



Stage-dependent Changes in Cognitive Intra-individual Variability: The Role of Amyloid Deposition and Network Segregation



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Background

- Cognitive intra-individual variability (IIV) reflects within-person variability in cognitive performance and is elevated in aging and Alzheimer's disease (AD).
- Increased cognitive IIV has been proposed as a sensitive marker of cognitive dysfunction beyond mean cognitive performance.
- However, stage-dependent changes in cognitive IIV and its relationship with AD pathology remain unclear.
- This study examined stage- and amyloid-related patterns of cognitive IIV and their associations with functional network segregation.

Methods

- 515 older adults (CN, MCI, AD dementia; age 55-90 years) were analyzed from the Korean Brain Aging Study for the Early Diagnosis and Prediction of Alzheimer's Disease (KBASE).
- Participants underwent Korean CERAD assessment and multimodal neuroimaging (resting-state fMRI and [¹¹C]PiB-PET).
- Cognitive IIV was defined as within-person dispersion across neuropsychological test performance independent of global cognition. Test scores were standardized using age-, sex-, and education-adjusted norms, residualized with respect to global cognition (CERAD TS z-score), and summarized as the within-individual standard deviation across cognitive domains.
- Amyloid positivity was defined as SUVR > 1.4 in any of four predefined cortical regions, and network segregation indices were derived from resting-state fMRI.
- Associations among cognitive IIV, cognitive stage, amyloid positivity, and network segregation were examined using general linear models.



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Results

- Cognitive IIV increased across cognitive stages from CN to MCI and AD dementia (**Figure 1**).
- Higher cognitive IIV was associated with low somatomotor network segregation (**Figure 2**).
- Cognitive IIV was modestly higher in amyloid-negative than amyloid-positive individuals after controlling for age and sex (**Figure 3A**).
- Amyloid positivity modified stage-dependent trajectories of cognitive IIV (**Figure 3B**).
 - Among **amyloid-negative individuals**, IIV increased from CN to MCI but plateaued from MCI to AD.
 - Among **amyloid-positive individuals**, IIV increased progressively from CN to MCI to AD.

Table 1.

	CN (n = 292)	MCI (n = 148)	AD (n = 75)	df	F	p-value
Age (years)	69.0 ± 8.0	73.5 ± 7.0	73.8 ± 7.2	2,512	23.2	< .001
Sex (male)	142 (48.6%)	51 (34.5%)	26 (34.7%)	2	10.3	.005
Education (years)	11.9 ± 4.8	10.2 ± 4.5	10.1 ± 5.2	2,512	8.6	< .001
APOE Positivity (count) (n = 514)	53 (18.2%)	58 (39.2%)	47 (62.7%)	2	62.3	< .001
Amyloid Positivity (count) (n = 506)	42 (14.5%)	71 (49.3%)	59 (80.8%)	2	119.5	< .001
IIV (mean)	0.8 ± 0.3	1.0 ± 0.3	1.1 ± 0.3	2,512	38.2	< .001
Somatomotor Functional Network Segregation Index (n = 490)	0.55 ± 0.1	0.52 ± 0.1	0.46 ± 0.1	2,487	8.9	< .001

Note. Values are presented as mean ± standard deviation for continuous variables and n (%) for categorical variables. Group differences were assessed using one-way analysis of variance (ANOVA) for continuous variables and χ^2 tests for categorical variables. Amyloid positivity was evaluated using logistic regression and likelihood ratio tests adjusting for age and sex.

Figure 1. IIV across cognitive stages

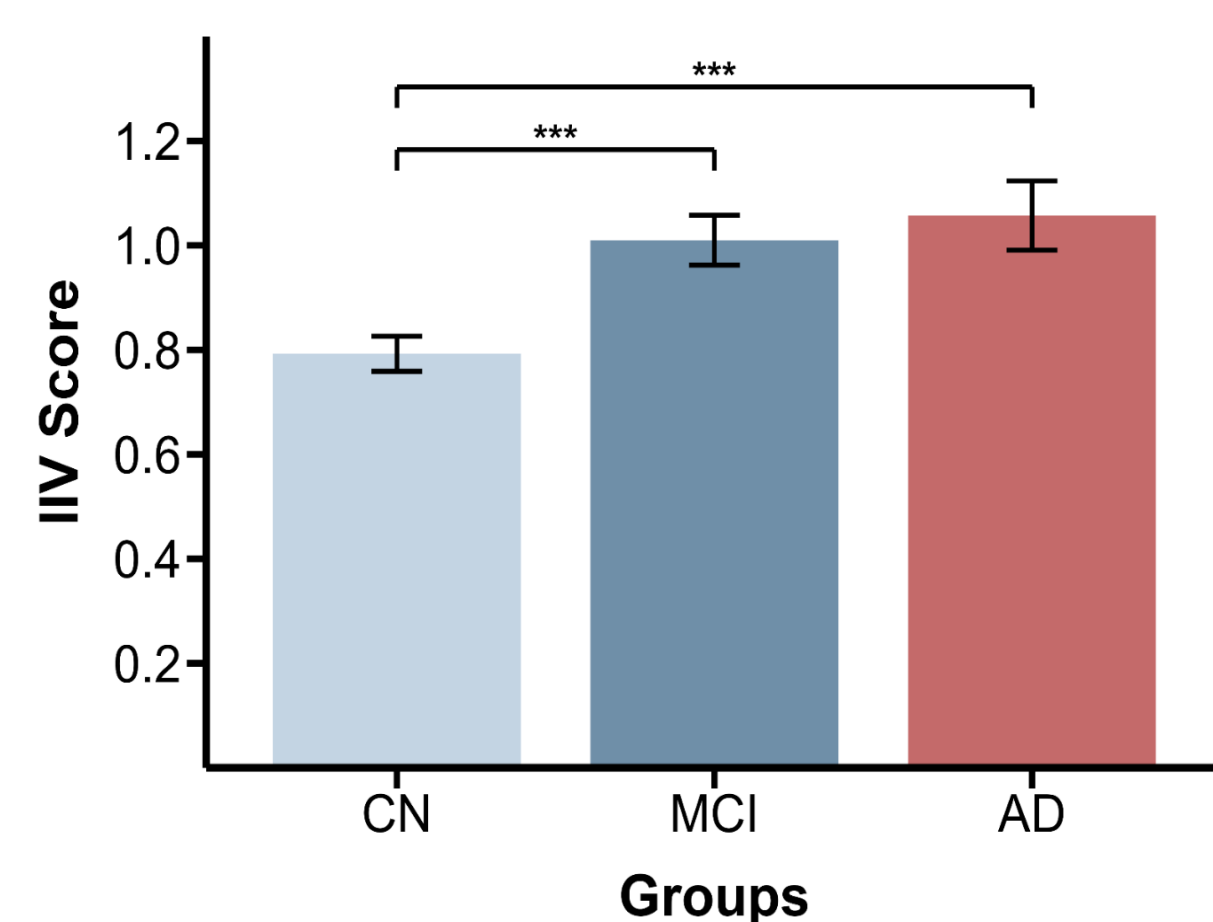


Figure 2. Somatomotor network segregation and IIV

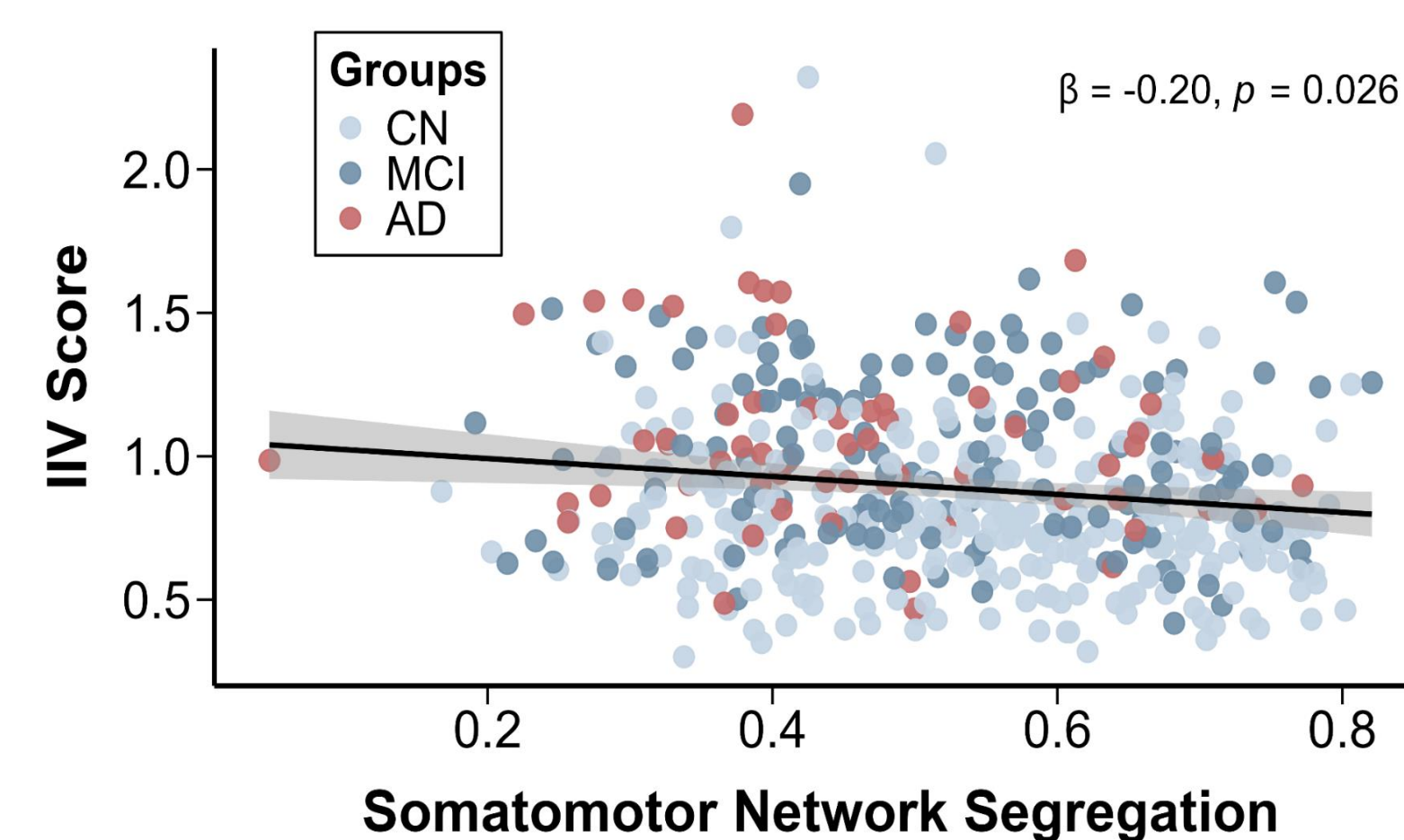


Figure 3A. Overall difference in IIV by Amyloid Status

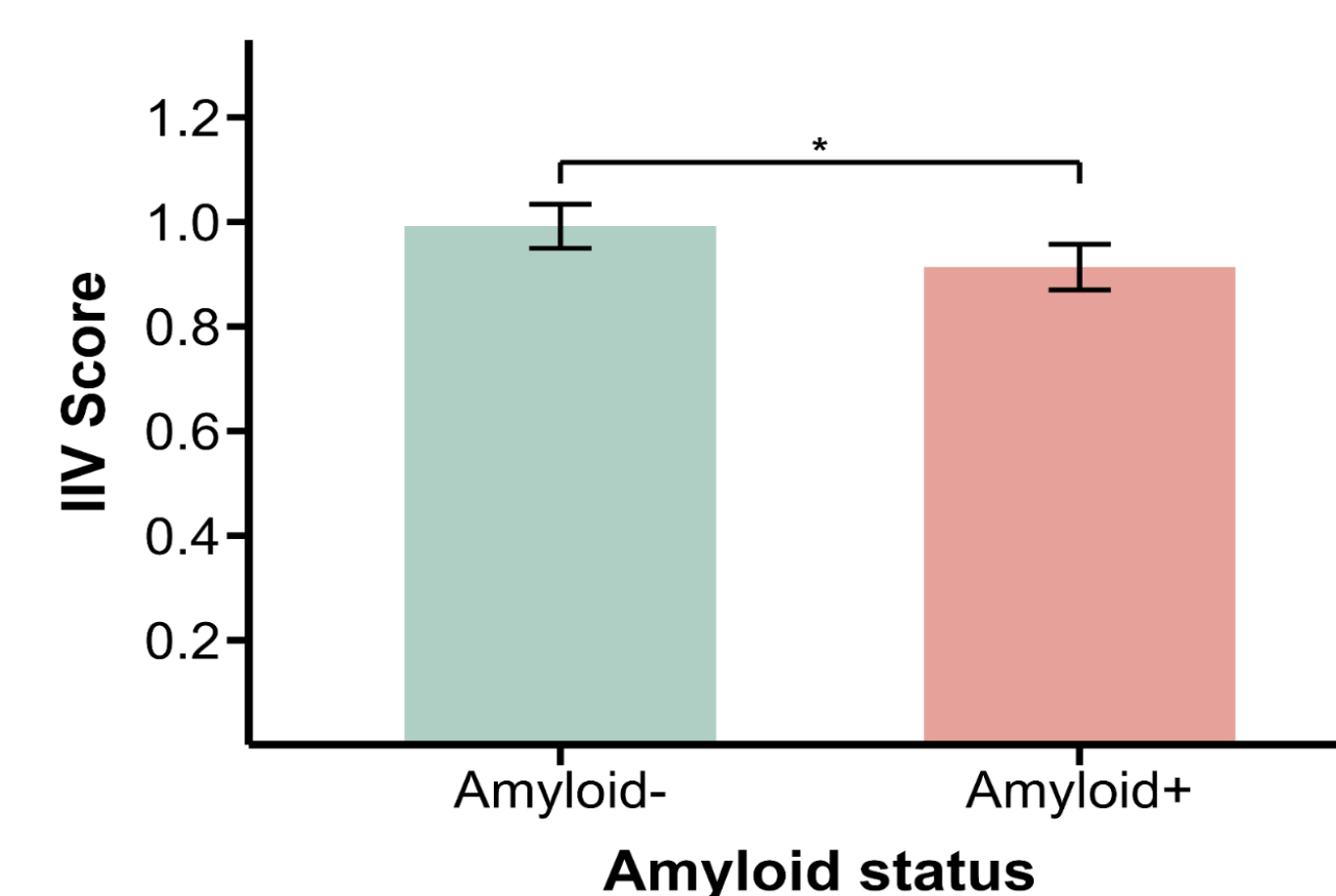
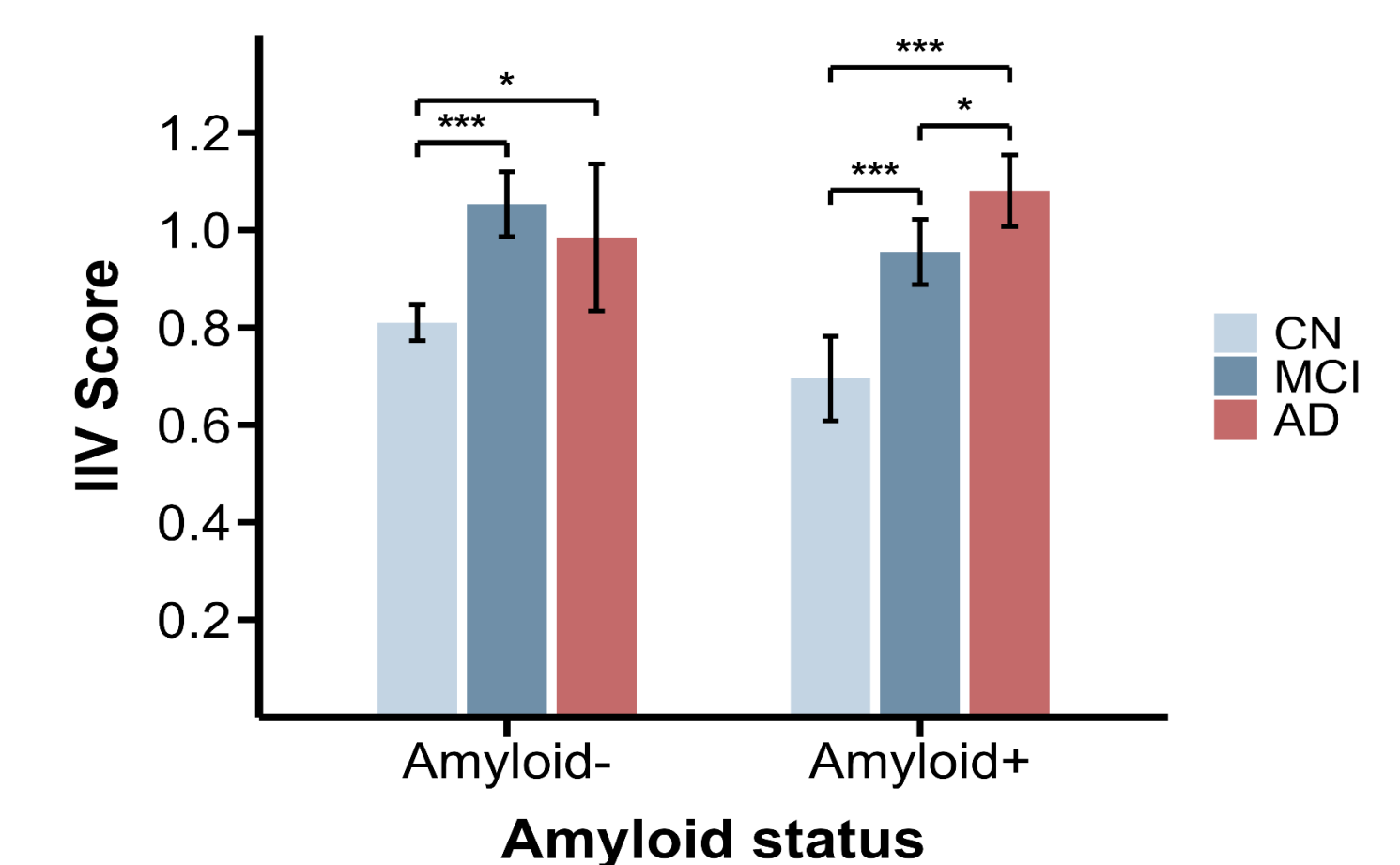


Figure 3B. Stage-dependent in IIV by Amyloid Status



Conclusion

- Cognitive IIV increased across cognitive stages and was associated with lower somatomotor network segregation, suggesting a link between cognitive variability and functional brain network organization.
- Pathological amyloid deposition modified stage-dependent trajectories of cognitive IIV, with progressive increases observed primarily in amyloid-positive individuals.
- These findings suggest that cognitive IIV may reflect both AD-related pathology and functional network alterations.

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