# EFFECT OF EMOTIONAL-PAINFUL STRESS ON Na,K-ATPase ACTIVITY IN HEART MUSCLE

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In emotional-painful stress (EPS), an excess of catecholamines induces activation of lipid peroxidation (LPO) in the myocardium [5]. This leads to injury to myocyte membranes and to disturbances of $Ca^{++}$ transport [2] and the contractile function of the heart [3]. These disturbances can be prevented by administration of the β-adrenoblocker inderal [6] or of LPO inhibitors [4] before stress.

The next step in the study of mechanisms of disturbances of cardiac function in stress is to consider the recently established fact that the adrenoreceptor–adenylate cyclase system, through which catecholamines exert their action, is located entirely in the sarcolemma [13] and, consequently, it is there that LPO activation and changes in phospholipid composition due to this process are most likely to take place. This, in turn, must lead to changes in activity of sarcolemmal lipid-dependent enzymes and, above all, of Na,K-ATPase, whose activity is highly dependent on the phospholipid environment [8].

To test this hypothesis, changes in Na,K-ATPase activity were investigated in heart muscle after EPS and the possibility of preventing these changes by administration of inderal before stress was examined.

## EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 180-200 g. The animals were divided into four groups: 1) control, 2) animals subjected to EPS, 3) animals receiving inderal, 4) animals receiving inderal and then subjected to EPS.

EPS was produced in the form of an anxiety neurosis by the usual method [7]. Exposure to the stressors lasted 6 h, and the animals were decapitated 2 h later. Inderal (from ICI, England) was injected in a dose of 1 mg/kg intraperitoneally 10 min before the beginning of stress.

To prepare the specimen in which Na,K-ATPase activity was determined, the animals' hearts were removed immediately after decapitation and freed from blood. The tissue was homogenized in the cold in a homogenizer of "Polytron" type (2 × 15 sec). After centrifugation at 2000g for 15 min, the residue was homogenized and treated with extracting solution (6 M NaI, 15 mM EDTA, 7.5 mM $MgCl_2$, 120 mM Tris-HCl; pH 8.3) at 4°C, which was added drop by drop with careful mixing in the ratio of 2:1 (by volume), and allowed to stand in the cold for 30 min. The sample was then centrifuged at 16,000g for 20 min. The residue was washed 3 times with 0.001 M EDTA solution, and after each washing it was centrifuged under the same conditions. The frozen residue was used for determination of Na,K-ATPase activity. For this purpose 50-70 μg of the preparation was incubated for 3 min in medium at 37°C; the reaction was induced by addition of ATP and it was stopped after 15 min with TCA solution to a final concentration of 5%. Phosphorus was determined by the method in [11] and protein by Lowry's method [10].

The incubation medium for determination of total ATPase activity contained 2 mM $MgCl_2$, 1 mM EDTA, 100 mM NaCl, 20 mM KCl, 50 mM Tris-HCl, pH 7.4 (37°C).

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activity of neuroleptics and it agrees with the results of experiments on radioligand binding [4], which demonstrated the high selectivity and stereospecificity of the effect of neuroleptics. The results indicate that neuroleptics have at least one other point of application in the dopamine system, for they not only influence dopamine receptors but they also interact stereospecifically and directly with the regulatory region of TH, which is responsible for substrate inhibition of the enzyme.

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