

Informant-reported mild behavioral impairment predicts informant-perceived cognitive decline independent of APOE ε4 and plasma p-tau217

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Background

Mild Behavioral Impairment (MBI) has emerged as a potential **early marker** of **neurodegenerative risk**, but its **relationship** with **subjective cognitive decline (SCD)** as perceived by informants remains poorly characterized, particularly in SCD community-based samples. We investigated whether **informant-reported MBI** was associated with **informant-reported cognitive concerns**, and whether this **relationship** was influenced by **APOE ε4** status or **plasma p-tau217**.

Methods

We analyzed baseline biomarker data and 12-month behavioral and cognitive assessments from the BRASCODE cohort. Informant-reported MBI was measured with the MBI Checklist, and informant-reported SCD was derived from a structured questionnaire.

Linear regression models tested the association between **MBI and SCD**, adjusting for age, sex, education, and global cognition.

Effect modification by APOE ε4 and plasma p-tau217 was examined using **interaction terms**.

Conclusion

In this SCD cohort, informants consistently perceived greater cognitive decline in individuals exhibiting more behavioral symptoms, independent of **APOE ε4** status or plasma p-tau217 levels. These findings suggest that MBI captures meaningful behavioral changes that influence informant concern even before biomarker abnormalities or measurable cognitive impairment emerge. MBI-related changes may therefore represent a salient early clinical signal in the preclinical spectrum of neurodegenerative disease.

Results

We included **117** individuals with SCD, with a mean (sd) age at baseline of 70.4 (4.5) and 14.1 (5.7) years of formal education. **Higher informant-reported MBI was robustly associated with greater informant-reported cognitive decline ($\beta = 0.12\text{--}0.15$, $p < 0.01$ across models)**. Neither **APOE ε4** carrier status ($p = 0.52$) nor plasma p-tau217 levels ($p = 0.28$) independently predicted SCD. Crucially, **neither APOE ε4 nor p-tau217 moderated the MBI–SCD association** (interaction $p > 0.35$ for both). **Objective cognitive performance was not associated with SCD**.

Table 1. Sociodemographic and clinical characteristics of the sample (n=117).

Variable	
Age, years mean (SD)	70.00 (5)
Female,n (%)	79 (69%)
Education, years mean (SD)	14 (6)
Race,n (%)	
White	108 (95%)
Brown	3 (2.6%)
Black	3 (2.6%)
APOE ε4, n (%)	37 (33%)
P-tau217, mean (SD)	0.49 (0.33)
Self-reported MCS, mean (SD)	7.34 (2.61)
Informant-reported MCS, mean (SD)	5.2 (3.3)
Self-reported MBI, mean (SD)	8 (11)
Informant-reported MBI, mean (SD)	6 (8)

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