SOME PRINCIPLES OF STRUCTURAL HOMEOSTASIS OF CARDIOMYOCYTES

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The results of quantitative analysis of the ultrastructural organization of the cardiomyocytes of man and animals (rabbit, rat, dog), by the point method, are described. A series of stereometric constants determining the structural homeostasis of the cardiomyocytes was found: the total volume of mitochondria (mt) and myofibrils (mf), forming the "cardiomyocytic constant" ($V_{mt} + V_{mf} = K_{st}$); the total increase in volume of mt and mf, equal to 0 ($dV_{mt} + dV_{mf} = 0$); adaptive reconstruction of mt and mf takes place within the range of 11% ($\Delta V_{mt} = \Delta V_{mf} = 11\%$); structural homeostasis of the cardiomyocytes is maintained by a change in the ultrastructural organization within limits set by the rule of "constancy of volumetric proportions" (80, 10, 10%), of which K_{st} accounts for 80%, the other organelles and inclusions (V_i) for 10%, and the cytoplasm (V_{cp}) for 10%. The possible universality of stereometric constants is postulated.

KEY WORDS: cardiomyocyte; stereometric constants; structural homeostasis.

The way in which the principles of structural homeostasis [4] operate cannot be understood without knowledge of the rules governing the intracellular organization and quantitative parameters of reparative processes [1]. An attempt to study these problems by stereometric analysis (SA) is described below.

EXPERIMENTAL METHOD

Stereometric analysis of the cardiomyocytes was undertaken in the following four series of observations: series I) rabbits aged 9 months, with 10 animals in each group: group 1) normal (M), 2) experimental atherosclerosis (X), 3) coarctation of the aorta (C), and group 4) XC. The duration of coarctation of the aorta was 1.5 months; series II) rats, six groups with five animals in each group, normal animals and after coarctation of the aorta for 6 months; series III) mongrel dogs, five animals aged 9 months; series IV) hearts (weighing 600-700 g) from five persons aged 70-75 years with a history of coronary atherosclerosis and essential hypertension (death from causes unrelated to heart failure).

SA of the cardiomyocytes of the left ventricle was carried out by a point method [1] under magnification of 3000×, with a rectangular test system with a constant of 0.91, and the total area investigated was 13,500-15,500 μ^2. The numerical data and the error of measurements were monitored graphically [2]. The following parameters of ultrastructural organization were studied: the coefficient of saturation of the cell with structural components and inclusions (K_i), the relative volumes of the mitochondria (V_{mt}) and myofibrils (V_{mf}), the total volume of these organelles ($V_{mt} + V_{mf}$), the total volume of the other structural components (nucleus, reticulum, etc.) and inclusions (glycogen, lipids, lipofuscin) in the cells, in %: $V_i = K_i - (V_{mt} + V_{mf})$, the relative volume of the basic cytoplasm of the cell (V_{cp}), and the mitochondrial/myofibrillary index (mt/mf).

EXPERIMENTAL RESULTS

The SA showed (Table 1) that the relative volumes of the energy-forming and contractile structures of the cardiomyocytes were distinguished by their variability (Nos. 1, 2, 3, 4, 10, 11, 12), possibly because of the different conditions under which the myocardium functioned. For each period of postnatal development (Nos. 1, 5, 6, 7, 8, 9, 11, 12) there was an optimal variant of volumetric proportions of these organelles. Coincidence of the values of these parameters in different representatives of the mammals for closely similar functional states of the myocardium (Nos. 1 and 7, 6 and 11, 3 and 10) can be explained by the general principles of ultra-

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TABLE 1. Results of Stereometric Analysis of Cardiomyocytes

Description of series	Group No.	Characteristics of group of observations	V_{mt} ±0.20	V_{mt} ±0.20	$V_{mt}+V_{mt}$ ±0.40	V_i ±0.40	K_i ±0.40	V_{cp} ±0.40	Index mt/mf ± 0.002
Rabbits	1	N	33,10	47,80	80,90	8,50	89,40	10,60	0,6925
	2	X	29,70	50,10	79,80	10,30	90,10	9,90	0,5928
	3	C	34,25	46,10	80,35	10,75	91,10	8,90	0,7429
	4	XC	40,60	39,60	80,20	10,20	90,40	9,60	1,0252
		Mean values			80,31	9,94	90,25	9,75	
		Whole-number values			80	10	90	10	
Rats	5	1 month	38,20	41,40	79,60	10,40	90,00	10,00	0,9227
	6	6 months	32,40	47,60	80,00	10,00	90,00	10,00	0,6807
	7	9 months	33,00	47,20	80,20	9,90	90,10	9,90	0,6991
	8	12 months	34,00	46,10	80,10	9,90	90,00	10,00	0,7375
	9	24 months	36,60	43,60	80,20	10,10	90,30	9,70	0,8394
	10	9 months (K)	35,30	44,80	80,10	10,10	90,20	9,90	0,7879
		Mean values			80,03	10,06	90,10	9,92	
		Whole-number values			80	10	90	10	
Dogs	11	9 months	32,00	48,00	80,00	10,00	90,00	10,00	0,6666
Man	12	70—75 years	39,40	40,70	80,10	9,60	89,70	10,30	0,9680

structural organization and analogous mechanisms of adaptive reactions. This is confirmed by the closely similar values of the stereometric parameters of the mitochondria and myofibrils of the elderly human myocardium and of the rabbit myocardium during experimental reproduction of chronic heart failure of atherosclerotic genesis (Nos. 4 and 12). Adaptive changes in the organelles of the cell (Nos. 10 and 8-9), caused by a change in the conditions of function of the organ (C), "shift" the values of the stereometric parameters toward older age groups ("aging" of the myocardium), a result which can be explained by the stereotyped character of repair processes during hyperfunction and age involution.

One other property of the structural organization of the cardiomyocytes was discovered, namely constancy of the combined volume (constant) of the energy-forming and contractile structures ($V_{mt} + V_{mf}$). This rule could be clearly detected in all series and groups of observations: The constancy of this stereometric parameter was preserved despite appreciable fluctuations in the values forming it. Several workers have given comparatively similar numerical values for this parameter for the cardiomyocytes of dogs, rabbits, and rats: 75-80 [3] and 82-83.4 [8-11].

The results of SA showed that the stereometric indices of structural organization of the cardiomyocytes (K_i, V_i, V_{cp}) in all groups of observations were similar and their variability can be explained by instrumental error of measurement ($\varepsilon \leq 1\%$). If the cell volume (V_{cell}) is taken at 100%, the total of the structural components (K_i) accounts for 90%, and of this sum 80% is accounted for by the combination of energy-forming and contractile structures ($V_{mt} + V_{mf}$) and 10% by the remaining structural components and intracellular inclusions (V_i). The remaining 10% of the cell volume is occupied by the basic cytoplasm (V_{cp}). This suggests that the regularity of volumetric proportions (80, 10, and 10%) of the structural organization of the cardiomyocytes reflects one of the principles of cellular homeostasis, namely the "preservation of optimal relations between the components of the cell" [6], and it probably is determinant in character.

A realistic idea of the level of energy provision (the mt/mf index) of the cell, incidentally, can be obtained by a study of the ultrastructural organization of the mitochondria [4]. The SA of electron micrographs shows that an increase in the volume of the mitochondrial fraction is accompanied by a change in the coefficient of ellipsoidality (rounding) and in the relative contribution of different classes of these organelles.

Structural homeostasis of the cardiomyocytes is controlled by several rules of ultrastructural organization, which determine the dynamics and limits of adaptive changes in the cells and the compensatory powers of the myocardium.

1. Adaptive reorganization of the principal structural-functional ensembles of the cardiomyocytes (mitochondria and myofibrils) obeys the following rules:

a) The total volume of the mitochondria and myofibrils is constant; this stereometric index of cell organization can accordingly be looked upon as a "cardiomyocytic constant" [7]:

$$V_{mt} + V_{mf} = K_{st}; \quad (1)$$

b) the volumes of these organelles satisfy a linear equation of the type:

$$V_{mt} + V_{mf} = 80; \quad (2)$$

c) the differential form of which indicates that the total increases in their volumes are equal in absolute value but opposite in sign:

$$dV_{mt} + dV_{mf} = 0; \quad (3)$$

d) the adaptive reorganization of these structures in different morpho-functional states of the myocardium takes place within a range of values limited to 11% of their volume:

$$\Delta V_{mt} = \Delta V_{mf} = 11\%. \quad (4)$$

2. Structural homeostasis of the cardiomyocytes is ensured by:

a) definite proportionality of the stereometric indices of the main components of the cell which have the value of stereometric constants (SC):

$$V_{cell} = K_{st} + V_i + V_{cp}, \text{ or}$$
$$100\% = 80\% + 10\% + 10\%; \quad (5)$$

b) constancy of the ratio of the stereometric indices of the structural components and of the "liquid" part of the cell:

$$K_i / V_{cp} = 9, \quad (6)$$

which determines the optimal volume of cytoplasm necessary for the functioning of the structures.

3. Equation (5) confirms, at the ultrastructural level, the basic principle of structural homeostasis [6] and it can be called "the law of constancy of volumetric proportions."

4. The stereotyped character of adaptive processes [6] suggests that adaptive reorganization of the cells of other organs obeys similar or closely similar rules.

5. The SA confirmed, at the structural level, the adequacy of the model of chronic cardiac failure of atherosclerotic genesis.

6. The rules of structural organization of the cardiomyocytes discovered (stereometric constants) are universal in character and are independent of the size or functional state of the myocardium.

These findings provide a fresh approach to the study of the principles of structural homeostasis, the mechanisms and ranges of adaptation, including age involution, and also corrective stimulation of regenerative processes, and this is a matter not only of theoretical, but also of great practical importance.

LITERATURE CITED

1. G. G. Avtandilov, Morphometry in Pathology [in Russian], Moscow (1973).
2. L. S. Blokh, Basic Graphical Methods of Analysis of Experimental Data [in Russian], Moscow–Leningrad (1951).
3. A. Wollenberger and W. Schulze, in: Physiology and Pathology of the Heart (ed. by M. E. Marshak) [Russian translation], Moscow (1963), p. 126.
4. V. S. Paukov, T. A. Kazanskaya, and V. A. Frolov, Byull. Éksp. Biol. Med., No. 4, 122 (1971).
5. D. S. Sarkisov, A. A. Pal'tsin, and B. V. Vtyurin, Adaptive Reorganization of Biorhythms [in Russian], Moscow (1975).
6. D. S. Sarkisov, in: Homeostasis [in Russian], Moscow (1976), pp. 133-190.
7. A. F. Yakovtsova, V. N. Ofitserov, V. D. Sadchikov, et al., in: Ultrastructure of the Cardiovascular System Under Normal and Pathological Conditions (Proceedings of a Symposium) [in Russian], Tbilisi (1976), p. 171.
8. M. Hagopial, P. Anversa, and A. V. Lond, J. Mol. Cell. Cardiol., 7, 357 (1975).
9. P. Y. Hatt, G. Berjal, J. Moravec, et al., J. Mol. Cell. Cardiol., 1, 235 (1970).
10. E. Page and L. P. McCallister, Am. J. Cardiol., 31, 172 (1973).
11. R. Poche, Ann. N. Y. Acad. Sci., 156, 34 (1969).