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Ceftriaxone Improves Learning and Memory Deficits by Promoting Glutamine Cycle in Early Stage of the APP/PS1 Transgenic Mouse Model for Alzheimer's Disease

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Alzheimer's disease (AD) is characterized by progressive impairment of learning, memory and cognitive functions. Glutamate as neurotransmitter plays an important role in learning, memory and cognition. The glutamate homeostasis and reutilization are associated with glutamate uptake by astrocytic glutamate transporter-1(GLT-1) and the subsequent glutamate-glutamine cycle. Increasing evidence showed the dysregulation of GLT-1 and glutamate-glutamine cycle in AD. Ceftriaxone (Cef) has been reported to up-regulate the expression and uptake activity of GLT-1. Therefore, the present study was undertaken to explore whether Cef can improve the learning and memory deficits of APP/PS1 mice at 7- and 6-month age by up-regulating the expression of GLT-1 and then promoting the glutamate-glutamine cycle by assaying the expression and activity of glutamate synthetase (GS) and the expression of system N glutamine transporter SN1, which are related to the glutamate-glutamine cycle. The learning and memory functions were examined by Novel object recognition and Morris water maze tests. The expressions of GLT-1, GS and SN1 in the hippocampus were assayed with immunohistochemistry and western blot analysis, and the GS activity was assayed with spectrophotometry. It was shown that Cef treatment in doses of 200 mg/kg and 300 mg/kg significantly improved the learning and memory deficits of the APP/PS1 mice and up-regulated the expression of GLT-1. Furthermore, the activity of GS and the expression of SN1 were significantly up-regulated as well after the Cef treatment. The above results suggested that Cef could improve the learning and memory deficits of the APP/PS1 mice in early stage of AD by promoting the glutamate-glutamine cycle.

Key words: Ceftriaxone, GLT-1, glutamate-glutamine cycle, APP/PS1 mice

Biography:

Wenbin Li is a Professor in the Department of Pathophysiology, Neuroscience Research Center, Hebei Medical University, China. He is now mainly interested in the fundamental study in the prevention and therapy of Alzheimer's disease, cerebral ischemia and the mechanism of cerebral ischemia tolerance.