Postgraduate Biophysical Seminars
Institute of Biochemistry and Biophysics, University of Tehran, Iran
1395-96a

The Amyloid β in Alzheimer's disease (AD)

Minoo Qafary*, Ali Akbar Moosavi-Movahedi

Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran

"Presented at the Postgraduate Biophysical Seminars, Autumn 95 (2016)"

Abstract

Introduction: Alzheimer's is known as a chronic Neurodegeneration disease that afflicts 36 million people worldwide. The amyloid β (Aβ) peptide aggregates in the brain to form progressively larger form ranging from oligomers to fibrils. The most well-established structural feature of amyloid fibrils is the cross-β motif, an extended β-sheet structure formed by β-strands oriented perpendicular to the long fibril axis. Amyloid fibrils and their accumulation as deposits in the neuropil can profoundly affect the functioning of the central nervous system, perhaps by neurotoxic mechanisms.

Methods: In this study, the applied techniques were solid-state Nuclear magnetic resonance spectroscopy (NMR), X-ray diffraction electron microscopy (negative and positive staining), the combination of discontinuous molecular dynamics and x-ray absorption spectroscopy (XAS) and density functional theory analysis of Aβ peptides complexed with Cu^{+2} in solution under a range of buffer conditions.

Results and discussion: Electron microscopy indicates that the peptides formed both twisted fibers of average diameter ~70 Å and pitch 460 Å, and straight fibers with the same diameter. Solid-state NMR techniques represent the first site specific of non-β-strand peptide conformations in an amyloid fibril. Simulations reveal that the peptide preferentially populates a helical structure in apolar organic solvent, while in pure water, the peptide adopts collapsed coil conformations and to a lesser extent β-hairpin conformations. The XAS spectra for truncated and full-length Aβ-Cu^{2+} peptides are similar. The presence of hydrophobic crowders reduces the antiparallel β-sheet.

Conclusion: amyloid fibrils cause neurotoxic effects in AD, Detailed structural studies of amyloid fibrils can elucidate which constituent polypeptides are more effective in toxicity and help our investigating on the prevention of these fibril formation and treatment of AD to be more effective.

Keywords: Amyloid β, fibrillation**,** Alzheimer's disease, Fibrillation, neurotoxicity

Reference:

Antzutkin, O. N., Balbach, J. J., & Tycko, R. (2003). Site-specific identification of non-β-strand conformations in Alzheimer's β-amyloid fibrils by solid-state NMR. Biophysical journal, 84(5), 3326-3335.
Benilova, I., Karran, E., & De Strooper, B. (2012). The toxic A [beta] oligomer and Alzheimer's disease: an emperor in need of clothes. Nature neuroscience, 15(3), 349-357.
Latshaw, D. C., & Hall, C. K. (2015). Effects of Hydrophobic Macromolecular Crowders on Amyloid β (16–22) Aggregation. Biophysical journal, 109(1), 124-134.
Malinchik, S. B., Inouye, H., Szumowski, K. E., & Kirschner, D. A. (1998). Structural analysis of Alzheimer's β (1–40) amyloid: protofilament assembly of tubular fibrils. Biophysical journal, 74(1), 537-545.
Streltsov, V. A., Titmuss, S. J., Epa, V. C., Barnham, K. J., Masters, C. L., & Varghese, J. N. (2008). The structure of the amyloid-β peptide high-affinity copper II binding site in Alzheimer disease. Biophysical journal, 95(7), 3447-3456.
Wei, G., & Shea, J.-E. (2006). Effects of solvent on the structure of the Alzheimer amyloid-β (25–35) peptide. Biophysical journal, 91(5), 1638-1647.