CHARACTERIZATION OF DIFFERENT Aβ OLIGOMER ASSEMBLIES IN ALZHEIMER AUTOPSY BRAIN TISSUE

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Recent studies suggest that soluble β-amyloid (Aβ) oligomers, rather than Aβ fibrils, may be the fundamental molecular pathogens that trigger synaptic dysfunction and memory deterioration observed in Alzheimer's disease (AD). However, we still don't know much about the abundance and the time course of different oligomeric Aβ assemblies in the brain, and how these may interact with neurotransmitter systems and affect synaptic functions during disease progression.

In the present study, we extracted various Aβ oligomers from autopsy frontal cortices of AD and age-matched control subjects. Aβ oligomer specific antibodies were used to detect the Aβ assemblies in serial extractions and correlated with ELISA measures of total Aβ1-40 and Aβ1-42 as well as the binding levels of ³H-PIB (fibrillar Aβ), ³H-Nicotine (nicotinic acetylcholine receptors, nAChRs) and choline acetyltransferase (ChAT) activity in the same subjects.

The predominant oligomeric Aβ assemblies detected were dodecamers, decamers, and pentamers, which showed an age-dependent expression in AD subjects (Bao et al., 2010). While a negative correlation was observed between the number of nAChRs and the total levels of Aβ oligomers and Aβ dodecamers in AD patients and control subjects, no correlation was observed between the different Aβ oligomer assemblies and fibrillar Aβ.

Our findings indicate that different Aβ oligomers may be linked to the neurodegenerative processes independent of Aβ fibrillar aggregation in the AD brain. Studies to characterize and compare the abundance of Aβ oligomers in AD APPswe transgenic mice are ongoing as well functional studies investigating which of these assemblies impair synaptic signaling.