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MORPHOFUNCTIONAL CORRELATIONS IN THE EXPERIMENTAL STUDY OF MYOCARDIOPATHIES UNDER THE STRESS OF FORCED RESTRAINT. NOTE II. THE INFLUENCE OF ADRENAL IMBALANCE

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Translation of "Corelatii Morfofunctionale in Studiul Experimental Al Miocardopatiilor din Timpul Stressului Prin Imobilizare Fortata," Revue Medico-Chirurgicale (Iasi) (Romania), No. 1, 1978, pp 87-91

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16. Abstract The experimental study carried out showed that in rats with adrenal imbalance, fasting and restraint produced the same biochemical alterations as in the controls. The morphologic alterations, as well as their electric expression, were more varied and evident in the animals with adrenal imbalance. Persistence of the microscopic and electrocardiographic alterations after 72 hours restraint in the animals subjected to unilateral adrenalectomy suggests chronic evolution of the myocardial lesions. This proves the necessity of intact adrenals for a good adaptability to stress.

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MORPHOFUNCTIONAL CORRELATIONS IN THE EXPERIMENTAL STUDY OF MYOCARDIOPATHIES UNDER THE STRESS OF FORCED RESTRAINT. NOTE II. THE INFLUENCE OF ADRENAL IMBALANCE

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In our previous studies [4, 12] we have pointed out, as did other authors [1, 10, 11], the role of stress states in the appearance of myocardiopathies. /87*

Many observations revealed that under adaptive stress conditions the demand for corticoids increases considerably [1, 2, 5, 6, 7, 8, 11]. On the basis of these data we believed it necessary to follow up in a new investigation the effect of restraint on the function and the structure of the myocardium under varying conditions of adrenal imbalance.

Method of Operation

The experiments were carried out with 70 male rats, with an average weight of 160 g, divided into 4 groups: Group I -- reference animals; Group II -- animals subjected to unilateral adrenalectomy; Group III -- animals subjected to bilateral adrenalectomy (bilateral adrenalectomy -- the adrenalectomy in the last two groups was carried out at the same time, 7 days before the experiment); Group IV -- animals, each of which, before being restrained, were administered 3 hydrocortisone injections in doses of 5 mg per 100 g of body weight.

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*Numbers in the margin indicate pagination in the foreign text.

Each group included animals in the following experimental conditions, from which the following series were sacrificed: normal feeding (N); fasting and thirsting for 44 hours (F + S); fasting, thirsting and restraint for 24 hours (I), at 72 hours before the start of the experiment (72 h). The mortality rate was followed up and the glycemia was determined by the Hagedorn Jensen method; in the urine 17-CS (Zimmermann method), 17-OH (Porter Zilber method), Na and K ions (Lundegardh and Lehnehknecht method), P (Brigge method), Mg (Kolhof method) were analytically determined; in addition, electrocardiographic studies were made (with the Cardior apparatus), morphological (hematoxylin eosin dying according to van Giessen and Simionescu) and histochemical examinations (using the Lie and Nielsen Selye technique for fuchsinophilics, the PAS method for mucopolysaccarides, the Hotchkiss-McManus method for glycogen) were carried out for studying the myocardium and the adrenal glands, using also histo-enzymatic methods for the myocardium (the Nachlas method for SDH, the Gomori-Bitenschi technique for the acid phosphatase and the Wachtein and Meisel method for the ATP-ase).

Results

The highest increase in the mortality during the restraint was encountered in animals subjected to bilateral adrenalectomy (75%), which, as a matter of fact, was noted also after fasting (33%) (Fig. 2). /88 The electrolyte eliminations exhibited similar variations in all of the experimental groups; however, it should be mentioned that the elimination of K, P and Mg was higher in animals with endocrine imbalance, in particular in those treated with hydrocortisone (Fig. 1). The glycemia decreased in the reference animals and in those subjected to unilateral adrenalectomy after fasting and restraint, while it was at a high level in animals subjected to bilateral adrenalectomy and in those treated with hydrocortisone (Fig. 2). The 17-CS eliminations decreased after adrenalectomy, and after fasting it obviously increased in these animals (Fig. 2); after restraint in the reference animals and in those treated with hydrocortisone the values decrease at the same proportion, growing 72 hours after the restraint was applied. The 17-OH elimination was not affected after endocrine imbalance; however, fasting favored the highest increase of the elimination in animals treated with hydrocortisone; after restraint, the values among the groups were identical.

The electrocardiographic examination of animals with adrenal imbalance revealed repolarizing modifications, in the sense of the decrease of the amplitude of the T waves. After fasting, we observed a microvoltage in all of the animals; this was especially marked in animals subjected to bilateral adrenalectomy. The restraint induced similar changes of the rhythm between the groups, with certain minor differences. Thus, we encountered changes of the rhythm (the frequency decreased from 250 to 150 beats/minute) of the behavior (grade I A-V blockage, intraventricular blockage), of the terminal phase (wide S waves, uneven ST segments); the repolarization was fast, with positive, sharp and symmetrical T waves, which in rare cases were negative; in most of the animals, a U wave was present. In a small number of animals treated with hydrocortisone we encountered atrial fibrillations or tachycardia.

Microscopic examination of the myocardium after fasting revealed protein dystrophy and fuchsinophilic reaction of the myocardial fiber (Fig. 3) in all of the groups, localized in the subepicardial zone in the reference groups and distributed throughout the whole surface in the other groups. Edema and plasmorrhagia were more evident in the group which was administered hydrocortisone. The glycogen content was often low. Associated restraint increased the zones of micronecrosis in all the groups, and in the animals with adrenal imbalance the striations of the myocardial fibers disappear; in many zones the fuchsinophilic character was found to be intense, the edema and plasmorrhagia were obvious (Fig. 4). In the animals treated with hydrocortisone the lesions affect also the supports. Microscopic examination of the adrenal glands in animals subjected to unilateral adrenalectomy and in the reference animals revealed, after fasting, hypertrophy with hyperplasia of the fasciculate zone and a nonhomogeneous repartition of the lipids, while in the animals treated with hydrocortisone a massive loading with lipids was observed (Fig. 5). After restraint, in the animals treated with hydrocortisone in the fasciculate zone a lipid depletion is encountered, while in the animals with unilateral adrenalectomy the cells were transformed into vacuolated spongiocytes (Fig. 6) and the lipid content increased. The medulla was intensively congestive (Fig. 7).

72 hours after the restraint, the microscopic and electrocardiographic aspects observed during the time of restraint persisted in the animals subjected to unilateral adrenalectomy.

Discussion

The relative similarity of the biochemical, electrocardiographic and morphological data observed after fasting or restraint between the groups subjected to adrenalectomy and the reference animals is attributed to the fact that the male rats which have subsidiary adrenals [3, 6, 9] were used in the experiments. However, the reduced capacity of these supernumerary glands to substitute for the functions of the adrenal glands caused perturbations in various metabolic processes, lowering the resistance of the organism (increased mortality) and affecting the power of adaptability with respect to a stressing agent. Activation of these subsidiary adrenal cells is not sufficient to satisfy the demands of the organism in glycocorticoids at the time of an attack when there is an excess of catecholamines from the extra-adrenal deposits. This probably causes the reduction of the energy metabolism, the increase of the permeability of the lysosome membrane with cytoplasmatic lysis through the action of proteolytic enzymes, thus structural modifications, which, together with the ionic imbalance which determines the decrease of the potassium gradient, change the electrical activity of the myocardium.

We attribute the higher resistance observed in animals subjected to unilateral adrenalectomy to a better adaptability to new conditions in comparison with animals with bilateral adrenalectomy, which would explain the importance of certain values of the adrenal hormones with respect to normal or unusual but more intensive stresses. /91

The fact that in the microscopic examination of the myocardium we found multiple pathologic elements, in comparison with the reference animals, in the animals subjected to unilateral adrenalectomy, leads us to state that the pathological modifications during the restraint are favored more by the excess of catecholamines and less by the endogenous corticoids. If by exogenous administration a certain corticoid dose is exceeded, it could be transformed into a noxious factor for the heart, blocking pyruvate oxidation, reducing the ATP synthesis, causing an enzyme insufficiency which could be followed by an ionic imbalance. Swingle et al. (cited by [6]) believe that the glucocorticoids could both improve or aggravate the overall state of the organism, just as we observed it in our own studies. E. Bajusz [1] showed that an excess of adaptive hormones could, under certain circumstances, cause disturbances or condition their generation.

Conclusions

In view of the investigation described in this communication, we may assume that facing a stressing action which determines a true disturbance of the homeostasis of the organism, both the excess and the reduction of adrenal hormones may favor the production of myocardial lesions and the reduction of the general resistance of the organism.

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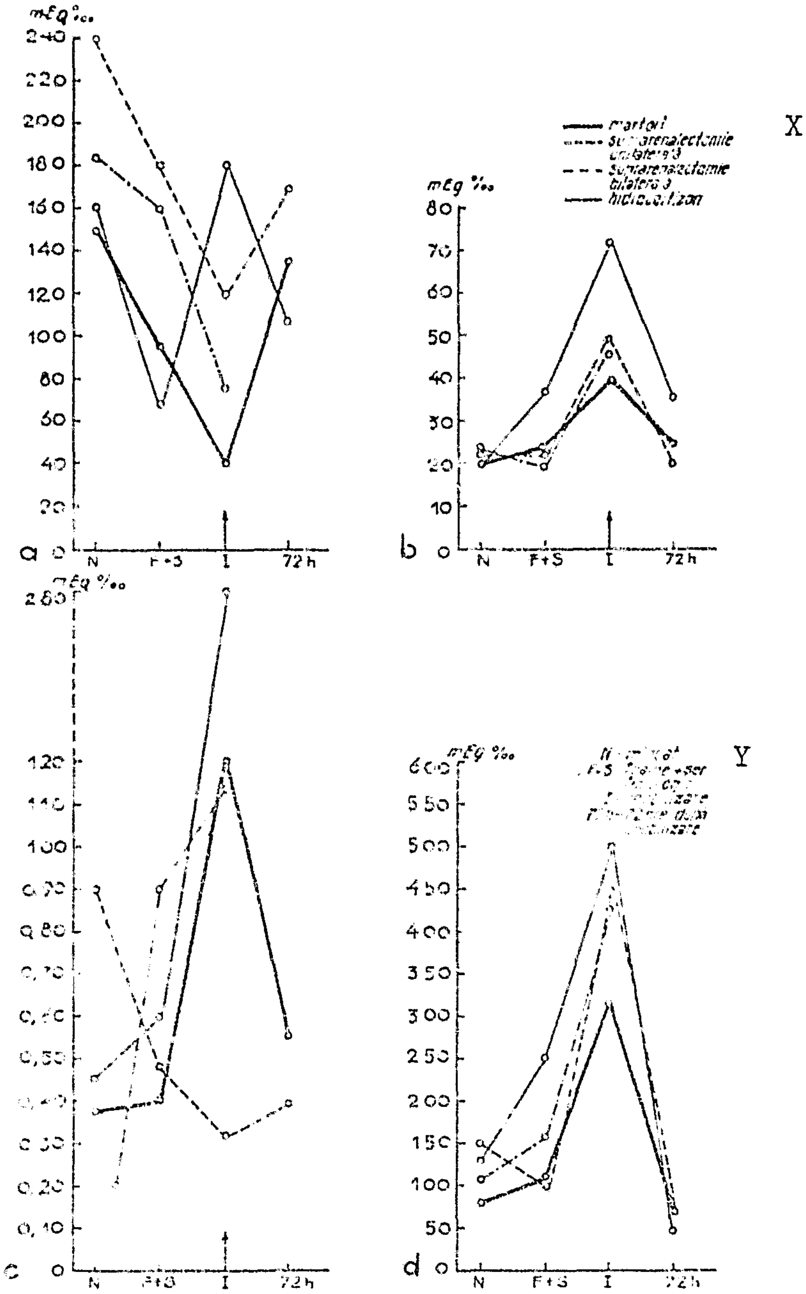

Figure 1. Average values of the elimination of Na (a), K (b), Mg (c), P (d) with the urine in male rats subjected to restraint on a background of adrenal imbalance.

Key: X
- ——— reference animals
- ----- unilateral adrenalectomy
- - · - · bilateral adrenalectomy
- —·—·— hydrocortisone

Y
- N: fed
- F + S: physiological fasting and thirsting
- I: restraint, 72h -- 72 hours after restraint

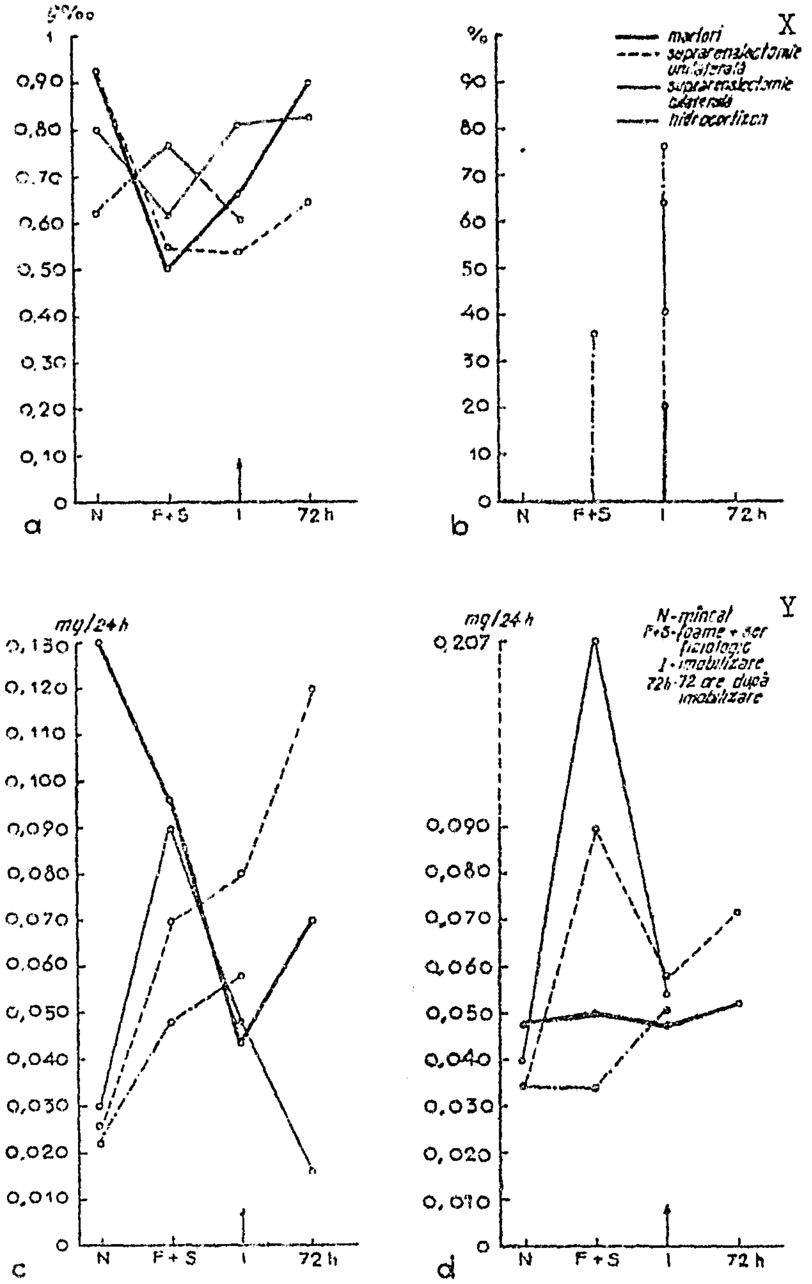

Figure 2. Average values of glycemia (a), urinary elimination of 17-CS (c), 17-OH (d) and the mortality expressed in percentages (b) in male rats subjected to restraint on a background of adrenal imbalance.

Key: X ——— reference animals
------ unilateral adrenalectomy
- · - · bilateral adrenalectomy
· · · - · hydrocortisone

Y N: fed
F + S: physiological thirsting and fasting
I: restraint, 72h -- 72 hours after restraint

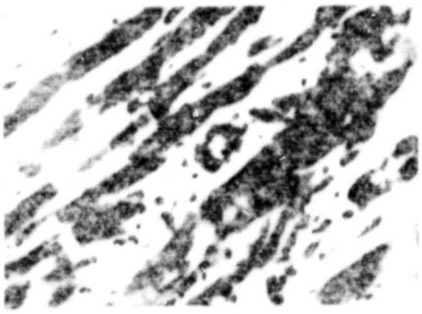

Figure 3. Myocardium
-- protein distrophy,
fuchsinophilic reaction

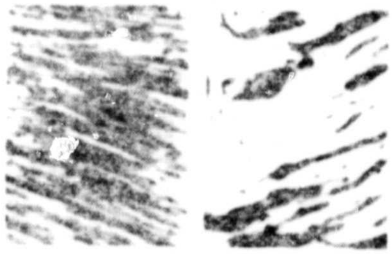

Figure 4. Myocardium
-- zone of micronecroses,
plasmorrhagia

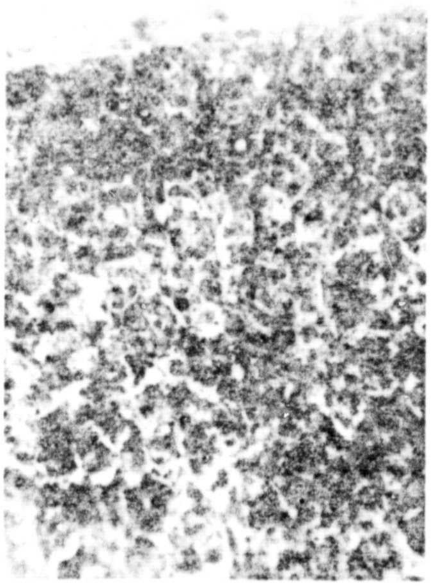

Figure 5. Adrenal gland
-- loading with lipids in
the cortical zone

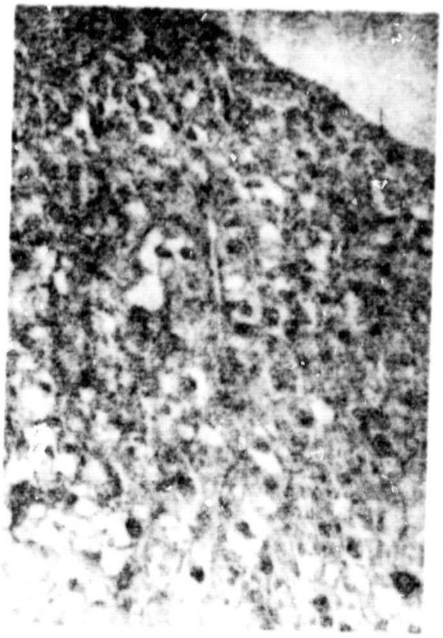

Figure 6. Adrenal gland -- spongiocyte aspect

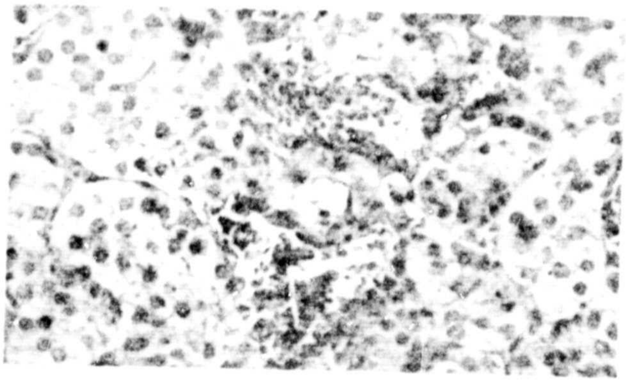

Figure 7. Adrenal gland -- medullar congestion