

Neuropsychological Profiles As Predictors
Of Clinical Progression In Subjective Cognitive Decline

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Introduction

Identifying features of subjective cognitive decline (SCD) that predict progression to mild cognitive impairment (MCI) or dementia is important, as some individuals with SCD may represent the preclinical stage of neurodegenerative diseases such as Alzheimer’s disease (AD).

This study aimed to evaluate whether baseline neuropsychological profiles predict clinical progression in SCD, with adjustment for Alzheimer’s biomarker status.

Methods

- We analyzed data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI; ADNI-1, ADNI-GO, ADNI-2, ADNI-3 and ADNI-4).
- Inclusion criteria
 - Participants with SCD at baseline
 - Initial diagnosis of cognitively normal
 - subjective cognitive complaints
 - Normal performance (≥ -1.5 SD) in all cognitive tests
- Cognitive function tests
 - Rey Auditory Verbal Learning Test (RAVLT), Trail making test (TMT), Boston naming test (BNT), Category fluency test (CFT)
- Amyloid biomarker evaluation
 - amyloid PET with SVUR ≥ 1.11 or CSF A β 42 < 680 pg/mL or CSF A β 42/A β 40 ≤ 0.068 .
- Participants with SCD at baseline were followed longitudinally for clinical progression.
- Statistical analysis
 - Cox proportional hazards regression models were conducted in two steps: without biomarker adjustment and with amyloid biomarker adjustment

Results

Table 1. Baseline characteristics of study participants

	All(n = 302)
Age, years, mean (SD)	70.54 (6.54)
Female, n (%)	191 (63.2)
Education, years,mean (SD)	16.66 (2.32)
Follow-up month, median (IQR)	48 (24-60)
APOE ϵ 4+, n(%)	95 (31.5)
MMSE, mean (SD)	29.14 (1.09)
MoCA, mean (SD)	25.99 (2.60)
CDR-SB >0, n (%)	29 (9.6)
RAVLT	
Immediate recall, mean (SD)	0.022 (0.939)
Delayed recall, mean (SD)	-0.007 (1.019)
Recognition, mean (SD)	0.030 (0.941)
Boston naming test, mean (SD)	0.043 (1.212)
Category fluency test (animal), mean (SD)	-0.028 (0.943)
TMT Part A, mean (SD)	0.105 (0.940)
TMT Part B, mean (SD)	0.018 (0.956)

Table 2. Baseline characteristics between the amyloid-positive (A+) and amyloid-negative(A-) SCD

	A+ SCD (n =89)	A- SCD (n = 191)	P-value
Clinical progression, n (%)	25 (28.1)	18 (9.4)	<0.001
Age, years, mean (SD)	72.32 (6.69)	70.03 (6.26)	0.006
Female, n (%)	60 (67.4)	113 (59.2)	0.234
Education, years, mean (SD)	16.47 (2.54)	16.77 (2.28)	0.327
Follow-up, month, mean (SD)	46.52 (27.05)	48.79 (26.05)	0.503
APOE ϵ 4+, n (%)	50 (56.2)	42(22.0)	<0.001
MMSE, mean (SD)	29.07 (1.07)	29.19 (1.08)	0.382
MoCA, mean (SD)	25.81 (2.63)	26.12 (2.55)	0.354
CDR-SB >0, n (%)	8 (9.0)	19 (9.9)	0.785
RAVLT			
Immediate recall	-0.038 (0.855)	0.041 (0.978)	0.514
Delayed recall	-0.030 (0.901)	-0.161 (1.079)	0.919
Recognition	0.094 (0.718)	-0.021 (1.055)	0.354
Boston naming test	0.148 (0.721)	-0.017 (1.422)	0.506
Category fluency test	0.014 (0.923)	-0.067 (0.898)	0.394
Trail making test			
Part A	0.160 (0.803)	0.156 (0.872)	0.969
Part B	-0.027 (1.038)	0.095 (0.917)	0.321

- Cox regression results in the overall SCD cohorts (n=302)
 - In multivariable analysis, older age (HR 1.078, 95% CI 1.017-1.143), lower baseline **MoCA scores** (HR 0.755, 95% CI 0.651-0.876), lower **RAVLT immediate recall** (HR 0.613, 95% CI ,0.425-0.883) and poor performance in **TMT Part B** (HR 0.759, 95% CI 0.562-0.926) significantly associated with clinical progression.
- Cox regression results after adjustment for amyloid status (amyloid biomarker available subset, n=280)
 - In multivariable analysis, older age (HR 1.074, 95% CI 1.014-1.137), lower baseline **MoCA scores** (HR 0.733, 95% CI 0.632-0.851), and lower **RAVLT immediate recall** (HR 0.624, 95% CI ,0.419-0.940) were significantly associated with clinical progression. In contrast, TMT Part B which was significant in the overall SCD cohorts, showed statistically not significant results (HR 0.629, 95% CI 0.388-1.018)

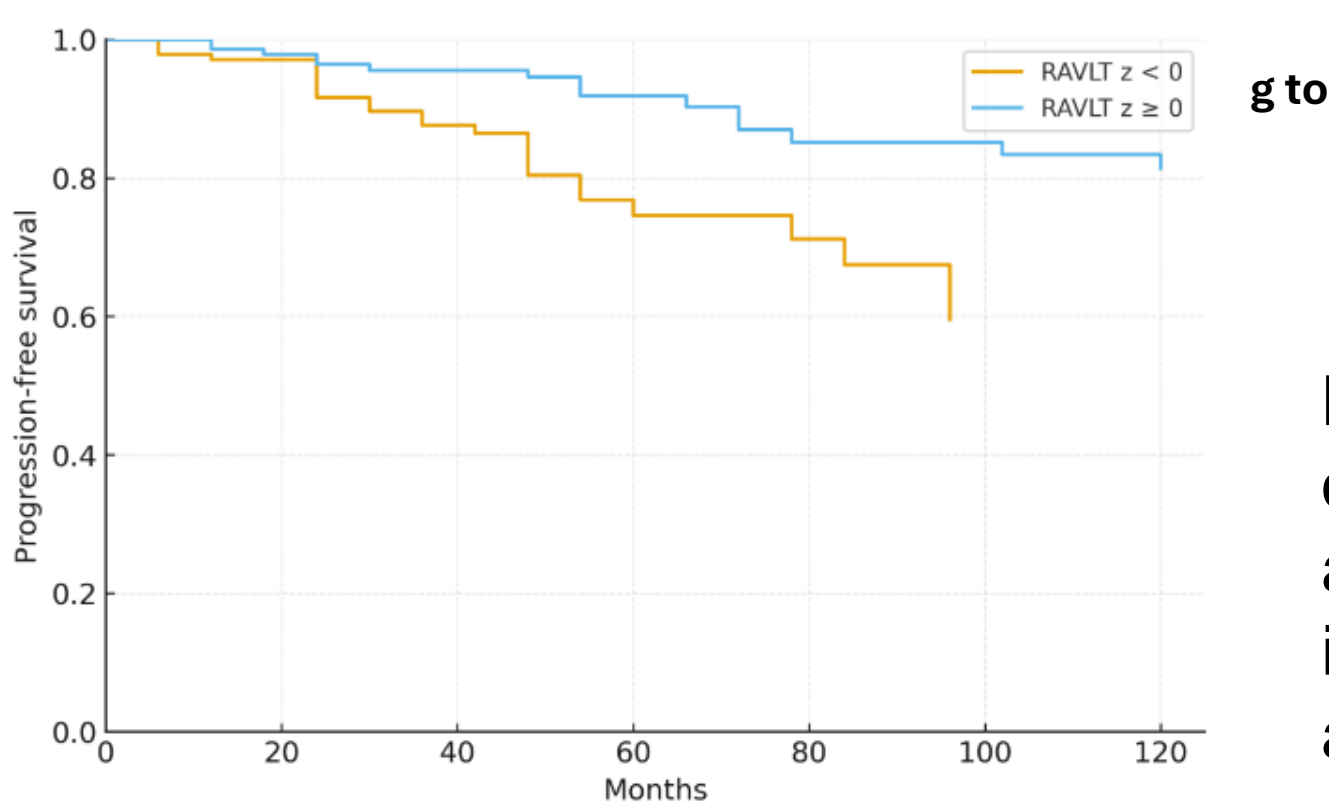


Figure. Kaplan-Meier curves of progression-free survival according to baseline RAVLT immediate recall scores in the amyloid-adjusted model

- Cox regression results in A+ subgroups (n=89)
 - In **A+ SCD subgroup (preclinical AD)**, older age (HR 1.092, 95% CI 1.048-1.152), and lower **RAVLT immediate recall** (HR 0.47, 95% CI ,0.253-0.892) were significantly associated with clinical progression.

Conclusion

Across all analytic models, baseline immediate recall consistently predicted clinical progression in SCD even after adjustment for amyloid biomarker and particularly among individuals in the preclinical stage of AD. These findings suggest that early memory encoding dysfunction may be an early marker of subsequent clinical progression.