

Clinical And Cognitive Differences In Subjective Cognitive Impairment Stratified By Ptau217 Status



Gabrielle Hromas, PhD^{1,2*}, Hanna Hausman, PhD^{1,2}, Chen-Pin Wang, PhD^{1,3}, Roman Fernandez, MS^{1,3}, Jennifer Del Bosque, BS¹, Denisse Garcia Cisneros, BA¹, Carlos A. Gaona, MD¹, Luis Gutierrez, MPH¹, Luis Mendez,MD¹, Rajeswar Kumar, MD¹, Amaya Seidl, BS¹, Anika Thomson, MBBS¹, Angel G. Velarde, BA¹, Jessica Zapata, BS¹, Monica Goss, PhD¹, Claudia Satizabal, PhD^{1,3}, Hector Adrian Treviño, PhD¹, Vanessa M. Young, PhD^{1,4}, Crystal Mendoza, MS¹, Juan Garcia, MBA¹, Gabriel de Erausquin, MD, PhD^{1,2}, Robin Hilsabeck, PhD^{1,2}, Bruce LeForce, MD^{1,2}, Stephanie Santiago-Mejias, PhD^{1,2}, Silvia Mejia-Arango, PhD⁵, Alicia Parker, MD^{1,2}, Arash Salardini, MD^{1,2}, Jeremy A. Tanner, MD^{1,2}, Amy Werry, PsyD^{1,2}, Tiffany Kautz, PhD¹, Joanne Curran, PhD⁶, Gladys Maestre, MD⁵, Sudha Seshadri, MD^{1,2}, Ashley LaRoche, BS¹, Campbell Sullivan, PsyD^{1,2}

¹Glenn Biggs Institute for Alzheimer's & Neurodegenerative Diseases, San Antonio, TX, USA, ²Neurology, University of Texas at San Antonio, San Antonio, TX, USA, ³Population Health Science, University of Texas at San Antonio, San Antonio, TX, USA, ⁴School of Social and Behavioral Sciences, University of Texas at San Antonio, San Antonio, TX, USA, ⁵Neurology, University of Texas Rio Grande Valley, Edinburg, TX, USA, ⁶Human Genetics, University of Texas Rio Grande Valley, Brownsville, TX, USA.

*Corresponding author: hromasg@uthscsa.edu

Introduction

- **Subjective Cognitive Impairment (SCI):** self-reported cognitive decline despite performing within normal limits on objective testing.
- In SCI, biomarker positivity may identify a subgroup with underlying Alzheimer’s disease pathology and increased risk for progression.¹
- This study examined whether individuals with SCI differ by p-tau217 status in demographic, dementia risk, mood, or cognitive factors.
- Hypothesis: biomarker positive individuals would exhibit higher burdens of dementia risk factors (e.g., older age, APOE ε4 carrier status). We also explored differences in cognitive and psychiatric status.

Materials & Methods

- This study utilized secondary data analysis from the South Texas Alzheimer’s Disease Research Center (STAC).
- Inclusion criteria: completion of the UDsv3, plasma p-tau217 assay, and SCI classification at the annual study visit.
- Clinical diagnoses were established through consensus conference review involving at least one neurologist and neuropsychologist. SCI diagnoses were tracked internally.
 - Participants and clinicians were blinded to p-tau217 status at the time of the study visit and diagnostic consensus.
- Wilcoxon rank-sum and Pearson’s chi-squared or Fisher’s exact tests examined differences in demographic and clinical risk factors between p-tau217 positive and negative groups (defined using NCRAD cutoff of 0.47).
- Linear regression, adjusting for age, sex, and education, evaluated the association between biomarker status and neuropsychological test performance with Box-Cox transformed scores used when appropriate.

Results

- The p-tau217 positive group was older than the negative group (75 vs. 67 yrs, $p=.007$). No other differences were identified in demographic or neurodegenerative risk factors.
- No clinically meaningful group differences were observed on measures of depression, neuropsychiatric symptoms, or UDsv3 neuropsychological testing. The p-tau217 positive group scored ~1 point higher on Number Span Backward (7.31 vs 6.39 points; $p=.032$).

Sample

**N=61 (mean age=69 yrs; 64% female; 52% Hispanic; mean education=15.57 yrs).
N=16 (26.2%) were p-tau217 positive.**

Participant Characteristics			
	Biomarker Negative (N=45)	Biomarker Positive (N=16)	P-value
Age	67 (10)	75 (7)	0.007
Years of Education	15.76 (2.3)	15.06 (3.64)	0.5
Sex	29 (54%) Female	10 (63%) Female	0.9
Ethnicity	26 (58%) Hispanic	6 (38%) Hispanic	0.2
Traumatic Brain Injury (TBI)	8 (17.7%) Positive	2 (12.5%) Positive	0.4
APOE 4 Carrier	10 (24%)	5 (38%)	0.3

Psychiatric Symptoms			
	Biomarker Negative (N=45)	Biomarker Positive (N=16)	P-value
Neuropsychiatric Inventory (NPI) Total	1.17 (1.36)	1/13 (1.51)	0.9
Geriatric Depression Scale (GDS-15) Total	2.27 (2.84)	0.93 (0.96)	0.13

Neuropsychological Testing

	Biomarker Negative (N=45)	Biomarker Positive (N=16)	P-value*
MoCA Total	26.21 (2.10)	25.13 (3.10)	0.66
Number Span Forward Total	7.41 (2.04)	7.81 (2.97)	0.52
Number Span Backward Total	6.39 (1.17)	7.31 (2.12)	0.03
HVLT Learning	26.5 (3.5)	24.8 (5.2)	0.75
HVLT Delay	9.19 (2.55)	8.29 (3.12)	0.71
Benson Figure Copy	15.66 (1.24)	15.88 (1.15)	0.37
Benson Figure Delay	11.98 (2.71)	12.19 (2.10)	0.23
Trails A	32” (13)	41” (14)	0.14
Trails B	77” (28)	110” (69)	0.39
F + L Words Total	27 (8)	28 (10)	0.29
Animals + Vegetable Total	34 (5)	35 (10)	0.25
MINT Total	29.89 (1.86)	29.75 (2.08)	0.77

Note: Unadjusted means and standard deviations are reported for all neuropsychological tests to aid clinical interpretation. *P values are based on adjusted linear regression models that included age, sex, and education as covariates. Analyses were conducted using Box-Cox transformed neuropsychological test scores to meet assumptions of normality.

Conclusions

- Within our sample, the biomarker-positive group was older than the negative group, consistent with expected biomarker trajectories.²
- Additional clinically meaningful differences in demographic, dementia risk factors, or cognitive or psychiatric status were not identified.
- Future directions include monitoring longitudinal changes.

1. Trieu, C., Van Harten, A. C., Van Leeuwenstijn, M. S., Schlüter, L. M., Boonkamp, L., Aladdin, A., ... & Van Der Flier, W. M. (2025). Longitudinal Blood-Based Biomarkers and Clinical Progression in Subjective Cognitive Decline. *JAMA Network Open*, 8(12), e2545862.
2. Mammel AE, Gonzalez-Ortiz F, Mousavi A, et al. Age-related increase in plasma p-tau217 in amyloid-beta-negative cognitively unimpaired individuals affects diagnostic interpretation. *Alzheimer's Dement*. 2026;22:e71532. <https://doi.org/10.1002/alz.71532>