THE MECHANISM OF PRESSOR AND DEPRESSOR RESPONSES TO ELECTRICALLY INDUCED CONVULSION

KIYOSHI TANAKA AND NOBORU KAN

Department of Pharmacology, Tottori University School of Medicine, Yonago

Received for publication March 3, 1952

Though no objection has been offered to the reports of various authors (1, 2, 3, 4), stating that the blood pressure changes distinctly during and after the electrically induced convulsion, the detailed mechanism of the change remains to be elucidate.

Recently Schoetensack and Hann (5) have given a new interpretation of the mechanism based on their experiment in cats. They found that the blood pressure simply rose and never fell below the normal level after electroshock in unanesthetized and curarized cats, while it was merely depressed in animals anesthetized with barbitalate. According to them, the pressor response was abolished by yohimbin and therefore it was attributed to the secretion of epinephrine, and the depressor response was potentiated by eserine and prevented by atropine, indicating that acetylcholine was liberated.

For the last several years we have been engaged in a research on the physiological changes induced by electroshock in experimental animals and have ascertained that the responses of blood pressure were not attributable solely to the liberation of chemical transmitters such as epinephrine or acetylcholine (6). The present report presents the results of our experiments and our view on the nature of the pressor and depressor responses to electroshock.

Method: Rabbits were used in every experiment. Electric current was applied through needle electrodes placed subcutaneously at the roots of both ears. Stimulation with 50 V. AC 1 sec. was sufficient to induce general tonic and clonic convulsion. Blood pressure was recorded on a smoked drum from the canule inserted in the carotid artery.

A. Typical Changes of Blood Pressure During and After Convulsion

In normal unanesthetized rabbits the change of blood pressure passes through the following four phases as shown in Fig. 1. Urethane narcosis has hardly any influence on the typical changes.

The 1st phase—a transient depressor response.

Right after the electric stimulation, a slight depressor response of short du-

FIG. 1. Four phases of typical pressure change due to electroshock.

ration often takes place. The drop is usually less than 10 mm Hg and the duration is shorter than 10 sec. This phase is sometimes totally lacking.

The 2nd phase—a mighty pressor response.

At the beginning of tonic convulsion the blood pressure takes a turn for a sudden and intense rise, reaching its maximum within 25 sec.. When the convulsion becomes clonic, the blood pressure begins to descend. The height is usually 50–100 mm Hg.

The 3rd phase—a postconvulsive depressor response.

When the convulsion is over, the blood pressure continues to drop till it comes down to 10–30 mm Hg below normal. This depressor phase lasts for 30–120 sec..

The 4th phase—a later pressor response.

Recovered from depression, the blood pressure is shifted on to a slow, slight but long lasting (2–5 min.) pressor phase. It is 10–20 mm Hg above normal.

B. Mechanism of the First Phase, "the Transient Depressor Response"

In an experiment with Nuki's cardiotaubour, we found remarkable bradycardia or even cessation of heart beat occurring immediately after the electric stimulation, and either symptom being abolished by atropine or after bilateral vagotomy (Fig. 2).

FIG. 2. Heart action (HA) and blood pressure (BP) changed by electroshock, [A] before and [B] after bilateral vagotomy.

The transient pressure fall of the first phase, therefore, must be the result of the powerful heart depression caused by central vagal stimulation.

C. Mechanism of the Second Phase, "the Mighty Pressor Response"

The following two factors are considered to be concerned with this phase.

1. The first mechanism, which must be the major factor, is increased resistance of blood vessels due to general tetanic convulsion. The following several experimental data will support this consideration.

(1) The pressure rise was almost eliminated when the convulsion had been prevented by curare as shown in Fig. 3.

FIG. 3. Pressure change due to electroshock applied after administration of curare; [A] after intravenous injection of 3 mg/kg curare, [B] 5 min. later, under artificial respiration.

We could hardly find such a case as was reported by Schoetensack and Hann, in which only the pressor response without the depressor phase can occur after the application of curare; we rather noticed that the depressor phase often became more distinct. This divergence of result may be due to the difference in experimental animals used: the unanesthetized cat and the anesthetized rabbit.

(2) The pressor reaction lessened when the convulsion was weakened by general anesthesia with ether, chloroform, alcohol or barbiturate, and the reaction was made marked by a violent convulsion occurring after the administration of morphine or sodium bicarbonate.

(3) In the Nolf's 3-manometer experiment, the fluctuation of the femoral peripheral pressure on the denervated and accordingly not convulsive side was lacking the mighty pressor phase though the later pressor phase was more obvious, while on the innervated side it underwent the same change as the carotid pressure (Fig. 4).

(4) Bastiani and Piotti (7) expressed their opinion that the compression of the visceral blood vessels in abdominal and thoracic organs due to tetanic convulsion might be the cause of the pressor response to electroshock. The compression they assumed may of course be regarded as a factor to increase the resistance of blood vessels, and the reduction in the pressor effect, observed in our experiment after removal of the majority of the abdominal organs, will support their opinion.

FIG. 4. Experiment with Nolf's 3-manometer; D: femoral peripheral pressure of denervated side; N: innervated side; C: carotid pressure.

2. The second mechanism of the pressor response consists in the direct stimulation of the vasomotor center. Since Hess's profound investigation of autonomic centers, there have been many studies on the vasomotor center. According to the results of these researches it may seem quite natural that the electrically stimulated vasomotor center should induce an active contraction of general blood vessels. The facts recognized in our experiment; namely, that the ear vessels which should not be influenced by muscle contraction were highly contracted during convulsion, and that curare did not completely abolish the pressor response, may be explicable by the central vasomotor stimulation.

D. Mechanism of the Third Phase, "the Postconvulsive Depressor Phase"

Many factors are conceivable in connection with this phase.

1. After convulsion the animal falls into a state of narcosis, accompanied by relaxation of all muscles. This may reduce the resistance of blood vessels and invite a pressure fall.

2. Stimulation of the vasodilator center is also possible. Kurozu's finding (8), that when stimulated simultaneously the parasympathetic vasodilator center is irritated later than the sympathetic vasoconstrictor center, corresponds with our experimental result that the depressor phase follows the mighty pressor phase.

3. Heart depression may be another factor. Hejtmancik (9) and Altschule (10) observed a remarkable reduction in heart rate in the human electrocardiogram during electroshock, and Wada (1) supposed the pressure fall to be due to cardiac depression.

In our experiment on the rabbit, however, bradycardia was insignificant in this depressor phase, while it was remarkable in the first and pressor phases, and furthermore it was abolished by atropine though the pressure fall was not

influenced by the drug. We can not, therefore, accept the view that heart depression is the chief factor in this phase.

4. Schoetensack and Hann assumed the liberation of acetylcholine to be the main factor in the pressure fall. We confirmed however that this depression was not prevented by atropine in the rabbit, while bradycardia completely disappeared after atropine administration or vagotomy (Fig. 2). On the other hand, the reduction of cholinesterase after electroshock reported by Neustadt (11), may be beneficial to the idea of acetylcholine accumulation. We should, therefore, suppose that acetylcholine may play some, if not, the chief role in the pressure fall.

E. Mechanism of the Fourth Phase, "the Later Pressor Response"

Two factors may be assumable in this phase.

1. Bilateral adrenalectomy or ergotamine administration abolished either this pressor phase or the depression of intestine motility, which usually appeared in this phase, but these managements did not affect the first pressor response during convulsion (Fig. 5). Epinephrine liberation is, therefore, most responsible for the appearance of this phase. Schoetensack's opinion, that the pressor response is due to epinephrine, is acceptable only so far as the fourth phase is concerned in our case.

FIG. 5. Blood pressure (BP) and intestine motility (IM) changed by electroshock: [A] before and [B] after bilateral adrenalectomy.

2. We noticed that this phase is distinct in anesthetized animals, and from our results reported before, indicating that electroshock has an awaking effect on animals anesthetized with urethane or alcohol (12), and that electroshock relieves animals from severe barbiturate poisoning (13), we can suggest the possibility of turning the vasomotor center from the state of depression to that of irritation as a result of the awakening from narcosis.

CONCLUSION

During and after electrically induced convulsion in rabbits, the blood pressure rises and falls through four phases. The mechanism of each phase is considered as follows:

1. The first transient depressor phase is due to the heart depression caused by stimulation of the vagal center.

2. The second mighty pressor phase is mainly the result of general convulsion which increases vessel resistance. Direct central vasomotor stimulation can also invite vessel contraction and consequently pressure rise.

3. The third depressor phase may be induced chiefly by decreased resistance of blood vessels in the narcotic state after convulsion. Stimulation of the vasodilator center, heart depression due to central vagal stimulation and acetylcholine liberation are considered to be side factors.

4. The fourth later pressor phase is ascribable to epinephrine secretion from the adrenal glands.

REFERENCES

- 1) WADA, J.: *Folia Psychol. Neurol. Japon.* **3**, 302 (1949)
- 2) KANAZAWA, T.: *Niigata Med. J.* **63**, 228 (1949)
- 3) ITO, S. *et al.*: *J. Tokyo Med. College* **8**, 48 (1950)
- 4) PIETTE, V.: *Ann. Soc. Roy. Sci. Med.* **3**, 5 (1950)
- 5) SCHOETENSACK, W. AND HANN, J.: *Arch. exper. Path. u. Pharmacol.* **213**, 102 (1951)
- 6) KAN, N.: *Folia pharmacol. japon.* **48**, 42 (1952)
- 7) BASTIANI, G. AND PIOTTI, O.: *Arch. di Sci. Biol.* **33**, 489 (1949)
- 8) KUROZU, T. *et al.*: *No-Kenkyu* **3**, 57 (1949)
- 9) HEJTMANEIK, M. R. *et al.*: *Amer. Heart J.* **37**, 790 (1949)
- 10) ALTSCHULE, M. D. *et al.*: *Arch. Neurol. Psychiat.* **58**, 653 (1947)
- 11) NEUSTADT, R. *et al.*: *Cit. f. Arch. Neurol. Psychiat.* **63**, 336 (1950)
- 12) TANAKA, K. AND KAN, N.: *Seitai no Kagaku* **2**, 237 (1951)
- 13) TANAKA, K. AND KAN, N.: *J. Yonago Med. Ass.* **3**, 22 (1951)