Decreased Tolerance to Acoustic Stress in Late Postresuscitation Period in Krushinsky-Molodkina Rats

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The effect of circulation arrest on the development of stress-induced injuries was studied in Krushinsky—Molodkina rats genetically predisposed to audiogenic seizure. Resuscitated rats were subjected to acoustic stress 1.5 month after circulation arrest. The severity of neurological disorders and the frequency and severity of intracranial hemorrhages increased, while excitability of the central nervous system remained unchanged during stress. Thus, the resistance to stress considerably decreased in rats survived a short-term circulatory arrest due to dysfunction of the autonomic nervous regulation of hemodynamics rather than enhanced excitability of the central nervous system.

Key words: *resuscitation; Krushinsky—Molodkina rats; acoustic stress; neurological disorders*

Resuscitation induces a variety of pathological processes in the organism manifested not only in the early, but also in the late postresuscitation period [4].

Most of these events involve the central nervous system (CNS). Our aim was to evaluate neurological status in the late postresuscitation period by studying organism's responses to audiogenic stress (AS).

MATERIALS AND METHODS

Experiments were carried out on Krushinsky—Molodkina (KM) rats weighing 180-200 g. Circulation arrest was produced by a 5-min mechanical occlusion of afferent and efferent cardiac vessels under ether narcosis and closed chest conditions [2]. Resuscitation consisted of closed chest cardiac massage, artificial ventilation, and intratracheal injection of epinephrine (0.1 mg/kg).

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Both resuscitated (1.5 months after AS) and intact rats of the same strain were subjected to AS in a Plexiglas chamber (45×50×60 cm) according to the L. V. Krushinsky protocol [3]. A loud acoustic signal (110 dB, 1.5 min) was followed by a series of sounds of alternating intensities (from 80 to 110 dB, 10 sec) with 10-sec intervals, and after a 3-min pause a loud acoustic signal (120 dB, 1 min) was presented again. The following parameters characterizing CNS excitability were studied during AS: pattern, latency, and intensity of seizures and locomotor disorders [8]. Mild (slight impairment of muscle tone not limiting animal motion), moderate (limb paresis with limitation of motion), and severe (almost complete immobilization) motor disturbances were distinguished. After completion of acoustic stimulation the rats were decapitated. The brain was removed and fixed in 10% formaldehyde. The areas of subdural and subarachnoid hemorrhages were measured on photographs. Intraventricular hemorrhages were determined on cross-sections.

The data were processed by Student's t and Fisher's tests and ANOVA F test.

Experiments were performed in accordance with Principles of Laboratory Animal Studies [7].

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RESULTS

Resuscitation was successful only if the circulation was stopped for no more than 5 minutes. After 8-10-min circulation arrest, cardiac function could be restored but spontaneous breathing was absent. Unlike KM rats, Wistar rats survived even 12-min cardiac arrest [6].

Circulation arrest reduced rat resistance to AS. Motor disturbances during AS (from minutes 1 to 10) were more severe ($p<0.05$) and neurological deficit developed more abruptly in resuscitated rats compared to the control (Fig. 1).

Morphological examination of the brain showed that cerebral hemorrhages in resuscitated rats exposed to AS occurred more often (Table 1) and subdural and arachnoid hemorrhages were more extensive (25.35±7.81 *vs.* 5.80±3.88 mm^2 in the control, $p=0.04$).

Parameters of CNS excitability in resuscitated rats during AS did not differ significantly from the control. The mean latencies of seizure in resuscitated and control rats were 3.1±0.2 and 3.6±0.4 sec, respectively, while seizure intensity score in both groups was 3.5±0.1. Despite the same level of convulsive activity, the enhanced severity of neurological deficit (impaired locomotion) and the higher occurrence and severity of intracranial hemorrhages induced by AS point to a decreased tolerance of resuscitated rats to stress.

Clinical death enhances convulsive activity of the brain by increasing the number epileptic neurons, rearrangements of interneuronal relationships, and the formation of epileptic neuronal networks [5]. We found that convulsive activity in resuscitated KM rats did not exceed the control level (judging from the latency and intensity of seizures) probably due to extremely high baseline convulsive activity in KM rats [3]. More extensive damage to the brain in resuscitated rats after AS probably results from impaired autonomic regulation. It was previously shown that cerebral hemorrhages in KM rats resulted from dramatic blood pressure rise during acoustic stimulation. Moreover, the area of hemorrhage closely correlated with the absolute increase in blood pressure [1]. It can be concluded that the higher frequency and more extensive hemorrhages induced by AS in resuscitated KM rats were a direct consequence of more pronounced rise in blood pressure compared to that in intact rats.

TABLE 1. Occurrence of Intracranial Hemorrhages (%) in KM Rats Exposed to AS

Type of hemorrhage	Control	Resuscitated
Subdural and subarachnoid	22.2	75**
Intraventricular	11.1	87.5*

Note: *$p<0.01$, **$p<0.05$ compared to the control.

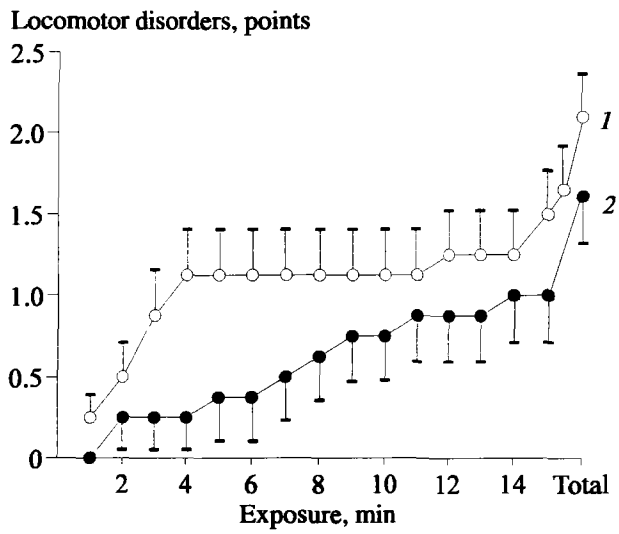

Fig. 1. Locomotor disorders in resuscitated (*1*) and control (*2*) KM rats exposed to audiogenic stress. Differences from the control are significant up to 10th min ($p<0.05$).

Our findings indicate that regulatory disorders persist in rats in the late postresuscitation period (1.5 month). These postresuscitation phenomena are determined by impaired autonomic nervous control of the hemodynamics rather than enhanced excitability of the central nervous system.

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