METHODS

Dynamics of the Recovery Period in Rats Exposed to Global Cerebral Ischemia

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Global cerebral ischemia-reperfusion was modeled by thermocoagulation of the vertebrobasilar arteries followed by occlusion of both carotid arteries. Behavioral parameters, neurological status, and mnesic functions in rats were studied during the recovery period. It is concluded that this model of ischemia is reproducible and can be used for studying ischemia-reperfusion damages to the brain.

Key Words: *cerebral ischemia; neurological status; behavioral reactions*

Recent studies showed that cerebral ischemia causes not only ischemic, but also reperfusion damages to the neuronal tissue. Therefore, ischemia should be considered as a complex two-stage process: injuries produced by acute ischemia are aggravated and become irreversible after restoration of the cerebral circulation [1]. In this respect, recovery of the higher nervous activity in rats during the reperfusion period (RP) following global cerebral ischemia (GCI) is of particular interest.

Here we studied behavioral parameters, neurological status, and mnesic functions in rats exposed to GCI followed by RP.

MATERIALS AND METHODS

Experiments were performed on 27 outbred male rats weighing 250-300 g kept in a vivarium. GCI and reperfusion were modeled as described elsewhere [4]. Thermocoagulation of the vertebrobasilar arteries was conducted at the C_1 level. Both carotid arteries were occluded 4 days later. The animals were narcotized intraperitoneally with 80-100 mg/kg calipsol. GCI was induced by 30-min occlusion of the carotid arteries on the next day 1 after the second operation. The efficiency of this procedure was confirmed by areflexia developed over the 1st min of ischemia and followed by dyspnea. Perfusion was restored by removal of the ligatures; adequate recirculation was verified visually. Sham-operated rats served as the control. Locomotor activity was assayed on days 1 and 2 of reperfusion in an Ugo Basile chamber. The rat was placed in a chamber (37×27×27 cm) with a transparent top. Locomotor activity was recorded for 10 min and expressed in arb. units. Open field behavior was studied on days 3 and 5; the latency of exit from the central square and horizontal (number of crossed squares), vertical (rearings),

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TABLE 1. Behavioral Parameters (% of Control) of Male Rats during Recovery after GCI

Parameter	Recovery, day	
	3	5
Latency	2033	861
Activity		
horizontal	10	43
vertical	20	35
exploratory	21	47

Note. All differences from the control are significant at $p<0.05$.

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and exploratory activities (number of explored holes) were recorded for 3 min. Conditioned passive avoidance behavior (CPAB) was studied; the rats were trained 1 h before ischemia and then the latency of entrance into dark compartment was recorded on day 7 of reperfusion. Neurological status (corneal, tail-flick, hind limb withdrawal, rotational, forelimb grasp, and acoustic startle reflexes) was examined over the first 7 days [2] and scored using a 3-point scale: normal (2), decreased (1), and absent (0). Muscle strength of forelimbs was measured by the force applied to hold the ring of a dynamometer during the forelimb grasp reflex [3]. These parameters remained practically unchanged during further observations. The results were analyzed by Student's *t* test and nonparametric Mann-Whitney test.

RESULTS

Mortality in our experiments was 25-30%. After thermocoagulation of the vertebrobasilar arteries, this parameter did not exceed 10%. During ischemia and RP, the mortality rates were practically similar.

Locomotor activity of some rats increased during early RP (by 3.1 and 2.1 times on days 1 and 2, respectively); on day 3, these animals died. In other rats, locomotor activity on days 1 and 2 decreased by 86 and 82%, respectively; there was no mortality in this group of animals.

The latency of exit from the central square of the open field sharply increased, while horizontal, vertical, and exploratory activities decreased during recovery (Table 1). On day 7, there were no significant differences in behavioral patterns between test and control animals.

In animals exposed to ischemia, neurological deficit and decreased muscle strength of forelimbs were found. These changes were most pronounced on days 3-4 (Fig. 1). However, the corneal and rotational reflexes were preserved. Hind limb withdrawal, tail-flick, and forelimb grasp reflexes then recovered. All

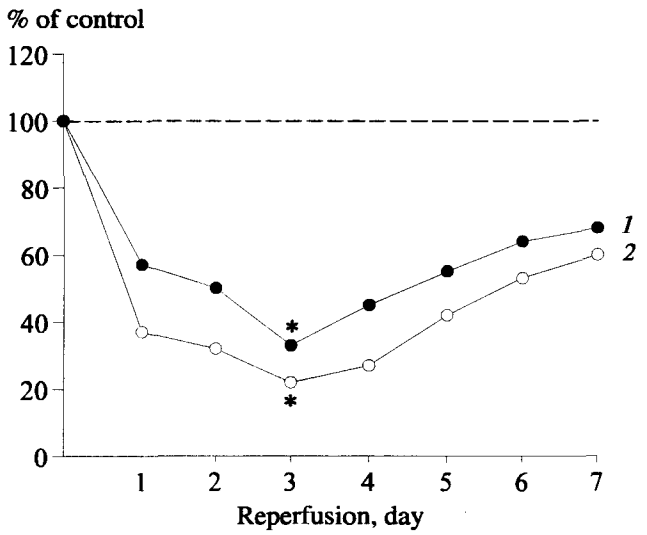

Fig. 1. Neurological status (*1*) and parameters of dynamometry (*2*) in rats exposed to global cerebral ischemia. *$p<0.05$ compared to the control.

rats exposed to ischemia lost the acoustic startle reflex. Passive avoidance learning was impaired in animals subjected to ischemia, which manifested in short latency of entrance into the dark chamber.

We conclude that this model of GCI is reproducible and can be used in pharmacological and pathophysiological experiments for studying ischemia-reperfusion injuries. Postischemic reperfusion causes disturbances in behavioral parameters, neurological status, and mnesic functions.

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