A SYSTEMATIC ANALYSIS OF MULTIPLE AB PATHOLOGIES IN ALZHEIMER'S DISEASE


¹Sanders Brown Center on Aging, ²Molecular and Cellular Biochemistry, University of Kentucky, Lexington, KY, ³Pennington Medical Research Center, Louisiana State University, Baton Rouge, LA, ⁴Center for Muscle Biology, University of Kentucky, Lexington, KY, USA

Introduction: Deposition of the amyloid-β (Aβ) peptide in neuritic plaques is a requirement for the diagnosis of Alzheimer's disease (AD). Despite progress in mapping the contribution of Aβ to neuronal dysfunction, lack of a detailed analysis of the interrelationship between the various pools and species of Aβ and the other common indices of AD pathology has hampered our understanding of disease development and progression.

Aims: Determining how these variables relate to one another is essential for understanding the etiology of AD and the continued development of reliable diagnostic biomarkers for AD, such as Pittsburgh Compound B (PiB).

Methods: We conducted a comprehensive analysis of the amount of Aβ40 and Aβ42 in different soluble pools, oligomeric Aβ, and fibrillar Aβ (as defined by PiB binding), as well as plaques (diffuse and neuritic) and neurofibrillary tangles (NFTs) in autopsy specimens from age-matched, cognitively normal controls, cognitively normal controls, amnestic MCI, preclinical AD (PCAD), and AD cases; we also included a subset of frontotemporal dementia cases (total N = 87).

Results: Higher order, oligomeric forms of Aβ were a surprisingly small proportion of the total amount of Aβ. The best single predictor of diffuse plaques was the amount of PiB binding, whereas the best predictor of neuritic plaques and tangles was formic acid soluble Aβ42.

Conclusions: Although PiB binding was able to distinguish some disease groups, binding in post mortem samples is driven largely by the number of diffuse plaques, a finding with important implications for the use of amyloid binding agents as diagnostic tools.