

# Abstract

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## **Folic acid deficiency increases brain cell injury via autophagy enhancement after focal cerebral ischemia.**

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**BACKGROUND:** Folic acid (FA) deficiency is not only associated with an increased risk of ischemic stroke, but also with increased oxidative DNA damage and brain injury after cerebral ischemia-reperfusion. However, the cellular and molecular mechanisms underlying FA deficiency-associated neuropathogenesis are not completely understood.

**OBJECTIVE AND METHOD:** In the present study, we tested the hypothesis that neuronal autophagy in focal cerebral ischemia rats may be involved in the mechanisms of FA deficiency-induced injury to neuronal cells.

**RESULTS:** The results demonstrated that, accompanied by obvious neuron damage, the expression of the autophagic markers LC3 and Beclin-1, and the formation of 8-OHdG (a marker of oxidative stress to DNA) and autophagosomes were significantly increased in the brain cortex after ischemia-reperfusion. FA deficiency further induced neuronal cell death, and significantly increased the formation of autophagosomes and the expression of LC3 and Beclin-1 in NeuN-positive cell bodies after ischemia-reperfusion. The elevated level of 8-OHdG was also observed in the ischemic cortex of FA deficiency-treated animals. Conversely, the neuronal cell injury, autophagosome accumulation and the effects of LC3 and Beclin1 overexpression caused by FA deficiency were partially blocked by an autophagic inhibitor 3-methyladenine.

**CONCLUSION:** These results suggest that FA deficiency progresses autophagic activation and aggravates the damage in rat brain cortex following focal cerebral ischemia-reperfusion. The oxidative injury may be involved in cell morphological damage and autophagy alteration caused by FA deficiency.

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