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**The Role of Peroxisome Proliferator-activated Receptor Gamma in Insulin Resistance Enhanced Alzheimer Disease Pathophysiology.**

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**Background:**

Alzheimer`s disease (AD) shares Pathophysiological features with type 2 diabetes (T2D). The nuclear receptor peroxisome Proliferator- activated receptor GAMMA (PPAR $\gamma$ ) is a ligand- activated transcription factor that regulates glucose and lipid metabolism and suppress inflammatory gene expression.

**Aim and hypothesis**

The potential therapeutic role of PPAR $\gamma$  on cognitive impairment and visuospatial memory in insulin resistance-induced AD using Pioglitazone; a PPAR $\gamma$  agonist.

**Methods**

AD was induced in 6 weeks old male rats by adding 6mg/L copper sulphate to drinking water for 8 weeks. Rats were randomly divided into 4 groups(n=10). (1) Normal control group on plain water, (2) AD control group, (3) Fructose drinking induced insulin resistance (IR) AD group, (4) Pioglitazone-treated group received orally (10mg/kg/day) at a volume of 2 ml/kg/day for the last 12 weeks of the 16 weeks period. Groups (3),(4) received 10% fructose solution in drinking water for 16 weeks after developing AD. Cognitive functions were assessed using discrimination index (DI) in object recognition test (ORT) and escape latency in Morris water maze(MWM) test. PPAR $\gamma$  was investigated for its role on  $\gamma$ -secretase and  $\alpha$  secretases as well as glucose homeostasis.

**Results**

PPAR $\gamma$  level was significantly elevated in IR-induced rats. However, Pioglitazone treatment was associated with restoration of PPAR $\gamma$  level to approximately normal values. Moreover, IR produced significant reduction in DI and prolongation of escape latency. Activation of PPAR $\gamma$  through Pioglitazone showed significant improvement in IR-induced dysfunctions in cognitive function and visuospatial memory in ORT and MWM tasks.

**Conclusion**

PPAR $\gamma$  agonists have a therapeutic potential in AD