

3rd International Conference on

NEUROPSYCHIATRY AND SLEEP MEDICINE

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8th International Conference on

NEUROLOGY AND BRAIN DISORDERS

September 21-22, 2018 | Philadelphia, USA

Brain insulin resistance: Targeting PI3K/AKT/GSK3- β pathway in an intracerebroventricular streptozocin-induced rat model of Alzheimer's disease

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Alzheimer's disease featuring dementia, cognitive deficits, and behavioral alterations is one of the most common prevalent neurodegenerative diseases affecting majorly elderly people termed as a sporadic AD. Global prevalence of AD is sharply increasing, expected to affect almost 115 million people by 2050. Downregulation of the insulin signaling pathway of PI3K-AKT plays a significant role in the pathophysiology of the AD. Intracerebroventricular streptozocin is used for the model of sporadic Alzheimer's disease being established. Animals are divided into various groups comprising normal control, sham control, diseased and drug-treated groups. Protocol lasts for 21 days, sacrificing animals on the 22nd day followed by isolation of serum and dissection of the cortex and hippocampus, preserving the same for further analysis. Behavioral studies, biochemical estimations, and molecular techniques are done for evaluating several parameters of control, diseased and treated groups of animals. Behavioral studies like Morris water maze, novel object recognition, and actophotometer are performed for cognition, memory and locomotor activity. Biochemical estimations for antioxidant activity are performed as glutathione reductase assay, catalase assay, glutathione S-transferase assay, lipid peroxidation assay, superoxide dismutase assay and protein carbonylation assay. Protein concentrations are determined by the biuret method. Cholinergic activity is determined by acetylcholinesterase assay. Inflammatory cytokines like TNF- α , IL-6 is determined by ELISA method. Mitochondrial dysfunction is evaluated estimating mitochondrial enzyme complex 1, 2, 3 and 4. Histopathology is done. Molecular techniques like western blotting for Akt protein and RT-PCR for PI3-K, AKT, p-AKT, NF- $\kappa\beta$ and GSK 3- β is performed for gene expression analysis.

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