Agmatine Protects Against Intracerebroventricular Streptozotocin-Induced Water Maze Memory Deficit, Hippocampal Apoptosis and Akt/GSK3β Signaling Disruption

Maryam Moosavi1, Amir Hossein Zarifkar1,2*, Yaghoub Farbood2, Mahin Dianat2, Alireza Sarkaki2, Rasoul Ghasemi3

1Department of Physiology, Shiraz University of Medical Sciences, Shiraz, Iran
2Department of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences (AJUMS), Ahvaz, Iran
3Department of Physiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Abstract

Intracerebroventricular streptozotocin (STZ) treatment has been described as a suitable model for sporadic Alzheimer’s disease (sAD). Centrally administered STZ decreases insulin and insulin receptors in the brain and interrupts PI3/Akt signaling pathway and GSK-3β. Additionally it raises Bax/Bcl-2 ratio and prompts hippocampal apoptosis. Agmatine, a polyamine derived from L-arginine decarboxylation, is recently shown to exert some neuroprotective effects. This study aimed to assess if agmatine reverses STZ-induced memory deficits and Akt/GSK-3β signaling disruption and apoptosis in the hippocampus. Adult male Sprague-Dawely rats weighing 200-250 g were used in this study. The canules were implanted bilaterally into lateral ventricle. STZ was administered on days 1 and 3 (3 mg/kg). Agmatine treatment (40 or 80 mg/kg) was started from day 4 in an every other day manner and continued till day 14. The animal’s learning and memory capability was assessed on days 15-18 using Morris water maze. After complement of the behavioral studies the hippocampi was isolated and the amounts of hippocampal cleaved caspase 3 (the landmark of apoptosis), Bax/Bcl-2 ratio, total and phosphorylated forms of GSK-3β and p-Akt were analyzed by western blot. The results showed that agmatine in 80 but not 40 mg/kg reversed the memory loss induced by STZ. Western blot analysis revealed that STZ induced elevation of caspase-3; Bax/Bcl-2 ratio and disrupted Akt/GSK-3β signaling in the hippocampus. Agmatine prevented apoptosis and Akt/GSK-3β signaling alteration induced by STZ. This study disclosed that agmatine treatment avert not only STZ-induced memory deterioration but also hippocampal apoptosis and Akt/GSK-3β signaling interruption.

Keywords: STZ, Agmatine, Learning and Memory, Apoptosis, Akt, GSK-3β

*Corresponding Author: Amir Hossein Zarifkar
E-mail: amirhosseinzarifkar13@yahoo.com