

# Oxidative stress promotes $\tau$ dephosphorylation in neuronal cells: The roles of cdk5 and PP1

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Oxidative stress has been demonstrated to produce modifications in several intracellular proteins that lead to alterations in their activities. Alzheimer's disease is related to an increase of oxidative stress markers, which may be an early event in the progression of the disease and neurofibrillary tangles formation. Abnormal phosphorylation of  $\tau$  has been implicated in the etiopathogenesis of Alzheimer's disease. By using phospho-specific antibodies, we analyzed the changes in  $\tau$  phosphorylation patterns after treatment of rat hippocampal and SHSY5Y human neuroblastoma cells with  $H_2O_2$ . We found that  $\tau$  isoforms were hypophosphorylated at the Tau1 epitope after 2 h in the presence of  $H_2O_2$ . The decrease in the phosphorylation levels of  $\tau$  protein were prevented by pretreatment with N-acetyl-L-cysteine. These changes were shown to depend on the activity of the cdk5/p35 complex, since a 3-fold increase in substrate phosphorylation and a 2-fold increase for the complex association were obser