ADAPTATION OF THE HEART TO PROLONGED STIMULATION OF THE SYMPATHETIC NERVES

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The heart may adapt itself to prolonged stimulation of either the sympathetic or the parasympathetic nervous system. Adaptation of the heart to prolonged nervous stimulation, especially sympathetic, has received little study. Work already carried out has demonstrated the short duration of the inotropic reaction of the heart to sympathetic stimulation, not exceeding 3-5 min [7]. Adaptation of the blood pressure and heart rate during reflex reactions has been studied by other authors [16, 20, 23]. Several investigations have been concerned with the adaptation of the heart to prolonged application of such factors as an increase in intracardial pressure or the action of sympathetic agents [3, 5, 9, 19, 24]. There are also reports that during adaptation of the frog's heart, a periodic replacement of the sympathetic effect by an inhibitory effect may be observed [12].

The object of the present investigation was to examine the role of the heart itself in the process of adaptation, the dynamics of the sympathetic effect on the heart, and also the relationship between the positive inotropic and chronotropic effects during stimulation of the sympathetic nerve.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on frogs (Rana ridibunda). The heart was isolated together with the medulla and the anterior portion of the spine on which the sympathetic chains of both sides lie, and was perfused with Ringer's solution by Straube's method. To obtain a sympathetic effect, the sympathetic chain was stimulated with platinum electrodes at the level of the second and third ganglia. Contractions of the heart were recorded by means of a light lever and an ink-writing device. The frequency of stimulation was constant (30 per sec), a rate considered to be optimal for stimulation of the sympathetic nerve [2, 4, 18], and the strength of the current was over threshold.

The results of 65 experiments (240 observations) were analyzed. During their analysis a difference was found in the adapatation of the positive inotropic and chronotropic effects, so that the data for each will be given separately.

In all cases in response to stimulation of the sympathetic nerve the heart reacted by a positive inotropic effect, and the increase in the amplitude of the contractions sometimes reached 400% by comparison with the initial level. During prolonged stimulation of the sympathetic nerve the reaction of the heart consisted of several phases: after a definite latent period (up to 40 sec) the cardiac contractions gradually increased in strength. The maximal inotropic effect lasted from 2 to 5 min. Later, despite continuing stimulation, the amplitude gradually fell. In these experiments complete adaptation, assessed from the inotropic effect of the heart, took place on the average after 30 min. Often the amplitude of these contractions did not return to normal even after 30 min. It was completely restored only after stimulation of the nerve was discontinued. A typical result of these experiments is shown in the figure, from which it can be seen that after a short latent period (5 sec), the amplitude of the cardiac contractions increased. The maximal effect (250%) persisted for 2 min, after which the amplitude gradually decreased, without reaching its initial level even after 30 min. After stimulation had been discontinued the amplitude of the contractions was restored, but before this, frequently it was below the initial level.

The result of some experiments showed that the inotropic effect on the heart during stimulation of the sympathetic nerve sometimes persisted for 112 min or more. In addition, the reaction of the heart to stimulation of the sympathetic nerve and the period of adaptation assessed from the inotropic effect were unequal in the same experiment, even though all the conditions remained identical throughout: during the first stimulation the positive inotropic reaction lasted longer than during the second, third, and subsequent stimulations.

In 32 experiments the effect of a stimulus of increasing strength (up to two or three times threshold strength) on the amplitude of the reaction of the heart and the duration of the adaptation time was studied. Results showed

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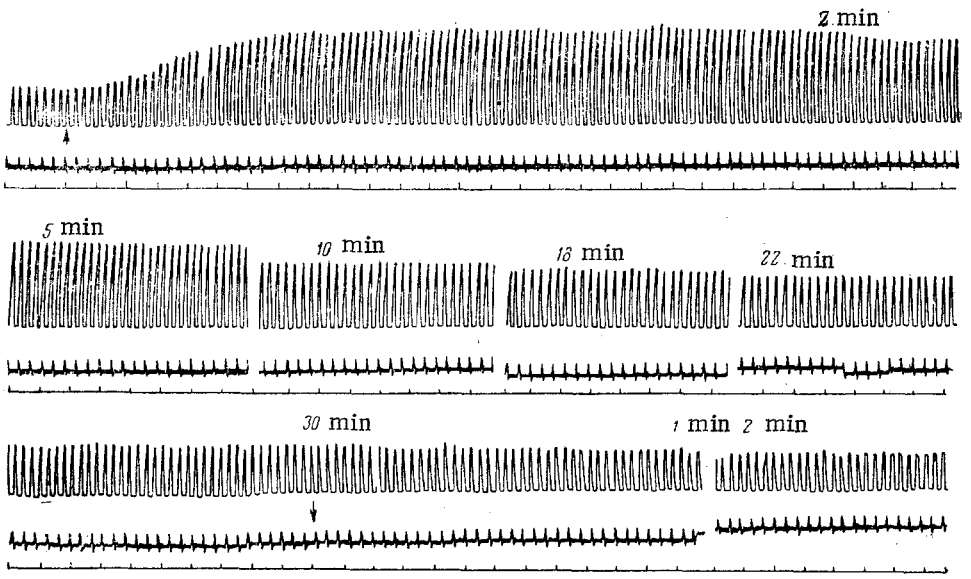

Adaptation of the heart during prolonged stimulation of the sympathetic nerve (experiment No. 50). Mechanogram of the heart. ↑↓ —beginning and end of stimulation; time marker—2 secs; strength of current—twice threshold.

that in these circumstances the inotropic effect was intensified and the period of adaptation lengthened. Consequently, the degree and duration of the effect dependend on the strength of stimulation.

The strength of the cardiac contractions was restored during prolonged stimulation of the sympathetic nerve and also by the destruction of the whole central nervous system of the frog, but in that case the positive inotropic reaction was approximately 40% stronger.

In 50% of cases the heart reacted to stimulation of the sympathetic nerve simultaneously by an increase in the amplitude of the contractions and in the frequency of the rhythm, the mean value of which was 5 beats/min. The results of these experiments showed that the chronotropic effect does not develop in phase with the inotropic. It begins before the latter and may persist unchanged until stimulation ceases. The time of persistance of the chronotropic effect was the same as that of the inotropic effect. After stimulation had been discontinued the rhythm returned to normal, but before this the rhythm was often slower than initially. In this respect, the results are in agreement with those obtained by other authors [16, 20, 23] studying the adaptation of the blood pressure during prolonged stimulation of the interoceptive zones and the afferent nerves. Similar phenomena are known in physiology as the "rebound" reactions or Sechenov's reactions [21].

The magnitude of the positive chronotropic effects depended on the original rhythm. With a slow original rhythm, stimulation of the sympathetic nerve caused a more marked increase in its rate.

As mentioned above, the frog's heart adapts itself to prolonged stimulation of the sympathetic nerve even after destruction of its connections with the central nervous system. This means that the principal processes responsible for the adaptation of the heart are localized in the heart itself, where complex neuro-humoral mechanisms are present.

The snail's heart, which possesses no intracardial nervous apparatus, is known to be incapable of adaptation when its connections with the central nervous system are severed [5, 9, 24]. Consequently, the ganglia situated in the walls of the heart are evidently peripheral reflex centers. This is shown by results demonstrating the snyaptic connections of the peripheral ganglia both with preganglionic nerve fibers and with axons of the peripheral sensory neurons [11, 21, 22]. According to some observations, the motor part of this reflex arc is composed of cholinergic fibers which supply all parts of the heart [6]. Intramural reflex arcs have also been described for the intestine [8]. In other investigations, great importance has also been attached to the nervous apparatus of the internal organs [15], and of the heart itself [13] in the self-regulation of the activity of the organ. Because of these findings, it is suggested that the intracardial nervous apparatus evidently plays an important role in the process of adaptation of the heart, but in the intact organism it is certainly dependent on the central nervous system, because the results of the present experiment showed that, after destruction of the central nervous system, the influence of the sympathetic nervous system was strengthened.

Likewise, of course, the importance of humoral factors in the mechanism of adaptation, described originally by A. A. Ukhtomskii, cannot be ignored. Evidence has now been obtained of the liberation of an acetylcholine-like substance in the heart in response to the action of adrenalin or stimulation of the sympathetic nerve [3, 10]. It is also known that oxidation products of the sympathins depress the activity of the heart, and especially of those systems responsible for the positive inotropic effect [7]. The present results, showing that after stimulation of the sympathetic nervous system was discontinued the amplitude and rhythm of the cardiac contractions were sometimes diminished, confirms this statement.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.