CONCENTRATION OF NUCLEIC ACIDS AND THEIR NUCLEOTIDE COMPOSITION IN VARIOUS AREAS OF THE DOG HEART WHEN EXTRACARDIAC PARASYMPATHETIC INFLUENCES ARE EXCLUDED

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A leading factor in the regulation of cardiac metabolism is the constant action of nerve impulses directed toward the heart by the extracardiac nervous system. The underlying mechanism of the diverse reactions of the heart to nervous activity apparently depends on minute processes of metabolism in the cardiac muscle and nerve tissue and also on changes in the form of their interaction. L. A. Orbeli [2] wrote of this mechanism: "The underlying mechanism of the nervous system influence should be viewed as a trophic one, which alters the fundamental physiological character of the tissue through basic changes in the physicochemical, colloidal, chemical, and physical make-up of the organ."

However, the question regarding the influence of the parasympathetic nervous system on cardiac muscle metabolism has been studied but little. The adaptational trophic effect of the parasympathetic nerves has been shown, in work by M. E. Raiskina [3] and by Raab [11] and others, to be manifested as a decrease in oxygen utilization by the cardiac muscle and also by increases in glycogen, creatinine phosphate, and the adenosine phosphates.

E. S. Troshanova [6] and V. A. Govyrin [1] and others have investigated the effect of vagus nerve severance upon the metabolism in the myocardium. They noted a marked decrease in glycogen content, and V. A. Govyrin also pointed out a decrease in ATPase activity in the tissue. Other workers established a clear decrease in the content of the contractile protein actomyosin after bilateral severance of the vagus nerve in the dog.

In consideration of the modern theory that nucleic acids carry out a decisive function in the protein synthetic mechanism, and considering also that the living animal constantly renews the cellular structures which provide the cell with nucleic acids and protein, we decided to study the changes which might occur in the nucleic acid concentration and in the nucleotide make-up of these substances during the very fundamental disturbance in physiological organization which takes place when the extracardiac parasympathetic influences are eliminated. We have found no reference to such work in the literature.

METHODS

The nucleic acid content and the nucleotide composition of the nucleic acids were investigated in different sections of the dog heart when the central parasympathetic effects were eliminated. To this end both branches of the vagus nerve in the neck were severed 4-5 cm below the sensory ganglion.

On the 4th day after operation the heart was removed from the ether-narcotized dog under artificial respiration, it was placed on ice quickly, repeatedly washed with cold physiological saline to remove blood completely, blotted dry with filter paper and then cut to separate the right and left ventricles and the right and left auricles. Individual measured samples were removed from each section of the heart and these were submitted to further treatment. All procedures described were carried out in the cold room at a temperature below 4°.

TABLE 1. Concentration of RNA and DNA Phosphorus in Various Sections of the Dog Heart after Bilateral Vagus Nerve Transection (in mg %)

Section of heart	RNA			DNA		
	normal	*P*	after transection	normal	*P*	after transection
Right ventricle	16,1 ± 0,34	< 0,05	15,7 ± 0,35	12,9 ± 0,29	< 0,02	12,4 ± 0,56
Left ventricle	19,4 ± 0,51	< 0,001	17,2 ± 0,32	14,7 ± 0,30	< 0,05	12,3 ± 0,17
Right auricle	14,7 ± 0,36	> 0,5	14,6 ± 0,53	11,8 ± 0,26	< 0,001	11,1 ± 0,42
Left auricle	13,3 ± 0,34	< 0,02	13,4 ± 0,51	10,9 ± 0,23	< 0,001	9,7 ± 0,42

The RNA and DNA contents were determined according to Schmidt and Thannhauser [14] using the spectrophotometer according to A. S. Spirin [4]. The results were expressed as milligrams percent of nucleic acid phosphorus. For determinations of nucleotide composition the method was used as described by A. S. Spirin and A. N. Belozerskii [4].

The RNA mononucleotides were separated by descending chromatography according to Magasanik and others [10]. The upper part of the paper containing guanylic and uridylic acids was cut out and submitted to ascending chromatography [17]. Chromatography of DNA was carried out in the Kirby [8] solvent. The spots were eluted and examined spectrophotometrically. The nucleotide contents were calculated by using the estimated coefficients given in the work by A. S. Spirin and A. N. Belozerskii [5]. The mononucleotides contained in RNA and the nitrogenous bases in DNA were expressed as mole percentages (the total moles of nucleotides or bases being taken as 100).

RESULTS AND DISCUSSION

As seen from Table 1, there was little change in the RNA content of the right ventricle and the right and left auricles 3 days after severing the vagus nerves. The quantity of RNA in the left ventricle was diminished by 11% on the average. The DNA phosphorus content of the right ventricle, right and left auricles did not change, but the DNA concentration in the left ventricle was diminished (16.3%). The nucleotide make-up of the total RNA in the right ventricle, and in the right and left auricles remained unchanged in dogs after vagotomy (Table 2). However, uniform and unchanged nucleotide composition alone does not indicate uniform structure of the RNA, since the latter may change because of shifting the order of the nucleotide residues or configuration of the molecule in different RNA fractions. The nucleotide composition of the RNA in the left ventricle was somewhat changed: decreased guanine nucleotide (by 14.5%) and minor decreases in the quantities of adenine (by 9%) and uracil nuclcleotides (by 10%). The ratio of purines to pyrimidines in all cases was close to unity.

The nucleotide content of DNA in contrast to the nucleotide content of RNA underwent extensive alterations (Table 3). Attention is drawn to the sharp increase (more than 2 times) in the content of thymidine nucleotide.

The ratio of purines to pyrimidines was disturbed. The specificity index (G + C)/(A + T), which is quite stable in different areas in the heart of intact animals (0.71-0.79), decreases by an average of 30% (0.49-0.57).

The indicated changes are observed in all areas of heart examined. This suggests that transection of the vagus nerve has its effect not only upon the cardiac left ventricle, which bears the major physiological and functional load, but also upon the organ as a whole. Most workers consider that the DNA is stable, that its concentration in the cell is constant, and that the DNA molecules once synthesized are not changed, the nucleotides contained in them are not exchanged and DNA disintegration takes place only after cell death.

However, recently there has been some work indicating that in numerous instances, involving either a physiological condition of an organ or under environmental influences on the organism, changes in DNA content [9, 12, 13, 15, 16] or in its structure [16] may occur. It was demonstrated that during ultraviolet treatment, at the beginning of radiation pairs of thymines are formed on the single polynucleotide chain; subsequent irradiation leads to suppression of DNA synthesis. Evidently, in our experiments, upon transection of the vagus nerves a marked change in the organism as a whole also appears; especially in the heart, and this results in some fundamental changes in the DNA molecule. The facts presented again point up the significance of the parasympathetic nervous system in regulating metabolic processes in the organism, particularly in regulating DNA synthesis.

TABLE 2. Nucleotide Composition of RNA in Various Areas of the Dog Heart after Bilateral Vagus Nerve Transection

Area of heart	Nucleotides in moles %								A + U/G + C		G + U/A + C		Purines/pyrimidines	
	guanylic		adenylic		cytidylic		uridylic							
	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection
Ventricle														
Right	30,5 ±0,39	28,2 ±0,31	20,0 ±0,40	21,5 ±0,36	29,9 ±0,40	31,3 ±0,29	19,54 ±0,35	18,5 ±0,4	0,64 ±0,016	0,67 ±0,0033	0,99 ±0,0031	0,90 ±0,0083	0,99 ±0,0022	0,99 ±0,035
	P <0,001		P <0,02		P <0,01		P <0,05		P <0,001		P <0,001		P <0,02	
Left	32,98 ±0,5	28,3 ±0,18	18,78 ±0,44	21,0 ±0,23	31,38 ±0,37	31,9 ±0,21	16,84 ±0,26	18,8 ±0,18	0,59 ±0,01	0,66 ±0,004	0,99 ±0,074	0,87 ±0,017	1,07 ±0,012	0,98 ±0,009
	P <0,001		P <0,001		P < 0,02		P <0,05		P <0,001		P <0,001		P <0,001	
Auricle:														
Right	29,4 ±0,39	29,1 ±0,2	20,8 ±0,28	20,3 ±0,25	29,6 ±0,37	30,8 ±0,2	20,4 ±0,40	19,8 ±0,22	0,69 ±0,012	0,67 ±0,004	0,99 ±0,01	0,97 ±0,009	1,07 ±0,022	0,98 ±0,14
	P <0,02		P <0,2		P < 0,01		P <0,001		P <0,001		P <0,01		P <0,001	
Left	30,00 ±0,70	28,4 ±0,32	19,8 ±0,79	20,9 ±0,22	30,0 ±0,48	30,9 ±0,12	19,95 ±0,76	20,0 ±0,21	0,63 ±0,04	0,68 ±0,01	0,99 ±0,018	0,93 ±0,09	1,01 ±0,044	0,98 ±0,006
	P <0,05		P <0,2		P < 0,01		P <0,05		P <0,02		P <0,01		P <0,05	

TABLE 3. Nucleotide Composition of DNA in Various Areas of the Dog Heart after Vagus Nerve Transection

Area of heart	Bases in DNA (in moles %)								G + C/A + T		G + T/A + C		Purine/pyrimidine	
	guanine		adenine		cytosine		thymine							
	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection	normal	after transection
Ventricle:														
Right	22,2 ±0,19	18,5 ±0,13	27,81 ±0,20	20,5 ±0,20	21,7 ±0,29	15,3 ±0,42	28,24 ±0,28	45,8 ±0,57	0,78 ±0,009	0,53 ±0,001	1,02 ±0,005	1,80 ±0,012	1,0 ±0,063	0,64 ±0,043
	P < 0,001		P < 0,001		P <0,001		P <0,001		P <0,001		P <0,001		P <0,001	
Left	22,27 ±0,25	19,1 ±0,23	28,07 ±0,19	20,7 ±0,24	21,87 ±0,12	17,1 ±0,14	28,22 ±0,31	43,1 ±0,31	0,79 ±0,003	0,57 ±0,007	0,99 ±0,001	1,64 ±0,024	1,0 ±0,005	0,66 ±0,006
	P < 0,001		P < 0,001		P <0,001		P <0,001		P <0,001		P <0,001		P <0,001	
Auricle:														
Right	20,83 ±0,36	19,9 ±0,25	28,91 ±0,34	19,0 ±0,29	20,60 ±0,35	13,7 ±0,12	29,82 ±0,56	47,5 ±0,32	0,71 ±0,002	0,51 ±0,001	1,01 ±0,003	2,07 ±0,03	0,99 ±0,007	0,64 ±0,011
	P < 0,02		P < 0,001		P <0,001		P <0,001		P <0,001		P <0,001		P <0,001	
Left	21,90 ±0,40	19,8 ±0,22	28,0 ±0,39	17,5 ±0,28	21,1 ±0,63	13,2 ±0,15	29,1 ±0,69	49,6 ±0,35	0,76 ±0,003	0,49 ±0,005	1,03 ±0,005	2,25 ±0,01	0,99 ±0,023	0,60 ±0,009
	P < 0,001		P <0,001		P <0,001		P <0,001		P <0,001		P <0,001		P <0,001	

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