EFFECT OF EMOTIONAL-PAINFUL STRESS ON RESISTANCE OF PORTAL VEIN CONTRACTILITY TO CHANGES IN CALCIUM CONCENTRATION AND TO ANOXIA

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Marked depression of contractility and adrenoreactivity of the portal vein is observed under the influence of severe emotional-painful stress (EPS) and this may play a role in the pathogenesis of arterial hypovolemia and of states resembling collapse [1, 3]. However, the effect of stress on resistance of the portal vein to acute anoxia and to changes in the calcium concentration in the surrounding fluid has not hitherto been studied. The object of the present investigation was accordingly to study the effect of anoxia and of various calcium concentrations on contractility of the portal vein in rats exposed to EPS.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-220 g were used. There were two groups of animals: control and exposed to EPS. EPS was produced by Desiderato's method [4] for 6 h. The rats were decapitated 2 h after the end of exposure to stress and the portal veins of the control and stressed animals were removed simultaneously and transferred to thermostatically controlled working chambers filled with oxygenated Krebs' solution at 32°C, pH 7.4, under an initial load of 500 mg [3]. The preparations remained under these conditions for 1 h before the beginning of the experiment in order to stabilize spontaneous contractile activity.

Spontaneous contractions were recorded on a two-channel apparatus (Ugo Basile, Italy), by means of which contractions of the control and experimental preparations could be recorded simultaneously.

To determine the response of the vascular smooth muscle to changes in the Ca^{++} ion concentration in the external solution, the original Krebs' solution was replaced by solution not containing calcium; the preparations remained in that solution until all spontaneous contractile activity had ceased. The solution was then replaced successively by solutions containing the following Ca^{++} concentrations: 0.35, 0.7, 1.4, 2.8, 3.5, 4.9, 6.7, and 8.1 mM. The preparations were kept in each of these solutions for 9 min until complete stabilization of spontaneous contractions.

To create conditions of anoxia the working solution was aerated with a mixture containing 96% N_2 and 4% CO_2, instead of the usual oxygenating mixture (96% O_2 + 4% CO_2) for 5 min. Contractions were recorded at the 2nd and 5th minutes of anoxia. The solution was then oxygenated and contractions recorded at the 2nd, 5th, 10th, and 20th minutes of reoxygenation.

In both tests the reaction was evaluated by the change in developed tension, the frequency of spontaneous contractions per minute, and the "intensity of functioning of structures" (IFS), i.e., the product of the developed tension and frequency of spontaneous contractions per unit weight of the organ.

The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

As a result of EPS the original parameters of portal vein contractility were considerably reduced (Table 1): The developed tension was reduced fivefold and ISF approximately by

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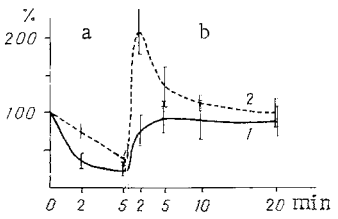

Fig. 1

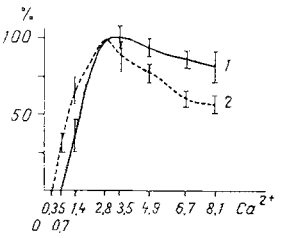

Fig. 2

Fig. 1. Effect of EPS on resistance of contractility of portal vein smooth muscle to anoxia (a) and reoxygenation (b). Abscissa, time (in min); ordinate, IFS (in % of initial value). 1) EPS; 2) control.

Fig. 2. Effect of EPS on sensitivity of portal vein contractility to changes in external calcium solution. Abscissa, Ca^{++} concentration (in mM); ordinate, IFS (in % of ISF in normal Ca^{++} concentration, namely 2.8 mM). 1) EPS; 2) control.

TABLE 1. Effect of Anoxia and Reoxygenation on Portal Vein Contractility under Normal Conditions and after EPS

Experimental conditions	Parameter studied	Initial parameters of contraction	Anoxia		Reoxygenation			
			2 min	5 min	2 min	5 min	10 min	20 min
Control	Developed tension, mg	127±19	72±12	44±11	114±16	156±22	155±32	150±33
	Frequency of contractions per minute	7,6±1,8	10±1,6	6,0±1,7	11±1,9	6,4±1,9	6,8±4,3	6,8±2,1
	IFS mg/mg·min	341±51	272±58	136±36	528±105	352±45	301±60	332±59
EPS	Developed tension, mg	25±4,7*	12±3,5*	4,1±1,1*	19±7,0*	30±6,6*	46±14	43±11
	Frequency of contractions per minute	12±1,8*	8,7±1,9	5,7±2,2	12±5,4	11±1,6*	9,3±2,4	8,1±1,2
	IFS mg/mg·min	124±21*	42±15*	13±5,4*	75±15*	86±25*	141±53*	122±36*

Legend. Here and in Table 2 asterisk indicates $P < 0.01$.

2.6 times. Acute anoxia led to deep depression of spontaneous activity of preparations of the vessels from both control and stressed animals. However, the results show that this depression developed more rapidly in experiments on portal veins of animals exposed to stress than the control, and recovery during reoxygenation took place more slowly in the veins of rats exposed to stress.

This becomes particularly clear if the response of the vascular smooth muscle to anoxia and reoxygenation was expressed as a percentage of its initial value. Figure 1 shows that at the 2nd minute of anoxia IFS for the brains of animals exposed to EPS fell to 34% of its initial level, whereas in the control it fell to only 14%. At 2nd and 5th minutes of reoxygenation IFS for the vascular smooth muscle of animals exposed to EPS recovered to 70 and 84% respectively of its initial value, whereas in the control it reached 199 and 126%.

Exposure to EPS thus considerably reduced the resistance of contractility of the portal vein smooth muscle to anoxia, i.e., to hypoxic energy deficiency [5]; this effect was evidently due to exhaustion of the energy reserves of the myocyte, due to stress, and a disturbance of processes of glycolysis and glycogenolysis [2].

The data given in Table 2 show that EPS causes an increase in sensitivity of the vascular smooth muscle to changes in the Ca^{++} concentration in the surrounding solution. For instance, the threshold of sensitivity of the vein preparation to calcium was lower in animals exposed to EPS than in the control: Spontaneous contractions of the control preparation appeared in a Ca^{++} concentration of 0.7 mM whereas after stress they appeared only when the concentration reached 1.4 mM. If contractility of the preparation in a normal Ca^{++} concen-

TABLE 2. Effect of Changes in Ca^{++} Concentration in External Solution on Portal Vein Contractility under Normal Conditions and after EPS

Experimental conditions	Parameter studied	Calcium concentration, mM								
		0	0,35	0,7	1,4	2,8	3,5	4,9	6,7	8,1
Control	Developed tension, mg	0	0	15±2,4	39±0,8	117±25	187±39	238±39	267±31	283±37
	Frequency of contractions per minute	0	0	18±0,5	18±1,9	10±1,2	5,5±0,8	3,6±0,2	2,3±0,3	2,2±0,3
	IFS, mg/mg·min	0	0	112±24	291±5,3	402±48	348±55	313±51	232±34	228±37
EPS	Developed tension, mg	0	0	0	4,0±0,9*	15±1,7*	22±3,3*	40±8,3*	46±7,2*	49±10*
	Frequency of contractions per minute	0	0	0	19±4,0	14±2,3*	11±2,3*	6,8±2,2*	6,8±1,5*	5,1±1,6*
	IFS, mg/mg· min	0	0	0	30±8,5*	81±17*	82±16*	71±14*	70±12*	64±14*

tration (2.8 mM) is taken as 100 (Fig. 2), it will be clear that IFS in a solution with reduced Ca^{++} concentration (1.4 mM) is 66 and 37%, respectively, for veins of control and stressed animals.

It can be tentatively suggested that this increase in dependence of portal vein contractility of animals exposed to EPS on the Ca^{++} concentration in the external solution is the result of reduced ability of membranes of the sarcoplasmic reticulum and sarcolemma to take up and accumulate Ca^{++} and of a disturbance of function of the membrane mechanisms responsible for active removal of Ca^{++} from the cell into the extracellular space [2].

One result of previous exposure to EPS is thus a decrease in resistance of the vascular smooth muscle to anoxia and an increase in its sensitivity to changes in the external calcium concentration. These changes may be due to a post-stress disturbance of the energy supply for the contractile apparatus of the myofibrils and injury to the membrane mechanisms of calcium transport.

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