

P009 Three histidine residues of amyloid beta peptide control the redox activity of transition metals

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It is unclear whether amyloid- β ($A\beta$) is a prooxidant or an antioxidant. We found that ascorbate oxidase activity and the intensity of ascorbate radicals measured using EPR spectroscopy, generated by free Cu(II), was decreased in the presence of $A\beta$, the major component of senile plaques. Specifically, the ascorbate oxidase activity was strongly inhibited (85% decrease) in the presence of $A\beta$ 1-16 or $A\beta$ 1-42, whereas it was only slightly inhibited in the presence of $A\beta$ 1-12 or $A\beta$ 25-35 (< 20% inhibition). Ascorbate-dependent hydroxyl radical generation by free Cu(II) decreased in the presence of $A\beta$ in the identical order of $A\beta$ 1-42, $A\beta$ 1-16 > $A\beta$ 1-12. Ascorbate oxidase activity and ascorbate-dependent hydroxyl radical generation by free Fe(III) were inhibited by $A\beta$ 1-42, $A\beta$ 1-16 and $A\beta$ 1-12. Our results suggest that His6, His13 and His14 residues of $A\beta$ 1-42 control the redox activity of transition metals present in senile plaques.