IONO-HUMORAL INTERRELATIONS DURING THE APPEARANCE AND
DEVELOPMENT OF VAGAL INHIBITION OF THE HEART

COMMUNICATION III. CHANGES IN THE EFFECT OF THE VAGUS
NERVE WITH ATROPINIZATION OF THE HEART

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In spite of the fact that data exist in the literature on the change in the effect of stimulating the vagus
nerve on atropinized visceral organs, until now the idea of the exclusion of the effect of the vagus nerve
by means of atropine has been widespread in physiology.

In Communication I we set forth experimental data on the effect of atropine on a mechanogram and elec-
trogram of the heart. It was established that atropine increases and stabilizes the resting potential of the heart
muscle, and does not alter the form and duration of the monophasic action potentials. The data of the report
showed a change in the effect of acetylcholine on an atropinized heart; under these conditions acetylcholine
proved to be incapable of changing in the usual way the rate of the restored processes taking place in the heart
following depolarization of cellular structures. These data permitted us to suggest that atropine, stabilizing
the resting potential of the heart muscle, must first of all disturb the normal process of an increase in polarizi-
bility of cellular structures during stimulation of the vagus nerve. Proceeding from the experimental data and
the theoretical conclusions of M. G. Udchnov [2, 3], we assumed that under these conditions the greatest changes
will be observed in the chronotropic index of vagal inhibition of the heart.

The present communication is devoted to an examination of the forms of the manifestation of the effect of
the vagus nerve on an atropinized heart.

EXPERIMENTAL METHODS

The experiments were conducted during all seasons of the year on frog hearts isolated according to A. F.
Samoilov's method. The use of the A. F. Samoilov preparation (the heart on a Straub cannula and in a
circular perfusion system, connected with the frog's head by the vagosympathetic trunks) permitted stimulation
of the nucleus of the vagus nerve in the medulla oblongata and the cephalic sympathetic ganglion. This method
made it possible to obtain pure vagus and sympathetic effects during parallel perfusion of the isolated heart.
Stimulation was accomplished by means of movable needle electrodes joined with a Dubois-Reymond coil; the
voltage in the primary circuit was 4 v. Cardiac mechanograms and electrograms maintained simultaneous re-
cording (see Communication I).

Following the recording of 3-5 normal vagal effects on a heart perfused with Ringer solution, atropine was
introduced into the cannula, and at varied time intervals repeated stimuli were applied to the medulla oblonga-
gata.
EXPERIMENTAL RESULTS

In all of the experiments, following atropinization of the heart the effect of vagal inhibition was replaced by a marked sympathicomimetic effect. The change in vagal effect after the injection of atropine into the heart in a concentration of $10^{-6}$ can be seen in Figure 1 (I and II). The sympathicomimetic effect is manifested in an increase in the strength of contractions and in the speed of the rhythmic activity of the heart. This effect is highly stable; in the experiment cited, 14 subsequent stimulations gave identical results (Figure 1, II). After 40 minutes the atropine solution was replaced with Ringer's solution and stimulation of the medulla oblongata was once again accompanied by an inhibitory effect (Figure 1, III).

![Figure 1](image)

Fig. 1. The change in vagal effect under the influence of atropine ($10^{-6}$). Vagal effect in conjunction with stimulation of the medulla oblongata before and immediately after the action of atropine (I), 1 hour after the action of atropine and following washing out with Ringer's solution (II). Distance between inductor coils -12 cm. Duration of stimulation -10 seconds.

During the course of the experiments we were faced with the question of the nature of the sympathicomimetic effect. In Figure 2, a, Segment I shows the typical inhibitory effect of stimulation of the medulla oblongata; a small increase in the amplitude and strength of the contractions of the heart is apparent in the aftereffect. In spite of differential stimulation of the fibers of the vagus nerve, one could assume that after the introduction of atropine precisely this sympathetic aftereffect is strengthened. Segments II and III show the development of a stable sympathicomimetic effect during stimulation of the medulla oblongata after the introduction of atropine (in the given experiment 12 identical results were obtained). Figure 2, b shows the change in the effect of stimulation of the cephalic sympathetic ganglion after atropinization of the heart; the introduction of atropine reduces the sympathetic effect (this phenomenon was observed in all of the experiments). Figure 2, c completely eliminates the possibility that the participation of sympathetic fibers in the development of sympathicomimetic effects is a result of stimulation of the vagus nerve. This kymogram was obtained on a permanently desympathetized frog heart; even in this case stimulation of the medulla oblongata after the introduction of atropine was accompanied by a marked sympathicomimetic effect.

In studying the relationships of the inotropic and chronotropic properties of vagal inhibition during atropinization of the heart, we established that stimulation of the medulla oblongata immediately after injection of atropine in concentrations of $10^{-6} - 10^{-8}$ is accompanied by the development of a positive chronotropic effect; the negative inotropic effect disappears after a certain period of atropine influence. Thus atropine affects first of all the chronotropic index of vagal inhibition. This regularity was particularly well-marked in the experiments with continuous perfusion of the heart.

This continuous perfusion is effected by a Straub cannula with a side outlet; introduced into the cannula is a small funnel with a fine, almost capillary outlet which passes freely into the horn of the cannula. The small funnel is filled with Ringer's solution, which is continuously renewed by means of drops falling from a large funnel fastened above the cannula; the excess fluid exits from the side outlet of the cannula. If an active substance (atropine, for example) is introduced into the small funnel, it will at once begin to be washed out by new drops of Ringer's solution. In this manner one can observe the change in vagal effect as atropine is washed out of the heart.