The protective effects of JNK inhibitor on β-amyloid-induced neuronal apoptotic factors and spatial memory behavior, using Morris water maze test

M. Ramin, P. Azizi, F. Motamedi, F. Khodagholi

Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Alzheimer’s Disease (AD) is a multi-factorial neurodegenerative disease characterized by neuronal death with gradual cognitive decline. β-amyloid plaques are important hallmarks of memory impairment in Alzheimer. One of the prominent factors having crucial impact in this process is MAPK. JNK, as a member of MAPK family has a pivotal role, especially in cell survival. We hypothesized that JNK inhibition may have protective effect in the process of memory impairment. Therefore, we performed Morris Water Maze (MWM) to investigate the possible impact of SP600125 as a JNK inhibitor on spatial memory in the rats treated with intra-CA1 injection of Aβ (30 ng/3 µl PBS per side). Our data indicated that intracerebroventricular (ICV) administration of SP600125 (30 µg/5 µl 1% DMSO in PBS) could significantly decrease escape latency in treatment group compared to control group (DMSO+Aβ treated rats; \(P<0.001\)). Furthermore, we evaluated the apoptotic factors in the hippocampus of the treated rats by using western blot analysis. Our study indicated that SP600125 could significantly decrease the expression of the apoptotic factors. The inhibitor led to the significant decrease in the amount of caspase-3 \((P<0.001)\), cyclooxygenase-2 \((P<0.01)\), and increase in Bcl2/Bax ratio \((P<0.01)\) in comparison with control group. Given the possible neuroprotective effects of SP600125 on Aβ-induced memory impairment along with its anti-apoptotic action, our results may open a new avenue for the treatment of AD.