PHYSIOLOGY

THE EFFECT ON CARDIOVASCULAR REFLEXES OF STIMULATING PERICARDIAL RECEPTORS

COMMUNICATION IV. THE EFFECT OF FORCED RESPIRATION ON REFLEXES ORIGINATING FROM STIMULATION OF THE PERICARDIAL CHEMORECEPTORS

B. S. Kulaev

From the Laboratory of General Physiology (Head – Active Member of the AMN SSSR V. N. Chernigovskii) of the Institute of Normal and Pathological Physiology (Director – Active Member of the AMN SSSR V. N. Chernigovskii) AMN SSSR, Moscow

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It has been shown previously [7, 8] that in most experiments a weak chemical stimulation of the pericardial receptors causes tachycardia and increased arterial pressure; stronger stimulation causes bradycardia and a reduced blood pressure. There is always a hyperpnea, which increases in proportion to the strength of the stimulation. It has been suggested that the two opposite effects were performed by different rates of afferent impulses from the cardiac and bulbar centers [5, 7, 8]. After denervation of the sinocarotid zone, both strong and weak chemical stimulation of the pericardial receptors caused only a constriction of the blood vessels, while the heart itself continued to give the two reactions as before [9]. It may be concluded that the regulatory effect on the heart is determined by the number of impulses reaching it at any one time [15, 18], whereas the vascular reaction is determined in the vasomotor center by either excitation or inhibition of the efferent elements by afferent impulses arriving at a high rate. In order to confirm this suggestion, it was important to develop an experiment on a cat which would allow increased afferent stimulation of the bulbar centers, so that any stimulation, even a weak one, applied to the pericardium would bring about only a depressor reaction, as was observed in rabbits [16, 17].

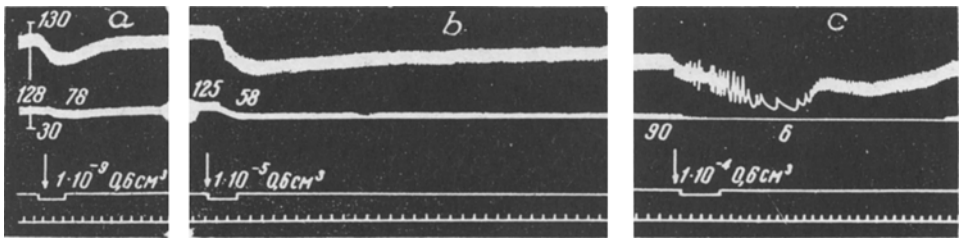

Fig. 1. Reduction in arterial pressure and bradycardia in response to stimulation of the pericardial receptors with different concentrations of nicotine. Cat. Urethane. Forced respiration. Value of the curves, from above downwards: pressure in the carotid artery (mercury manometer), ditto (membrane manometer), stimulus marker (⊕– application of nicotine), time marker (5 seconds); a) reflex induced by injection of 0.6 ml of $1 \cdot 10^{-9}$ nicotine solution; b) ditto, 0.6 ml of $1 \cdot 10^{-5}$ nicotine; c) ditto, 0.6 ml of $1 \cdot 10^{-4}$ nicotine. Figures above the membrane manometer trace indicate heartbeats per minute.

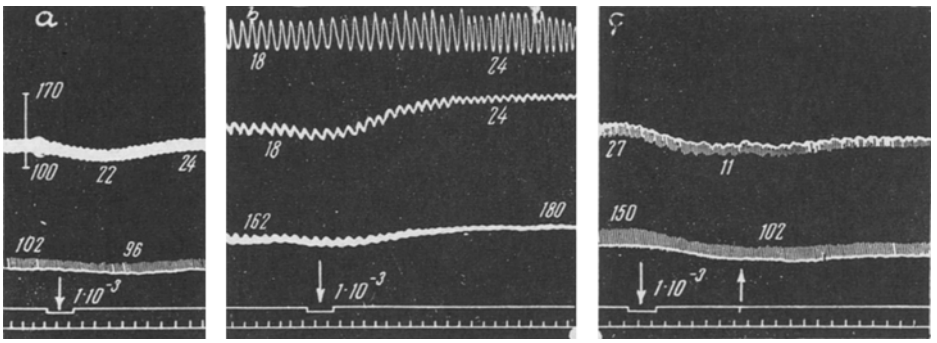

Fig. 2. Cardiovascular changes induced by stimulation of the pericardial receptors with $1 \cdot 10^{-3}$ nicotine solution. a) forced respiration, b) natural respiration, and c) forced respiration resumed; ↓— nicotine washed out. Curves, from above downwards, for a and c: pressure in carotid artery (mercury manometer); ditto (membrane manometer), stimulus marker, time marker (5 seconds); for b) uppermost curve — respiration, figures below the curve of arterial pressure indicate the number of arterial pressure waves of the second order per minute.

We have succeeded in developing just such an experiment on cats, by using artificial respiration which must evidently induce powerful stimulation of the mechanoreceptors of the lungs.

Afferent effects from the lungs on the cardiovascular system have been investigated repeatedly. Weak electrical stimulation of the pulmonary branches of the vagus nerves induces tachycardia and raises the arterial pressure [19, 29, 30], whereas strong stimulation causes bradycardia and a reduced blood pressure [19, 21, 30]; a small increase in the inspired volume of the lungs causes tachycardia and increased arterial pressure, while a greater increase causes bradycardia and a reduced blood pressure [19, 27, 30, 31]. Reducing the pressure in the pulmonary vessels causes tachycardia and a pressor reaction, while increasing it causes bradycardia and a fall in blood pressure [10, 11, 20, 22, 32]. Weak chemical stimulation of the mediastinal pleura, where the receptors are most concentrated than in any other portion of the respiratory system [14, 28], causes tachycardia, raised blood pressure, and hyperpnea, while weak stimulation causes bradycardia, reduced blood pressure, and inhibition of respiration [4].

The afferent pathways of all these reflexes and the efferent routes of cardiac and pulmonary reflexes run through the vagi and have their center in the medulla, while the efferent pathways of the vasomotor reactions run in the sympathetic system. This means that reflex effects from the lungs on the cardiovascular system are closely related both functionally and morphologically to reflexes from the pericardium and sinocarotid zone. It might be possible, therefore, that the conditions of the vasomotor center might be considerably modified by changing the rate of flow of afferent pulmonary impulses.

In all, 60 experiments were carried out.

The method of investigation was described in part I of this series [7].

RESULTS

In all experiments in which forced ventilation of the lungs was used, application of nicotine to the pericardial receptors caused only a depressor reaction and bradycardia, whatever the concentration (Fig. 1, a, b, c).

The transition from the pressor reaction with natural breathing [5, 7, 12] to the exclusively depressor reaction with artificial respiration takes place very rapidly. Fig. 2 shows the effect of three successive stimulations with $1 \cdot 10^{-3}$ nicotine solution applied at different time intervals. The first and third stimuli were applied during forced respiration, and caused a depressor reaction and bradycardia (Fig. 2, a, c); the second stimulation, applied between the first and the third, during the interval with natural respiration, caused a pressor reaction and tachycardia (Fig. 2, b).

In cases when animals with previous denervation of the carotid sinus were transferred to artificial respiration, and when only very intense pressor reactions were observed [9], the transition lasted somewhat longer, and it was possible to observe the intermediate stages. These can be seen in Fig. 3, where a series of kymograms from such an experiment are shown.

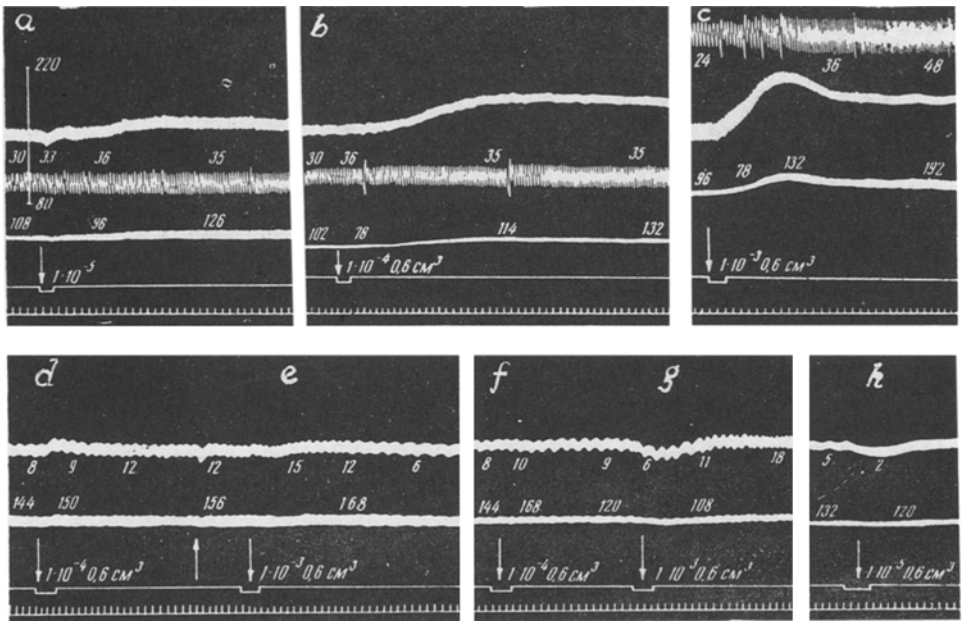

Fig. 3. Changes in the cardiovascular reactions in response to stimulation of the pericardium with various concentrations of nicotine during transition from natural (a, b, c) to forced respiration (2-3) in an animal with previous denervation of the sinocarotid reflexogenous zone. Curves, from above downwards, for a and b: arterial pressure in carotid artery (mercury manometer), respiration, arterial pressure (membrane manometer), stimulus marker (↓ –injection of nicotine), time marker (5 seconds), for c – respiration, arterial pressure in carotid artery (mercury manometer), ditto (membrane manometer), stimulus marker (↓ – injection of nicotine), time marker (5 seconds), for d, e, f, g, h curves as in Fig. 2,c.

This transition from pressor to depressor reactions can be observed also in animals with intact carotid sinuses, but in this case the transition occurs much more quickly, and the depressor reaction and bradycardia are very marked.

It is important to note one typical phenomenon shown very clearly in Figs. 2 and 3. Immediately after the transition to forced respiration, second order blood pressure waves scarcely differing from those due to natural respiration can be clearly seen. In some experiments, at low natural rates of respiration (18 per minute) these second order waves were more frequent and smaller in amplitude than those recorded with natural respiration (Fig. 2), while in other experiments when the natural breathing rate was higher (30 per minute), the waves were smaller in amplitude and lower in frequency (Fig. 3). However, in both cases the waves did not coincide with the rhythm of the forced respiration, but had their own rhythm which evidently reflected the activity of the respiratory center as affected by pericardial stimulation: the frequency increased in the first few minutes after the onset of forced respiration (see Fig. 3, d, e), it was slowed subsequently (see Fig. 2, a, c and Fig. 3, h), and at the intermediate stages it was increased in response to weak and reduced in response to strong stimulation (Fig. 3, f, g). During this time, the rate of forced respiration was kept constant. With natural respiration, chemical stimulation of the pericardial receptors caused only an increase in the rate of respiration [5, 7] and an increase in the second order waves (Fig. 2, b).

In experiments in which action potentials from the vagus were recorded on a cathode ray oscillograph, we succeeded in showing that the discharge rats from the lungs increases several fold, and that the increased frequency is maintained during forced breathing. The increased rate of flow of impulses following reflex hyperpnea during natural breathing did not as a rule reach such a high value.

Our experiments have shown that cats in whom artificial respiration was applied represent the opposite model to that which we obtained with previous denervation of the sinocarotid zone. Those in whom forced respiration was applied showed a considerable increase in the flow of afferent impulses in the vagi, as well as depressor reactions and bradycardia in response to pericardial chemical stimulation at all intensities.

The possibility that the changed gaseous constitution of the blood might have some effect on the reactions has been discussed [2], and was convincingly refuted by I. de Burg Daly and M. Scott [23]. However, these authors

did not take into account the fact that stabilization of impulses from the lungs by forced respiration is the result of increasing the rate to a value higher than that which occurs in reflex hyperpnea and maintaining it for a longer period. It is percisely these afferent impulses which in our experiments brought about the controlled condition of the bulbar and cardiac centers which enabled any cardiac receptor stimulation to cause a fall in blood pressure, bradycardia, and inhibition of the respiratory center (insofar as the latter could be inferred from reduction in the frequency of the second order waves). Reflex hyperpnea during natural respiration cannot, according to our results, be considered to be a certain cause of a secondary reflex tachycardia, because strong stimulation evoked both hyperpnea and bradycardia; evidently, the same thing occurs on stimulation of the carotid chemoreceptors [3].

Stimulation of the carotid chemoreceptors by hypoxia during natural respiration as a rule brings about the same changes as does stimulating them with low concentrations of drugs [1, 3, 26], whereas high concentrations of drugs cause a high rate of afferent impulsation, a far greater hyperpnea, bradycardia, and a reduction of arterial pressure [3]. Therefore, the relationship between the cardiac reaction and the intensity of reflex hyperpnea as demonstrated by I. de Burg Daly and M. Scott is valid only for the weakest stimulation of the carotid chemoreceptors, and corresponds to what was found by W. Douglas and has co-workers [24, 25], during the transition from weak to moderate electrical stimulation of the sinocarotid nerves; however, it does not apply to stronger pharmacological action on the chemoreceptors [3] or to strong electrical stimulation of the sinus nerves [24, 25].

In studying the reflex effects on heart rate of electrical stimulation of the branchial nerves in fish [6], we have found that weak stimulation of any branchial nerve causes tachycardia, and a stronger stimulation, bradycardia. Simultaneous stimulation of any two of these nerves causes a bradycardia even when stimulation of either of them separately at the same intensity caused a tachycardia. Similar results were obtained by M. G. Udel'nov and his co-workers [15, 18] on frogs by stimulating different afferent nerves and reflexogenous zones. They showed that the involvement of a comparatively small number of vagus fibers supplying the heart causes tachycardia and that bradycardia results when a large number of fibers are involved.

I. de Burg Daly and M. Scott [23] imitated hyperpnea by an extremely high rate of forced respiration; they induced what was evidently a partial inhibition of the bulbar vagal centers, so causing a tachycardia.

Increase of afferent impulses from the lungs during forced breathing causes a fall in arterial pressure to occur in response to any chemical stimulation of the pericardial receptors, and this results not only from a bradycardia, but also from an inhibition of the vasomotor center through summation of the afferent effects from both lungs and heart.

The changes which we have found in the second order arterial pressure waves indicate that the same process applies to respiratory regulation. The bradycardia, reduction in arterial pressure, and apnea, form what is known as the Betsol'd-Yarish triad, which from our results, should be regarded as the result of summation in the bulbar centers of the increased flow impulses from the thoracic receptors, and should not be attributed to specific depressor influences.

Thus, at a certain optimal level of the combined afferent inflow, weak stimulation of the caridac receptors causes an increased arterial pressure and tachycardia, while a strong stimulation causes a fall in pressure and bradycardia. Reduction of the general afferent inflow level through a reduction of the contribution of any of the thoracic reflexogenous zones causes an increase in arterial pressure and has the effect that any stimulation of the cardic receptors will produce only pressor reactions. Increase in the afferent flow rate will produce the opposite effect.

SUMMARY

Acute experiments were performed on cats with the employment of artificial respiration. In these animals the chemical stimulation of pericardial receptors provoke only depressor reactions of the arterial blood pressure, bradycardia and inhibition of waves of the second order.

The pressor reactions reappear after the restoration of natural respiration. Such relations are also observed in animals with previously denervated sinocarotid zones.

Proofs are given of the fact that the depressor reaction and bradycardia during artificial respiration are due to the increased flow of pulmonary afferent impulses.

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*In Russian.

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