Antecedent biomarkers of presymptomatic stages of Alzheimer’s disease: Results from the Wisconsin Alzheimer’s Disease Research Center (ADRC) and other studies

There is converging evidence from animal and clinical studies that Alzheimer’s disease (AD) pathology starts several decades before the onset of clinical symptoms. It is widely projected that systematic characterization of antecedent biomarkers of presymptomatic stages of AD will significantly enhance our understanding of the pathobiology of AD, and lead to the discovery of effective diagnostic, treatment and prevention strategies for the disease. Results from several prospective cohort studies to date suggest that biomarkers of amyloid deposition and metabolism in the brain, as measured by neuroimaging and cerebrospinal fluid (CSF) assays are likely the earliest changes, followed by neuronal death, cortical atrophy, and eventually onset of clinical symptoms. The overarching scientific focus of the NIA/NIH-funded Wisconsin ADRC in the United States is to identify antecedent biomarkers of preclinical stages of AD in asymptomatic at risk adults, and study their progression prospectively as some subjects convert from asymptomatic to symptomatic stages of the disease. To that end, the ADRC supports two renowned cohorts, namely the Wisconsin Registry for Alzheimer’s Prevention (WRAP) and IMPACT, comprised together of over 2,000 middle-aged, asymptomatic adults (mean age at enrollment: 53 years) with a parental history of AD. These adults participate in prospective collection of extensive socio-demographic, cognitive, medical, neuroimaging (structural and functional MRI, ASL, DTI, FDG PET, amyloid PET) and CSF collection. Over 44% of the study participants carry the APOE4 allele, and 67% have consented for a brain autopsy to date. This presentation will summarize novel findings from several Wisconsin ADRC-supported and other relevant studies targeting biomarkers of presymptomatic stages of AD. Data will be presented to demonstrate that a subset of asymptomatic subjects with a parental history of AD show evidence of disease onset as indicated by amyloid deposition, reduced glucose uptake and cortical atrophy in areas of the brain commonly affected by AD pathology. Moreover, these structural and functional changes in the brain are associated with alterations in CSF levels of Aβ42, p-tau and total tau suggestive of amyloid deposition and neurodegeneration. Overall, this presentation will underscore the significance of studying changes in AD pathology-related biomarkers over time as the disease progresses from presymptomatic to symptomatic stages. Such studies will eventually lead to a better understanding of the neurobiology of AD and lead to the discovery of disease-modifying therapies, novel prevention strategies and eventually a cure.

Biography

Sanjay Asthana received his medical degree at the University College of Medical Sciences, University of Delhi in New Delhi, India and completed his residency training in internal medicine at the University of Saskatchewan School of Medicine. He obtained his Geriatric Fellowship training at the Johns Hopkins University School of Medicine and completed an additional Senior Staff Fellowship in Alzheimer’s disease research at the Laboratory of Neurosciences of the National Institute on Aging (NIA), National Institutes of Health (NIH) in Bethesda, Maryland. The primary focus of his research is to identify novel antecedent biomarkers for preclinical stages of Alzheimer’s disease (AD). Additionally, he is internationally recognized for his research on estrogen and related hormones for the treatment of AD. For over 20 years, his research program has been supported by multiple peer-reviewed grants from NIH, the US Department of Veterans Affairs, and various philanthropic organizations.

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