ROLE OF ACETYLCHOLINE IN THE MECHANISM OF NERVOUS AUTOREGULATION OF THE HEART

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The action of acetylcholine (AC) in concentrations of 10^{-18} to 10^{-6} g/ml and of perfusion fluid taken from a donor heart at various times of development of vagal inhibition on ganglionic and synaptic transmission in the heart was studied. AC in low concentrations (10^{-18} to 10^{-16} g/ml) and the perfusion fluid taken during the first 5-10 sec after arrest of the donor heart were found to facilitate transmission in the ganglia. Higher concentrations of AC (10^{-10}-10^{-6} g/ml) and perfusion fluid taken 0.5-2 min after arrest of the donor heart inhibited the transmission of impulses. It is postulated that AC liberated in the heart during the development of vagal inhibition may play the role of humoral feedback factor and, by facilitating or inhibiting transmission in ganglionic synapses, may regulate their activity and lead to appropriate changes in the intensity of the parasympathetic effect of the heart.

Investigations have shown that the intramural nervous system of the heart plays an important role in organizing ultimate regulation of various aspects of cardiac function [1, 2, 4, 6]. Under certain conditions it can also function as an independent autoregulatory system [1, 3, 5]. There is reason to suppose that the intracardiac nervous system, as the intramural component of the extracardiac regulatory system, can change its state and its functional activity depending on the quantitative characteristics of preganglionic nervous influences. Its state and activity may perhaps also depend on intracardiac afferent and humoral factors coupled with the development of regulatory effects.

The effect of various concentrations of acetylcholine (AC) and of the perfusion fluid from a donor heart taken at various phases of development of vagal inhibition was investigated.

EXPERIMENTAL METHOD

Experiments were carried out on a preparation from the sinus region of the heart of Rana temporaria. The vago-sympathetic trunks approaching the ganglionic synaptic system in this region were dissected. The intracardiac nerves running along the atrial septum (the septal nerves) from the sinus ganglia also were mobilized.

Functional activity of the ganglionic structures of the intracardiac nervous system was judged from the parameters of the discharge arising in the septal nerve in response to stimulation of preganglionic fibers in the extracardiac part of the vago-sympathetic trunk. The extracardiac nerves were stimulated with square pulses at 2-4 Hz. Activity in the intracardiac nerve was recorded with bipolar electrodes and UBP2-03 amplifier on a loop oscillograph. Recordings were made before and after application of the perfusion fluid or AC solution in concentrations of 10^{-18} to 10^{-16} g/ml to the region of the sinus. The energies of the corresponding spike volleys recorded in the septal nerve were compared. The energy was measured as the total length of the oscillations of the volley and expressed in conventional units. The frequency, amplitude, and total duration of the volley were thereby automatically allowed for. Ringer's solution was applied to the region of the sinus in the control series.

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TABLE 1. Changes in Activity in Septal Nerve in Response to Stimulation of Vago-Sympathetic Trunk (in conventional units)

Series of experiment	$M \pm m$	n	P
Control	+0,01±0,32	33	
AC			
10^{-18}—10^{-16} g/ml	+3,1±1,0	27	<0,01
10^{-10}—10^{-6} g/ml	—3,3±1,1	29	<0,01
Perfusion fluid taken during vagal inhibition of donor heart			
At beginning of inhibition	+5,3±2,5	12	<0,05
Later	—5,2±0,9	63	<0,001

Note: Statistical analysis carried out by the difference method.

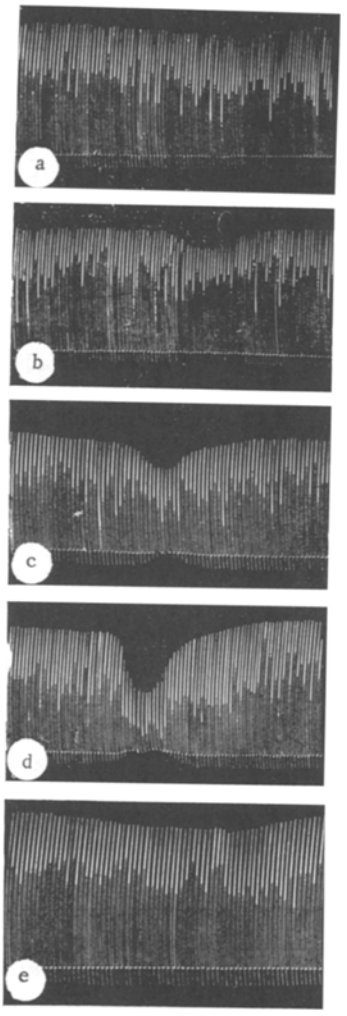

Fig. 1. Action of perfusion fluid taken from donor heart at different times after cardiac arrest on the recipient heart: a) action of perfusion fluid taken 5 sec after arrest of the donor heart; b) 50 sec; c) 1 min 10 sec; d) 2 min after arrest; e) action of AC in concentration of 10^{-12}g/ml.

EXPERIMENTAL RESULTS AND DISCUSSION

In the experiments of series I the effect of exogenous AC in different concentrations was studied. The results showed that, depending on the AC concentration, it could exert a directly opposite action on the effectiveness of transmission of excitation in the ganglionic synapses of the intracardiac nervous system: low concentrations of AC (10^{-18} to 10^{-16} g/ml) had a facilitatory action, but higher concentrations (10^{-10} to 10^{-6} g/ml) had an inhibitory action (Table 1).

The next series of experiments showed that perfusion fluid taken from the donor heart in the various phases of development of vagal inhibition had a definite action on the function of the ganglionic synapses of the recipient heart: perfusion fluid taken 30 sec or more after the beginning of vagal inhibition had an inhibitory effect, while perfusion fluid taken at the beginning of inhibition (5-10 sec) had a facilitatory effect (Table 1). The main active factor in the perfusion fluid was evidently AC. The dual character of the effects of the perfusion fluid can perhaps be explained by the accumulation of AC during the development of inhibition. As a result, perfusion fluid containing low concentrations of AC at the beginning of inhibition facilitated transmission, but the gradual increase in the AC concentration had the result that perfusion fluid taken later during inhibition began to have an inhibitory action. The AC concentration in the perfusion fluid taken at the various phases of inhibition was tested on another recipient heart isolated by Straub's method. These experiments showed that the longer the time elapsing after the beginning of inhibition of the heart before the perfusion fluid was taken, the greater the negative inotropic action of the perfusion fluid on the recipient heart (Fig. 1). In this series of experiments the hypothesis that AC accumulation in the perfusion fluid during the development of vagal inhibition was thus confirmed.

The results suggest that AC, appearing in the tissues and perfusion fluid of the heart in concentrations depending on the depth of the inhibitory effect, may act on the ganglionic synapses of the heart and modify their functional activity in either direction. The actual direction of these changes is evidently determined by the AC concentration applied. In this particular case AC thus plays the role of a unique feedback factor adapting extracardiac influences to suit the course of development of the regulatory act.

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