Alzheimer disease (AD) and related tauopathies are characterized by progressive neurodegeneration involving abnormal phosphorylation of the microtubule associated protein tau. Glycogen synthase kinase (GSK3) is one of the main tau kinases and it modifies tau phosphorylation in those sites related with paired helical filaments formation. GSK3 activity is repressed by the canonical Wnt signaling pathway. Recent studies have found increased levels of the negative modulator of the Wnt pathway, DKK1 in brain of AD's patients. However, the role of Wnt signaling inhibition on GSK3 activity and its consequences on tau hyperphosphorylation during aging has not been studied. Thus, the aim of this study is to investigate the effects of DKK1 and the specific inhibitor of GSK3 (6BIO), on tau phosphorylation in some sites relevant for AD (pSer199/202; pSer214) in a model of metabolically active hippocampal slices from young (3 months) and aged rats (18 months). We found that in young rats DKK1 diminished the phosphorylation on Ser199/202, whereas in aged rats an important increase in the same epitope was observed. With respect to the tau epitope pSer214 we didn't found a significant difference in young or aged hippocampus. The GSK3 inhibitor induced a considerable decrease in Ser199/202 phosphorylation but no differences were observed in Ser214. These results support a site and age dependent GSK3 regulation of tau phosphorylation. Supported by PAPIIT IN219509