Assessment of Cognitive Functions and Some Markers of Synaptic Plasticity in Diabetic Rats

Thesis

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بسم الله الرحمن الرحيم

(الحمد لله الذى هدانا لهذا و ما كنا

لنهتدى لولا ان هدانا الله)

صدق الله العظيم

(الاعراف: الاية ٤٣)

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Shaimaa Nasr Amin

Dedicated to:
My Parents

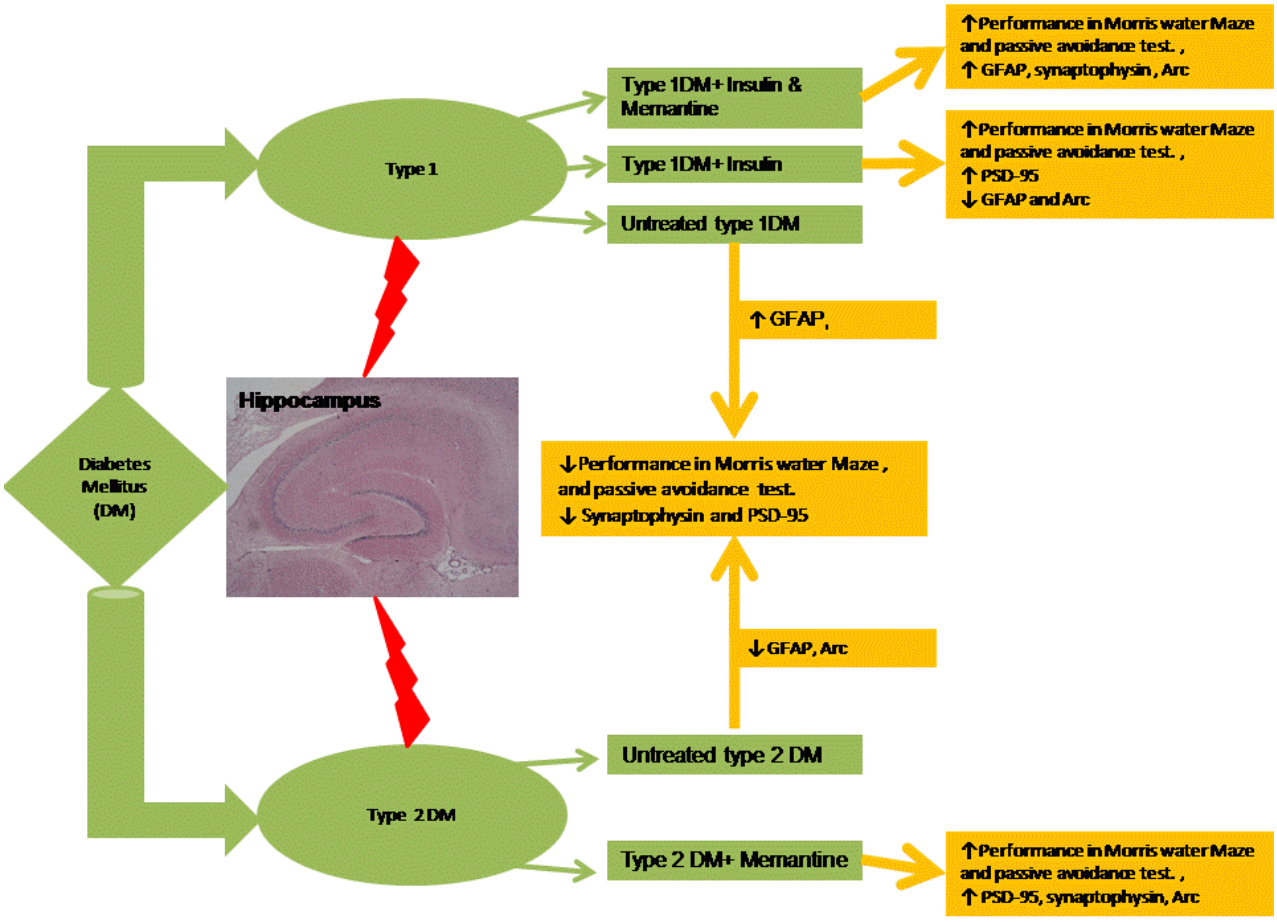
Abstract

Cognitive dysfunction is a common complication of diabetes mellitus however, less addressed and recognized. This study aimed to investigate the effect of type 1 and 2 diabetes on cognitive functions and related markers of hippocampal synaptic plasticity and the possible impact of blocking N-methyl-d-aspartate (NMDA) receptors by memantine. Seven rat groups were included in this study: non-diabetic, non-diabetic-memantine, type 1 diabetic groups: Untreated, treated with insulin alone and treated with insulin and memantine and type 2 diabetic groups: untreated and memantine treated. Cognitive functions were assessed by Morris Water Maze and passive avoidance test and immunohistochemistry was used for detection of hippocampus pre and post-synaptic markers: synaptophysin and postsynaptic density protein-95(PSD-95) respectively, learning and memory plasticity marker: activity regulated cytoskeletal associated protein (Arc) and the astrocytes reactivity marker: glial fibrillary acidic protein (GFAP). Both type 1 and 2 untreated diabetic groups showed significantly impaired cognitive performance with concomitant decrease in synaptophysin and PSD-95 compared to the non-diabetic group. In addition type 2 group showed a significant decrease in hippocampus GFAP and Arc compared to the non-diabetic group. Treating type 1 diabetic group with insulin alone significantly improved cognitive performance and PSD-95 and significantly decreased GFAP and Arc compared to untreated type 1 group. Blocking NMDA receptors by memantine (30 mg/kg/day) for 3 weeks significantly increased cognitive performance, synaptophysin, GFAP and Arc in type 1 insulin-memantine group compared to type 1-insulin group and significantly increased synaptophysin, PSD-95 and Arc in type 2-memantine group compared to untreated type 2 diabetic group. In conclusion, cognitive functions are impaired in both types of diabetes mellitus and can be improved by blockage of NMDA receptors which may spark future therapeutic role of these receptors in diabetes-associated cognitive dysfunction.

Key words:

Diabetes, cognitive functions, glial fibrillary acidic Protein, synaptophysin, postsynaptic density protein-95, activity regulated cytoskeletal associated protein.

Graphical abstract



DM=Diabetes mellitus; **GFAP**=Glial Fibrillary Acidic Protein; **PSD-95**=Post Synaptic Density Protien-95; **Arc**=Activity Regulated Cytoskeletal Associated Protein.

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