

Predictive Models for Alzheimer’s Disease Pathology Risk: Participant–Informant Reported ECog-12 Scores and Discrepancy

Inhee Shim^{1,2}, Adam Diaz³, Melanie Miller³ Michael Weiner^{2,3,4,5}, Sarah Farias⁶, Rachel Nosheny^{2,3,4}, for the Alzheimer’s Disease Neuroimaing Initiative (ADNI)*

¹Department of Psychiatry, Dongnam Inst. of Radiological & Medical Sciences, Busan, Republic of Korea
²Department of Psychiatry and Behavioral Sciences, University of California San Francisco, San Francisco, California, United States
³Northern California Institute for Research and Education, San Francisco, CA, United States
⁴Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States.
⁵Department of Medicine, University of California San Francisco, San Francisco, CA, United States.
⁶Department of Neurology, University of California Davis, Sacramento, CA, United States.

Informant-reported ECog-12 strongly predicts AD pathology across disease stages; beyond severity, the participant–informant discrepancy (awareness gap) resolves biomarker heterogeneity within equivalent strata — enabling sharper risk stratification and prevention-trial enrichment.

INTRODUCTION

- Early AD pathology often precedes measurable cognitive decline — scalable tools are needed to flag high-risk individuals.
- ECog-12 (participant [PT] and informant [study partner, SP] report) and the SP–PT discrepancy may reflect awareness changes linked to AD pathology.
- Aim:** test whether ECog-12 scores and discrepancy predict biomarker-defined AD risk and stratify high-risk individuals.

Variable	Unimpaired (n=504)	Impaired (n=355)
Age, years	72 (65, 77)	75 (69, 80)
Female	324 (64.3%)	167 (47.0%)
APOE ε4 carrier	171 (34.1%)	164 (46.3%)
CDR-SB	0.0 (0.0, 0.0)	1.5 (1.0, 3.0)
Diagnosis (MCI / DEM)	–	279 / 76
ECog-12, SP	1.08 (1.00, 1.25)	1.75 (1.33, 2.50)
ECog-12, PT	1.33 (1.08, 1.58)	1.58 (1.33, 2.17)
ECog-12 discrepancy	−0.17 (−0.42, 0)	0.08 (−0.42, 0.67)
Amyloid PET +	118 (29.3%)	157 (63.1%)
Plasma p-tau217 +	54 (10.7%)	160 (45.1%)

Median (Q1, Q3) or n (%). All between-group comparisons p<0.05. SP, study partner (informant); PT, participant.

METHODS

- ADNI-4**; N=859 (CU 504, MCI 279, dementia 76); ECog-12 + p-tau217 + amyloid PET within 180 days.
- Biserial correlations (ρ) of SP/PT vs biomarker status (Fig 1A); logistic regression for positivity & diagnosis (impaired = MCI or dementia); SP–PT discrepancy via natural cubic spline → ribbon plots (Fig 1B).
- Visualization:** predicted risk as a 2-D SP-score × discrepancy heatmap (Fig 2); AT-group distribution across strata as stacked bars (Fig 3).

Figure 1. Biological validity of ECog-12 scores/discrepancy

A. Box plots of ECog-12 scores for negative and positive biomarker positivity. (a) SP, (b) PT.

B. Natural cubic spline plots of predicted odds of biomarker positivity vs ECog-12 discrepancy. (a) Amyloid PET, (b) p-tau217, (c) combined.

RESULTS

- SP ECog-12 linked to biomarker positivity more (p=0.36) than PT (p=0.24) (Fig 1A).
- SP–PT discrepancy independently associated; non-linear, U-shaped (Fig 1B).
- Diagnostic discrimination — AUROC: 0.872 (SP), 0.776 (PT), 0.819 (discrepancy).
- Heatmaps (Fig 2):** nonlinear by score — low–mid: SP<PT linked to positivity; mid: parabolic rise from SP≈PT into SP>PT; high: elevated regardless of discrepancy.
- AT shift (Fig 3):** within equal scores, greater SP>PT shifts A–T→A+T+ (A+T+ 58.8% mid, 78.3% high); A–T– dominant at low scores.

Figure 2. Heatmaps of Predicted Odds of Biomarker Positivity Based on ECog-12 Scores and Discrepancies

A. Combined. B. Amyloid PET. C. p-tau217. SP-score thresholds: low <1.54, mid 1.54–2.83, high ≥2.83; green→red = low→high risk.

CONCLUSIONS

- ECog-12 scores and the SP–PT discrepancy are scalable, non-invasive markers for AD pathology risk stratification.
- Combining subjective cognitive complaints with biomarker-informed estimation can flag individuals at risk for underlying AD pathology.
- Next:** validate in diverse populations; extend to remote and digital settings.

Figure 3. Distribution of A/T (Amyloid-PET/plasma p-tau217 positivity) Across Ecog-12 Scores and Discrepancy

Stacked bar chart showing the distribution of A/T status across ECog-12 scores (low, mid, high) and discrepancy (low, mid, high). Legend: A+T+ (blue), A+T- (green), A-T+ (orange), A-T- (dark blue).

REFERENCES

1. Jack CR Jr, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimers Dement*. 2024;20(8):5143–69.

2. Tomaszewski Farias S, et al. Development and validation of a short form of the Everyday Cognition scales (ECog-12). *Alzheimers Dement*. 2011;7(6):593–601.

3. Manjavong M, et al. A short Everyday Cognition scale predicts clinical progression and cognitive decline. *Alzheimers Dement*. 2024;20(12):8651–60.

4. Janelidze S, et al. Plasma p-tau217 and Aβ42/40 to predict early brain Aβ accumulation in people without cognitive impairment. *JAMA Neurol*. 2024;81(9):947–57.

5. Nosheny RL, et al. Dyadic cognitive report and subjective cognitive decline in early AD research and trials. *Alzheimers Dement (N Y)*. 2022;8(1):e12357.

6. Aaronson A, et al. Self- and informant-report cognitive decline discordance and MCI diagnosis. *JAMA Netw Open*. 2025;8(4):e255810.

7. López-Martos D, et al. Dyadic perspective in subjective reports and objective cognitive decline in preclinical Alzheimer's. *Alzheimers Dement*. 2024;20(Suppl 3).

8. Pérez-Blanco L, et al. Predicting progression to dementia using dyadic patterns of subjective reporting: the CompAS study. *Front Aging Neurosci*. 2024;16:1319743.

9. Kuhn E, et al. Informant-reported memory decline and cognitive/brain deterioration across the Alzheimer clinical continuum. *Neurology*. 2023;100(24):e2454–65.

10. Sánchez-Benavides G, et al. Informant- and self-reported subjective cognitive decline predict amyloid-β PET in cognitively unimpaired individuals. *Alzheimers Dement (Amst)*. 2020;12(1):e12127.

11. Mimmack KJ, et al. Dimensions of self-awareness of memory function and clinical progression in cognitively normal older adults. *JAMA Netw Open*. 2023;6(4):e239964.

12. Caselli RJ, et al. Subjective cognitive decline: self and informant comparisons. *Alzheimers Dement*. 2014;10(1):93–8.

CONTACT

Inhee Shim

ihshim1224@dirams.re.kr

Dongnam Inst. of Radiological & Medical Sciences, Busan, Republic of Korea