INTRACELLULAR Ca^{++} TRANSPORT IN THE MYOCARDIUM OF DOGS WITH EXPERIMENTAL INFORMATIONAL NEUROSIS

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In recent decades the frequency of ischemic heart disease of psychogenic origin has increased, and this phenomenon is associated with the fact that man spends his life under conditions of prolonged emotional stress and resulting disturbance of regulation of higher brain functions [6]. A definite correlation has been shown to exist between changes in myocardial contractility and activity of membrane transport systems in emotional-painful stress [2, 3] and during stimulation of the posterior hypothalamus [1].

The aim of this investigation was to study intracellular Ca^{++} transport in the myocardium of dogs with experimental informational neurosis (EIN), i.e., in a state of disturbed higher nervous activity arising through the need to process a large volume of information with insufficient time for the purpose, and with a high level of motivation of behavior.

EXPERIMENTAL METHOD

Experiments were carried out on 24 adult dogs aged from 2 to 5 years. Ten of these dogs (control 1) spent the whole time under natural conditions of unrestrained motor activity. In seven dogs (control 2), which were kept under normal conditions in the animal house for 8-9 months before the beginning of the investigation, motor-food conditioned reflexes were formed, but no experimental neurosis was produced in them. In the other dogs (experimental), kept under the same animal house conditions, motor-food conditioned reflexes also were formed, after which EIN was induced in them by sharply reducing the time intervals between succession of the individual conditioned stimuli, thus creating an unfavorable combination of number of conditioned stimuli (volume of information) to be analyzed and learned, the time factor allowed for this work, and the level of motivation. The experimental dogs developed a well-marked EIN at the 3rd-7th months. The animals were killed in the 8th-9th month. Details of the technique of inducing neurosis in the animals were described previously [5].

The fragmented sarcoplasmic reticulum (FSR) was isolated from the dogs' myocardium by the method in [7] and mitochondria by the method in [10].

Efficiency of binding and uptake of Ca^{++} by FSR and mitochondria [7] and also the efficiency of EGTA-initiated Ca^{++} release from previously "loaded" (in the presence of potassium oxalate) vesicles of FSR [9] were determined with the use of $^{45}Ca^{++}$ and millipore filtration (pore diameter 0.4 μ). Radioactivity of the samples was measured on a "Delta-300" liquid scintillation counter (from Searle, The Netherlands).

The content of endogenous Ca^{++} in FSR and the mitochondria was determined wtih an AAS-1 atomic absorption spectrophotometer (from Carl Zeiss, East Germany) by the method in [4].

EXPERIMENTAL RESULTS

In the animals of control group 2 no changes in uptake (Fig. 1), binding, or release of Ca^{++} from FSR could be found (Table 1) and no change likewise in Ca^{++} accumulation by the mitochondria (Fig. 2) compared with these parameters in the dogs of control group 1.

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TABLE 1. Binding, Release, and Content of Ca^{++} (in nmoles/mg protein) in FSR and Mitochondria during EIN (M ± m)

Experimental conditions	Binding of Ca^{++}	Release of Ca^{++} from FSR		Ca-concentration	
	FSR	loading	unloading	in FSR	in mitochondria
Control 1	47,7±1,7* (8)	1487*±25* (6)	194±24*** (6)	81,8±8,7 (8)	62,3±6,5 (9)
Control 2	43,5±4,5*** (7)	1433±71* (7)	212±22** (7)	80,5±3,2 (7)	77,5±4,5 (7)
EIN	31,0±3,1 (7)	909±39 (7)	106±23 (7)	76,5±6 (7)	75±8,5 (7)

Legend. *P < 0.001, **P < 0.01, ***P < 0.05 compared with EIN. Number of animals given between parentheses.

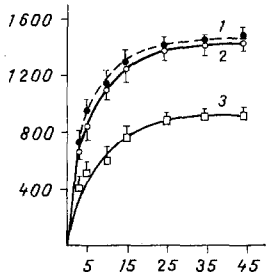

Fig. 1

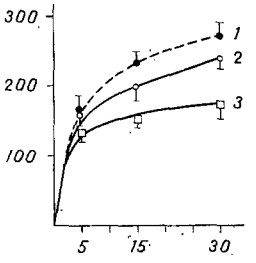

Fig. 2

Fig. 1. Uptake of Ca^{++} by FSR of dog myocardium. 1, 2) Corresponding control groups, 3) EIN. Incubation medium: 20 mM Tris-maleate buffer, pH 6.8, 0.1 M KCl, 10 mM $MgCl_2$, 2 mM ATP, 5 mM potassium oxalate, 50 μM $^{45}CaCl_2$, FSR 0.05 mg protein/ml (37°C). Abscissa, time (in min); ordinate, uptake of Ca^{++} (in nmoles/mg protein).

Fig. 2. Uptake of Ca^{++} by mitochondria isolated from dog myocardium. Incubation medium: 20 mM Tris-maleate buffer, pH 6.8, 0.1 M KCl, 10 mM $MgCl_2$, 2 mM ATP, 100 μM $^{45}CaCl_2$, 5 mM sodium succinate, 4 mM mitochondrial P_i (0.1-0.3 mg protein/ml). Remainder of legend as to Fig. 1.

Meanwhile, in animals in a state of EIN, considerable disturbance of the Ca^{++}-accumulating capacity of FSR and the mitochondria was observed. For instance, the ability of FSR to bind Ca^{++} was reduced by 35% compared with control 1, and by 29% compared with control 2. The rate of uptake of Ca^{++} and the maximal calcium "capacity" of the FSR vesicles were 37-38% lower than in control 2. The quantity of Ca^{++} released from FSR under these circumstances in response to addition of EGTA (at the 45th minute of uptake) was reduced by half (Table 1). However, if the quantity of released Ca^{++} is expressed as a ratio of the quantity taken up (direct correlation exists between these values [8, 9]), it is found that the induced release of Ca^{++} from FSR was unchanged during necrosis (12% of the quantity taken up was released) compared with controls 1 and 2 (13 and 15% of Ca^{++} taken up was released respectively).

The ability of the mitochondria to accumulate Ca^{++} was 35% lower than in control 1 and 25% lower than in control 2, even though the initial rate of Ca^{++} uptake was not significantly altered (Fig. 2).

The concentration of endogenous calcium in FSR and the mitochondria of dogs in a state of EIN was unchanged compared with that in the two controls (Table 1).

Disturbances of Ca^{++} transport combined with changes in the contractile properties of the system of contractile proteins may perhaps lie at the basis of the weakening of cardiac activity in human patients with informational neuroses and concussion.

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PREVENTION OF ADRENALIN-INDUCED HEART LESIONS BY THE ANTIOXIDANT IONOL

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Activation of lipid peroxidation arises in the heart in emotional-painful stress and the contractile function of the myocardium is disturbed [3-5]. Preliminary administration of antioxidants prevents both these phenomena [1, 6]. Since the principal harmful factor in stress is generally considered to be an excess of catecholamines, it was decided to study whether disturbances of the contractile function of the heart caused by injection of large doses of catecholamines can be prevented by means of antioxidants.

The aim of this investigation was to evaluate quantitatively the disturbances of cardiac contractility induced by injection of a large dose of adrenalin and to discover whether these disturbances can be prevented by the antioxidant ionol.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 200-250 g. There were four series of experiments: I) control, II) subcutaneous injection of 50 mg/kg adrenalin, III) intraperitoneal injection of 50 mg/kg ionol daily for 3 days, IV) injection of ionol before adrenalin. The heart was removed from the rats under urethane anesthesia 48 h after injection of adrenalin or the last injection of ionol. The contractile function of the papillary muscle of the left ventricle was investigated. The posterior papillary muscle was isolated and placed in a constant-temperature chamber containing oxygenated Krebs–Henseleit solution (pH 7.4, 29°C, 5.5 mM glucose). The muscle contracted for 1 h under isotonic conditions under the influence of electrical stimulation with a frequency of 20 pulses/min, and a weight of 250 mg was attached to it. The optimal load at which the muscle was stretched to a length permitting maximal isotonic shortening of the preparation was then determined. The length of the muscle was recorded by measuring displacement of a lever of the apparatus to which the muscle was attached. This displacement was measured with a capacitive transducer and recorded on a "Disa" indicator by means of a "Crossor" camera. The amplitude of contraction in each experiment was expressed as a percentage of the initial length of the muscle. The maximal rate of contraction and relaxation of the muscle was calculated graphically in conventional units per second.

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