Potassium and Sodium Ions in the Nerve Tissue of Emotionally Overstrained Rabbits

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UDC 616.8-018-008.924.1]-02:613.863]-092.9-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 8, pp. 129-131, August, 1994
Original article submitted December 12, 1993

Measurement of K^+ and Na^+ concentrations in samples of individual brain nuclei and in ganglia of the autonomic nervous system from rabbits subjected to severe emotional stress (ES) through aperiodic stimulation of ventromedial hypothalamic nuclei and electrocutaneous stimulation revealed significantly altered levels of these ions in locus ceruleus samples from animals predisposed to ES-induced cardiovascular disorders and in samples of neurons of the caudal part of the brainstem from those resistant to such disorders.

Key Words: *emotional stress; resistance; K^+ and Na^+ ions; brain nuclei*

It has been shown that the stability of cardiovascular functions in animals is determined by characteristics of neurotransmitter processes in the brain. Catecholamine levels in individual brain nuclei have been found to differ in animals differing in their resistance to emotional stress (ES) [5], which suggests that such animals also differ with regard to synaptic transmission of excitation in these brain structures. Synaptic processes are known to be associated with the presence of K^+ and Na^+ ions in neurons and their redistribution precisely at moments when the functional activity of these cells increases. In this study, we focused our attention on the distribution of K^+ and Na^+ ions in individual nervous system structures of animals differing in their resistance to ES.

MATERIALS AND METHODS

The study was conducted on two groups of rabbits (4 animals in each) differing in the responses of arterial blood pressure (BP) and heart rate to the severe ES produced by aperiodic stimulation of ventromedial hypothalamic nuclei and by electrocutaneous stimulation. One group was characterized by slight variations in BP ("resistant" rabbits) and the other by a progressive fall in BP (rabbits "predisposed" to cardiovascular disorders). Rabbits of this second group died with signs of acute heart failure. Five intact rabbits served as controls.

The brains of all animals were frozen and used to obtain a total of 300 micron sections of the following brain structures: (1) lateral reticular nucleus of the medulla oblongata (dorsal part) - A_1; (2) a group of nuclei in the region of the solitary tract - A_2; reticular formation (RF) of the medulla oblongata; (4) locus ceruleus and "subcerulean" area (nSC); (5) RF of the midbrain; (6) RF of the pons; (7) substantia nigra; (8) perifornicate area; (9) frontal cortex; (10) nucleus caudatus; and (11) preoptic area.

Additionally, the superior cervical and stellate sympathetic ganglia and the nodose ganglion of the vagus were examined. K^+ and Na^+ levels in the samples were determined by flame photometry [4]. The results were treated statistically by Student's t test.

RESULTS

Measurements of K^+ and Na^+ concentrations revealed their elevated levels in locus ceruleus

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0007-4888/94/0008-0816$12.50

TABLE 1. Levels of K and Na Ions (g−eq/mg Protein) in Brain Structures from Rabbits with Emotional Stress ($M \pm m$)

Brain structure	K			Na		
	"predisposed" rabbits (n=4)	"resistant" rabbits (n=4)	control rabbits (n=5)	"predisposed" rabbits (n=4)	"resistant" rabbits (n=4)	control rabbits (n=5)
A_1	2.4±0.39	3.5±0.88	1.7±0.5	2.6±0.2	3.7±0.7*	1.5±0.5
A_2	2.5±0.4	0.8±0.5	14.0±0.7	3.1±0.4	3.0±1.7	12.2±5.8
Reticular formation of medulla oblongata	4.7±1.4	3.5±1.3	2.7±1.7	4.1±1.6	4.2±1.7	2.1±0.6
Locus ceruleus + nSC	2.8±0.5*	2.9±1.9	1.2±0.6	2.8±0.4*	5.0±1.7	1.0±0.4
Reticular formation of midbrain	3.2±2.0	3.4±1.5	2.9±0.4	5.8±3.6	2.1±0.8	1.9±0.2
Reticular formation of pons	2.5±0.3	2.7±0.3	2.0±0.1	2.8±1.0	1.8±0.5	1.3±0.1
Sibstantia nigra	6.6±4.6	1.3±0.7	2.4±0.6	9.1±6.0	2.8±2.2	1.6±0.3
Perifornicate area	2.6±0.6	3.2±0.6	3.0±0.8	4.4±1.8	4.6±1.6	2.2±0.6
Caudate nucleus	1.6±0.4	2.2±0.3	2.3±0.7	3.0±1.1	2.7±0.4	2.1±0.7
Preoptic area	2.3±0.6	2.8±0.5	2.6±0.5	2.5±0.4	2.2±0.8	2.0±0.1
Superior cervical sympathetic ganglion	2.0±0.2	1.1±0.3	2.0±0.5	3.5±0.8	2.1±1.9	3.3±0.3
Nodose ganglion	1.3±0.1	2.6±1.6	1.2±0.1	3.2±0.7	8.9±0.3	4.3±0.8
Stellate synpathetic ganglion	0.9±0.4	1.2±0.1	1.4±0.3	3.1±0.4	3.9±0.6	5.8±3.2
Cortex	2.1±0.5	2.6±0.6	2.1±0.3	1.8±0.1	2.7±0.5	2.2±0.2

Note. The asterisk indicates a significant difference from the control group at $p<0.025$.

samples from rabbits predisposed to cardiovascular disturbances. Samples from "resistant" rabbits contained near-normal K^+ and Na^+ levels in this locus, but had significantly elevated Na^+ levels in the A_1 area. The concentrations of both electrolytes in most central and autonomic nervous system structures were close to their control values (Table 1). For some structures, namely the substantia nigra, perifornicate area, and nodose ganglion, a tendency toward alterations in K^+ and Na^+ levels in response to ES was discernible, and it should be noted that such alterations were unidirectional in most of the samples studied. This phenomenon may be due to altered permeability of the blood-brain barrier (BBB) in certain brain structures as a result of ES. In our previous experiments on stressed rats, increased BBB permeability to a high-molecular-weight dye (trypan blue) was shown by the preoptic area of the hypothalamus, the RF of the midbrain, and the catecholamine-synthesizing groups A_1 and A_2 [5]. In brain samples from rats stressed by immobilization, increased BBB permeability was noted in the RF of the brainstem, and ruptured vessels with components of endothelial cells lying in their lumens were seen in some samples. In the present study, brainstem structures (RF of the midbrain and medulla oblongata) contained appreciably altered electrolyte levels (Table 1). In the midbrain RF, substantia nigra, and nodose ganglion from rabbits differing in responses of the cardiovascular system to stress, the concentration of only one of the two electrolytes was altered. A reduction in extracellular K^+ is known to be an energy-dependent process in which Na,K-ATPase takes part, and the observed differences in Na^+ and K^+ levels between animals differing in their resistance to stress appear to be associated with differences in the metabolic processes by which the brain is supplied with energy.

Earlier experiments in our laboratory revealed that a leading role in responding to a stress-producing factor is played by the locus ceruleus [1,2]. The resistance of animals to stress and the response of BP to it were found to be dependent on catecholamine levels in the major norepinephrine-synthesizing nuclei of the brain, i.e., the locus ceruleus and nSC [1]. In the present study, too, these structures of the midbrain RF were implicated in mediating the effects of the stress-producing factor: locus ceruleus and nSC samples from rabbits predisposed to cardiovascular disorders contained K^+ and Na^+ at elevated levels. In a previous study, stress reactions were shown to involve the participation of cellular structures in the caudal brainstem, namely of group A_1 neurons, which was manifested in altered epinephrine levels [1]. The study reported here revealed changes in K^+ and Na^+ concentrations in this area, indicating that neurons of the caudal brainstem region were in-

volved in the development of the stress reaction in the animals with stable cardiovascular functions.

The altered electrolyte levels detected in this study in certain brain nuclei appear to be a reflection of profound metabolic changes in the cellular brain structures responsible for mediating the stress-producing stimulus. The measurements of K^+ and Na^+ concentrations performed in individual brain nuclei support the notion that characteristics of synaptic transmission are the major determinants of the cardiovascular system's resistance to stress.

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Antiulcerogenic Effects of Benzylpenicillin in Acutely Stressed Rats

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UDC 615.281:616.33-002.44

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 118, № 8, pp. 131-133, August, 1994
Original article submitted December 6, 1993

The antibiotic benzylpenicillin was found to produce dose-dependent antiulcerogenic effects in rats when administered immediately before their exposure to acute stress (swimming for 1 h) that led to gastric mucosal ulceration. Such effects were not observed in rats given benzylpenicillin 48 h before stress exposure. The results of this study suggest that in acutely stressed animals benzylpenicillin may activate as yet unidentified mechanisms which afford protection to the gastric mucosa and which are not associated with the longer-lasting antimicrobial effects of this antibiotic.

Key Words: *ulcerogenesis; acute stress; benzylpenicillin*

Stress-induced gastric mucosal lesions have customarily been considered to result from an imbalance between protective and aggressive factors and to involve directly a number of neurohumoral mechanisms [7,9]. The properties of various pharmacological agents that influence neurohumoral processes and ulcerogenesis are therefore under intensive study [4,6]. Some benefit in the treatment of gastric ulcer is afforded by certain antibiotics, including benzylpenicillin (BP), which is usually attributed to their antimicrobial properties - their action on microorganisms which have recently been incriminated as possible culprits in the pathogenesis of gastric mucosal lesions [15]. There is also evidence that BP possesses neurotropic properties [1,3,5,8,13]. This calls for studies to find out whether BP and its analogs can exert antiulcerogenic effects via central and/or peripheral mechanisms.

MATERIALS AND METHODS

A total of 240 random-bred white rats of both sexes weighing 150-200 g were used. Before the experiments they had been fasted for 48 h but given free access to water. Immediately (1 min) or 48 h before exposure to acute stress, test rats were injected intraperitoneally with 0.2 ml of BP so-

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0007-4888/94/0008-0818$12.50