitude of the cardiac contractions for either the conditioned or the unconditioned stimulus. On the other hand, in response to a conditioned signal given after the 6th day, or to an unconditioned stimulus after the 19th day, there was a greater change in the amplitude of the contractions than had occurred before the operation.

SUMMARY

Conditioned reflex changes of the rate and intensity of the cardiac contractions were altered by the removal of the adrenal medulla. Studies were made on chronic preparations of dogs having a pericardial fistula. The conditioned cardiac reflexes were reduced or disappeared completely at the third, fourth, and fifth postoperative days. The amount by which the amplitude of the contractions changed in response to the stimulus was different on the

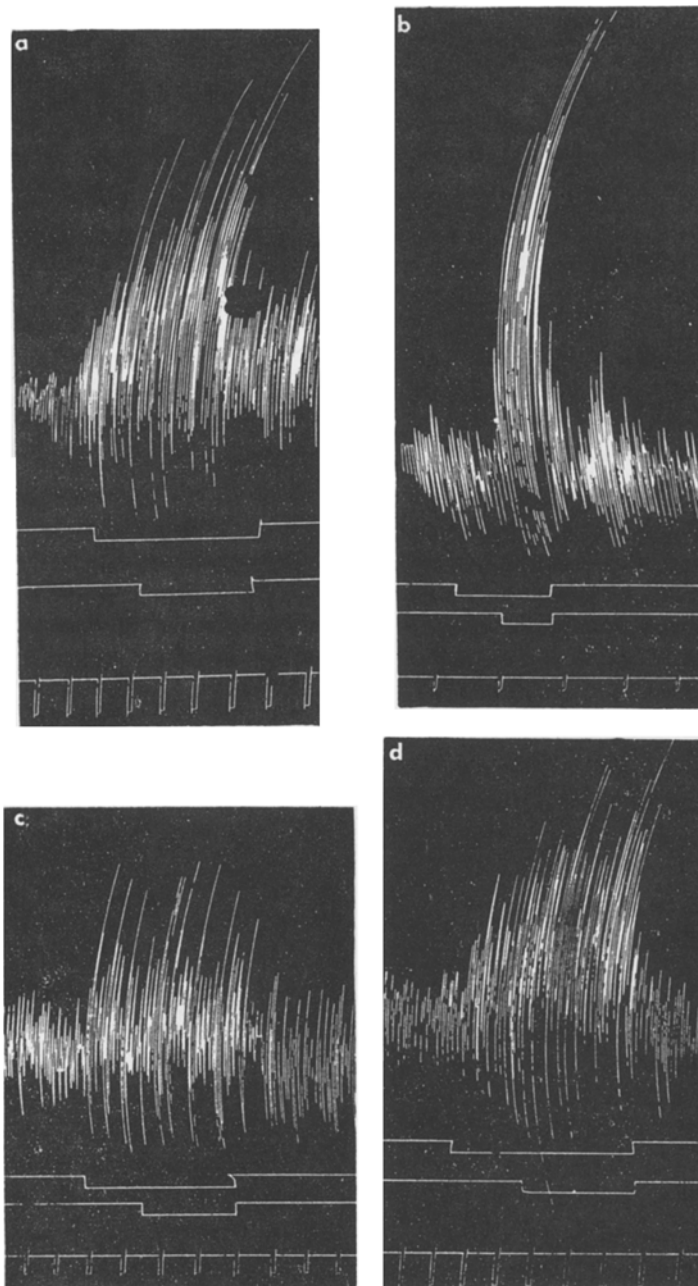


Fig. 3. Change in cardiac activity in response to conditioned and unconditioned stimuli at different times after removal of the adrenal medulla. a) Before operation; b) on the 4th day after operation; c) on the 11th day; d) on the 26th day. Curves, from above downwards: cardiac contractions; conditioned stimulus marker; unconditioned stimulus marker; time marker (3 seconds).

fifth and sixth postoperative days. The changes were phasic: first there was a reduction, then an intensification, and finally a gradual re-establishment of the preoperative level. In response to an unconditioned stimulus, the failure of the normal increase in cardiac contractions was more marked and prolonged. The removal of the adrenal medulla had no significant effect upon the elicitation of an increased heart rate.

LITERATURE CITED

1. B. B. Voznesenskii, Byull. Éksptl. Biol. i Med., 49, 4 (1960) p. 15.
2. M. M. Karimova, Zhurn. Vyssh. Nerv. Deyat., 6, 3 (1956) p. 415.
3. A. V. Kibyakov, On the Nature of the Regulatory Influence of the Sympathetic Nervous System [in Russian] (Kazan', 1950).
4. A. V. Kibyakov and L. V. Tukhvatullina, Byull. Éksptl. Biol. i Med., 26, 9 (1948) p. 231.
5. A. V. Kibyakov and L. V. Tukhvatullina, Byull. Éksptl. Biol. i Med., 26, 11 (1948) p. 347.
6. A. V. Kibyakov and Z. V. Urazaeva, Byull. Éksptl. Biol. i Med., 32, 7 (1951) p. 28.
7. O. D. Kurmaev, Byull. Éksptl. Biol. i Med., 27, 3 (1949) p. 186.
8. N. P. Sinitsyn, Byull. Éksptl. Biol. i Med., 39, 3 (1955) p. 74.
9. Z. V. Urazaeva, in book: The Physiological Role of the Mediators [in Russian] (Kazan', 1959) p. 125
10. M. I. Yakovleva, Fiziol. Zhurn. SSSR, 3 (1960) p. 291.

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.
