Sub-lethal levels of amyloid ?-peptide oligomers decrease non-transferrin-bound iron uptake and do not potentiate iron toxicity in primary hippocampal neurons

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Two major lesions are pathological hallmarks in Alzheimer's disease (AD): the presence of neurofibrillary tangles formed by intracellular aggregates of the hyperphosphorylated form of the cytoskeletal tau protein, and of senile plaques composed of extracellular aggregates of amyloid beta (Ab) peptide. Current hypotheses regard soluble amyloid beta oligomers (AbOs) as pathological causative agents in AD. These aggregates cause significant calciumderegulation and mediate neurotoxicity by disrupting synaptic activity. Additionally, the presence of high concentrations of metal ions such as copper, zinc, aluminum and iron in neurofibrillary tangles and senile plaques, plus the fact that they accelerate the rate of formation of Ab fibrils and A?Os in vitro, suggests that accumulation of these metals in the brain is relevant to AD pathology. A common cellular response to AbOs and transition metals such as copper and iron is the generation of oxidative stress, with the ensuing damage to cellul