Structural Characterization of Brain Zinc Metal Complexes of β-Amyloid Oxidation for Alzheimer's Disease by XANES/EXAFS Spectroscopy

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Transition-metal ions, such as Zn(II) can contribute to the neuropathology associated with βAP fibrils by affecting the rate of fibril formation, by modifying fibril morphology, and by direct chemical reaction with βAP. Administration of metal ions chelator decreases deposition of βAP in the brains of transgenic mice and releases soluble βAP from prefored amyloid deposits, supporting the hypothesis that Zn(II) are incorporated in AD plaque architecture in vivo. Advances in selective chelation therapy to combat AD require that details of the binding sites of relevant Zn(II) be known and that the mechanism through which Zn ions participate in fibrillization events be better understood.

βAP shows a high affinity to Zn(II) and binding of these metals promotes βAP aggregation. Increasing in the brain metal concentrations of Zn ions greatly facilitate pathological protein aggregation processes. Some reports have shown that Zn ions induce aggregation in vitro of solubleβAP, at pH 7.4, and that this reaction is totally reversible with metal chelation. In addition, Cu(II) favors βAP aggregation when working at pH 6.8 and similarly the process may be reversed by removing the metals. Free Cu ions are known to promote potentially neurotoxic oxidation processes of biological substrates. Moreover, the peptide efficiently reduces Cu(II) to Cu(I), a process which ultimately generates hydrogen peroxide in aerobic solution. In vitro investigation of βAP with Cu(II) continues to be used as a model for the role of metals in fibril formation in vivo. The Zn(II) ions coordination environments in βAP will be a key point for the important pathway of the pathology to AD. Thus, the main objective of the present work was to investigate the fine structures and oxidation states of S species bound with Zn atoms accumulated in the catalytic transformations of βAP for AD by EXAFS and XANES spectroscopies. The binding sites of Zn(II) with S ligands and that the mechanism through which Zn(II) participate in fibrillization events were also studied.

The EXAFS spectra may provide the bond distance of Zn atoms and oxidation states of S species bound with Zn species in catalytic transformations of βAP for AD. These results may offer a further study on the catalytic mechanism and distribution of Zn heavy metals in catalytic transformations of βAP for AD. The surface of βAP might consist of biopolymer such as polysaccharides, proteins, and lipids, which act as a basic binding site of Zn(II). The functional groups within the wall of βAP provided the sulfate (SO_4^{2-}), thiol (mercaptan) or sulfhydryl (mercapto, R-SH) groups that can bind Zn(II). Especially, thiol or sulfate functional groups are stronger sites bound with znic ions and may form Zn-SH or $ZnSO_4$ complex. The binding sites of Zn(II) with S ligands and that the mechanism through which metal ions participate in fibrillization events may be evaluated by EXAFS spectroscopy. The Cu and S EXAFS spectra indicated that the Cu-S species with bond distances of 1.99 Å and 2.04 Å, respectively. Coordination numbers of the Cu-S species from Cu and S EXAFS spectra were 2.2 and 2.4, respectively. Especially, thiol or sulfate functional groups are stronger sites bound with Zn(II) and may form Zn-SH or $ZnSO_4$ complex. The Zn and S EXAFS spectra indicated that the Zn-S species with bond distances of 2.05 Å and 2.13 Å, respectively were found in Figure 1.. Coordination numbers of the Zn-S species from Zn and S EXAFS spectra were 2.3 and 2.5, respectively. The uptake of Zn(II) can take place by entrapment in the βAP structure and subsequent sorption onto the binding sites present in the structure in the catalytic transformations of βAP for AD. However, by the EXAFS spectra, highly significant correlation occurred between the individual heavy metal on its available percentage in the catalytic transformations of βAP for AD may be also studied.

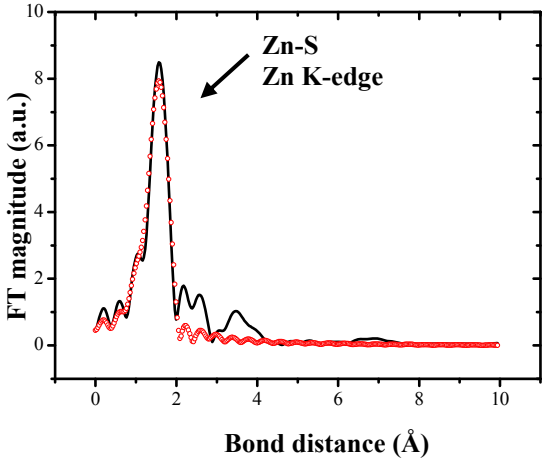

Figure 1. Fourier transform of Zn-S for znic K edges EXAFS that the S species bound with Zn atom catalyzed transformations of βAP for AD. The best fitting of the EXAFS spectra are expressed by the circle lines.