REFLEX CHANGES IN THE ACTIVITY OF THE CARDIOVASCULAR SYSTEM PRODUCED BY CHEMICAL STIMULATION OF PERICARDIAL RECEPTORS

COMMUNICATION II. ON THE EFFECT OF COMPLETE OR PARTIAL EXCLUSION OF PERICARDIAL RECEPTORS ON CIRCULATION AND RESPIRATION

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It is known that stimulation of pericardial receptors in rabbits with nicotine has a depressor effect [6, 7], whereas exclusion of these receptors with novocain – a stable pressor effect on the blood pressure [6, 7, 11]. In a previous communication [3] we showed that both pressor and depressor reactions can be produced by chemical stimulation of pericardial receptors in cats. In some experiments only pressor and in others only depressor reactions were observed. However, in the majority of the animals it was possible to produce both reactions; pressor reactions were produced by relatively weak concentrations of nicotine and depressor reactions by higher concentrations. We expressed our conjecture that the character of the reaction of the cardiovascular system to stimulation of pericardial receptors is determined not by the specificity of different receptors conducting pressor or depressor effects, but by the number of receptors all of which are similar in so far as the effect on the cardiovascular system is concerned.

The purpose of this investigation was to determine which reactions of the cardiovascular and respiratory systems in cats are produced by excluding the pericardial receptors and how the reactions are influenced by stimulation of these receptors after their partial exclusion with small doses of novocain.

EXPERIMENTAL METHOD

Fundamental steps of the method are described in a previous communication [3]. Substances used for exclusion of receptors were dissolved in a Ringer-Locke solution (novocain – up to 1 or 2%, acetic acid – up to 3% concentration) and injected intrapericardially.

EXPERIMENTAL RESULTS

Injection of 1 – 2 ml of 2% novocain into the pericardial cavity usually excludes the pericardial receptors completely and, regardless of the character of resulting reactions, produces a rise in blood pressure and in cardiac and respiratory rate. It was found that in a number of instances stimulation and exclusion of receptors produced identical reactions by the cardiovascular system. Identical changes in the respiratory rate were produced in all experiments by both stimulation and exclusion of pericardial receptors.

In Fig. 1 is shown a kymogram in an experiment on a cat which reacted with a rise in blood pressure and in cardiac and respiratory rate to any, even the strongest (Fig. 1, a), chemical stimulation of pericardial receptors. Treatment of the pericardium with novocain caused similar, but somewhat less marked, changes following which the introduction of nicotine in the same concentration as before produced no effect. From

the point of view of current understanding this result can be explained only by assuming that nicotine stimulated certain – in this case pressor – receptors, and novocain excluded receptors sending tone-depressing impulses.

It is known that stimulation of chemoreceptors of the reflexogenic zone of the carotid sinus results in a rise of blood pressure, whereas increased stimulation of mechanoreceptors of this zone produces a reflex fall in general blood pressure. It was shown [12] that certain chemicals can stimulate not only chemo- but also mechanoreceptors in the zone of the carotid sinus. By analogy one may assume that in our experiments small doses of nicotine stimulated only the chemoreceptors, but larger doses stimulated the pericardial mechanoreceptors too (or increased their excitability) inasmuch as impulses from mechanoreceptors cause a fall in blood pressure [1, 5, 10]. If one were also to assume that the reflex tonus of pericardial mechanoreceptors is higher than that of chemoreceptors, it would be possible to explain the rise in blood pressure and in the cardiac and respiratory rates resulting from the treatment of the pericardium with novocain as due to exclusion of mechanoreceptors, and the origin of analogous effects resulting from treatment of the pericardium with nicotine as due to stimulation of chemoreceptors. In order to verify this assumption we selected E. Gernand's [9] method of selective exclusion of chemoreceptors with 0.5 M acetic acid.

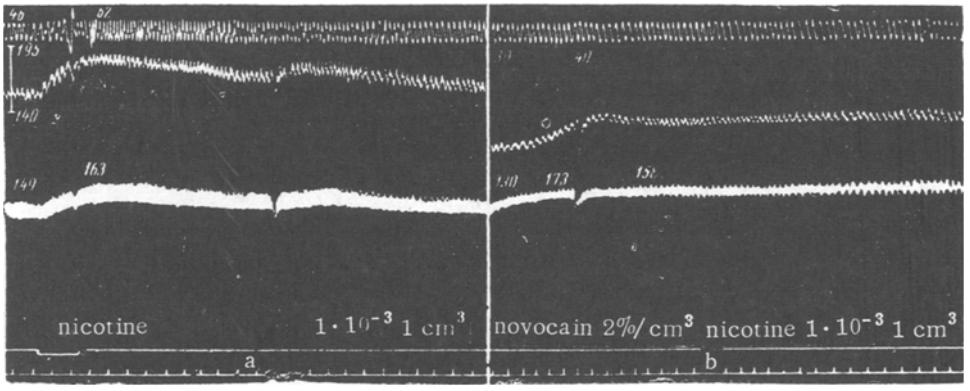

Fig. 1. Rise in blood pressure produced by stimulation of pericardial receptors with nicotine (a) and by exclusion with novocain (b). Meaning of tracings (from above down): respiration, blood pressure (mercury manometer), blood pressure (membranous manometer), record of stimulation, time record (2 seconds). Numerals along the respiration and blood pressure (membranous manometer) tracings indicate the respiration and pulse rates per minute.

It was found that treatment of the pericardium with one ml of 3% (0.5 M) acetic acid excludes irreversibly the possibility of reflex reactions to chemical stimulation of pericardial receptors and produces a lasting rise in blood pressure and in cardiac and respiratory rates strongly resembling the reaction to exclusion of pericardial receptors with novocain (compare Fig. 2,a and b; or Fig. 3). The difference is that the action of 3% acetic acid is manifested in a steeper growth of the reaction (Fig. 2,a) or in a greater intensity of the reaction in its initial stage (Fig. 3, e). The subsequent course of the reaction to acetic acid fully coincides with the reaction to novocain. Differences in the initial stages of the reactions can be explained as due to the effect of the brief but intense outburst of impulse which was observed consistently by E. Gernand during the first instants of the action of 3% acetic acid and before the exclusion of chemoreceptors. In our experiments, as in those of E. Gernand, mechanoreceptors preserved their excitability; this manifested itself in a momentary fall in blood pressure in response to rapid injection into the pericardial cavity of 10 ml of Ringer-Locke solution. Such effects were invariably observed when the stimulant was washed away (see Fig. 3, e).

Therefore, selective exclusion of pericardial chemoreceptors also produces strong rise in blood pressure and in cardiac and respiratory rate. This was observed in experiments on cats with various reactions of the cardiovascular system to chemical stimulation. If pressor reactions are linked with chemoreceptors, one could logically expect that their selective exclusion, at least in those experiments in which chemical stimulation always caused pressor reactions, must result in fall in blood pressure and in bradycardia.

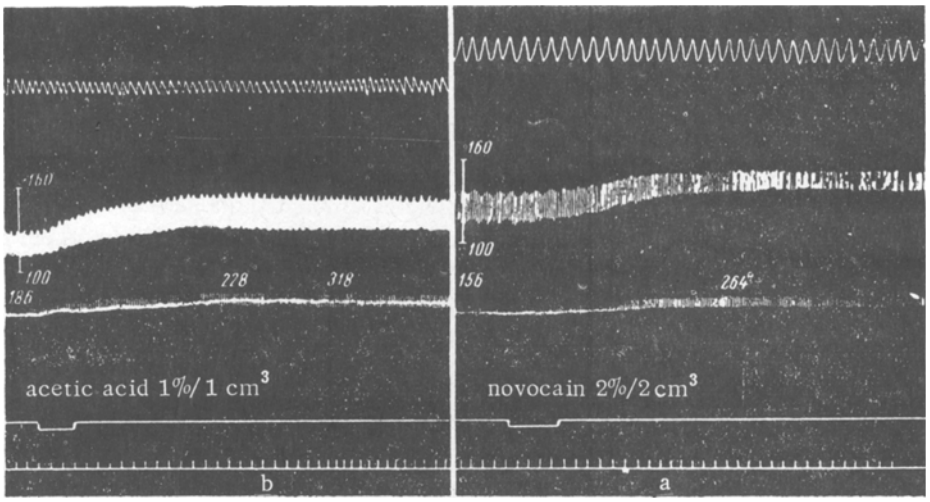

Fig. 2. Rise in blood pressure produced by exclusion of chemoreceptors (a) or all receptors (b) of the pericardium. Designations same as in Fig. 1.

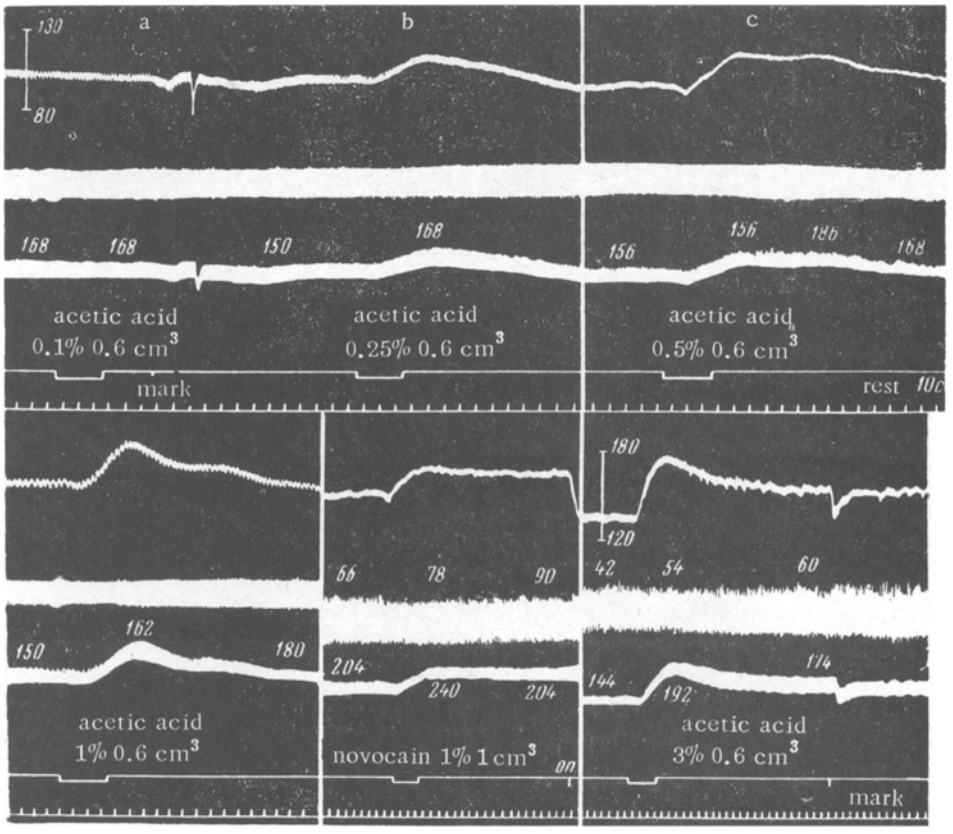

Fig. 3. Pressor reactions of blood pressure produced by treating the pericardium with acetic acid and with novocain. Meaning of tracings (from above down): blood pressure (mercury manometer), respiration, blood pressure (membranous manometer). The remaining designations same as in Fig. 1.

Treatment of the pericardium with acetic acid of lesser concentration (0.1 – 1%) reveals distinctly its stimulating action while its paralyzing action weakens and becomes reversible; however, it always manifests

itself, sharply limiting the duration of the impulse caused by the initial stimulation as a result of which pressor reactions accompanied by tachycardia are observed almost always in response to increasing concentrations of acetic acid (see Fig. 3). In these instances the effect of weak stimulation combined with subsequent effect of brief exclusion of receptors cannot produce a depressor reaction and bradycardia.

Subsequent experiments showed that treatment of the pericardium with novocain in amounts insufficient to completely exclude pericardial receptors but able to cause lowering of sensitivity of this reflexogenic zone, usually results in distinct rise of blood pressure and of cardiac and respiratory rate.

Under similar conditions, treatment of the pericardium with nicotine in low concentrations produces no effect on circulation and respiration. The effect produced by larger doses of nicotine was found to be weaker and similar to effects arising in response to small doses of nicotine prior to treatment of the pericardium with novocain. In experiments in which chemical stimulation of pericardial receptors produced only pressor or only depressor reactions, partial exclusion of these receptors with novocain was followed by weakening in intensity of the reactions to strong stimulation and by preservation of their original pressor or depressor character. In those experiments in which small doses of nicotine produced pressor reactions and tachycardia, and larger — depressor reactions and bradycardia, following treatment of receptors with a small dose of novocain large concentrations of nicotine produced not depressor reactions as prior to treatment with novocain, but pressor reactions, i.e. the same reaction as that produced in response to weak stimulation prior to treatment with novocain. Thus, by either decreasing the concentration of the stimulant or by preserving it but decreaing the sensitivity of the reflexogenic zone, we can convert the reaction of the cardiovascular system to chemical stimulation of pericardial receptors from depressor to pressor.

The facts described do not permit the consideration of the reflex rise in blood pressure and in cardiac and respiratory rates, resulting from the effect of novocain on the pericardium of cats, as a consequence of the exclusion of receptors which have a specific depressor effect on blood pressure, and thus cast doubt on the classification of receptors as pressor and depressor.

The assumption that the ability to send pressor effects is the function of chemoreceptors and the ability to send depressor effects produced by large concentrations of nicotine is the function of mechanoreceptors, is ruled out by experiments involving selective exclusion of pericardial chemoreceptors with acetic acid (0.5 M solution), in which a rise in blood pressure rather than a fall is observed as in exclusion of all pericardial receptors with novocain.

Against ascribing to individual receptors the ability to determine the direction of regulatory displacements caused by their stimulation are the experiments with partial exclusion of pericardial receptors with small doses of novocain. In the experiments we performed on cats which reacted to all stimulations of pericardial receptors with only pressor or only depressor reactions, we are convinced that novocain weakens both to the same extent. For this reason attention is drawn to the results of such experiments on animals in which weak concentrations of nicotine produced pressor reactions and high concentrations — depressor reactions. The fact that, after lowering of sensitivity of the reflexogenic zone of the pericardium with novocain, those concentrations of nicotine which called forth a fall in blood pressure and bradycardia now produced a rise in blood pressure and tachycardia, definitely speaks in favor of the assumption that impulses of individual receptors do not carry specifically pressor or depressor signals, but having arisen from a stimulation of a given intensity they determine the one or the other reaction on the part of the cardiovascular system. From experiments in which low concentrations of acetic acid were used, it becomes apparent that the duration of the volley of impulses which must be sufficiently great to give rise to a depressor reaction is an important characteristic of the signal significance of impulses from pericardial receptors. Analysis in receptors is limited, apparently, by differences in intensity and duration of the stimuli and by their ability to involve in the reaction of excitation a larger or smaller number of receptors; at the same time the character of efferent effects is determined by changes in the condition of nerve centers depending on the quantity of temporary and spatial distribution of afferent impulses entering the nerve centers [2].

Similarity of reactions to stimulation and exclusion of pericardial receptors can apparently be understood in the light of V. N. Chernigovskii's presentations [7, 8] that interoceptive impulses not only bring about these or those reflex reactions but also participate in formation of tonus in nerve centers, and not only those centers in which the reflex arc of their own reflexes is closed, but also in adjacent centers which effect the

vascular tonus in other areas [4], the heart rate, the respiratory rate, etc., i.e. those centers which, according to the type of combined reflexes [8], affect the vasomotor center as a whole and certain adjacent centers. Therefore, a rise in blood pressure and in cardiac and respiratory rates takes place when the total number of impulses entering the vasomotor center from the receptors of the pericardium and the reflexogenic zones of the carotid sinus, aorta and lungs is decreased.

SUMMARY

Exclusion of all pericardial receptors by novocain or only of its chemoreceptors by 0.5 M acetic acid brings about the rise of the blood pressure and increases the frequency of the heart beat in all cats. This takes place irrespective of whether the stimulation of these receptors by nicotine caused the rise of the blood pressure and tachycardia, depression and bradycardia, or (depending on the strength of stimulation) both reactions. Exclusion of the pericardial receptors, as well as their chemical stimulation, resulted in the increased frequency of respiration. After decrease of the sensitivity of the pericardial reflexogenic zone by small doses of novocain, reactions to small doses of nicotine disappeared, while those to large ones became weaker in animals in which all doses of nicotine cuased only pressor or only depressor reactions. In animals in which weak stimulation brought about a pressor reaction and strong stimulation a depressor one, pressor reactions resulted after strong stimulation following decrease of the sensitivity of receptors by novocain.

The conclusion is drawn that reflex reactions caused by exclusion of pericardial receptors cannot be explained by exclusion of afferent tone depressing impulses.

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