Effect of Locus Coeruleus Stimulation on Ocular Hypertension and Pathology of Pulmonary Surfactant during Chronic Emotional Stress

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In chronic experiments on rabbits and rats, parameters of eye homeostasis (intraocular pressure and ocular hydrodynamics) and lungs (water balance and surface-active properties of surfactant) were studied during electrical stimulation of the locus coeruleus against the background of chronic stress induced in rabbits by repeated electrical stimulation of the ventromedial nucleus and in rats by daily immobilization on a platform. Stimulation of the locus coeruleus eliminated ocular hypertension of hypothalamic origin and stress-induced disturbances in surface activity, blood volume, and water balance in the lungs.

Key Words: *locus coeruleus; stress; intraocular pressure; surfactant; water balance*

Structures of the hypothalamus-limbicoreticular complex including ventromedial hypothalamic nucleus (VMHN) are involved in the development of stress reaction [5]. Activity of the autonomic nervous system during stress is partially controlled by the locus coeruleus (LC). Among other functions this structure improves organism's resistance to stress [1].

MATERIALS AND METHODS

The study was carried out on rabbits (n=24) and rats (n=51). In rabbits, chronic emotional stress was induced by repetitive electrical stimulation of VMHN (every other day for 30 days). Rectangular pulses (2-5 V, 0.5 msec, 70 Hz) were applied for 1 h. Intraocular pressure and ocular hydrodynamics (rates of production and outflow of intraocular fluid) were recorded by the method of simplified tonography [4] with a TNC-100 tonometer (load weight 7.5 g). Stress in rats was induced by daily 2-h immobilization on a platform for 10-30 days. The parameters of pulmonary surfactants and pulmonary water balance were assessed as described elsewhere [2,3]. In some experiments, stress was combined with electrical stimulation or bilateral destruction of LC. Intact or sham-operated animals comprised the control group. The data were processed statistically using Student's t test.

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RESULTS

In rabbits, electrical stimulation of VMHN produced a sustained increase in intraocular pressure resulting from enhanced production and reduced outflow (on week 3) of intraocular fluid (Table 1). Electrical stimulation of LC increased intraocular pressure on week 1, which was caused by increased production of intraocular fluid and was accompanied by compensatory increase in its outflow. Combined stimulation of VMHN and LC decreased or normalized true intraocular pressure, *i.e.* completely abolished of the effect of stress. Both minute volume of intraocular fluid and outflow coefficient returned to normal.

Chronic immobilization stress decreased surface activity of pulmonary surfactant and pulmonary blood volume and induced accumulation of extravascular fluid (Table 2). Electrical stimulation of LC produced similar changes, but the content of alveolar phospholipids considerably increased. Stimulation performed against the background of immobilization stress

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TABLE 1. Effect of Stimulation of VMHN and LC on Intraocular Pressure and Ocular Hydrodynamics (*M*±*m*)

Period of experiment	Electrical stimulation of VMHN			Electrical stimulation of VMHN and LC		
	true intraocular pressure, mm Hg	outflow coefficient, mm^3/min/mm Hg	minute volume of intraocular fluid, mm^3/min	true intraocular pressure, mm Hg	outflow coefficient, mm^3/min/mm Hg	minute volume of intraocular fluid, mm^3/min
Before stimulation	19.28±0.69 20.01±0.72	0.12±0.02 0.13±0.01	1.18±0.23 1.35±0.22	19.28±0.69 20.01±0.72	0.12±0.02 0.13±0.01	1.18±0.23 1.35±0.22
Week 1	23.57±0.66* 21.35±0.56	0.09±0.01 0.13±0.01	2.25±0.31* 1.32±0.15	18.58±0.27 20.17±0.75	0.16±0.01 0.27±0.03*	1.29±0.38 3.95±0.59*
Week 2	23.83±0.72* 22.32±0.69**	0.07±0.02 0.12±0.03	2.21±0.37** 1.84±0.26	18.43±0.12 19.58±0.69	0.15±0.02 0.21±0.02*	1.21±0.19 2.68±0.17*
Week 3	26.09±0.82* 23.17±0.54*	0.06±0.02** 0.11±0.02	2.46±0.13* 2.44±0.29*	18.35±0.28 18.42±0.25**	0.27±0.06** 0.18±0.01*	2.39±0.29* 1.28±0.19
Week 4	27.43±0.79* 25.25±1.03*	0.07±0.02 0.13±0.03	2.92±0.31* 2.21±0.21*	18.35±0.94 18.32±0.37**	0.19±0.07 0.17±0.01**	1.69±0.63 1.37±0.13
After stimulation	23.81±0.88* 23.78±0.65*	0.08±0.01 0.12±0.02	2.21±0.12* 2.59±0.32*	19.02±0.31 19.58±0.58	0.13±0.01 0.13±0.03	1.31±0.87 1.41±0.15

Note. *p<0.01, **p<0.05 compared to the control. Nominator and denominator show parameters of right and left eyes, respectively.

removed the pulmonary manifestations of the stress except adrenal hypertrophy. Bilateral destruction of LC normalized the weight of adrenals, but did not eliminate pulmonary changes.

These findings attest to opposite effects of electrical stimulation of LC under control conditions and against the background of emotional stress. It shows that LC modulates physiological functions during stress, which agrees with assumed homeostatic role of this cerebral structure [1]. There are indications that LC is a neuronal focus of genetic tolerance to emotional stress [6], which agrees with the data on decreased stress resistance in animals with damaged ascending noradrenergic pathways [7]. Probably, LC is involved in the genesis of normal stress reaction, which does not surpass the limits of general adaptation response and does not transform into distress. Therefore, stimulation of LC can prevent the development of abnormalities in the brain [1] and peripheral organs under conditions of severe stress.

TABLE 2. Effect of Chronic Stress, Electrical Stimulation of LC and Bilateral Electrolytic Destruction of LC on Surfactant Characteristics, Pulmonary Blood Volume, and Fluid Balance

Parameter	Control	Stress	Electrical stimulation of LC	Stress+electrical stimulation of LC	Stress+destruction of LC
Pulmonary blood volume, %	8.67±0.94	5.96±1.06***	4.45±0.63**	10.75±2.64^{+++}	6.43±1.98
Total fluid, %	78.39±0.87	80.06±0.66	79.64±0.87	80.97±1.50	80.50±0.91
Intravascular fluid, %	7.19±0.78	4.95±0.88	3.62±0.52**	8.92±2.19	5.33±1.64
Extravascular fluid, %	72.58±0.98	75.74±0.51***	75.95±1.24	73.69±1.68	72.49±2.91
Minimal surface tension, mN/m	19.65±0.46	25.87±0.46*	24.93±1.40**	18.49±0.99^{+}	22.83±0.58**
Maximum surface tension, mN/m	35.08±0.47	38.57±0.73*	37.71±0.95***	33.51±0.49^{+}	37.60±0.37*
Stability index	0.560±0.018	0.390±0.025**	0.410±0.036***	0.580±0.044^{++}	0.490±0.024
Phospholipids, μmol/g	37.61±5.07	28.49±4.66	151.98±16.62*	27.71±4.44	21.22±2.88***
Cholesterol, μmol/g	12.69±2.99	11.14±1.79	7.13±1.10*	7.46±1.58***	19.05±6.98
Phospholipids/cholesterol	2.99±0.36	3.09±0.54	23.59±4.19*	4.70±0.71**	1.06±0.14*
Weight of adrenals, %	0.021±0.001	0.027±0.001**	0.029±0.003**	0.032±0.005***	0.021±0.002^{+++}

Note. *p<0.001, **p<0.01, ***p<0.05 compared to the control. ^{+}p<0.001, ^{++}p<0.01, ^{+++}p<0.05 compared to stress.

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