Glial-neuronal crosstalk in Alzheimer's: Unmasking the real culprit

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Sporadic Alzheimer's disease (SAD) is a progressive neurodegenerative disorder with dysfunctional insulin signaling and energy metabolism. Growing evidence supports that impairment in brain insulin responsiveness, glucose utilization and energy metabolism may be a major cause of amyloid precursor protein mishandling. A support for this notion comes from the studies where streptozotocin (STZ) induced brain insulin resistance in murine model, resulting into the SAD like brain pathology with cognitive decline. To understand dialogue exchange between glia and neuron, glial-neuronal co-culture has been modelled for sporadic Alzheimer's disease and studied for status of insulin signaling pathway using real time RT-PCR and immunoblotting for different signaling markers. Furthermore, Intracerebroventricular streptozotocin rat model has been used and checked for cognitive deficits (using Morris water maze) and histopathological changes senile plaques and taupathy) along with disturbed insulin signaling by immunoblotting. Culture study indicated that along with alterations in insulin signaling pathway, expression of hallmark genes of Alzheimer's i.e. APP and BACE1 was more in co-cultured neurons as compared to monoculture. Results from animal study suggested a remarkable decrease in insulin receptor and p-GSK3βser9/t-GSK3β expression. Behavioral data indicated significant loss of cognitive abilities which may be due to axonal thinning of CA1 neurons showed in Histological staining. Findings from this study suggested neuronal vulnerability and compromised insulin signaling in case of sporadic Alzheimer's disease along which was further confirmed using animal model by behavioral, histopathological and molecular paradigm.