

Non-core CSF Biomarkers Reveal Strong Associations With Core AD Biomarkers And Cognition In SCD And MCI

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CSF non-core biomarkers were not useful for distinguishing SCD from MCI, but showed robust stage-specific associations with core AD biomarkers and cognitive performance, supporting their value as complementary indicators of early disease biology.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Alzheimer’s disease (AD) is characterized by a long preclinical and prodromal phase, during which molecular and synaptic alterations precede cognitive decline. WELL ESTABLISHED CORE AD BIOMARKERS CSF BIOMARKERS • Aβ42 • Total tau (T-tau) • Phospho-tau (p-tau181) PLASMA BIOMARKERS • Aβ42 • Total tau (T-tau) • Phospho-tau (p-tau181/217) INCREASING ATTENTION TO NON-CORE CSF BIOMARKERS NEURODEGENERATION • Neurofilament light chain (NFL) SYNAPTIC DYSFUNCTION • Neurogranin • Visinin-like protein 1 (VILIP-1) COPATHOLOGIES • Alpha-synuclein (α-synuclein) Provide complementary information about disease biology and heterogeneity in AD. CSF PLASMA Understanding their relationships with core biomarkers and cognitive performance in Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI) may improve biological characterization in early AD.	STUDY DESIGN & PARTICIPANTS Cross-sectional study SCD Subjective Cognitive Decline MCI Mild Cognitive Impairment Group comparisons adjusted for age and education BIOSPECIMEN COLLECTION Cerebrospinal fluid (CSF) BIOMARKER ASSESSMENT NON-CORE CSF BIOMARKERS • Neurofilament light chain (NFL) • Neurogranin • Visinin-like protein 1 (VILIP-1) • Alpha-synuclein CORE BIOMARKERS (PLASMA AND/OR CSF) • Aβ42 • Aβ40 • Total tau (t-tau) • Phospho-tau181 (p-tau181) • Phospho-tau217 (p-tau217) COGNITIVE ASSESSMENT Neuropsychological tests covering multiple cognitive domains (including executive function and memory) STATISTICAL ANALYSIS MANCOVA Spearman correlations	1. NO GROUP DIFFERENCES No significant differences in CSF non-core biomarker concentrations between SCD and MCI. 2. SCD: ASSOCIATIONS WITH AD PATHOLOGY α-synuclein ↔ CSF p-tau181/Aβ42 $p = 0.897, p = 0.003$ α-synuclein ↔ VILIP-1 $p = 0.857, p = 0.007$ 3. MCI: ASSOCIATIONS WITH COGNITION Neurogranin ↔ VILIP-1 $p = 0.821, p = 0.001$ Neurogranin → Executive Function $p = -0.538, p = 0.001$ VILIP-1 → Executive Function $p = -0.492, p = 0.001$	CSF NON-CORE BIOMARKERS SCD Subjective Cognitive Decline (n = 11) MCI Mild Cognitive Impairment (n = 53) NFL Neurogranin VILIP-1 α-Synuclein No significant differences in CSF non-core biomarker concentrations between SCD and MCI. SCD Associations with AD pathology α-Synuclein CSF p-tau181/Aβ42 VILIP-1 Strong associations with core AD pathology (tau and amyloid). MCI Associations with cognition Neurogranin VILIP-1 Executive Function Associations with synaptic dysfunction and poorer executive function.	1. Jack CR Jr et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimers Dement. 2018. 2. Jack CR Jr et al. Revised criteria for diagnosis and staging of Alzheimer's disease. Alzheimers Dement. 2024. 3. Zetterberg H, Bendlin BB. Biomarkers for Alzheimer's disease. Mol Psychiatry. 2021. 4. Hansson O. Biomarkers for neurodegenerative diseases. Nat Med. 2021. 5. Dulewicz M et al. Neurogranin and VILIP-1 in AD. Int J Mol Sci. 2020. 6. Bellomo G et al. Alpha-synuclein copathology in AD. Alzheimers Dement. 2024. CONTACT Presenter: Isadora Stabille FCM - UNICAMP Campinas, Brazil ALZHEIMER'S ASSOCIATION AAIC 26