Participant and Study Partner Prediction and Identification of Cognitive Impairment in Preclinical Alzheimer's Disease: Study Partner vs. Participant Accuracy

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Objectives

We sought to:

- Determine if study partners provide additional information, in relation to preclinical AD study participants, in predicting future cognitive decline or assessing current cognitive performance
- Describe association between study partner and participant subjective cognitive scores (ECog) and objective cognitive scores (ADAS13)
- Assess whether amyloid status modifies observed effects

Introduction

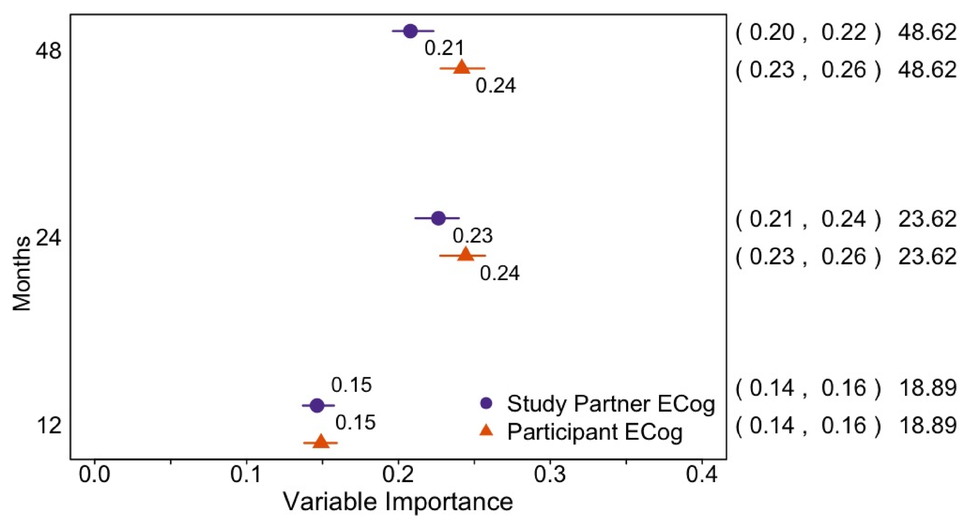
- Preclinical Alzheimer's disease (AD) trials require cognitively unimpaired participants to enroll with a study partner
- Study partner requirement is a significant barrier for study enrollment[1,2]
- Preliminary studies indicate that self-reports from cognitively normal participants may better predict future outcomes than do study partners[3,4], but they have not examined how amyloid status affect these relationships

Methods

- 335 cognitively normal participant-partner dyads in the AD Neuroimaging Initiative with Everyday Cognition (ECog) scores
- Assessed participant and study partner ECog scores as subjective assessment of performance, and participant Alzheimer Disease Assessment Scale-cognitive subscale (ADAS13) as objective measure of cognitive performance and change in cognition
- We used random forest models and Linear Mixed Effects (LME) to model ADAS13 scores as a function of participant and/or study partner ECog scores over time
  - Adjusted for potential confounding factors: APOE4 status, amyloid status, baseline age, years of education, and sex

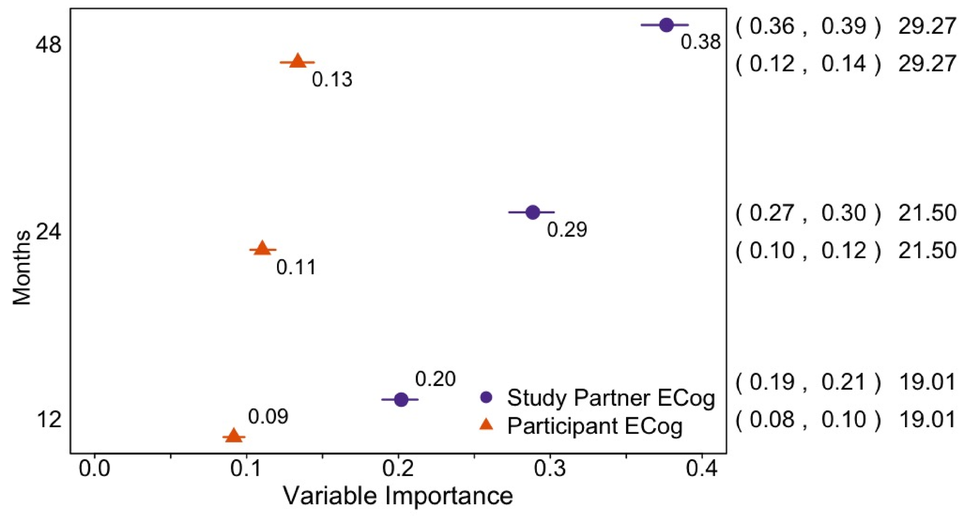
Results

Figure 1: Prospective Prediction Models



- In random forest models predicting ADAS13 12 months from baseline, we observed no difference in the estimated mean variable importance (eMVI) associated with baseline study partner ECog compared to the baseline participant ECog
- In models predicting ADAS13 48 months after baseline, the eMVI associated with baseline study partner ECog was slightly lower than that associated with baseline participant ECog

Figure 2: Cross-Sectional Prediction Models



- In cross-sectional models, study partner eMVI was twice as large as participant eMVI at 12 months, and three times as large at 48 months

Results (cont.)

- We did not observe qualitative differences by amyloid status in any model

	Prospective Prediction Model		Cross-Sectional Prediction Model	
	Coefficient	95% CI	Coefficient	95% CI
Participant ECog	0.16	(-0.50, 0.79)	0.06	(-0.44, 0.56)
Study Partner ECog	0.72	(0.07, 1.36)	0.67	(0.11, 1.23)
Amyloid Status	-0.10	(-1.41, 1.20)	-0.04	(-1.37, 1.30)

Table 1: Subset of LME coefficients for prospective and cross-sectional prediction models at 12 months from baseline.

	Prospective Prediction Model		Cross-Sectional Prediction Model	
	Coefficient	95% CI	Coefficient	95% CI
Participant ECog	0.24	(-1.06, 1.54)	0.66	(-0.17, 1.48)
Study Partner ECog	1.18	(-0.39, 2.75)	1.37	(0.78, 1.96)
Amyloid Status	1.58	(-0.76, 3.91)	0.83	(-1.43, 3.08)

Table 2: Subset of LME coefficients for prospective and cross-sectional prediction models at 48 months from baseline.

Conclusions

- While cognitively normal participants may be capable of providing consent and accurately informing on their own cognitive abilities at study start, study partners perform are better at cross-sectionally recognizing cognitive status, and this difference in performance increases over time
- **Our results provide evidence to support the continuation of the study partner requirement to ensure trial data integrity in preclinical AD trials**

References

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