Therapeutic Actions of the Thiazolidinediones in Alzheimer's Disease

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Alzheimer's disease (AD) is a multifactorial metabolic brain disorder characterized by protein aggregates, synaptic failure, and cognitive impairment. In the AD brain is common to observe the accumulation of senile plaques formed by amyloid-beta (A?) peptide and the neurofibrillary tangles composed of modified tau protein, which both lead to cellular damage and progressive neurodegeneration. Currently, there is no effective therapy for AD; however several studies have shown that the treatments with the peroxisome proliferators activated receptor-gamma (PPAR?) agonists known as thiazolidinedione drugs (TZDs), like rosiglitazone and pioglitazone, attenuate neurodegeneration and improve cognition in mouse models and patients with mild-to-moderate AD. Furthermore, studies on animal models have shown that TZDs inhibit neuroinflammation, facilitate amyloid-? plaque clearance, enhance mitochondrial function, improve synaptic plasticity, and, more recently, attenuate tau hyperphosphorylation. How TZDs may improve or reduce these pathologic signs of AD and what the mechanisms and the implicated pathways in which these drugs work are are questions that remain to be answered. However, in this review, we will discuss several cellular targets, in which TZDs can be acting against the neurodegeneration.