EFFECTS OF ROSIGLITAZONE ON TAU PHOSPHORYLATION IN TYPE-2 DIABETES RAT MODEL


Increasing evidence supports an association between Alzheimer's disease (AD) and diabetes. Rosiglitazone, a peroxisome proliferator-activated receptor-γ (PPARγ) agonist, which is an anti-diabetic agent against type 2 diabetes, is currently in Phase III clinical trials in AD patients because rosiglitazone reduces β-amyloid (Aβ) pathology and inflammation. However, few studies have investigated whether rosiglitazone affects tau phosphorylation, another critical pathological feature of AD. Thus, we investigated it using OLETF type 2 diabetic rats and streptozotocin-injected type 1 diabetic mice. Interestingly, rosiglitazone reduced tau phosphorylation only in the hippocampus of OLETF type 2 diabetes rats, and not in that of STZ-injected type 1 diabetes mice. The activity of JNK was reduced in the hippocampus of rosiglitazone-treated OLETF rats, correlating with a reduction in tau phosphorylation, however, which was not correlated with GSK3b activity. Phosphorylation of insulin receptor substrate at serine and activation of some stress kinases was reduced in rosiglitazone-treated OLETF rats, suggesting reduction of insulin resistance. In human tau-transfected SH-SY5Y neuronal cell line, reduction of tau phosphorylation was also associated with reduction of JNK activity, not of GSK3b activity. Hence, rosiglitazone could be used in reducing tau phosphorylation through JNK inactivation for therapeutic effects in type 2 diabetes related Alzheimer's disease.