It can thus be concluded that changes in the EEG of animals developing in neurosis are a correlate of disturbances of brain metabolism and, in particular, of the processes of utilization of the energy of high-energy compounds.

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ADAPTIVE CHANGES IN RAT MYOCARDIUM DURING PERIODIC COOLING

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Investigations [2, 3] have shown that the immigrant population of the Far North develops hypertrophy of the right ventricle during adaptation to extremal environmental conditions. According to one study [5], when rats were cooled to a temperature of 5°C a significant increase in weight of the heart took place in the 4th week of the experiment on account of hypertrophy of both ventricles. However, no other data on organometric changes in the heart during cooling of animals to lower temperatures could be found in the literature.

The object of this investigation was to study the heart of rats during periodic measured cooling by morphometric and correlation analysis.

EXPERIMENTAL METHOD

Experiments were carried out on 55 noninbred male albino rats weighing initially 190 ± 10 g. The control group consisted of 15 rats. For 6 h daily for 1 week, 40 rats isolated from each other were kept in a Foutron (East Germany) climatic chamber at temperatures of +4°, 0°, −5°, −12°, and −20°C. The animals were killed 5-10 at a time by decapitation each week. Autopsy and separate weighing of the heart were carried out by Avtandilov's method [1] in the present writers' modification: Before the ventricles were opened, both atria were separated. The area of the inner surface of the ventricles was calculated by weighing replicas of them on paper. The material was then fixed in Lillie's solution. Pieces of tissue were embedded in paraffin wax. Histological sections were stained with hematoxylin–eosin, picrofuchsin and fuchselin, and by the PAS reaction. By means of an ocular hexagonal grid, the

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TABLE 1. Increase in Body Weight of Rats and Weight of Parts of Their Heart (in %)

Time of experiment, weeks	Body weight	PWH	WRV	WLV
Control	100	100	100	100
1 (4 °C)	102	104	105	105
2 (0 °C)	103	106	116	102
3 (—5 °C)	113	119	116	107
4 (—12 °C)	122	132	142	119
5 (—20 °C)	102	125	132	114

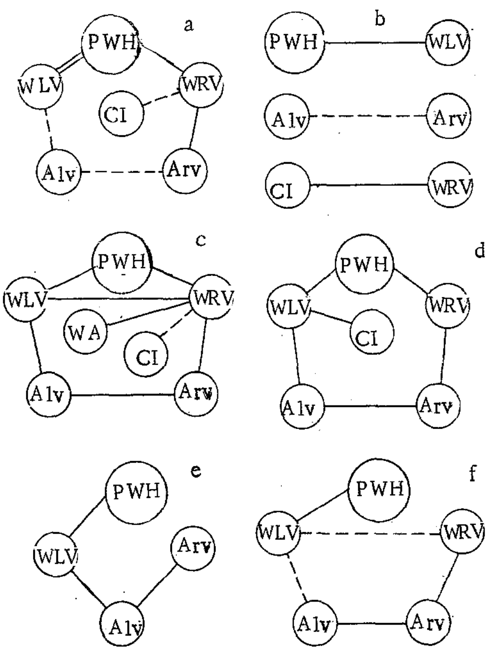

Fig. 1. Schemes of correlations of organometric parameters of rat heart during periodic measured cooling: a) control; b) 1st week (4°C); c) 2nd week (0°C); d) 3rd week (—5°C); e) 4th week (—12°C); f) 5th week (—20°C). PWH) Pure weight of heart, WRV) weight of right ventricle, WLV) weight of left ventricle, WA) weight of atria, Arv) area of inner surface of right ventricle, Alv) area of inner surface of left ventricle, CI) cardiac index.

bulk density of cardiomyocytes (V_m), capillaries (V_c), and connective tissue (V_t) were determined separately for each ventricle in the preparations, and the diameters of the cardiomyocytes (D_m) and of their nuclei (D_n) were measured by means of an ocular micrometer. The ratios V_m/V_c and D_n/D_m were then calculated. The numerical data were subjected to statistical correlation and variance analysis on the Nairi-K-computer, using algorithms suggested in [4]. Correlations were assessed as follows: coefficient of correlation up to 0.5 — weak correlation; 0.5-0.69 — average; 0.7-0.89 — strong; 0.90-0.99 — functional. Graphic schemes were prepared for assessment of these correlations. Altogether 28 parameters of the heart were measured and calculated and correlation analysis was carried out on 46 pairs of features.

EXPERIMENTAL RESULTS

The gain in weight of the animals during 5 weeks of the experiment averaged 83 ± 3 g for the experimental rats but only 29 ± 3 g for the controls. Analysis of the weight of the right ventricle (WRV) showed that in the fourth week of the experiment at —12°C it was significantly increased compared with the control group, and was 297 ± 7 mg (control 209 ± 19 mg).

TABLE 2. Changes in Histometric Parameters of Right Ventricle

Time of experiment, weeks	V_m, %	V_c, %	V_m/V_c	Dm	Dn	D_n/D_m
Control	81±0,4	13,6±0,6	6,2	9,8±0,2	7:2±0,2	0,74
1 (4 °C)	85±0,5	10,2±0,3	8,4	12,3±0,4	7,7±0,2	0,63
2 (0 °C)	87±0,6	8,3±0,2	10,5	13,6±0.7	9,2±0,7	0,68
3 (−5 °C)	88±0,5	8,1±0,2	11,3	14,9±0,5	8,7±0,2	0,59
4 (−12 °C)	86±0,8	9,9±0,6	9,1	14,2±0,5	9,4±0,2	0,66
5 (−20 °C)	88±1,0	11,2±0,9	7,9	15,2±0,3	8,4±0,1	0,56

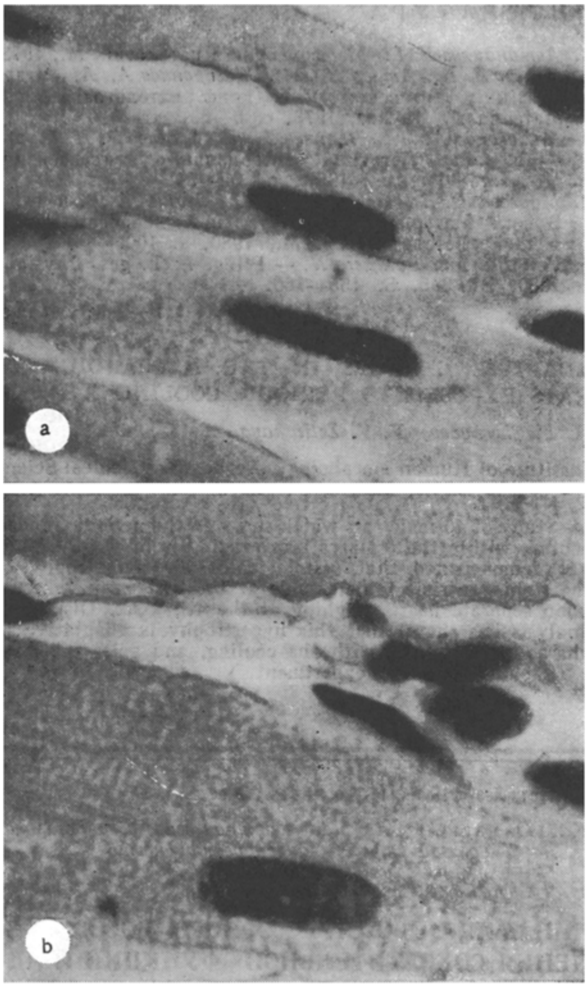

Fig. 2. Myocardium of right ventricle of rat: a) control; b) hypertrophy of cardiomyocyte with increase in volume of nucleus and sarcoplasm (1st week of adaptation to cold at 4°C). Stained with hematoxylin and eosin, ocular 10, objective 100.

The relative parameter represented by WRV as a fraction of the pure weight of the heart (PWH) was increased from 25 ± 2% in the control to 28 ± 1% in the same week of the experiment. There was a significant increase in the ventricular index and a decrease in Fulton's index compared with the control. The internal area of the right ventricle (Arv) was significantly increased by the fourth week of the experiment compared with the control and the first week of the experiment. Since PWH and WRV increased simultaneously in the animals as a result of their natural growth, the gain in weight of parts of the heart taking place both on account of growth and on account of adaptive changes was analyzed. In Table 1 the increase in PWH, WRV, and the weight of the left ventricle (WLV) for each week of the experiment relative to the control group is given as a percentage in Table 1.

It will be clear from these data that the increase in WRV took place more rapidly than the increase in WLV starting with the second week of the experiment, and reached a maximum in the fourth week. Analysis of variance showed that the effect of exposure to cold on the increase in WRV is much greater than on the increase in WLV. Fisher's index for the right ventricle was 31.4 and for the left 4.6, and the strength of the effect η^2 was 76 ± 2.4 and 32.1 ± 6.9% respectively.

Morphometric investigation on histological preparations of the right and left ventricles showed a significant increase in V_m of the right ventricle starting with the second week of the experiment, accompanied by a simultaneous decrease in V_c. A significant increase in D_m and D_n was observed as early as after the first week (4°C) of the experiment (Table 2). Measurements made by the same scheme in the left ventricle revealed no significant changes in these parameters.

During correlation analysis in the first week of the experiment severance and weakening of the correlations were observed. Each parameter studied was connected with only one parameter (Fig. 1b). In the second week of exposure to cold, strengthening and an increase in number of the correlations were observed mainly on account of those with WRV (Fig. 1c). In the fourth week the total number of correlations was reduced and, what is particularly characteristic, there were no correlations whatever with WRV (Fig. 1e), although it is at this time that hypertrophy of the right ventricle first comes to light. By the fifth week of the experiment the level of correlations was almost the same as in the control. The following sequence of correlations can thus be distinguished: severance in the first week, an increase in their strength and number in the second week, absence of correlations between WRV and other parameters in the fourth week, and recovery of correlations in the fifth week.

During periodic measured general cooling of the animals, in the initial periods there was an increase in area of the inner surface of the right ventricle, which evidently correlated primarily with hypervolemia of the pulmonary circulation, and histologically a significant increase was found in the diameter of the cardiomyocytes and their nuclei (Fig. 2b). However, organometric investigations revealed hypertrophy of the right ventricle, but not before the fourth week of the experiment. This hypertrophy was due to an increase of pressure in the pulmonary circulation. Severance of the correlations in the first week of the experiment indicates that the animals react to what for them is a new state (general cooling) by a stress reaction, and also by changes in the hemodynamics, especially in the pulmonary circulation. Later intracardiac correlations become stabilized, evidence that the heart is working during this period under the greatest strain at a new morphological and functional level. To some degree this may be connected with the nonspecific stress reaction reflecting Selye's stabilization phase. The absence of correlation with the weight of the right ventricle in the 4th week of the experiment coincides with the beginning of marked hypertrophy of the right ventricle, i.e., the heart during this period is stabilizing at a new level of adaptation. By the fifth week of the experiment, in our opinion, the animals are adapted to exposure to cold, and it is this which largely facilitates the development of hypertrophy of the right ventricle.

In rats exposed to periodic measured cooling, hypertrophy of the right ventricle can thus be detected histologically in the first week, and by separate weighing, in the four week. Analysis of variance showed that this hypertrophy is adaptive in character, correlates with cooling, and stabilizes by the fifth week of the experiment.

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