

**Supplemental Materials for “The association between hippocampal subfield volumes and education in cognitively normal older adults and amnesic mild cognitive impairment patients” by Kang et al.**

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## **Supplemental Methods**

### ***1. Neuropsychological evaluation***

Cognitive status was assessed by neuropsychological testing at the Seoul St. Mary's Hospital, The Catholic University of Korea. The cognitive functions of all the subjects were assessed with the Korean version of Consortium to Establish a Registry for Alzheimer's Disease (CERAD-K), including Verbal Fluency (VF), 15-item Boston Naming Test (BNT), MMSE-K, Word List Memory (WLM), Word List Recall (WLR), Word List Recognition (WLRc), Constructional Praxis (CP), and Constructional Recall (CR). The CERAD is the standardized clinical and neuropsychological assessment battery for the evaluation of patients with Alzheimer's disease. The results were reviewed by a neuropsychologist to determine whether there was evidence of cognitive impairment.

The VF score is the number of animal names that the subject speaks for himself for one minute. The score range of BNT is from 0 to 15 points. The score range of MMSE-K is from 0 to 30 points. The score range of WLM is from 0 to 30 points. The score range of WLR is from 0 to 10 points. The score range of WLRc is from 0 to 10 points. The score range of CP is from 0 to 11 points. The score range of CR is from 0 to 11 points.

### ***2. APO E genotyping***

DNA was isolated from blood using the QIAmp Blood DNA Maxi Kit protocol (Qiagen, Valencia, CA). Genotypes for two APOE SNPs, rs429358 (E\*4) and rs7412 (E\*2) were determined using TaqMan SNP genotyping assays (Applied Biosystems, Foster City, California).

### **3. The definition of early and late mild cognitive impairment**

(i) Late mild cognitive impairment defined by the report on memory impairment and performance on delayed verbal recall (CERAD-K Word List Recall) below 1.5 SD of the norm, (ii) Early mild cognitive impairment defined by the report on memory impairment and performance on delayed verbal recall (CERAD-K Word List Recall) between 1.0 SD and 1.5 SD below the norm.

## **Supplemental Results**

### **1. The stepwise regression analyses**

#### **1.1 Relationship between education and hippocampal subfield volumes**

##### **1.1.1 Lt. parasubiculum, both groups**

Result of Stepwise Backward Regression

Analysis of Variance Table

*Model 1: left parasubiculum ~ age + education*

*Model 2: left parasubiculum ~ age + gender + education + APOE genotype*

	<b>Res.Df</b>	<b>RSS</b>	<b>Df</b>	<b>Sum of Sq</b>	<b>F</b>	<b>Pr(&gt;F)</b>
1	65	11673.14				
2	63	11406.79	2	266.35	0.74	0.4833

Finally Selected Model

Result of Multiple Regression Analysis

	<b>Beta</b>	<b>lwr</b>	<b>upr</b>	<b>SE</b>	<b>std.Beta</b>	<b>lwr</b>	<b>upr</b>	<b>SE</b>	<b>t value</b>	<b>p</b>
(Intercept)	117.44	72.69	162.19	22.41					5.24	< 0.001
age	-0.72	-1.31	-0.12	0.30	-0.27	-0.5	-0.05	0.11	-2.41	0.019
education	-0.83	-1.44	-0.22	0.31	-0.31	-0.53	-0.08	0.11	-2.70	0.009

$R^2=0.1601$ ,  $adj.R^2=0.1343$ ,  $F=6.2$ ,  $p=0.003$ ,  $AIC =550.87$

Res. Df, residual degrees of freedom; RSS, residual sum of squares; Df, degree of freedom; Sq, squares;

Pr(>F), Probability of F value.

### 1.1.2 Lt. presubiculum, both groups

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left presubiculum ~ age + education

Model 2: left presubiculum ~ age + gender + education + APOE genotype

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	65	132668.1				
2	63	131895.6	2	772.5	0.18	0.832

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	553.66	402.79	704.52	75.54					7.33	< 0.001
age	-3.43	-5.43	-1.43	1.00	-0.38	-0.6	-0.16	0.11	-3.43	0.001
education	-2.47	-4.54	-0.40	1.04	-0.26	-0.48	-0.05	0.11	-2.38	0.02

$R^2=0.2027$ ,  $adj.R^2=0.1782$ ,  $F=8.26$ ,  $p < 0.001$ ,  $AIC = 716.15$

### 1.1.3 Lt. subiculum, both groups

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left subiculum ~ age + education

Model 2: left subiculum ~ age + gender + education + APOE genotype

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	65	247721.8				
2	63	246508.9	2	1212.94	0.15	0.8567

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	868.76	662.61	1074.91	103.22					8.42	< 0.001
age	-5.90	-8.64	-3.17	1.37	-0.46	-0.67	-0.25	0.11	-4.31	< 0.001
education	-3.28	-6.11	-0.45	1.42	-0.25	-0.46	-0.04	0.11	-2.32	0.024

$R^2=0.2604$ ,  $adj.R^2=0.2376$ ,  $F=11.44$ ,  $p < 0.001$ ,  $AIC = 758.61$

### 1.1.4 *Lt. paraboliculum*, aMCI group

Analysis of Variance Table

Model 1: *left parasubiculum* ~ age + gender + education + APOE genotype

Model 2: *left parasubiculum* ~ age + gender + education + APOE genotype

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	4685.8				
2	30	4685.8	0	0		

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	136.31	64.82	207.79	35.00					3.89	0.001
age	-0.99	-1.95	-0.02	0.47	-0.32	-0.63	-0.02	0.15	-2.09	0.045
gender	8.63	-1.91	19.17	5.16	0.25	-0.04	0.55	0.15	1.67	0.105
education	-1.21	-2.23	-0.19	0.50	-0.37	-0.67	-0.07	0.15	-2.43	0.021
APOE genotype	-7.48	-17.72	2.76	5.01	-0.23	-0.52	0.07	0.15	-1.49	0.146

$R^2=0.3581$ ,  $adj.R^2=0.2725$ ,  $F=4.18$ ,  $p=0.008$ ,  $AIC =282.72$

### 1.1.5 *Lt. paraboliculum*, aMCI group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: *left subiculum* ~ age + education + APOE genotype

Model 2: *left subiculum* ~ age + gender + education + APOE genotype

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	31	120000.3				
2	30	119200.9	1	799.46	0.2	0.657

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	994.71	639.35	1350.07	174.24					5.71	< 0.001
age	-7.28	-12.03	-2.53	2.33	-0.46	-0.75	-0.17	0.15	-3.13	0.004
education	-5.22	-10.25	-0.20	2.47	-0.31	-0.59	-0.02	0.14	-2.12	0.042
APOE genotype	-51.14	-101.23	-1.05	24.56	-0.3	-0.58	-0.02	0.14	-2.08	0.046

$R^2=0.3933$ ,  $adj.R^2=0.3346$ ,  $F=6.7$ ,  $p=0.001$ ,  $AIC =394.22$

## 1.2 Relationship between cognitive functions and hippocampal subfield volumes

### 1.2.1 CERAD-K Word List Recall, Control Group

#### 1.2.1.1 Lt. parasubiculum, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left parasubiculum ~ age + APOE genotype + WLR

Model 2: left parasubiculum ~ age + gender + education + APOE genotype + WLR

	<b>Res.Df</b>	<b>RSS</b>	<b>Df</b>	<b>Sum of Sq</b>	<b>F</b>	<b>Pr(&gt;F)</b>
1	29	4219.51				
2	27	4100.11	2	119.4	0.39	0.6787

Finally Selected Model

Result of Multiple Regression Analysis

	<b>Beta</b>	<b>lwr</b>	<b>upr</b>	<b>SE</b>	<b>std.Beta</b>	<b>lwr</b>	<b>upr</b>	<b>SE</b>	<b>t value</b>	<b>p</b>
(Intercept)	177.51	96.80	258.22	39.46					4.50	< 0.001
age	-1.16	-2.10	-0.22	0.46	-0.46	-0.82	-0.1	0.18	-2.51	0.018
APOE genotype	-9.57	-20.97	1.82	5.57	-0.27	-0.57	0.04	0.16	-1.72	0.096
WLR	-6.13	-9.68	-2.57	1.74	-0.65	-1.01	-0.29	0.18	-3.53	0.001

$R^2=0.3242$ ,  $adj.R^2=0.2543$ ,  $F=4.64$ ,  $p=0.009$ ,  $AIC =263.73$

### 1.2.1.2 Lt. presubiculum, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left presubiculum ~ age + WLR

Model 2: left presubiculum ~ age + gender + education + APOE genotype + WLR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	51168.26				
2	27	49405.91	3	1762.35	0.32	0.8101

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	682.83	414.19	951.46	131.54					5.19	< 0.001
age	-3.85	-7.01	-0.69	1.55	-0.45	-0.8	-0.1	0.18	-2.49	0.018
WLR	-20.89	-32.82	-8.97	5.84	-0.64	-1	-0.29	0.18	-3.58	0.001

$R^2=0.3065$ ,  $adj.R^2=0.2602$ ,  $F=6.63$ ,  $p=0.004$ ,  $AIC =344.08$

### 1.2.1.3 Lt. subiculum, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left subiculum ~ age + WLR

Model 2: left subiculum ~ age + gender + education + APOE genotype + WLR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	79895.44				
2	27	70849.75	3	9045.7	1.15	0.3473

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	858.80	523.12	1194.48	164.36					5.22	< 0.001
age	-4.82	-8.77	-0.88	1.93	-0.49	-0.87	-0.1	0.19	-2.50	0.018
WLR	-15.72	-30.62	-0.81	7.30	-0.42	-0.8	-0.04	0.19	-2.15	0.039

$R^2=0.1927$ ,  $adj.R^2=0.1389$ ,  $F=3.58$ ,  $p=0.04$ ,  $AIC =358.78$

### 1.2.1.4 Rt. presubiculum, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: *right presubiculum* ~ *age* + *WLR*

Model 2: *right presubiculum* ~ *age* + *gender* + *education* + *APOE genotype* + *WLR*

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	51834.81				
2	27	48226.75	3	3608.07	0.67	0.5759

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	583.75	313.37	854.13	132.39					4.41	< 0.001
age	-3.28	-6.45	-0.10	1.56	-0.42	-0.8	-0.03	0.2	-2.11	0.044
WLR	-12.76	-24.76	-0.75	5.88	-0.43	-0.82	-0.04	0.2	-2.17	0.038

$R^2=0.1656$ ,  $adj.R^2=0.11$ ,  $F=2.98$ ,  $p=0.066$ ,  $AIC =344.51$

### 1.2.1.5 Rt. subiculum, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: *right subiculum* ~ *age* + *WLR*

Model 2: *right subiculum* ~ *age* + *gender* + *education* + *APOE genotype* + *WLR*

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	66354.60				
2	27	61134.16	3	5220.44	0.77	0.5217

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	898.75	592.84	1204.66	149.79					6.00	< 0.001
age	-5.31	-8.90	-1.71	1.76	-0.57	-0.94	-0.2	0.19	-3.02	0.005
WLR	-14.33	-27.92	-0.75	6.65	-0.41	-0.78	-0.04	0.19	-2.16	0.039

$R^2=0.2405$ ,  $adj.R^2=0.1899$ ,  $F=4.75$ ,  $p=0.016$ ,  $AIC =352.66$



## 1.2.2 CERAD-K Word List Recognition, Control Group

### 1.2.2.1 Lt. CA1, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left CA1 ~ gender + education + WLRC

Model 2: left CA1 ~ age + gender + education + APOE genotype + WLRC

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	29	95537.57				
2	27	92372.32	2	3165.25	0.46	0.6345

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	290.25	124.83	455.66	80.88					3.59	0.001
gender	40.63	-7.56	88.81	23.56	0.3	-0.04	0.64	0.17	1.72	0.095
education	2.90	-0.98	6.78	1.90	0.26	-0.07	0.59	0.17	1.53	0.137
WLRC	28.73	10.37	47.09	8.98	0.48	0.19	0.78	0.15	3.20	0.003

$R^2=0.3644$ ,  $adj.R^2=0.2987$ ,  $F=5.54$ ,  $p=0.004$ ,  $AIC=366.69$

### 1.2.2.2 Lt. CA3, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left CA3 ~ WLRC

Model 2: left CA3 ~ age + gender + education + APOE genotype + WLRC

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	31	14005.46				
2	27	13052.57	4	952.89	0.49	0.741

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	88.51	28.95	148.08	29.21					3.03	0.005
WLRC	12.47	5.84	19.10	3.25	0.57	0.28	0.86	0.15	3.84	0.001

$R^2=0.3218$ ,  $adj.R^2=0.2999$ ,  $F=14.71$ ,  $p < 0.001$ ,  $AIC=299.32$

### 1.2.2.3 Lt. CA4, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left CA4 ~ WLRc

Model 2: left CA4 ~ age + gender + education + APOE genotype + WLRc

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	31	23578.30				
2	27	21196.76	4	2381.54	0.76	0.561

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	115.72	38.43	193.00	37.89					3.05	0.005
WLRc	15.21	6.60	23.81	4.22	0.54	0.25	0.84	0.15	3.60	0.001

$R^2=0.2954$ ,  $adj.R^2=0.2726$ ,  $F=12.99$ ,  $p=0.001$ ,  $AIC =316.51$

### 1.2.2.4 Lt. GC-DG, Control group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: left GC-DG ~ APOE genotype + WLRc

Model 2: left GC-DG ~ age + gender + education + APOE genotype + WLRc

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	34513.86				
2	27	31987.37	3	2526.49	0.71	0.554

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	133.70	37.31	230.09	47.20					2.83	0.008
APOE genotype	22.50	-8.92	53.93	15.39	0.23	-0.08	0.53	0.16	1.46	0.154
WLRc	16.83	6.18	27.48	5.22	0.5	0.2	0.81	0.16	3.23	0.003

$R^2=0.2809$ ,  $adj.R^2=0.233$ ,  $F=5.86$ ,  $p=0.007$ ,  $AIC =331.09$

### 1.2.2.5 *Lt. subiculum, Control group*

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: *left subiculum* ~ *APOE genotype* + *WLRc*

Model 2: *left subiculum* ~ *age* + *gender* + *education* + *APOE\_genotype1* + *WLRc*

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	78738.69				
2	27	73099.10	3	5639.58	0.69	0.5635

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	272.12	126.53	417.71	71.29					3.82	0.001
<i>APOE genotype</i>	47.85	0.39	95.31	23.24	0.34	0.02	0.66	0.16	2.06	0.048
<i>WLRc</i>	16.22	0.14	32.31	7.88	0.34	0.02	0.66	0.16	2.06	0.048

$R^2=0.2044$ ,  $adj.R^2=0.1513$ ,  $F=3.85$ ,  $p=0.032$ ,  $AIC =358.3$

### 1.2.2.6 *Lt. total hippocampus, Control group*

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: *left total hippocampus* ~ *WLRc*

Model 2: *left total hippocampus* ~ *age* + *gender* + *education* + *APOE genotype* + *WLRc*

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	31	3247719				
2	27	2828408	4	419310.99	1	0.4244

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	1882.69	975.64	2789.73	444.74					4.23	< 0.001
<i>WLRc</i>	150.21	49.21	251.20	49.52	0.48	0.17	0.79	0.16	3.03	0.005

$R^2=0.2289$ ,  $adj.R^2=0.204$ ,  $F=9.2$ ,  $p=0.005$ ,  $AIC =479.05$

### 1.2.2.7 Rt. CA4, Control group

Result of Stepwise Backward Regression

#### Analysis of Variance Table

Model 1: right CA4 ~ gender + education + WLRc

Model 2: right CA4 ~ age + gender + education + APOE genotype + WLRc

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	29	19645.39				
2	27	19127.14	2	518.24	0.37	0.697

Finally Selected Model

#### Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	161.46	86.45	236.47	36.67					4.40	< 0.001
gender	19.70	-2.15	41.55	10.68	0.34	-0.02	0.7	0.18	1.84	0.075
education	1.53	-0.22	3.29	0.86	0.32	-0.03	0.68	0.18	1.78	0.085
WLRc	9.18	0.85	17.51	4.07	0.36	0.05	0.68	0.16	2.26	0.032

$R^2=0.2841$ ,  $adj.R^2=0.21$ ,  $F=3.84$ ,  $p=0.02$ ,  $AIC=314.49$

### 1.2.2.8 Rt. total hippocampus, Control group

Result of Stepwise Backward Regression

#### Analysis of Variance Table

Model 1: right total hippocampus ~ age + WLRc

Model 2: right total hippocampus ~ age + gender + education + APOE genotype + WLRc

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	30	2903657				
2	27	2590957	3	312699.66	1.09	0.3717

Finally Selected Model

#### Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	3752.70	1837.95	5667.45	937.56					4.00	< 0.001
age	-19.10	-39.77	1.57	10.12	-0.3	-0.61	0.01	0.16	-1.89	0.069
WLRc	113.01	12.86	213.17	49.04	0.37	0.05	0.68	0.16	2.30	0.028

$R^2=0.2796$ ,  $adj.R^2=0.2316$ ,  $F=5.82$ ,  $p=0.007$ ,  $AIC=477.35$

### 1.2.3 CERAD-K Constructional Recall, aMCI Group

#### 1.2.3.1 Lt. GC-DG, aMCI group

Result of Stepwise Backward Regression

##### Analysis of Variance Table

Model 1: left GC-DG ~ education + CR

Model 2: left GC-DG ~ age + gender + education + APOE genotype + CR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	32	49308.70				
2	29	45777.43	3	3531.28	0.75	0.5336

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	270.29	234.75	305.82	17.44					15.49	< 0.001
education	-3.75	-6.87	-0.63	1.53	-0.38	-0.68	-0.08	0.15	-2.45	0.02
CR	7.55	1.96	13.14	2.74	0.43	0.12	0.73	0.15	2.75	0.01

$R^2=0.262$ ,  $adj.R^2=0.2159$ ,  $F=5.68$ ,  $p=0.008$ ,  $AIC =361.09$

#### 1.2.3.2 Rt. CA4, aMCI group

Result of Stepwise Backward Regression

##### Analysis of Variance Table

Model 1: right CA4 ~ education + CR

Model 2: right CA4 ~ age + gender + education + APOE genotype + CR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	32	37898.05				
2	29	35757.42	3	2140.64	0.58	0.6337

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	257.78	226.63	288.93	15.29					16.86	< 0.001
education	-2.50	-5.24	0.24	1.34	-0.3	-0.61	0.02	0.16	-1.86	0.072
CR	6.24	1.34	11.14	2.41	0.41	0.1	0.73	0.16	2.59	0.014

$R^2=0.2123$ ,  $adj.R^2=0.1631$ ,  $F=4.31$ ,  $p=0.022$ ,  $AIC =351.88$

### 1.2.3.3 Rt. GC-DG, aMCI group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: right GC-DG ~ gender + education + CR

Model 2: right GC-DG ~ age + gender + education + APOE genotype + CR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	31	54838.15				
2	29	52643.64	2	2194.51	0.6	0.5531

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	314.98	262.91	367.04	25.53					12.34	< 0.001
gender	-24.15	-60.37	12.08	17.76	-0.22	-0.53	0.1	0.16	-1.36	0.184
education	-3.41	-6.76	-0.06	1.64	-0.32	-0.62	-0.02	0.15	-2.07	0.046
CR	7.59	1.32	13.85	3.07	0.4	0.08	0.71	0.16	2.47	0.019

$R^2=0.295$ ,  $adj.R^2=0.2267$ ,  $F=4.32$ ,  $p=0.012$ ,  $AIC =366.81$

### 1.2.3.4 Rt. presubiculum, aMCI group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: right presubiculum ~ education + CR

Model 2: right presubiculum ~ age + gender + education + APOE genotype + CR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	32	91858.77				
2	29	85751.19	3	6107.58	0.69	0.5664

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std.Beta	lwr	upr	SE	t value	p
(Intercept)	270.36	221.86	318.85	23.81					11.36	< 0.001
education	-5.18	-9.44	-0.92	2.09	-0.38	-0.68	-0.08	0.15	-2.48	0.019
CR	11.16	3.53	18.79	3.75	0.45	0.16	0.75	0.15	2.98	0.005

$R^2=0.2825$ ,  $adj.R^2=0.2377$ ,  $F=6.3$ ,  $p=0.005$ ,  $AIC =382.87$

### 1.2.3.5 Rt. total hippocampus, aMCI group

Result of Stepwise Backward Regression

Analysis of Variance Table

Model 1: right total hippocampus ~ education + CR

Model 2: right total hippocampus ~ age + gender + education + APOE genotype + CR

	Res.Df	RSS	Df	Sum of Sq	F	Pr(>F)
1	32	8509529				
2	29	7828342	3	681186.97	0.84	0.4825

Finally Selected Model

Result of Multiple Regression Analysis

	Beta	lwr	upr	SE	std. Beta	lwr	upr	SE	t value	p
(Intercept)	3295.09	2828.32	3761.86	229.16					14.38	< 0.001
education	-41.72	-82.73	-0.72	20.13	-0.33	-0.64	-0.02	0.16	-2.07	0.046
CR	93.67	20.24	167.10	36.05	0.41	0.1	0.72	0.16	2.60	0.014

$R^2=0.2252$ ,  $adj.R^2=0.1767$ ,  $F=4.65$ ,  $p=0.017$ ,  $AIC =541.37$

## 2. Mediation Analyses

### 2.1 The proposed mediator: Left GC-DG

Indirect effect of education on CERAD-K CR score

	Effect	Boot SE	BootLLCI	BootULCI
Left GC-DG	.0047	.0369	-.0547	.1008

Boot, bootstrapping; SE, standard error; LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval.

Normal Theory tests for indirect effect

	Effect	SE	Z	p
Left GC-DG	.0047	.0358	.1320	.8950

SE, standard error.

## 2.2 The proposed mediator: Right CA4

Indirect effect of education on CERAD-K CR score

	<b>Effect</b>	<b>Boot SE</b>	<b>BootLLCI</b>	<b>BootULCI</b>
Right CA4	.0154	.0298	-.0337	.0880

Boot, bootstrapping; SE, standard error; LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval.

Normal Theory tests for indirect effect

	<b>Effect</b>	<b>SE</b>	<b>Z</b>	<b>p</b>
Right CA4	.0154	.0311	.4956	.6202

SE, standard error.

## 2.3 The proposed mediator: Right GC-DG

Indirect effect of education on CERAD-K CR score

	<b>Effect</b>	<b>Boot SE</b>	<b>BootLLCI</b>	<b>BootULCI</b>
Right GC-DG	.0116	.0313	-.0414	.0895

Boot, bootstrapping; SE, standard error; LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval.

Normal Theory tests for indirect effect

	<b>Effect</b>	<b>SE</b>	<b>Z</b>	<b>p</b>
Right GC-DG	.0116	.0308	.3761	.7069

SE, standard error.



#### **2.4 The proposed mediator: Right presubiculum**

Indirect effect of education on CERAD-K CR score

	<b>Effect</b>	<b>Boot SE</b>	<b>BootLLCI</b>	<b>BootULCI</b>
Right presubiculum	-.0086	.0309	-.0915	.0433

Boot, bootstrapping; SE, standard error; LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval.

Normal Theory tests for indirect effect

	<b>Effect</b>	<b>SE</b>	<b>Z</b>	<b>p</b>
Right presubiculum	-.00086	.0308	-.2807	.7790

SE, standard error.

#### **2.4 The proposed mediator: Right total hippocampus**

Indirect effect of education on CERAD-K CR score

	<b>Effect</b>	<b>Boot SE</b>	<b>BootLLCI</b>	<b>BootULCI</b>
Right total hippocampus	-.0045	.0261	-.0351	.0732

Boot, bootstrapping; SE, standard error; LLCI, lower limit of confidence interval; ULCI, upper limit of confidence interval.

Normal Theory tests for indirect effect

	<b>Effect</b>	<b>SE</b>	<b>Z</b>	<b>p</b>
Right total hippocampus	.0045	.0273	.1643	.8695

SE, standard error.

## Supplemental Tables

**Table S1. Non-amnestic cognitive functions of the study participants**

	<b>Control Group (n=39)</b>	<b>aMCI group (n=38)</b>	<b>P value</b>
<b>CERAD-K VF</b>	14.3 ± 3.7 (8-24)	12.5 ± 3.4 (7-21)	<b>0.033*</b>
<b>CERAD-K BNT</b>	11.8 ± 2.7 (5-15)	10.8 ± 2.4 (5-15)	0.093
<b>CERAD-K CP</b>	9.9 ± 1.5 (6-11)	9.7 ± 1.6 (5-11)	0.461

CERAD-K, the Korean version of Consortium to Establish a Registry for Alzheimer's Disease; VF, Verbal Fluency; BNT, 15-item Boston Naming Test; CP, Constructional Praxis. \* $p < 0.05$

**Table S2. Clinical Characteristics of amnestic mild cognitive impairment subjects**

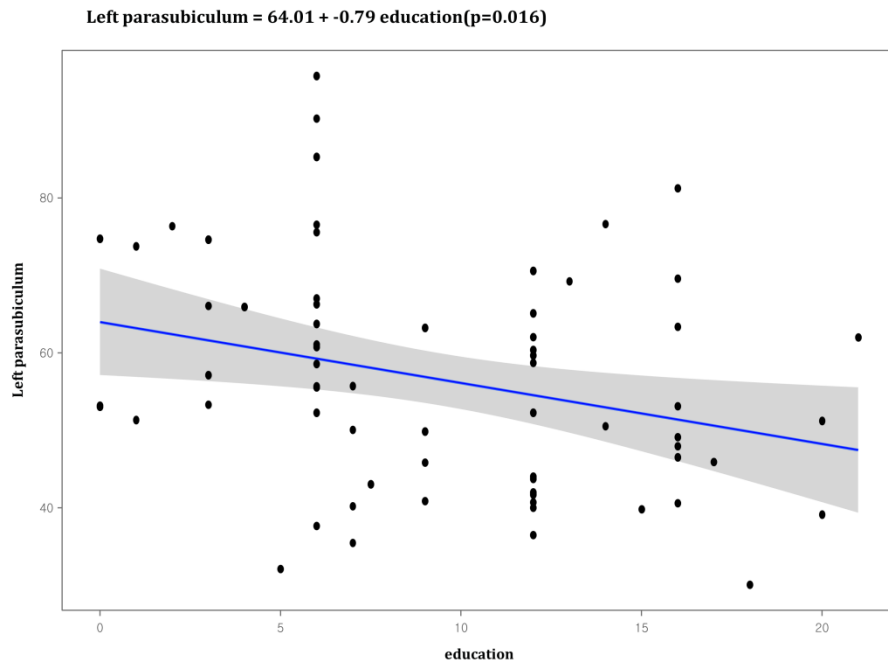
	<b>aMCI group (n=38)</b>
<b>Early/late aMCI (n, %)</b>	21 : 17 (55.3 : 44.7)
<b>aMCI, Single/Multiple domain (n, %)</b>	4 : 34 (10.5 : 89.5)
<b>CERAD-K WLM Impairment (n, %)</b>	23 (60.5)
<b>CERAD-K WLR Impairment (n, %)</b>	34 (89.5)
<b>CERAD-K WLRc Impairment (n, %)</b>	24 (63.2)
<b>CERAD-K CR Impairment (n, %)</b>	22 (57.9)

CERAD-K, the Korean version of Consortium to Establish a Registry for Alzheimer's Disease; WLM, Word List Memory; WLR, Word List Recall; WLRc, Word List Recognition; CR, Constructional Recall.

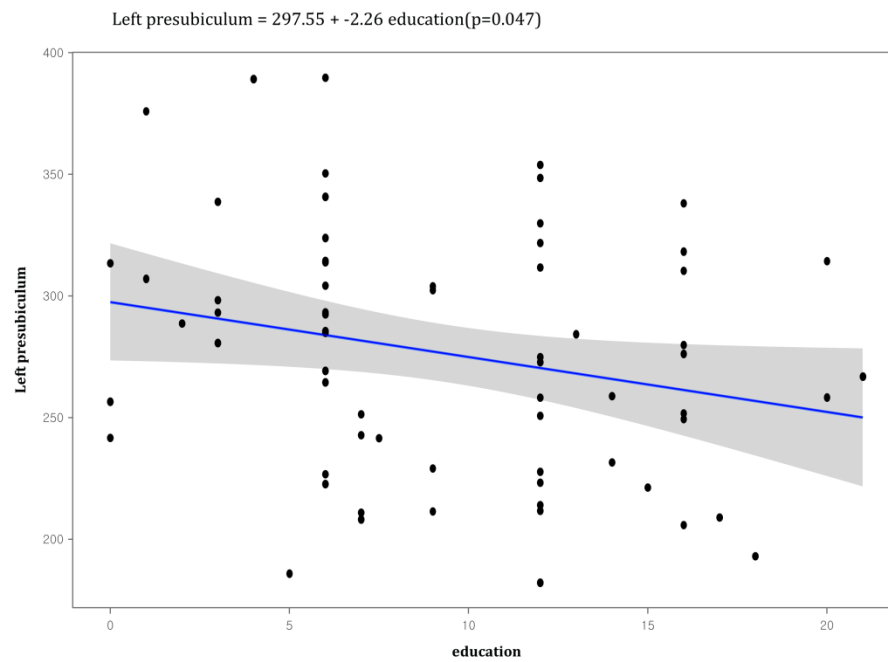
## Supplemental Figures

**Figure S1. Relationship between hippocampal subfield volumes and education (plots of simple regression)**

**(A) Relationship between education and Lt. parasubiculum in both groups**

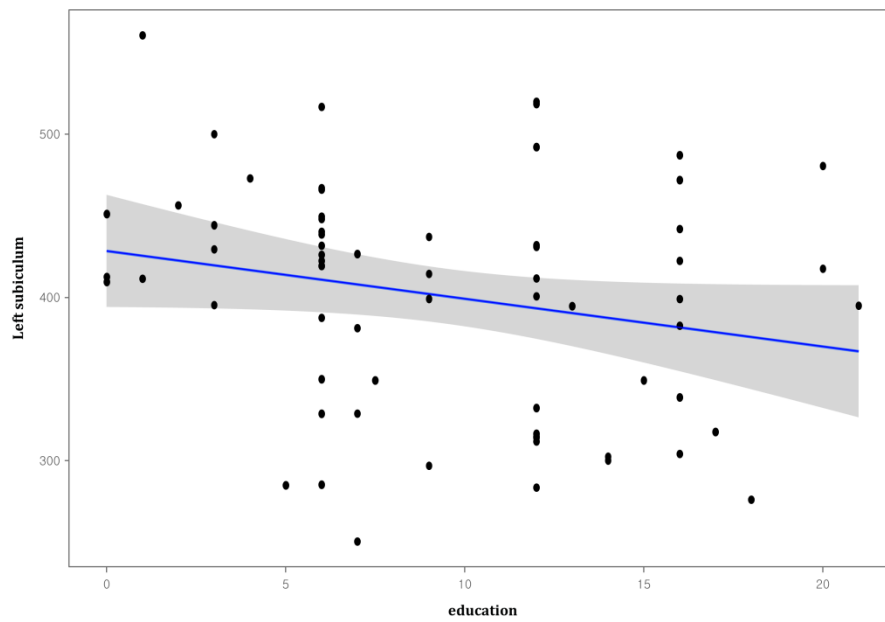


**(B) Relationship between education and Lt. presubiculum in both groups**



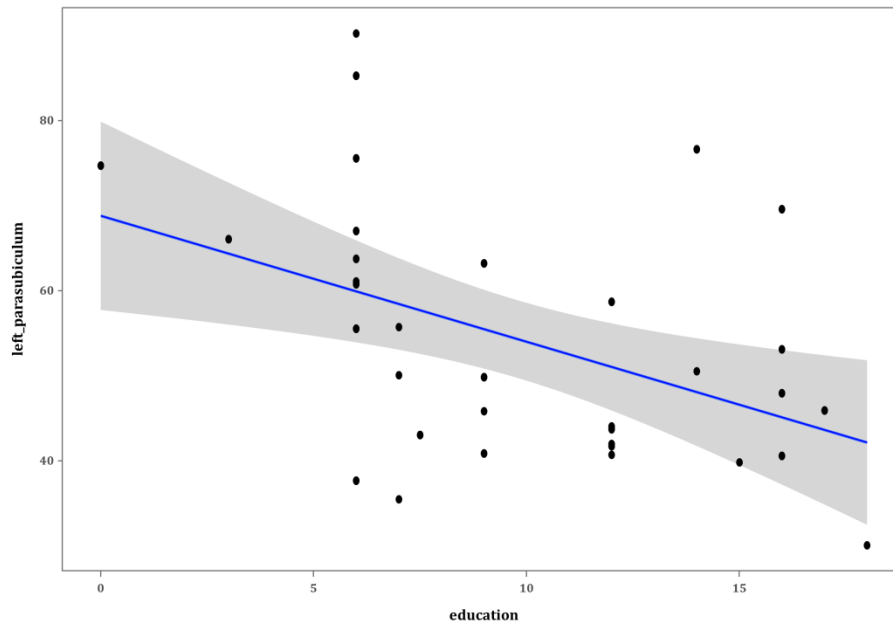
### (C) Relationship between education and Lt. subiculum in both groups

$$\text{Left subiculum} = 428.52 + -2.93 \text{ education} (p=0.07)$$

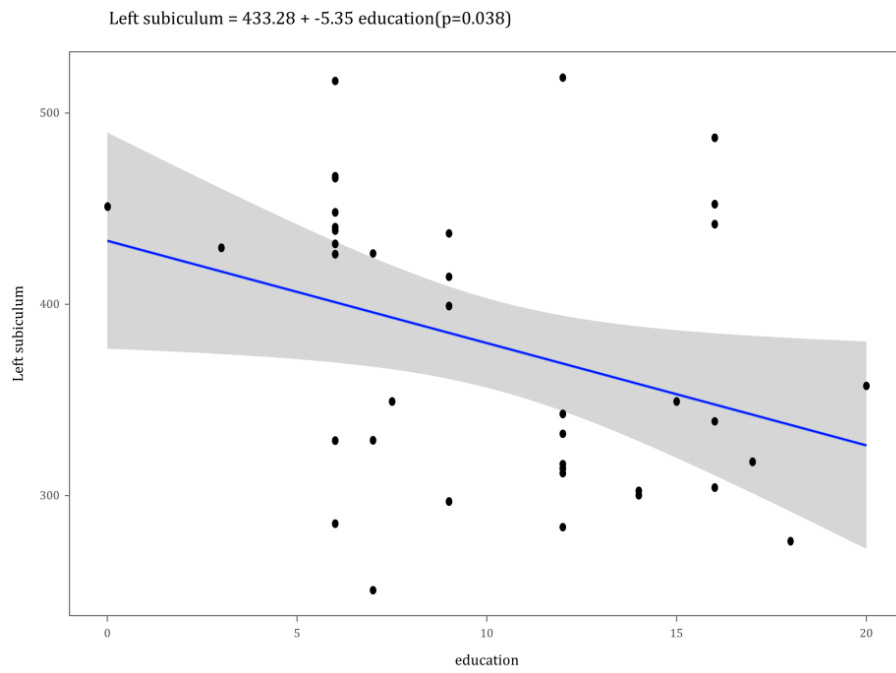


### (D) Relationship between education and Lt. parasubiculum in aMCI group

$$\text{left\_parasubiculum} = 68.81 + -1.48 \text{ education} (p=0.006)$$



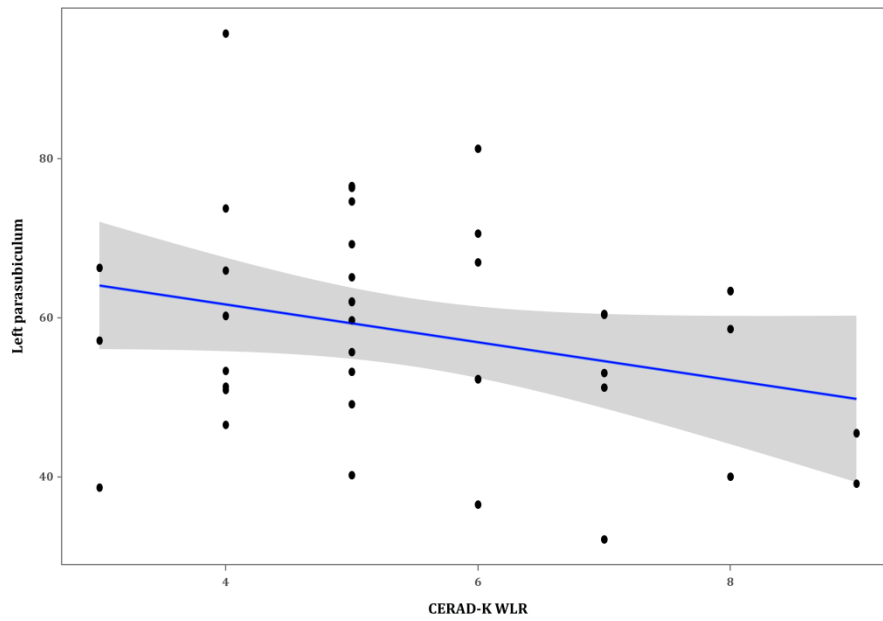
**(E) Relationship between education and Lt. subiculum in aMCI group**



**Figure S2. Relationships between cognitive functions and hippocampal subfield volumes (plots of simple regression)**

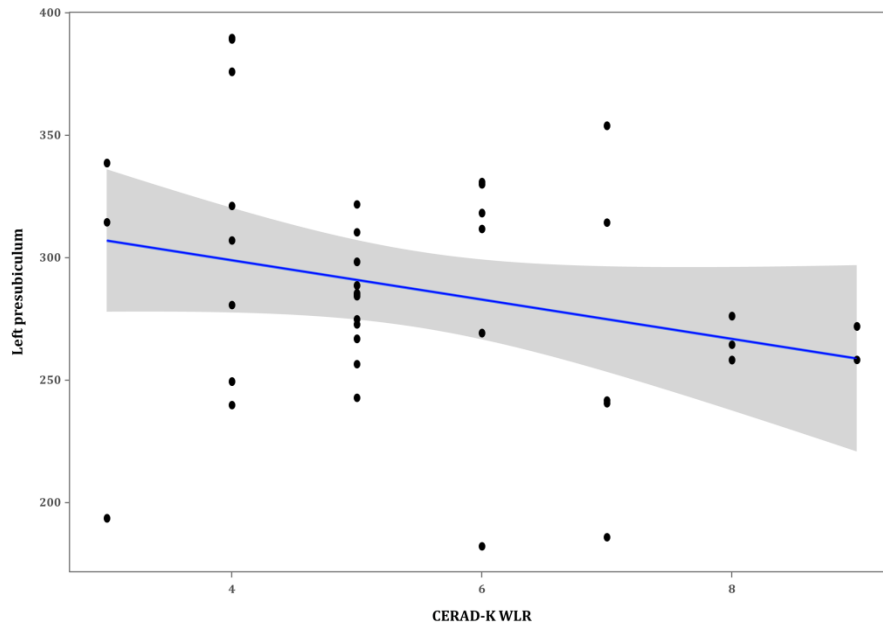
**(A) Relationship between CERAD-K WLR and Lt. parasubiculum in control group**

Left parasubiculum =  $71.2 + -2.38 \text{ CERAD-K WLR}$  ( $p=0.085$ )



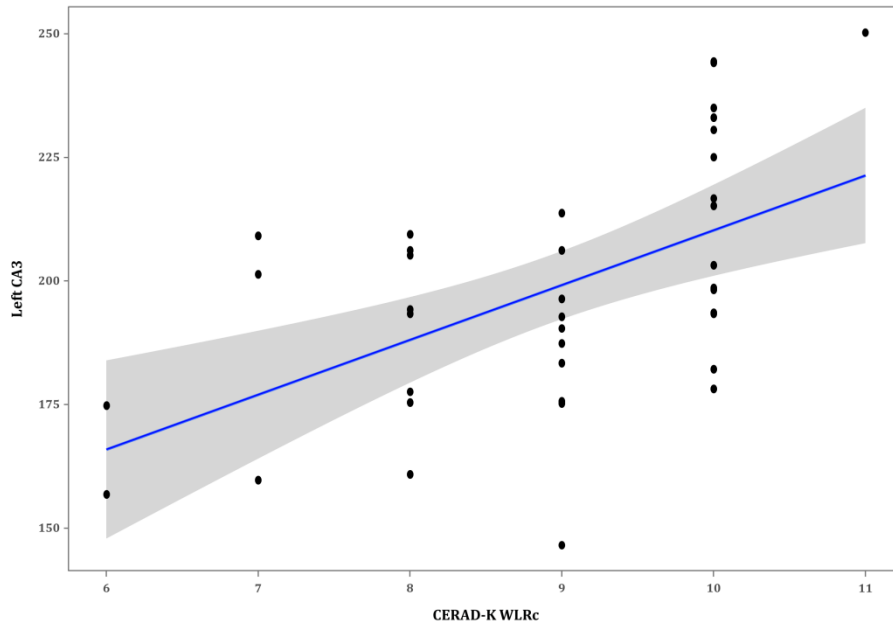
**(B) Relationship between CERAD-K WLR and Lt. presubiculum in control group**

Left presubiculum =  $331.13 + -8.02 \text{ CERAD-K WLR}$  ( $p=0.109$ )



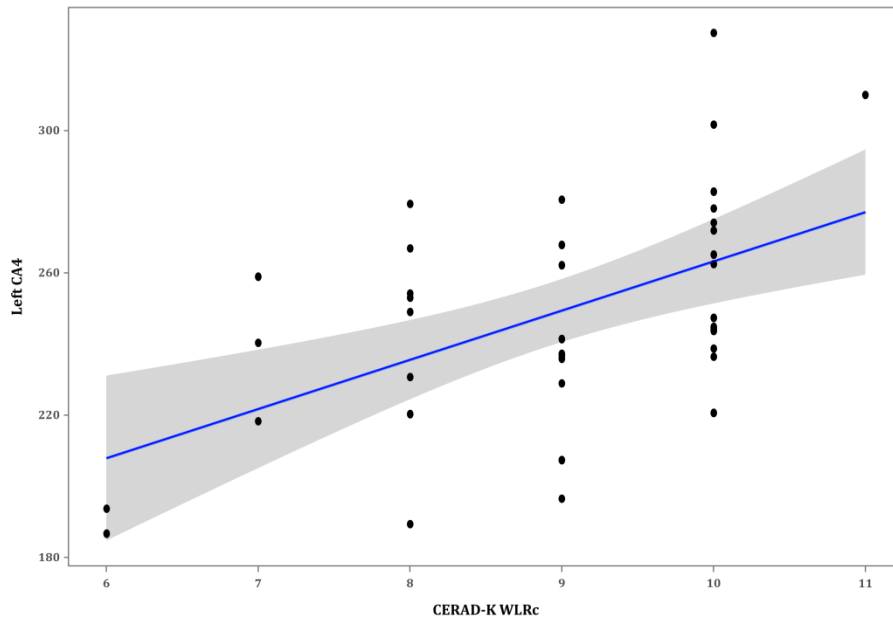
**(C) Relationship between CERAD-K WLRc and Lt. CA3 in control group**

$\text{left\_CA3} = 99.41 + 11.08 \text{ CERAD-K WLRc}$  ( $p < 0.001$ )



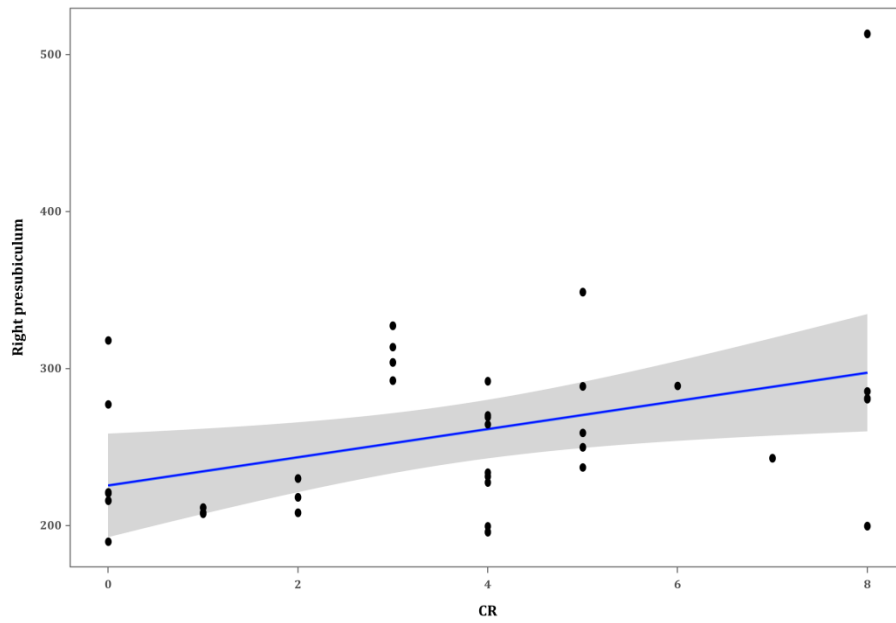
**(D) Relationship between CERAD-K WLRc and Lt. CA4 in control group**

$\text{Left CA4} = 124.95 + 13.83 \text{ CERAD-K WLRc}$  ( $p < 0.001$ )



**(E) Relationship between CERAD-K CR and Rt. presubiculum in aMCI group**

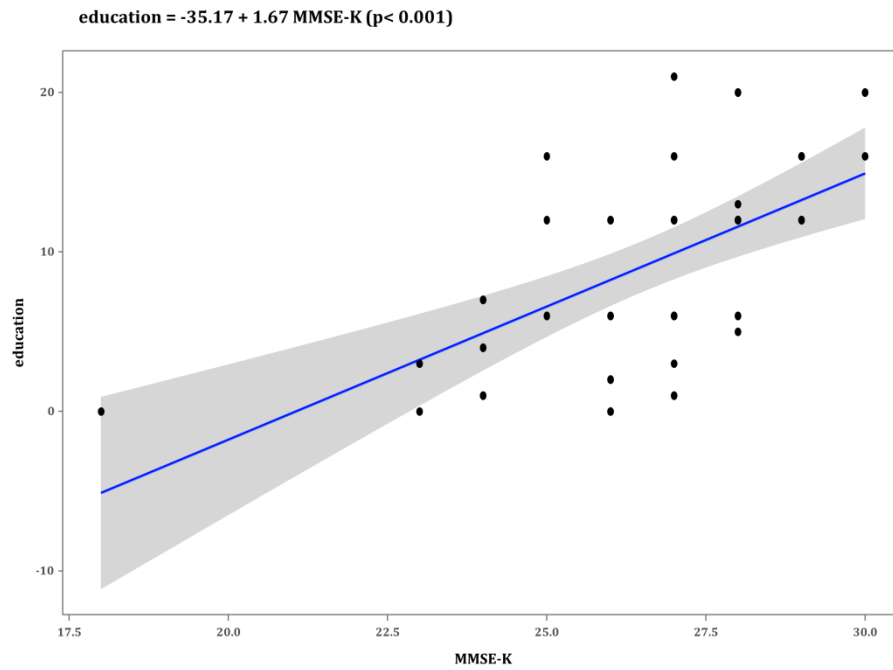
Right presubiculum = 225.63 + 8.97 CR(p=0.02)



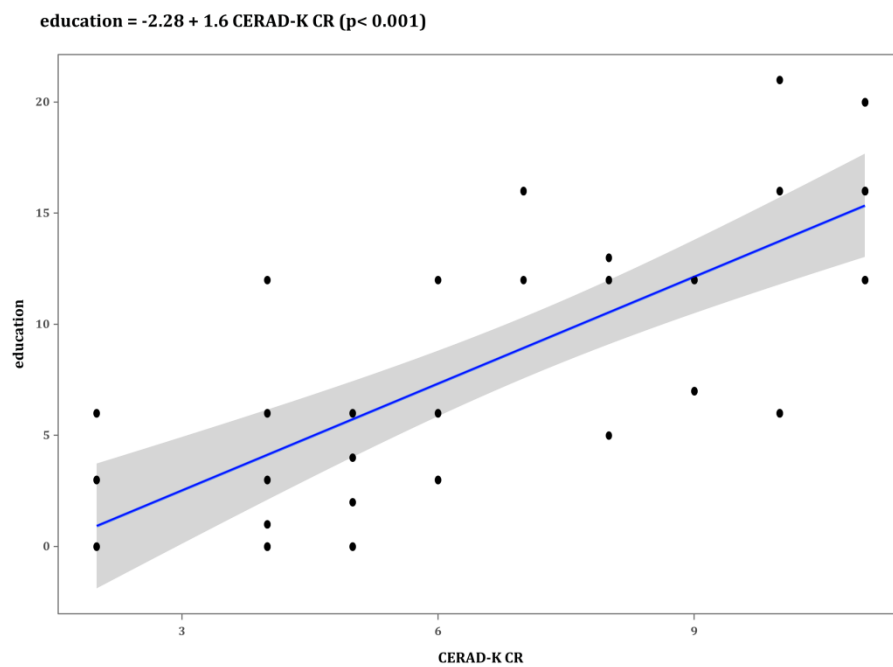


**Figure S3. Relationships between cognitive functions and education (plots of simple regression)**

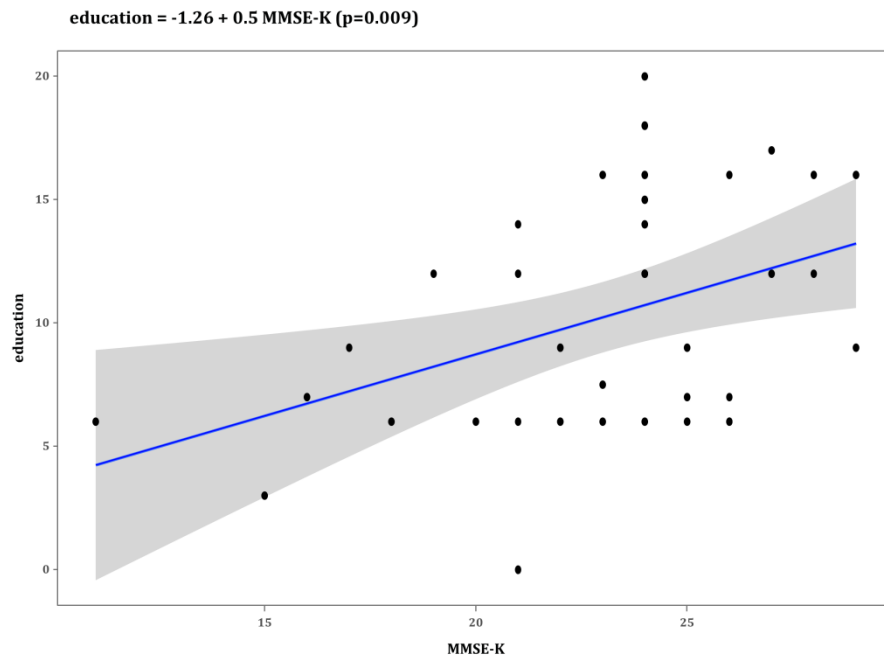
**(A) Relationship between education and MMSE-K in control group**



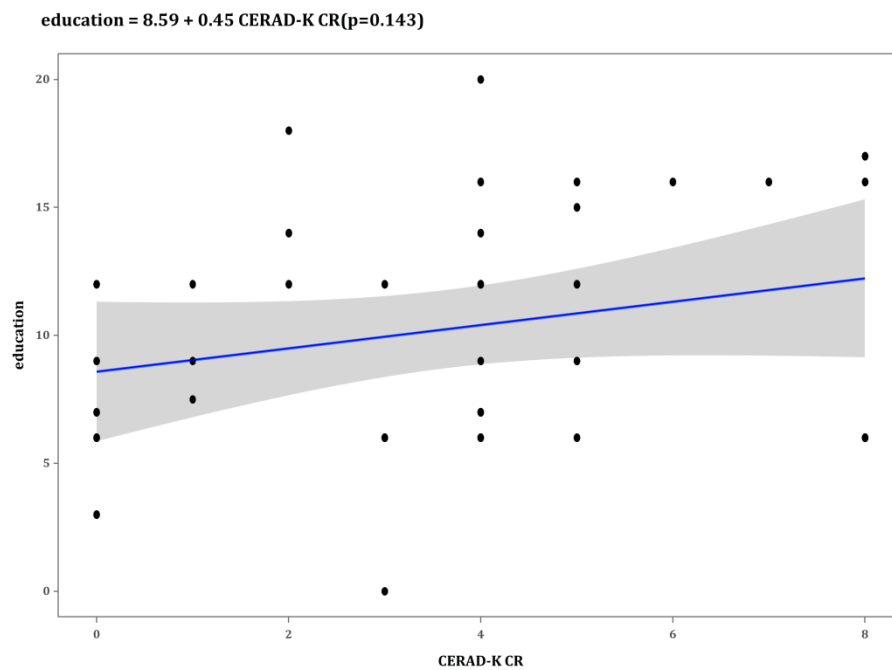
**(B) Relationship between education and CERAD-K CR in control group**



**(C) Relationship between education and MMSE-K in aMCI group**



**(D) Relationship between education and CERAD-K CR in aMCI group**



CERAD-K, the Korean version of Consortium to Establish a Registry for Alzheimer's Disease; MMSE-K, The Korean version of mini mental status examination; WLR, Word List Recall; WLRc, Word List Recognition; CR, Constructional Recall