

Association between cognitive complaints and Alzheimer's disease biomarkers in at-risk individuals : An item by item analysis in the INSIGHT-preAD cohort



Mila Chardon¹²³, Laurent Cleret de Langavant¹²⁴, Philippe Remy¹²⁴, Federica Cacciamani¹²

¹ Mondor Biomedical Research Institute, INSERM U955, Interventional Neuropsychology Lab (NPI), Paris Est Créteil University, Créteil, France

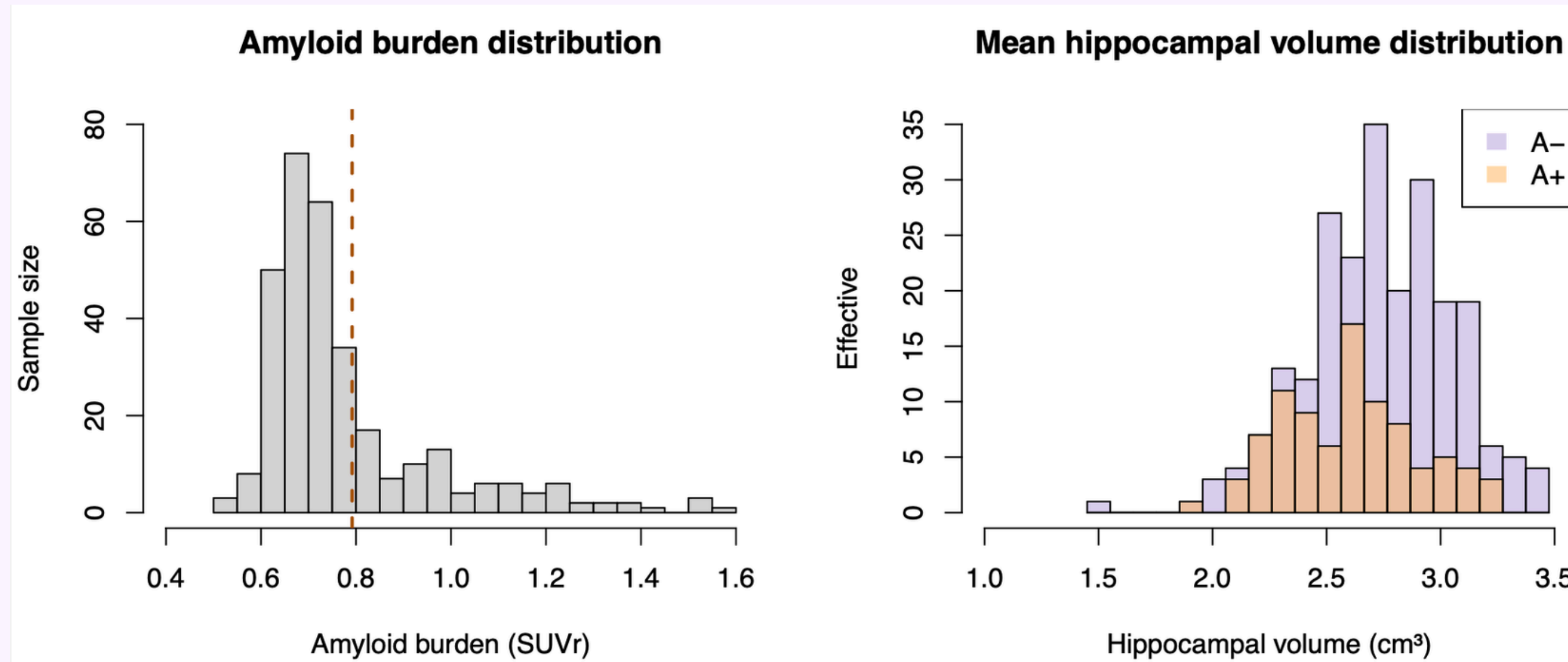
² Department of Cognitive Studies, École Normale Supérieure, PSL University, Paris, France

³ Sorbonne Université, Paris, France

⁴ Henri Mondor University Hospital, Neurology Department, AP-HP, Créteil, France



- No SCD item was significantly associated with amyloid burden.
- No SCD item was significantly associated with hippocampal volume.
- Item-level SCD assessment may have limited utility for identifying preclinical AD pathology in asymptomatic at-risk older adults.

INTRODUCTION	METHODS	RESULTS	CONCLUSION
Background: Alzheimer's disease (AD) begins with the accumulation of amyloid proteins in the brain. This leads to neurodegeneration with atrophy developing in specific brain regions, particularly in the hippocampus. These abnormalities are detectable well before the first cognitive impairments identified by neuropsychological tests. Cognitive complaints, or subjective cognitive decline (SCD)¹, may constitute a potential early indicator of AD. However, cognitive complaints encompass a wide range of symptoms. Aim: To examine, cross-sectionally, in asymptomatic at-risk individuals, the association between various cognitive complaint items and two AD biomarkers, brain amyloid burden and hippocampal volume.	Participants (INSIGHT-preAD cohort)²: • 317 cognitively normal participants with cognitive complaints, • Aged between 70 and 85 years, • 27.2% amyloid-positive. Measures: • Amyloid burden: PET, • Mean hippocampal volume: MRI, • Cognitive complaints: 47 SCD items drawn from the HABC-M and additional cohort-specific items. Distribution of amyloid burden and mean hippocampal volume in the sample  Note : The red line represents the 0.792 SUVR threshold determining amyloid positivity. Statistical analysis: • Multivariate regression models: association between SCD items and biomarkers, adjusted for confounding variables (age, sex, education level), • Interaction: association between SCD items and amyloid status on mean hippocampal volume.	Multivariate model: No significant association was found between biomarkers and each SCD item (all adjusted p-values > 0.27 for amyloid burden; > 0.97 for mean hippocampal volume). Interaction: No significant effect was found in the association between SCD items and amyloid status on mean hippocampal volume. The strongest association was observed for the item regarding the belief in having a brain disease, without reaching statistical significance ($\beta = 0.23$, 95% CI = [0.04-0.42], p-adjusted = 0.13).	In asymptomatic at-risk participants, no subjective complaint item was able to predict amyloid burden or hippocampal atrophy. Therefore, SCD questions do not appear to be reliable tools for very early detection in this type of population. It would be interesting to examine informant-reported SCD at the item level. REFERENCES 1. Jessen F, Amariglio RE, van Boxtel M, Breteler M, Ceccaldi M, Chételat G, et al. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. <i>Alzheimers Dement J Alzheimers Assoc.</i> nov 2014;10(6):844-52. doi:10.1016/j.jalz.2014.01.001 2. Dubois B, Epelbaum S, Nyasse F, Bakardjian H, Gagliardi G, Uspenskaya O, et al. Cognitive and neuroimaging features and brain β-amyloidosis in individuals at risk of Alzheimer's disease (INSIGHT-preAD): a longitudinal observational study. <i>Lancet Neurol.</i> avr 2018;17(4):335-46. doi:10.1016/S1474-4422(18)30029-2