Characterization of Oxidant Properties of Cupric-Amyloid b Peptide Complex and its Ability to Generate Hydroxyl Radials by the Reaction with Hydrogen Peroxide

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A growing body of evidence supports an important role of oxidative stress in the pathogenesis of Alzheimer?s disease. Recently, a number of papers showed a synergetic neurotoxicity of amyloid b peptide and cupric ions. We hypothesized that complexes of cupric ions with neurotoxic amyloid b peptides can stimulate copper-mediated free radical formation. It was found that copper-mediated oxidation of cyclic hydroxylamines was significantly increased in the presence of neurotoxic amyloid b peptides. Moreover, neurotoxic Ab (1-42), Ab (1-40), and Ab (25-35) stimulated copper-mediated oxidation of ascorbate, while nontoxic Ab (40-1) did not. Once cupric ion is reduced to cuprous ion, it can be oxidized by oxygen to generate superoxide radical, or it can react with hydrogen peroxide to form hydroxyl radical. It was found that hydrogen peroxide greatly increased the oxidation of cyclic hydroxylamines and ascorbate by cupric-amyloid b peptide complexes, implying redox cycling of copper ions. Using spin-trapping technique, we have shown that toxic amyloid b peptides caused a four-fold increase in copper-mediated hydroxyl radical formation.

The data obtained led to the conclusion that toxic Ab peptides indeed stimulates copper-mediated oxidation of ascorbate and generation of hydroxyl radicals. Therefore, cupric-amyloid b peptide-stimulated free radical generation may be involved in the pathogenesis of Alzheimer’s disease.