Evolution of Amyloid Structure Across Alzheimer's Disease Stages

Alzheimer's disease (AD) is a neurodegenerative disorder that is pathologically characterized by the accumulation and aggregation of amyloid beta (Aβ) protein in the brain. These aggregates, known as plaques, are insoluble deposits that inhibit neuronal function and ultimately lead to cognitive decline. Previous in-vitro work shows that Aβ fibrils are the dominate component of plaque cores and these species can exhibit both parallel and antiparallel β-sheet secondary structures. However, little is known regarding if a correlation between plaque core composition and AD progression exists and if there are any additional heterotypical findings from plaque cores across various regions of the brain. In this study, we apply discrete frequency infrared (DFIR) imaging to diseased human brain tissue to quantitatively explore plaque core composition across AD stages. IR imaging is an excellent technique for identifying protein secondary structural heterogeneities within tissues; it combines IR spectroscopy with optical microscopy resulting in IR spectra with respective spatial information. This study also utilizes multivariate curve resolution (MCR) to deconvolute imaging data collected from over 180 Aβ plaque cores. The results from this work provide evidence that localized β-sheet content increases as AD stage increases and that this phenomenon is not limited to a particular region of the brain. The study presented here expands on our recent work and highlights additional heterogeneities within Aβ plaque cores.