Lithium reduces post-resuscitation damage of the hippocampus in rats

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A well-known drug for the treatment of bipolar disorders, lithium chloride, has a neuroprotective effect in conditions associated with acute and chronic circulatory disorders.

The aim of the study was to investigate the effectiveness of lithium chloride to prevent the hippocampal damage in the post-resuscitation period.

Material and methods.

Cardiac arrest in adult male rats for 10 minutes was evoked by intrathoracic clamping of the vascular bundle of the heart, followed by resuscitation. 4,2% LiCl solution (40 mg/kg) was administered 1 hour before cardiac arrest, on the 1st and 2nd day after resuscitation (20 mg/kg). Untreated animals received equivalent doses of saline. Sham-operated rats served as controls. The number of viable neurons in the CA1 and CA3/CA4 fields of the hippocampus was estimated in brain sections stained with cresyl violet by day 7 post-resuscitation. In a separate series of experiments, at the same terms, the levels of total/phosphorylated glycogen synthase kinase (GSK) 3 β , a molecular target of lithium, were investigated in brain tissue using Western blot analysis.

Results.

Fig. 1. Decrease in the number of viable neurons in the CA1 field of the hippocampus after cardiac arrest - by 37.5% (** $p < 0.001$; ANOVA), in the CA3/CA4 field - by 12.9% (* $p < 0.05$). Lithium treatment increased the number of viable neurons in resuscitated rats - in the CA1 field by 37% (* $p < 0.01$), in the CA3/CA4 field - by 11.5% (# $p \leq 0.1$) compared to untreated animals.

Fig. 2. Lithium caused an increase in phosphorylated form of GSK3 β : by 180% versus control (* $p < 0.05$; Mann-Whitney *U*-test), and by 150% compared to untreated animals (# $p < 0.05$).

Conclusion. Lithium chloride administration resulted in neuroprotection in neuronal populations of the hippocampus post-resuscitation. This effect may be due to a modulation of GSK3 β activity. Lithium is extremely promising for the prevention and treatment of neurodegenerative disorders caused by ischemia-reperfusion.