EFFECT OF TONE OF THE VAGUS NERVE ON MOLECULAR ORGANIZATION OF THE MYOCARDIAL SARCOPLASM

A. A. Gurvich and V. F. Eremeev

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Spectra of mitogenetic radiation of the rabbit's heart studied experimentally in vivo show that an unbalanced molecular organization is specific for the sarcoplasm of its fibers. An increase in vagal tone increases the degree of orderliness. This phenomenon is regarded as the first stage of the action of the vagus nerve on structures of the heart.

The results of previous investigations of the spectra of mitogenetic radiation of skeletal muscles and heart muscle in experiments in vivo show that a highly labile molecular organization, maintained by the energy of metabolism, i.e., an unbalanced molecular organization, is specific for the sarcoplasm [1-4]. However, the degree of orderliness, i.e., predominance of an organized or, on the contrary, a disorganized state, like the character of the organization, evidently varies depending on the functional state of the muscle systems. This is seen especially clearly if spectra of radiation of the heart under normal conditions and after partial destruction of its innervation are compared. At the same time, individual variations in the spectra of different animals are also observed in a physiologically normal state, i.e., when the normal innervation is preserved and no external factors are acting. However, comparison of all the findings shows that, despite their variability, discrete types of spectra can be distinguished, and it is accordingly possible to speak of different types of organization of the molecular substrate. In the normal state, the myocardium is characterized by bands of average width, indicating a definite orderliness of the substrate. However, this orderliness is not maximal, but is capable of being increased.

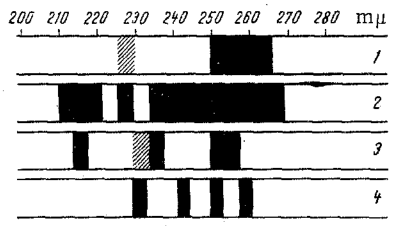

Fig. 1. Spectra of radiation of rabbit's heart during electrical stimulation of vagus nerve at different strengths: 1) nerve on electrodes, no stimulation; 2) stimulation: 0.5 V (subthreshold), 40 Hz, 1 msec; 3) stimulation: 1 V (threshold), 40 Hz, 1 msec; 4) stimulation: 1.5 V (abovethreshold), 40 Hz, 1 msec.

The predominance of narrow bands, indicating a low degree of molecular orderliness, is typical of the substrate of the myocardium after spinal and, in particular, vagal deafferentation [5,6]. The presence of wide bands, i.e., a high level of orderliness, is found when the tone of the nervous centers, especially centers of vagal innervation, is raised. Hence the need for the investigation described below.

It must be emphasized at once that the concept of width of the band is somewhat conventional, because a wide band most probably means the grouping together of a large number of narrow bands, whereas the narrower band means grouping of fewer narrow bands. However, from the manner in which this parameter of the spectra is seen to depend on the character of the agents used, the full meaning of this not absolutely exact term will be clear.

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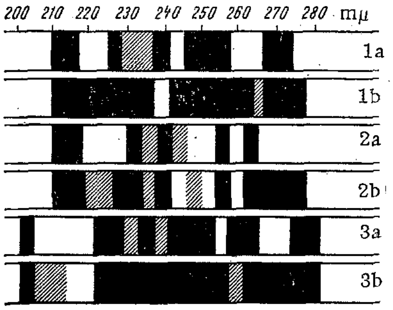

Fig. 2

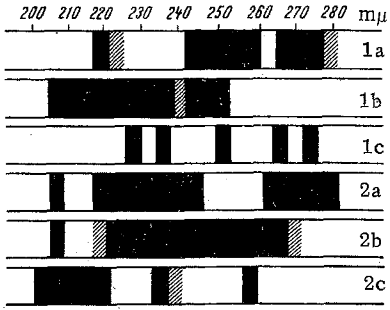

Fig. 3

Fig. 2. Spectra of radiation from heart of three rabbits during electrical stimulation of nerve: 1a, 2a, 3a) nerve on electrodes without stimulation; 1b, 2b, 3b) stimulation: 0.5 V (subthreshold), 40 Hz, 1 msec.

Fig. 3. Emission spectra of heart of two rabbits during mechanical and temperature stimulation of nerve: 1a, 2a) nerve on ligature at normal temperature; 1b, 2b) nerve slightly stretched, normal temperature; 1c, 2c) same degree of stretching of nerve, cooling to 10°.

EXPERIMENTAL METHOD

Experiments were carried out on unanesthetized rabbits. A small segment of the vagus nerve (right or left) was exposed in the neck, and under artificial respiration the thorax was opened from the side and part of the pericardium removed opposite the apex of the heart. By gentle traction on the edge of the pericardium the heart was centered with the apex of the left ventricle in front of the slit of a quartz spectrograph, and throughout the experiment it was periodically moistened with warm physiological saline. The surrounding tissues were screened. Biological detectors of mitogenetic radiation (a yeast culture on solid nutrient medium) were placed in front of the outlet slit of the spectrograph during the exposure.

EXPERIMENTAL RESULTS

The spectra were studied during electrical stimulation of the vagus nerve and during slight stretching of the nerve produced by a glass tube placed underneath it. In addition, spectra of the heart were recorded in the absence of stimulation of the nerve.

In one of the first series of experiments, the relationship between the character of the spectra and the intensity of electrical stimulation was established. Clear widening of the bands compared with their normal width for the particular rabbit was obtained in response to subthreshold stimulation (0.5 V; Fig. 1). Stronger, but still subthreshold stimulation (1 V) caused the appearance of several narrower than normal bands. Above-threshold stimulation (1.3-1.5 V), causing slowing of the heart or even its arrest, was associated with still further narrowing of the bands.

This series of measurements is interesting because an increase in the degree of orderliness is specific for the primary change in the substrate. The sharp change ("inflection") in the process occurring during stronger stimulation is probably connected with the rapid onset of secondary processes. Further experiments were therefore undertaken with weak subthreshold stimulation of the vagus nerve (Fig. 2). The marked widening of the spectral bands under these circumstances is obvious, despite individual differences between the control spectra.

The spectra of radiation of the heart during stretching of the vagus nerve were recorded both when the temperature of the nerve was normal and during its cooling to 10°C (cold water was passed through the tube; Fig. 3). Stretching the nerve while it remained at the normal temperature led to the appearance of wide bands corresponding in width to the bands obtained during subthreshold electrical stimulation. Cooling of the nerve was associated with the appearance of a series of much narrower bands in the emission spectrum of the heart.

These results supplement those obtained previously [4] and provide a firm basis for the concept of different types of spectra and an increase in the orderly state of the molecular substrate of the sarcoplasm with an increase in tone of the vagus nerve. From the point of view of molecular processes, the concept of continuity of the transition from neuroplasm to sarcoplasm must therefore be introduced.

Some observations can now be made regarding the connection between the phenomena described above and electrophysiological and biochemical data [7, 8]. In the first place, stimulation of the nerve brings about the liberation of acetylcholine from its bound state, and free acetylcholine is a substance which reacts unusually rapidly with specific enzymically active protein. In other words, the acetylcholine appearing through structural changes in the substrate in turn induces structural (evidently conformational) changes in some specific proteins. Under these circumstances, as recent work has shown, the action of acetylcholine is not confined to synaptic junctions, but it is also an essential link in the mechanism of change of permeability of cell membranes, both surface and intracellular. This mechanism, moreover, operates rapidly and reversibly. One of the first stages in the action of acetylcholine is its combination with receptor protein, present in the membrane, and this is followed by the development of conformational changes in part of the membrane. The increase in membrane permeability to ions and the increase in electrical activity thus arising are evidently secondary processes. From the writers' point of view, it is the leading role of structural changes in these processes which is of the greatest interest. That is why a connection must be sought between phenomena discovered by different methods and studied from different points of view. It follows from the foregoing description that the main general conclusion to be reached is that the physiological "background" of the nervous and muscular systems is unquestionably associated with the continuous formation of labile (disturbed and restored) molecular orderliness, which increases or decreases depending on the character of the forces applied. As was mentioned at the beginning, there is evidence to show that the labile orderliness of the neuroplasm and sarcoplasm must be described as unbalanced. Unbalanced molecular constellations are supported by the energy of metabolism and, because of this, are maintained at a raised energy level. Orderliness of excited molecules, creating systems of common energy levels, despite its dynamic character, must facilitate the spread of states which arise locally. It is in this way that the reaction of the substrate of heart muscle fibers to changes in the state of the nervous system innervating the heart, as mentioned above,* must be regarded.

On the basis of the foregoing account, the following hypothesis appears likely. Weak electrostatic interactions, similar to the interaction between acetylcholine and specific proteins, are established between molecules of active acetylcholine arising through stimulation of the nerve and structural elements of the substrate. These interactions cause the constellations to be combined into more general systems of common energy levels. The continuously maintained unbalanced molecular organization gives this process its chain character, leading to an increase in orderliness in the heart muscle. This increase in orderliness, associated with an undoubted reorientation of elements in the organized systems, leads to conformational changes in the more stable membrane structures. However, the rapid development of secondary processes, inducing reactions of the contractile elements, takes place only with an increase in the strength of stimulation.

It can be concluded from the essence of these remarks that the first result of stimulation of the vagus nerve is an increase in molecular orderliness in the nerve and in the myocardium. Weaker but constant tone of the vagus nerve in the absence of stimulation is perhaps responsible for the initial and continuous formation of the molecular organization. It is also probable that unbalanced molecular orderliness is essential for the regulation of metabolism and, in particular, it may play a decisive role in the more economic utilization of the energy of oxidative processes in the myocardium during an increase in tone of the vagus nerve.

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*Changes in the emission spectrum of the heart during cooling of a nerve, leading to reversible disturbance of the molecular orderliness of the neuroplasm, spreading to the sarcoplasm, must be regarded from the same point of view.