ROLE OF THE ACETYLCHOLINE – CHOLINESTERASE SYSTEM IN THE MECHANISM OF ADAPTATION OF THE DOG'S HEART TO SYMPATHETIC INFLUENCES

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During prolonged sympathetic stimulation of the dog's heart the acetylcholine (AC) concentration and cholinesterase activity in the blood are increased, returning to normal again 2-3 min after stimulation ceases. After vagotomy and in the presence of an AC deficiency caused by partial depancreatization, the time taken for cardiac activity to recover from prolonged stimulation of the sympathetic nerves was considerably lengthened. Compensatory injection of AC into these animals undergoing the operation helped to restore the normal values of these indices quicker.

The restoration of cardiac function after prolonged stimulation of the extracardiac nerves is a phenomenon of adaptation. The adaptation is more marked in rate and degree after sympathetic stimulation if the parasympathetic system is intact and the recovery of the inotropic function always takes place before recovery of the chronotropic function [5, 6].

This paper describes the results of an investigation of changes in the acetylcholine (AC) concentration and in the activities of pseudocholinesterase (PCE) and acetylcholinesterase (ACE) in the blood during prolonged stimulation of sympathetic nerves.

EXPERIMENTAL METHOD

Acute experiments were carried out on 38 adult dogs under morphine–hexobarbital anesthesia. Mechanical contractions of the left ventricle and the ECG in lead II were recorded. The sympathetic fibers were stimulated after leaving the node with square pulses (30 Hz, 1 msec) with a current not exceeding twice the threshold strength continuously for 5 min. Experiments were carried out with the vagus nerve intact, after vagotomy of the heart, and after partial depancreatization [2, 3]. Blood for analysis was taken initially, during sympathetic stimulation, and 3 min after the end of stimulation. Activity of the cholinesterases was determined by Hestrin's method [9] and the AC content by testing on the isolated frog lung by Corsten's method [8] in Khamitov's modification [7].

EXPERIMENTAL RESULTS

During prolonged stimulation of the sympathetic nerve with the vagus nerves intact (Table 1) complete recovery of the inotropic function was observed in 85% of experiments in about 2 min and the heart rate was restored by 50% in a period of about 3 min. Restoration of the strength of contractions to the initial level took place in the vagotomized heart in only 2 experiments in about 2 min, and the heart rate was not restored. In the experiments of series I, during stimulation of the sympathetic nerves the AC concentration in the blood rose significantly, as also did the PCE activity ($P < 0.05$); after stimulation had ceased these processes returned to normal. ACE activity in the blood did not change significantly during prolonged stimulation of the sympathetic nerve. Consequently, with the vagus nerves intact, AC plays an important role in the mechanism of adaptation of the heart for its concentration remained higher than the hydrolytic activity of the

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TABLE 1. Changes in AC Concentration and Cholinesterase Activity in the Blood during Prolonged Sympathetic Stimulation of the Heart (N ± m)

Experimental conditions	Number of animals	Positive inotropic effect (in percent)	Positive chronotropic effect (in percent)	Blood AC concentration (in g/ml)			PCE activity (in mg AC/ml/h)		
				initial	during adaptation	aftereffect	initial	during adaptation	aftereffect
Intact heart	27	210±15 $P<0,05$	167±7 $P<0,05$	$4 \cdot 10^{-9,6 \pm 0,6}$	$4 \cdot 10^{-8,1 \pm 0,6}$	$4 \cdot 10^{-9,1 \pm 0,7}$	5,25±0,6	6,7±0,7	5,9±0,7
After vagotomy	21	212±17 $P<0,05$	140±3 $P<0,05$	$4 \cdot 10^{-10 \pm 0,6}$	$4 \cdot 10^{-10 \pm 0,6}$	$4 \cdot 10^{-9,3 \pm 0,7}$	5,4±1,1	4,8±0,8	

cholinesterases. In the vagotomized heart, a slight increase in the AC concentration was found only after the end of stimulation (Table 1).

Extirpation of the greater part of the pancreas weakens the function of the cholinergic innervation of the heart [1, 4, 7] and disturbs AC synthesis. In the present experiments (11 animals), after incomplete depancreatization and prolonged stimulation of the sympathetic nerves for 5 min in no case was the inotropic function restored (mean positive inotropic effect 174%). The positive chronotropic effect in these experiments was well defined (78 ± 8 beats/min; $P < 0.05$), but the time taken for restoration of the heart rate also was significantly lengthened: it was restored by 36% in only 3 experiments. Injection of AC into depancreatized animals 1-2 h before the experiment largely restores the effect of the vagus nerve [3]. After intravenous injection of 2 ml (0.1 mg/kg) AC into the depancreatized animals 2 h before the experiment a significantly quicker recovery of the inotropic and chronotropic functions was observed: restoration of the amplitude of the cardiac contractions was observed in 75% of the experiments in a period of 1 min 18 sec, whereas the rhythm of contractions was restored in 45% of the experiments although the response of the heart to stimulation of the sympathetic nerve after compensatory injection of AC did not differ significantly from the control.

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