MORPHOLOGICAL AND FUNCTIONAL CRITERIA FOR THE CHOICE OF NERVES TO REINNERVATE THE TRANSPLANTED HEART

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During transplantation the heart loses its nervous connections with the CNS, which under ordinary conditions continuously monitors the actions of that organ [8]. The denervated heart, however, responds inadequately to functional loads, giving rise to myocardial damage [2, 11]. As yet, however, no technique of reinnervation of the donated heart has been developed. This is due, first, to the fact that despite numerous investigations into the innervation of the heart, the nerves approaching the organ directly have not been studied, nor has the effect of each of them on myocardial function been established.

The aim of this investigation was to discover, among all the cardiac nerves, groups of nerves capable of maintaining adequate activity of the heart under conditions of changing functional loads on the cardiovascular system.

EXPERIMENTAL METHOD

Two series of investigations were carried out. In series I the anatomy of the cardiac nerves was studied in cadavers of 25 dogs by combined macro- and microdissection. In series II, different cardiac nerves were divided in bilaterally thoracotomized dogs maintained on artificial respiration. In control experiments the cardiac nerves were isolated from the surrounding tissues but not injured. Next, in both experimental and control series, artificial respiration was stopped for 3 min and cardiac activity studied during and after asphyxia. The electrocardiogram and blood pressure (BP) in the femoral and subclavian arteries were recorded on a type MKh-01 monitor. The cardiac output (CO) was calculated by the usual methods [4]. The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

The experiments showed that nerves of the vagosympathetic and sympathetic trunks, and also branches of the vagus nerves joined together into plexuses, which formed the nerves that approach the heart directly. The largest of these nerves passed along the ascending aorta and pulmonary trunk to areas of the myocardium in the region of the coronary vessels. In addition, large precardiac nerves crossed the left pulmonary artery along the transitional fold of the pericardium, wound around the left caudal pulmonary vein, and emerged on the dorsal surfaces of the atria and ventricles of the heart. The remaining precardiac (extracardiac) nerves approached the atria (Fig. 1).

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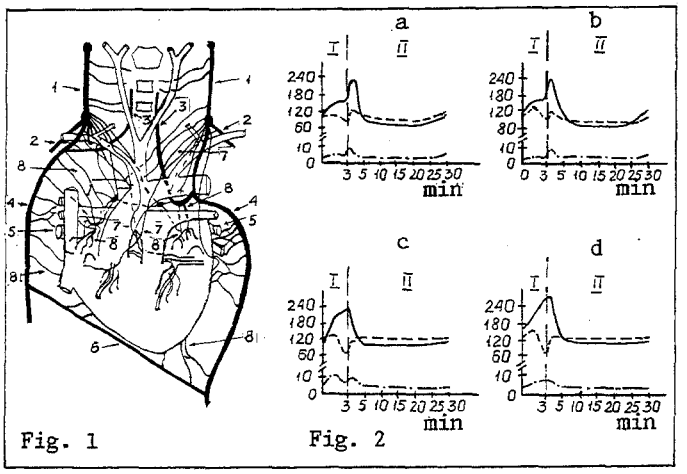

Fig. 1 Fig. 2

Fig. 1. Diagram showing arrangement of extracardiac nerves of a dog: 1) vago-sympathetic trunks; 2) sympathetic trunks; 3) recurrent laryngeal nerves; 4) vagus nerves; 5) caudal pulmonary veins; 6) branch connecting vagus nerves; 7) precardiac nerves running along ascending aorta and pulmonary trunk; 8) precardiac nerves approaching atria.

Fig. 2. Changes in hemodynamics during asphyxia in dogs with extracardiac nerves variously divided: a) all precardiac nerves divided; b) nerves running to heart along ascending aorta and pulmonary trunk, and also along transitional fold of pericardium to dorsal surface of heart divided; c) precardiac nerves approaching atria divided; d) normally innervated heart. I) Period of asphyxia, II) period after asphyxia. Continuous line represents BP. broken line HR, line of dots and dashes CO.

The experiments of series II showed that the heart rate (HR) of animals with undisturbed innervation of the heart rose by 19% at the first minute of axphyxia. It then gradually fell, and by the 3rd minute it was 56% of its initial value. The basic mechanism of compensation of heart failure is known to be slowing of the contractions and relaxation of the myocardium [5]. The bradycardia during prolonged asphyxia in the present experiments was probably due to a protective reaction of the body to myocardial hypoxia. Meanwhile, during asphyxia there was a sharp increase of both BP and CO. After restoration of breathing all parameters of the hemodynamics gradually decreased in magnitude and returned completely to normal after 3-5 min (Table 1).

In animals with a completely denervated heart, on the development of asphyxia HR did not increase, and by the 3rd minute it had fallen by only 19%. We know from data in the literature that during functional loads HR of the denervated heart usually does not increase [10]. The decrease in HR toward the 3rd minute of asphyxia was less marked than in the control, indicating disturbance of the adaptive mechanisms of work of the denervated heart, which, as previous investigations have shown, weakens its capacity for self-regulation [7].

Reactions to functional loads are known to be delayed in the denervated heart [9]. In our experiments we also noted that BP and CO increased during asphyxia more slowly in animals with a denervated heart than in the control.

TABLE 1. Changes in Parameters of Hemodynamics during Asphyxia in Dogs with Extracardiac Nerves Variously Divided

Parameter studied	Group of expt.	Background	Duration of asphyxia, min		Period after asphyxia, min			
			1	3	1	5	10	30
HR	a	110±5,8	110±6,1	89±4,3	139±4,8	119±5,8	105±4,4	117±6,4
	b	117±4,6	138±5,8	91±7,6	122±6,1	109±5,2	98±3,6	114±4,2
	c	121±4,8	145±5,6	67±4,2	122±6,8	123±4,8	128±4,3	122±5,2
	d	124±5,2	148±6,1	69±3,8	124±5,1	127±5,4	124±4,8	127±4,7
Systolic BP, mm Hg	a	113±8,9	147±9,6	152±11,6	240±12,7	100±5,2	87±6,4	106±7,2
	b	122±5,4	151±4,6	164±10,2	236±15,9	119±4,8	91±5,4	119±5,2
	c	112±4,6	176±5,6	238±6,4	214±11,2	108±6,8	110±5,2	116±5,6
	d	129±4,9	178±7,5	270±12,4	255±10,4	123±4,7	126±4,2	125±4,7
CO, liters/min	a	2,2±0,4	3,6±1,2	3,2±0,8	8,6±2,2	1,8±0,6	1,2±0,4	2,2±0,8
	b	2,1±0,4	3,9±0,6	3,5±0,8	7,5±0,5	1,6±0,2	0,9±0,3	1,9±0,3
	c	4,1±0,2	9,8±0,8	5,7±0,6	9,3±1,4	4,0±0,6	4,2±0,4	4,4±0,4
	d	3,8±0,2	4,8±0,3	5,8±0,4	5,2±0,4	3,8±0,6	3,8±0,8	3,8±0,8

Legend. a) All precardiac nerves divided; b) nerves running to heart along ascending aorta and pulmonary trunk, and also along transitional fold of pericardium on to dorsal surface of heart divided; c) precardiac nerves approaching atria divided; d) normally innervated heart.

After restoration of breathing in animals with a completely denervated heart HR, BP, and CO rose sharply (Fig. 2). In animals with an innervated heart this phenomenon was not observed. It can therefore be tentatively suggested that it was not due to the demands of the body. It was most probably associated with the fact that by this time myocardial hypoxia was abolished and the heart was able to react to stimulating substances which had accumulated in the blood. After division of nerves the peripheral segments of the divided nerve chain become more sensitive to mediators and, in particular, to adrenalin and noradrenalin [3, 6]. When self-regulation of the heart is disturbed, these substances can therefore lead to a sharp increase in contractile activity of the myocardium.

The uneconomic work of the denervated heart during and after asphyxia led to inhibition of its function toward the 10th minute of the recovery period and to lowering of the parameters of the hemodynamics below the background values. These parameters were not fully restored to normal until the 30th minute, i.e., 6-10 times slower than in the innervated heart.

Division only of those nerves which ran to the heart along the ascending aorta and pulmonary trunk, and also of nerves running toward the dorsal surface of the heart along the transitional fold of pericardium had the effect that during and after asphyxia the changes in the hemodynamics were similar to those observed in animals with a completely denervated heart. The exception was HR, which rose at the 1st minute of asphyxia from 117 ± 4.6 to 138 ± 5.8 ($p < 0.05$).

In cases when the above-mentioned nerves of the animals were left intact, but all extracardiac nerves approaching the atria were divided, parameters of the hemodynamics during and after asphyxia were modified, largely in the same way as in the animals with an innervated heart. The rise of HR in this and the previous experiments was evidence that different nerves are responsible for this function of the heart. Duplication of regulatory mechanisms is one of the main features of the architecture of physiological functions [1].

Hence, of all the nerves that approach the heart, the largest run along the ascending aorta and pulmonary trunk, and also along the transitional fold of the pericardium, along which they cross the left pulmonary artery along their way to the dorsal surface of the heart. These nerves can maintain adequate cardiac activity in response to an increase in functional loads on the cardiovascular system. It is probably these nerves that should be used in the first place for reinnervating the transplanted heart.

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