

ITEM-LEVEL TRAJECTORIES OF SELF- AND STUDY PARTNER-REPORTED COGNITIVE COMPLAINTS IN PRECLINICAL ALZHEIMER'S DISEASE: DATA FROM THE A4 STUDY

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Background

- Subtle cognitive and functional changes emerge before measurable impairment in AD, making subjective reports a key source for early detection.
- Self- and study partner reports of cognitive complaints differ in their predictive value of disease progression.¹
- Overall complaint burden increases over time, but the specific trajectories of individual complaints as reported by participants and study partners remain unexplored.²

Aim

This study investigated item-level trajectories of cognitive and functional complaints in cognitively unimpaired older adults and their study partners participating in the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease Study (A4 study).

Methods

- Sample:** 833 cognitively unimpaired, amyloid-positive participants of the A4 study and their study partners.
- Materials:** Cognitive Function Index (CFI; 15 items assessing cognitive and functional complaints over the past year).
- Design:** Longitudinal study with 6 assessments over 4.5 years at ~50-week intervals.
- Analyses:** Logistic regression models estimated item-level endorsement trajectories over time, with time × reporter interactions to compare self (as reference) vs. study partner reports. Exploratory analyses stratified by amyloid tertiles to examine trajectories across levels of amyloid burden.

Characteristic	Participants	Study Partners*
Age	71.5 ± 4.4	66.0 ± 11.1
Female Sex	494 (59.3%)	500 (60.0%)
Years of Education	16.6 ± 2.7	
Retired	623 (74.8%)	
Race		
White	789 (94.7%)	
Asian	18 (2.2%)	
Black or African American	14 (1.7%)	
Other	12 (1.4%)	
Amyloid burden (Centiloids)	65.4 ± 31.3	
APOE ε4 Carrier	512 (61.5%)	
PACC	0.1 ± 2.7	
Same Household as Participant		68.1%
Relation to Participant		
Spouse		531 (63.7%)
Relative		143 (17.2%)
Friend		141 (16.9%)
Hours Spent Together (per week)		75.8 ± 60.4
Total	833	833

Table 1: Baseline Characteristics of Participants and Study Partners.
* 199 participants switched study partners at the study. Only the first study partner was included in the demographics

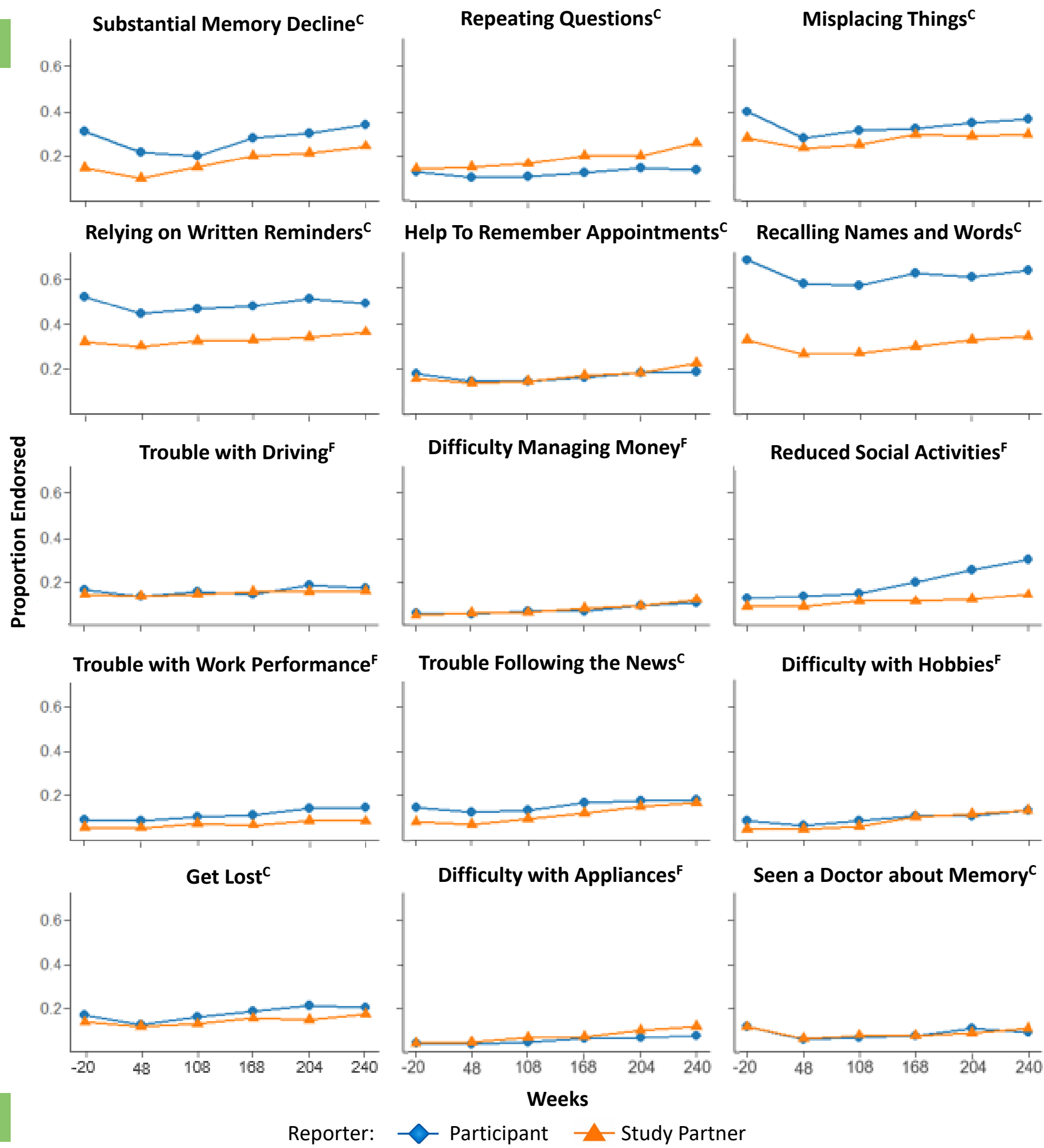


Figure 1: Item endorsement over time, with separate lines for participants (blue) and study partners (orange). Superscripts indicate cognitive (c) and functional (f) complaint items. Baseline measurement occurred 20 weeks before the start of treatment in the A4 trial.

Results

- Odds of endorsement increased over time for 11 of 15 CFI items, with most changes emerging from week 204 onward.
- Significant time × reporter interactions were observed for multiple cognitive items ($OR_{interaction} = 1.47-1.93$), with relatively stable self-reports but increasing study partner endorsements over time, e.g., see **“Repeating Questions”**.
- Endorsement of functional complaints increased from week 204 onward for both reporters ($OR_{time} = 1.37-2.36$).
- Functional items showed no time × reporter interactions, indicating similar self- and study partner endorsement trajectories, e.g., **“Difficulty with Hobbies”**.
- “Reduced Social Activities”** was the only item where *only* participant endorsement increased.
- Effects were strongest in the highest amyloid tertile ($OR_{time} = 2.14-3.51$), with a time × reporter interaction for **“Following the News”** ($OR_{interaction} = 2.13$).

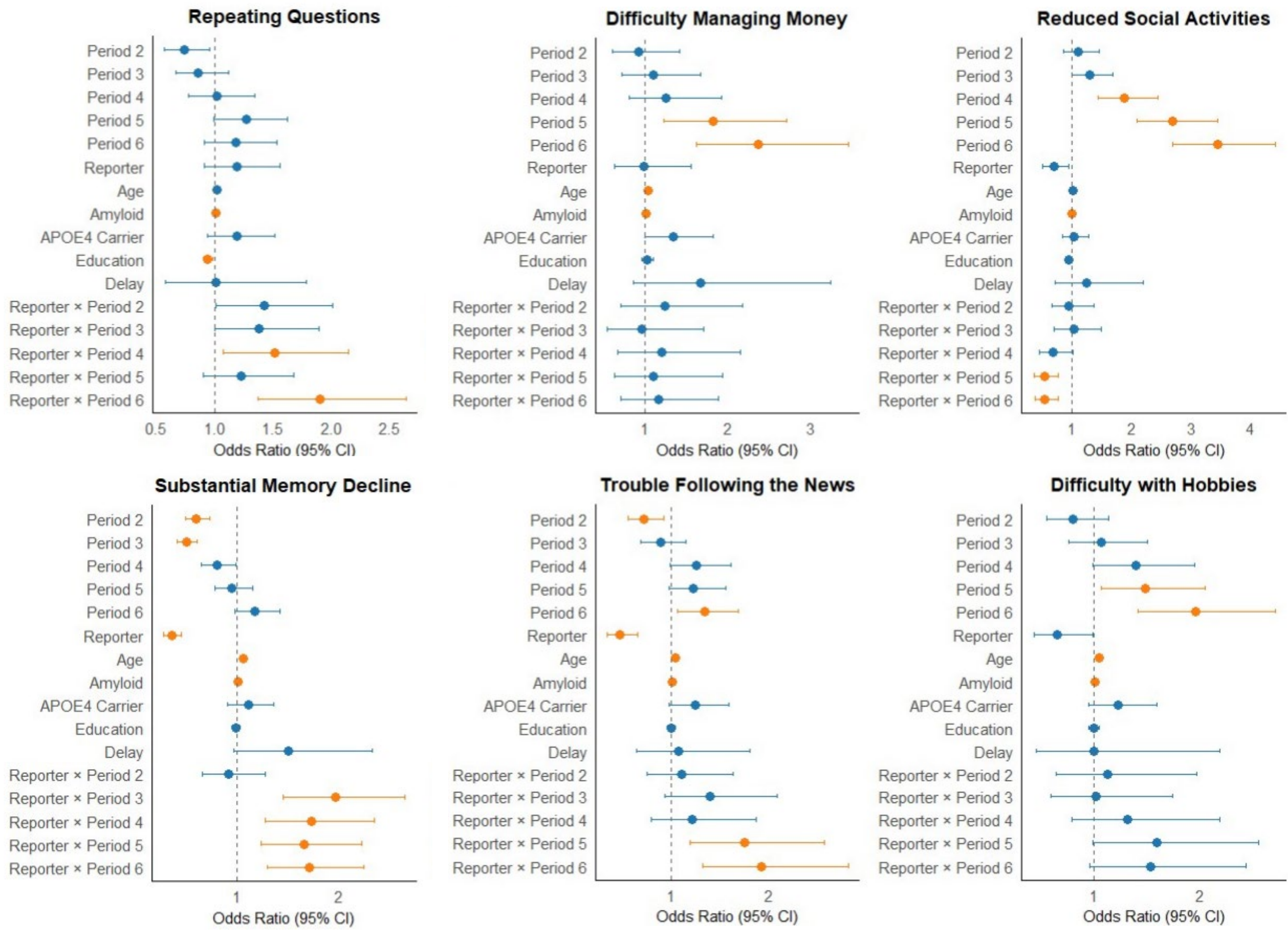


Figure 2: Odds Ratios and 95% Confidence Intervals (CI) by Predictor and CFI item. Significant effects (FDR-adjusted $p < .05$) are shown in orange; non-significant effects in blue.

Conclusion

- Study-partner endorsement of cognitive complaints increased over time, while endorsement of functional complaints showed more agreement over time between reporters, with modest increases overall.
- Participants and study partners may provide complementary perspectives on emerging symptoms.
- Understanding the sequence of changes in specific complaints can improve expectation management

1) Dubbelman MA, Sikkes SAM, Ebenau JL, et al. Changes in Self- and Study-Partner Perceived Cognitive Functioning in Relation to Amyloid Status and Future Clinical Progression: Findings from the SCIENCE Project. *Alzheimer's Dement.* 2023;29:33-2942.

2) Amariglio RE, Grill JD, Rentz DM, et al. Longitudinal Trajectories of the Cognitive Function Index in the A4 Study. *J Prev Alzheimers Dis.* 2024;11(4):838-845.