

# Altered epigenetic age acceleration associated with cognitive aging : A longitudinal pilot study

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## Introduction

Epigenetic age acceleration (EAA) has emerged as a promising biomarker of aging-related conditions. This longitudinal pilot study aimed to identify a biomarker for cognitive aging by examining the EAA differences between successful cognitive aging (SCA) and normal cognitive aging (NCA) among Korean community-dwelling older adults.

## METHODS

We classified participants into two groups: SCA (above the 50th percentile in all domains of cognitive function, n = 13) and NCA (n = 13). Universal epigenetic age acceleration, intrinsic epigenetic age acceleration (IEAA), extrinsic epigenetic age acceleration (EEAA), and cognitive functions were measured at baseline and after two years. Man-Whitney U test and partial correlation tests were used to analyze cognitive functions and EAA.

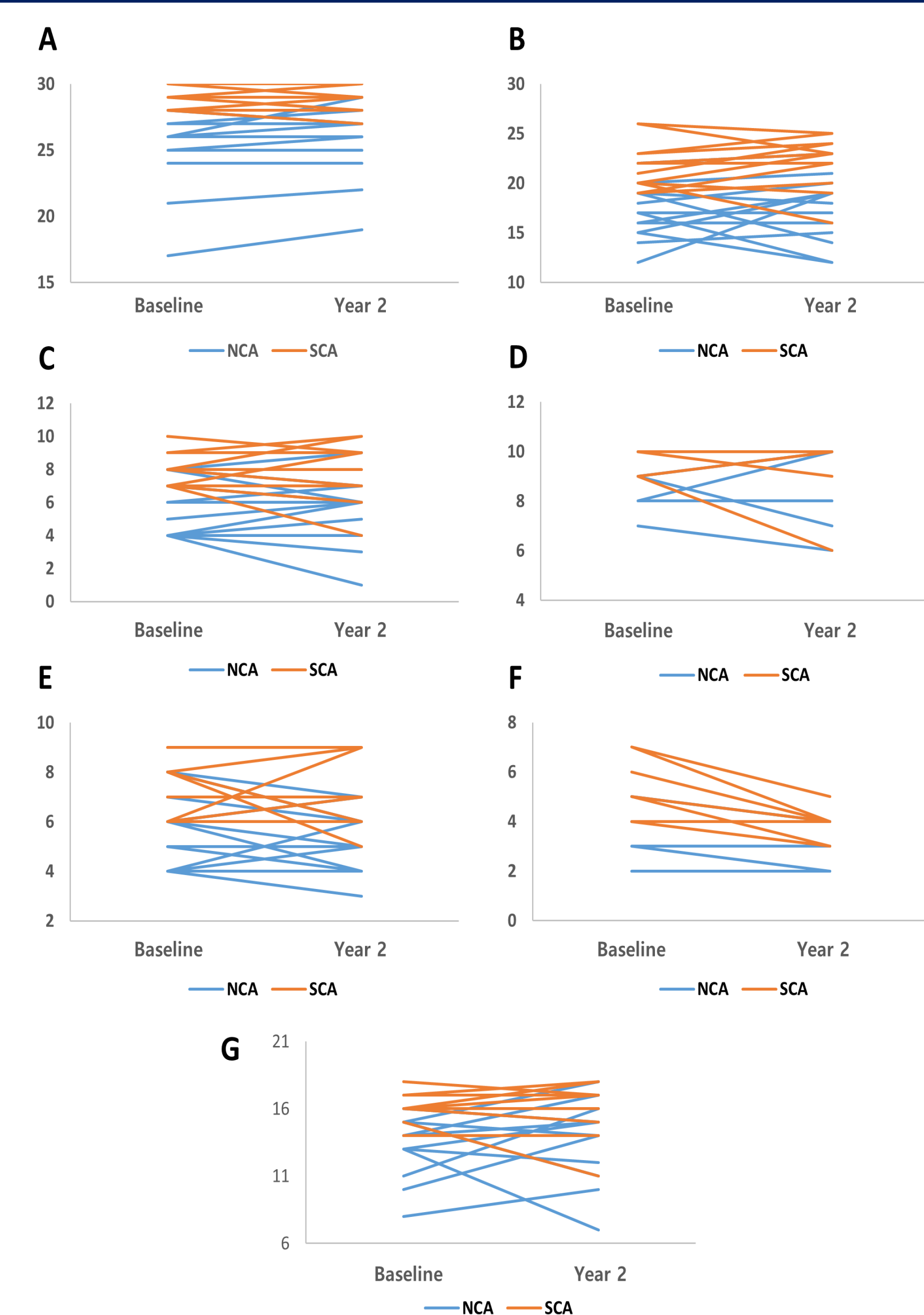
## RESULTS

The trajectories at baseline and after two years showed that 85% of participants of the SCA group has been changed to the NCA group after two years. There was a significant mean difference between SCA and NCA groups in EEAA ( $Z = -2.128$ ,  $p = .034$ ). EEAA was also negatively correlated with digit span backward test after controlling number of comorbidities ( $r = -0.52$ ,  $p = .030$ ).

**Table 1.** Descriptive summary of successful and normal cognitive aging and their trajectories at baseline and after two years

Variables	Categories	Baseline (n = 26)	Year 2 (n = 26)
SCA		13 (50.0%)	3 (11.5%)
NCA		13 (50.0%)	23 (88.5%)
Trajectories	SCA → SCA		2 (7.7%)
	SCA → NCA		11 (42.3%)
	NCA → SCA		1 (3.8%)
	NCA → NCA		12 (46.2%)

Note: SCA, successful cognitive aging; NCA, normal cognitive aging; MCI, mild cognitive impairment



**Figure 1.** Individual neuropsychological test scores for all baseline (2017) and two-year follow-up measures by groups. (A) Mini-Mental State Exam (MMSE-KC), (B) Word List Memory, (C) Word List Recall, (D) Word List Recognition, (E) Digit Span Forward, (F) Digit Span Backward, (G) Frontal Assessment Battery.

**Table 2.** Comparison of neuropsychological test and epigenetic age acceleration between groups over time

Categories	Group	Baseline M ± SD	Year 2 M ± SD	Mean difference	Z	p
Universal age acceleration	NCA	1.42 ± 5.72	2.10 ± 6.12	0.68 ± 4.04	-0.385	.724
	SCA	-2.07 ± 3.58	-1.45 ± 4.33	0.62 ± 2.38		
IEAA	NCA	1.09 ± 5.35	2.83 ± 5.08	1.74 ± 3.10	-0.436	.687
	SCA	-2.73 ± 3.21	-1.19 ± 4.34	1.54 ± 2.31		
EEAA	NCA	3.75 ± 4.30	-1.35 ± 4.13	-5.10 ± 2.83	-2.128	.034
	SCA	0.26 ± 3.75	-2.66 ± 3.51	-2.92 ± 2.22		

Note: † Mann-Whitney U test; MMSE-KC, Mini-Mental State exam in the Korean version; IEAA, intrinsic epigenetic age acceleration; EEAA, extrinsic epigenetic age acceleration

**Table 3.** Partial correlation between the neuropsychological tests and epigenetic age acceleration controlling comorbidities.

Variables	1	2	3	4	5	6	7	8	9	10
1. Universal Age Acceleration	1.00	0.88**	0.00	-0.06	0.00	-0.16	0.15	0.22	-0.17	0.18
2. IEAA		1.00	-0.07	0.12	0.08	-0.03	0.25	0.03	-0.13	0.20
3. EEAA			1.00	-0.25	-0.02	0.03	0.04	-0.16	-0.52*	-0.22
4. MMSE-KC				1.00	-0.16	0.44*	0.42*	-0.16	-0.05	0.34
5. Word List Memory					1.00	0.40	-0.27	-0.40*	0.29	0.08
6. Word List Recall						1.00	0.48*	-0.33	0.06	0.15
7. Word List Recognition							1.00	-0.06	-0.22	0.17
8. Digit Span Forward								1.00	-0.12	0.13
9. Digit Span Backward									1.00	-0.23
10. FAB										1.00

Note: IEAA, intrinsic epigenetic age acceleration; EEAA, extrinsic epigenetic age acceleration; MMSE-KC, Mini-Mental State exam in the Korean version; FAB, frontal assessment battery; \*,  $p < 0.05$ ; \*\*,  $p < 0.01$

## CONCLUSIONS

We found that EEAA was associated with cognitive aging. We suggest EEAA can be used as a biomarker for the early detection of cognitive decline in Korean community-dwelling older adults.