THE ANALYSIS OF REFLEX CHANGES IN THE CARDIOVASCULAR SYSTEM DURING STIMULATION OF THE CHEMORECEPTORS OF THE PERICARDIUM

COMMUNICATION 1. THE ROLE OF THE HEART AND OF VARIOUS VASCULAR REGIONS IN THE FORMATION OF THE DEPRESSOR REACTION

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According to reports in the literature [1, 2, 9, 10], during stimulation of the chemoreceptors of the pericardium with nicotine solutions changes may be observed in the level of the general arterial pressure: depressor, pressor, or combined depressor-pressor. The lowering of the arterial pressure is accompanied by bradycardia, and its elevation by tachycardia. In a previous communication [5] we also described similar changes in the arterial pressure and heart rate during stimulation of the chemoreceptors of the pericardium with nicotine. In our experiments we also found changes in the strength of the cardiac contractions and in the tone of the blood vessels of certain internal organs in the course of this reaction.

Accordingly, we were interested to discover the causal relationship between the manifestation of the depressor reaction and the changes in the state of the vascular tone in different parts of the vascular system during stimulation of the chemoreceptors of the pericardium with nicotine solutions.

EXPERIMENTAL METHOD

Acute experiments were carried out on cats under urethane anesthesia (1 g/kg). After artificial respiration had been instituted, the animal's chest was opened widely and a short incision made in the pericardium at the apex of the heart. A small hook with an attached thread was inserted into the apex of the heart, and the frequency and strength of the cardiac contractions recorded by an Engelmann lever through a system of pulleys. The peripheral vascular resistance (tone) in various parts of the vascular system was determined by means of a perfusion pump of our own modification [6]. In some experiments we used a method of measuring the volume velocity of the blood flow [4]. The general arterial pressure was recorded in the carotid artery by means of a mercury manometer.

The chemical agents used to stimulate the pericardial receptors were solutions of nicotine ($10^{-6}-10^{-3}$) and acetylcholine ($10^{-6}-10^{-4}$), introduced into the cavity of the pericardium by means of a syringe. Experiments were conducted on 43 animals.

EXPERIMENTAL RESULTS

During the depressor reaction of the general arterial pressure caused by the introduction of nicotine solutions into the pericardial cavity, changes were observed in the rate or amplitude of the cardiac contractions. A slowing of the heart rate always took place when the arterial pressure was lowered, and in individual experiments the frequency of the contractions ranged from 24 to 66 per minute. In response to stimulation of the pericardial chemoreceptors the strength of the cardiac contractions was increased, decreased, or unaffected. It should be pointed out that the lowering of the arterial pressure and the slowing of the heart rate began simultaneously; the strength of the cardiac contractions changed at the same time, being either increased or decreased. In some cases no changes were observed in the strength of the cardiac contractions. The return of the strength of the cardiac contractions to its initial level took place much sooner than the restoration of the heart rate and the level of the arterial pressure.

These findings showed that the depressor reaction of the arterial pressure during stimulation of the pericardial chemoreceptors with nicotine solutions takes place through the intermediary of the heart, which in this case slows its rhythm, whereas changes in the strength of the cardiac contractions may not always be found in the course of this reaction.

With the object of elucidating the changes in the tone of the blood vessels in the various vascular regions during the lowering of the arterial pressure caused by introduction of nicotine solutions into the pericardial cavity, we studied the state of the vessels of the hind limbs, the pelvic organs, the kidneys, small intestine, spleen, lungs, neck, and head. We found that during the depressor reaction a lowering of the tone took place only in the blood vessels of the spleen and small intestine and, more rarely, of the kidneys, although these changes were not always well defined, and in some experiments they were not present at all.

The inconstancy of the changes in tone of the blood vessels in different organs led us to conduct experiments in which individual vascular regions were isolated (by ligating the main arterial and venous trunks) from the general circulation, in order to discover their role in the production of the depressor reaction. Despite the results showing a lowering of the tone of the blood vessels of the spleen, small intestine, and kidneys, the exclusion of these organs from the general circulation, whether successively or simultaneously, did not abolish the depressor reaction of the arterial pressure to stimulation of the pericardial chemoreceptors. Not even after the successive exclusion of the vascular regions of the femoral, iliac, renal, mesenteric, splenic, subclavian, and carotid arteries in the same experiment was the depressor effect abolished. Only after partial exclusion of the lungs from the general circulation was there a marked decrease in the magnitude of the depressor reaction. After exclusion of three-quarters of the total lung tissue this reaction of the arterial pressure almost disappeared (Fig. 1). Because hemodynamic disturbances could sometimes be observed in these experimental conditions, the problem of the part played by the pulmonary vessels in the lowering of the arterial pressure in response to stimulation of the pericardial chemoreceptors could only be solved by the application of different methods of investigation.

The results of experiments to determine the tone of the pulmonary vessels and to exclude the vascular fields of the lungs from the general circulation were slightly contradictory: on the one hand, no changes were observed in the tone of the pulmonary arteries during the depressor reaction of the blood pressure, and on the other hand the exclusion of three-quarters of the lungs from the general circulation almost completely abolished this reaction. An explanation must be sought in the changes in the velocity of the blood flow in the pulmonary vessels.

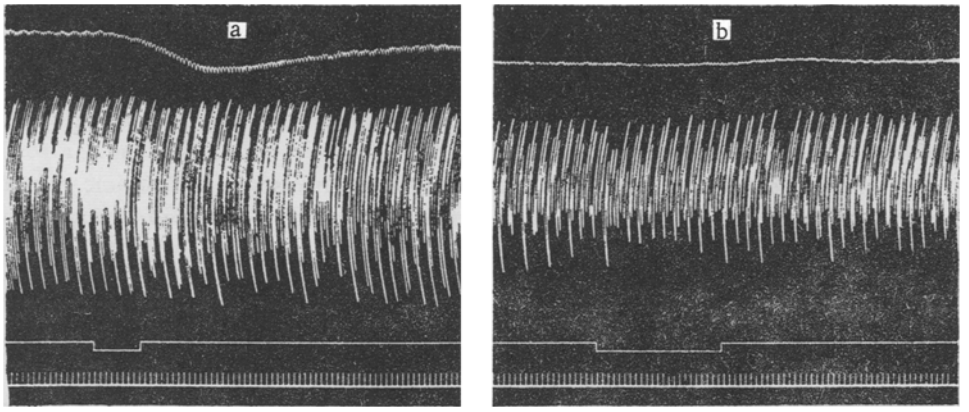

Fig. 1. Changes in the general arterial pressure and activity of the heart in response to stimulation of the pericardial chemoreceptors with nicotine (0.5 ml, 10^{-3}) before (a) and after (b) exclusion of three-quarters of the lungs from the general circulation. Significance of the curves (from top down): arterial pressure; strength of cardiac contractions; marker of introduction of stimulus; time marker (2 sec).

Recording of the volume velocity of the blood flow in the pulmonary arteries and veins showed that it began to fall before the change in the general level of the arterial pressure took place (Fig. 2). In the pulmonary arteries, on the other hand, the volume velocity of the blood flow either remained unchanged or was reduced, but this decrease was apparent immediately after the general arterial pressure had begun to fall.

Hence the experiments in which the lungs were excluded from the general circulation and the experiments in which the volume velocity of the blood flow in the pulmonary vessels was recorded showed that the pulmonary vessels are concerned in mechanisms of the depressor reaction of the arterial pressure. The character and the site of the changes in the velocity of the blood flow in the pulmonary vessels were evidence of the retention of blood by the lungs during stimulation of the pericardial chemoreceptors by nicotine, which explained the absence of changes in the tone of the pulmonary arteries. The pulmonary arteries are vessels of the elastic type; elastic elements may be seen to predominate in them up to arteries about 1 mm in diameter [13]. In the pulmonary veins, muscle elements predominate, and in the large veins the muscle fibers form thick muscle bundles. At the points of division of the venous trunks, the muscular and elastic layers are considerably thickened. The muscle fibers of the large veins pass directly into the wall of the left atrium [11, 16]. The small vessels of the lungs are much wider than the capillaries in other organs [3]. On account of these anatomical peculiarities, the pulmonary vessels, according to

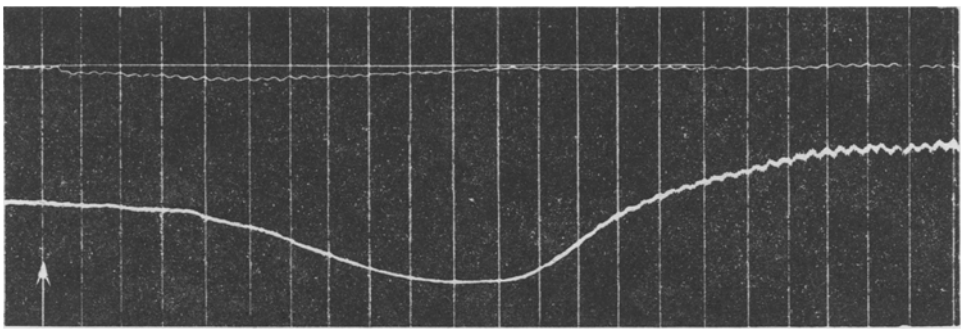

Fig. 2. Changes in the volume velocity of the blood flow in a pulmonary vein and the general arterial pressure during stimulation of the pericardial chemoreceptors with nicotine (0.5 ml, 10^{-3}). Significance of the curves (from top down): zero line; velocity of blood flow; arterial pressure; time marker (2 sec). The arrow marks the beginning of stimulation.

the literature, can accomodate 25% of the total blood volume without any change in the pressure in the pulmonary artery [12] and in the state of its tone [14, 15]. In our experiments we also observed no change in the tone of the pulmonary arteries. During the depressor reaction of the arterial pressure caused by stimulation of the pericardial receptors by nicotine solution, functional changes take place in the pulmonary veins, and the slowing of the blood flow in these vessels contributes to the retention of blood by the lungs.

In face of the results showing the importance of the pulmonary vessels in the depressor reaction of the general arterial pressure following the introduction of nicotine into the pericardial cavity, it was necessary to investigate the pathways of the reflex connections between the pericardium and the pulmonary vessels. In order to study the afferent pathways of this reflex, the pulmonary branches of the vagus nerve were divided bilaterally in the thorax below the origin of the cardiac branches. After division of these nerves the depressor reaction of the arterial pressure in response to stimulation of the pericardial receptors by nicotine was considerably diminished, and in some experiments it almost completely disappeared (Fig. 3). It follows from our experiments that the afferent pathway of the reflex from the pericardial receptors to the pulmonary vessels during the depressor reaction of the general arterial pressure lies in the vagus nerves, and that the latter contain vasodilator fibers of the pulmonary vessels. Despite statements to the contrary, we found similar reports in the literature [8].

Reports in the literature and our own findings indicate that the afferent pathways of the reflexes from the pericardial chemoreceptors lie in the vagus and depressor nerves, for blocking the pericardial receptors with novocaine, like division of the vagus and depressor nerves in the neck, abolishes the changes we have described in the general arterial pressure.

In addition to stimulating the pericardial receptors with nicotine solutions, we also conducted experiments in which acetylcholine was used for stimulation. A depressor reaction of the arterial pressure was also observed in these experiments, but the mechanism of the lowering of the arterial pressure was rather different in this case from that when nicotine was used. Denervation of the pulmonary vessels, like exclusion of the lungs from the general

circulation, in association with the introduction of acetylcholine solutions into the pericardial cavity, did not abolish the depressor reaction of the general arterial pressure.

It was found that the depressor reaction in these cases was related to both reflex and resorptive effects of acetylcholine on the pericardium. The reflex changes mainly affected the activity of the heart, and took the form of a slowing of the heart rate. Depending on the degree of excitability of the receptor apparatuses of the pericardium, the reflex reaction developed either at the moment of introduction of the acetylcholine or after the lapse of 3-4 sec after application of the stimulus. Preliminary injection of novocaine into the pericardial cavity abolished the reflex

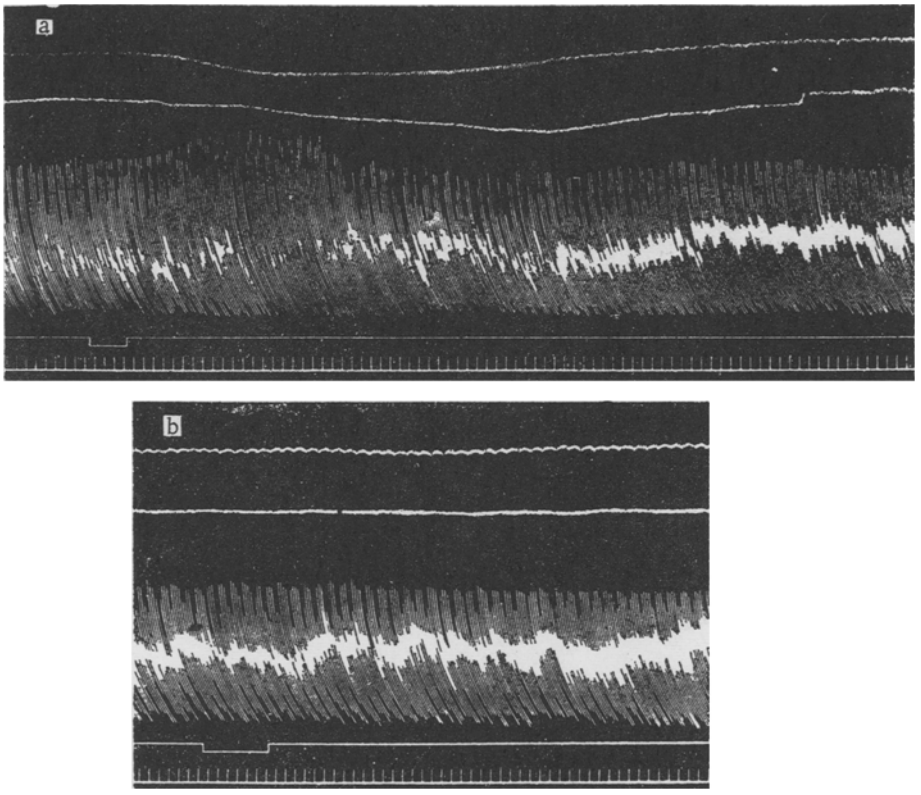

Fig. 3. Character of the changes in the general arterial pressure, the strength of the cardiac contractions, and the tone of the splenic vessels before (a) and after (b) division of the pulmonary branches of the vagus nerves. Significance of the curves as in Fig. 1. Second curve from the top—tone of the splenic vessels.

changes in cardiac activity in response to stimulation of the pericardial receptors, and the fall in the arterial pressure in this case was due entirely to resorptive influences, arising after a long latent period (12-20 sec). The resorptive action of acetylcholine was manifested as a lowering of the tone of the blood vessels of the striped muscles and the abdominal organs. Support for the view that a reflex link is concerned in the depressor reaction to introduction of acetylcholine into the pericardial cavity was given by experiments in which small doses of acetylcholine solutions were preliminarily injected into the general blood stream. Against this background the resorptive effects of the acetylcholine introduced into the pericardial cavity could not be demonstrated, and only the reflex changes in the activity of the heart took place.

It may thus be concluded from our experimental results that during stimulation of the pericardial chemoreceptors with nicotine solutions, the depressor reaction of the arterial pressure takes place with the direct participation of the heart (mainly by a slowing of the heart rate) and of the pulmonary vessels, in which the blood is retained. Although changes in the strength of the cardiac contractions and in the state of the vascular tone in other organs may develop in the course of this reaction, they are not essential to it. The afferent pathways for this reflex lie in the vagus nerve. The most marked reactions of the arterial pressure are observed when they are caused by simultaneous changes in the heart rate and the state of the pulmonary vessels.

The differences in the changes in the strength of the cardiac contractions in response to stimulation of the pericardial chemoreceptors by nicotine may be associated with differences in the level of excitability of the nervous apparatuses regulating the activity of the heart, as reported in the literature [1, 7].

During stimulation of the pericardial chemoreceptors by acetylcholine solutions, the depressor reaction of the arterial pressure is associated both with reflex influences (slowing of the heart rate) and with resorptive effects (a lowering of the tone of the peripheral vessels).

SUMMARY

Acute experiments were conducted on cats under urethane anesthesia. A study was made of the frequency and strength of cardiac contractions, as well as of the vascular resistance in various organs with nicotine and acetylcholine solutions acting upon the pericardial receptors. In depressor reaction occurring in response to the pericardial administration of nicotine, there always occurred a deceleration of the cardiac rhythm, whereas the strength of the cardiac contractions either diminished, increased or remained unchanged. A study of the vascular resistance of the posterior extremities, organs of the pelvis minor, kidneys, small intestine, spleen, lungs, neck and head demonstrated that reduced resistance was observed only in the vessels of the spleen, intestine and kidneys. However, the resistance changes in the mentioned organs were not always distinct and were even absent in a number of cases. Experiments with a temporary exclusion of various vascular areas from the general circulation demonstrated that the development of depressor reaction consequent upon the nicotine action, upon the pericardial receptors is connected with changes in the pulmonary vessels. There is deminished circulation rate in the venous vessels preceeding the arterial pressure reduction; as to the arteries the circulation rate remains unchanged or decreased after the arterial pressure shifts. The efferent route of this reflex passes in the vagus. With stimulation of the pericardial chemoreceptors by acetylcholine solutions depressor reaction is connected both with the reflex effects (decelerated cardiac rhythm) and the resorptive ones (reduction of peripheral resistance).

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