عنوان مقاله:

Mechanism underlying the effects of doxepin on β-amyloid -induced memory impairment in rats

محل انتشار:

مجله علوم پایه پزشکی ایران, دوره 20, شماره 9 (سال: 1396)

تعداد صفحات اصل مقاله: 6

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خلاصه مقاله:

Objective(s): In previous studies, researchers observed that doxepin could improve cognitive processes and has protective effectson the central nervous system. Thus, this study was designed to analyze the effects of doxepin on β-amyloid (Aβ)-induced memory impairment and neuronal toxicity in ratand to explore the underlying mechanism. Materials and Methods: Rats were treated with Aβ۱-۴۲ and doxepin was injected to validate its effects on cognitive function. The Morris water maze test was performed to detect memory function. Aβ۱-۴۲-treated SH-SY۵Y human neuroblastoma cell line was also used to detect the effects of doxepin and to explore the underlying mechanism. Western blotting analysis was used to detect the protein expression levels of PSD-۹۵, synapsin ۱, p-AKT and p-mTOR in rats. Results: After treated with ۱ mg/kg of doxepin, Aβ۱-۴۲-treated rats showed markedly lower escape latency and higher platform-finding strategy score. Low doses of doxepin significantly reversed the effects of Aβ۱-۴۲ on the protein expression levels of PSD-۹۵, synapsin ۱, p-AKT and p-mTOR in rats. In vitro experiment showed the consistent results. Besides, PI۳K inhibitor (LY۲۹۴۰۰۲) treatment could markedly reversed the effects of doxepin on Aβ۱-۴۲-treated SH-SY۵Y cells. Conclusion: Our results demonstrated that doxepin could protect against the Aβ۱-۴۲-induced memory impairment in rats. The protective effect of doxepin was associated with the enhancement of PSD-۹۵ and synapsin ۱ expression via PI۳K/AKT/mTOR signaling pathway.

کلمات کلیدی:

Alzheimer’s disease, Doxepin, Memory injury, PI۳-K/AKT/mTOR- signaling, β-amyloid۱-۴۲