tem, is compensated not only on account of ipsilateral connections of KA which remain intact, but also through switching of the nervous sytem to a different level of control of the voluntary motor act, which itself requires weaker participation of somatosensory feedback, namely feedback exerted on a centrally programmed level of control. Extralemniscal projections of KA under these circumstances can form and correct this program, and can also provide afferentation from the effect. By developing and widening these views, we can take a general look at the process of compensation in the CNS from certain novel standpoints. What do we understand by this process? Traditional ideas regard it as a process of activation of nervous formations or conduction systems not previously involved in the realization of a particular function, or activation, as we might say, of the reserves of the brain. At the same time, however, another principle may be involved, namely the switching to a different level of control of nervous structures and connections which previously had been concerned in the realization of that particular function, i.e., what we indeed can observe in compensation of processes controlling motor activity may also take place in any other compensatory reorganization of the nervous system. Views similar to these have also been expressed in [7].

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EFFECT OF TAURINE ON Ca,Mg-ATPase ACTIVITY AND PLATELET AGGREGATION IN MAN

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The role of calcium ions in realization of the dynamic properties of platelets is currently receiving considerable attention. Functioning of the contractile system of platelets, triggering the reaction of their release, prostaglandin synthesis, and regulation of the cyclic nucleotide system — these processes determining the level of platelet aggregating activity, changes in which are associated in turn with the pathogenesis of several hematologic and cardiovascular diseases and syndromes, are all connected with mobilization of intracellular calcium. Calcium metabolism in platelets, compared with its metabolism in cells of the myocardium and striated muscle tissue, has received less study. However, there are indications that factors in the regulation of calcium metabolism in excitable cells, such as the ATP-dependent transport system, Ca-binding proteins, and so on, actively function in platelets also [9].

The sulfoamino acid taurine is considered to be an effector of calcium metabolism in excitable tissues [1, 10]. It has also been found that platelets constitute a unique depot of taurine in the blood, for its concentration in them is 400 times higher than in plasma [4]. Taurine was shown previously to have an activating effect on energy-dependent calcium transport in excitable cells and it has been suggested that this is a universal effect for cells of different types [1, 2].

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TABLE 1. Effect of Some Drugs on Ca,Mg-ATPase Activity of Human Platelets

Experimental conditions (n = 5)	Enzyme activity, per cent
Control	100
Taurine (25 mM)	145
Trifluoperazine (0.01 mM)	45
Trifluoperazine (1.0 mM)	0
Trifluoperazine (0.01 mM) + taurine	55
Trifluoperazine (1.0 mM) + taurine	0
Colchicine (0.5 mM) *	130
Colchine + taurine *	130
β-alanine (15 mM)	102
β-alanine + taurine	114
Verapamil (0.5 mM) *	105
Verapamil + taurine *	120

Note. "Asterisk" indicates intact platelets. Here and in Table 2: n) number of experiments.

TABLE 2. Effect of Taurine on Rate of Aggregation of Human Platelets (M ± m; n = 10)

Experiment conditions	Aggregation rate, relative units	
	Spontaneous	Induced
Control	2,1±0,6	62,8±9,8
Taurine	1,0±0,3	30,3±5,8

The aim of this investigation was to test this hypothesis in relation to platelets, activation of whose function is closely linked with calcium ions.

EXPERIMENTAL METHOD

To isolate platelets, blood from healthy blood donors was collected in siliconized tubes containing 1/10 by volume of 3.8% sodium citrate solution. All subsequent procedures were carried out at 4° C is siliconized glassware immediately after blood taking. The citrated blood was centrifuged at 200 g for 10 min. Platelet-enriched plasma was separated and centrifuged at 1800 g for 20 min. The residue of platelets was washed with 0.85% NH_4Cl solution, equal in volume to the platelet-enriched plasma, and recentrifuged and resuspended in solution containing 30 mM KCl, 5 mM $MgCl_2$, 10 mM potassium oxalate, 20 mM Tris-HCl, pH 7.0. The platelets were fragmented on an ultrasonic disintegrator (20 kHz, 30 sec).

Activity of Ca, Mg-ATPase and Na,K-ATPase was determined as the increase in inorganic phosphate (P_i) removed from ATP under optimal conditions. The incubation medium for determination of Ca,Mg-ATPase activity contained (in mM): ATP 2.5, $MgCl_2$ 5.0, ouabain 0.15, EGTA 1.0, Tris-HCl 23.0, pH 7.5. The corresponding medium for determination of Na,K-ATPase activity contained (in mM): ATP 2.5, $MgCl_2$ 5.0, NaCl 75.0, KCl 12.5, $CaCl_2$ 0.05, ouabain 0.15, Tris-HCl 21.0, pH 7.5. Incubation continued for 20 min at 37° C and P_i was determined colorimetrically [6]. Enzyme activity was expressed in micromoles P_i/h/mg protein. Depending on the concrete aims of the experiment, 25 mM taurine, 1.0 or 0.01 mM trifluorperazine, 0.5 mM colchicine, 15 mM β-alanine, or 0.5 mM verapamil was added to the incubation medium. Protein was determined by Lowry's method [8]. The calcium concentration was determined on an ASS-1 atomic adsorption spectrometer and calculated in micromoles Ca^{++}/mg platelet protein or /ml platelet-deprived plasma.

Spontaneous platelet aggregation and aggregation induced by 3.5 μM ADP were assessed as the fall in intensity of scattering of light by platelet-rich plasma by the method in [5]. The results were subjected to mathematical analysis on the Hewlett Packard 9845T computer system.

EXPERIMENTAL RESULTS

Taurine (25 mM), when added to the incubation medium, increased Ca,Mg-ATPase activity of the platelet suspension by 45%. Meanwhile Na,K-ATPase activity was inhibited. Similar results were obtained by the use of sonicated platelet preparations, the only difference being that the initial enzyme activity was much higher than that of the intact cells. This was evidently due to fragmentation of the membranous structures of the platelets by ultrasound and with the consequently greater accessibility of the active centers of the enzymes. The results are in agreement with those of an investigation of the action of taurine on excitable cells [2], and it provides some confirmation of the hypothesis that its effect on the Ca^{++} transport system is universal in different types of cells [1].

The study of dependence of Ca,Mg-ATPase activity on the ratio between calcium concentrations in the platelets and blood plasma showed the existence of positive correlation between these parameters ($r = 0.87$). This may be indirect confirmation of the earlier hypothesis that the stimulating action of taurine on Ca,Mg-ATPase activity is based on its ability to potentiate calcium immobilization by membrane structures [2].

Transport Ca-ATPase of excitable cells and erythrocytes, and also actomyosin ATPase have been shown to be activated by a complex of calmodulin and Ca^{++} [11]. It has been suggested that calmodulin, firmly bound with the membrane, is a constituent subunit of transport Ca-ATPase [3]. To investigate whether calmodulin is necessary for taurine to exert its activating action on platelet Ca,Mg-ATPase, trifluoperazine, which forms a biologically inactive complex with calmodulin, was added to the incubation medium. Under these circumstances a sharp decline was observed in activity of the enzyme, or even its total inhibition, in the presence of a high concentration (1 mM) of trifluoperazine (Table 1). When this fact is evaluated, it must evidently be recalled that the selective action of trifluoperazine on Ca,Mg-ATPase is manifested in low concentrations of the drug.

The fact that the action of taurine on Ca,Mg-ATPase is virtually not exhibited in the presence of trifluoperazine is evidence that functionally active calmodulin is essential for taurine to exert its stimulating effect.

Ca,Mg-ATPase activity was increased by 30% on incubation of the platelet suspension with colchicine, which promotes depolymerization of microtubules. In this case also, taurine did not exhibit its activating action on the enzyme. Thus integrity of the cytoskeleton is an essential condition for the action of taurine, and to some degree this in specific, because replacement of taurine by its structural analog β-alanine was not accompanied by any change in Ca,Mg-ATPase activity.

Preincubation of platelets with the calcium antagonist verapamil, which blocks the calcium channels of the outer cell membranes, reduced activation of Ca,Mg-ATPase by taurine by half. In this connection it will be noted that although verapamil prevents penetration of calcium from the extracellular medium through the plasma membrane, and taurine promotes calcium immobilization by the intracellular membranes, the end result of their action is the same, namely a fall in the calcium concentration in the cytoplasm. In this sense taurine can be regarded as an intracellular calcium antagonist. The effect of calcium antagonists on the dynamic properties of platelets and, in particular, on their ability to aggregate, is well known [7]. It is natural to suggest that taurine also possesses activity in this respect. In fact, exposure of platelet-rich blood plasma with 25 mM taurine reduced the mean level both of spontaneous aggregation and of aggregation induced by 3.5 μM ADP (Table 2).

It can be concluded from these results that taurine takes part in energy-dependent calcium transport in platelets. The effect of taurine on platelet aggregation is evidence that it may have a modulating role on the stage between the humoral stimulus and intracellular calcium translocation, with a consequent change in the dynamic properties of the platelets.

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