Differential Effects of Body Mass Index on Domain-Specific Cognitive Outcomes After Stroke

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Abstract

Background

We aimed to investigate the association between body mass index (BMI) and domain-specific cognitive functions in post-ischemic stroke survivors.

Methods

A total of 335 ischemic stroke patients were included in the study after completion of the Korean-Mini-Mental Status Examination (K-MMSE) and the K-VCIHS neuropsychological protocol at 3 months after stroke. Frontal lobe functions were analyzed using semantic/phonic fluency, processing speed, and mental set shifting. Our study participants were categorized into four groups according to BMI quartiles

Results

The K-MMSE scores at 3 months differed significantly between the groups after adjustment for covariates with univariate p-value less than 0.1 (p = 0.003). Global cognitive function in stroke survivors in the Q1 BMI group was significantly lower than those in Q2 and Q4 BMI groups (K-MMSE scores, Q1: 22.9 ± 6.7 vs. Q2: 25.2 ± 5.2 and Q4: 25.1 ± 4.3). Controlled oral word association test findings indicated that phonemic and semantic word fluency was lower in Q4 BMI group participants than in Q2 BMI group participants (p = 0.012, and p=0.012 respectively).

Conclusions

BMI might differentially affect cognitive domains after ischemic stroke. Although being underweight may negatively affect global cognition post-stroke, obesity could induce frontal lobe dysfunctions, specifically phonemic and semantic word fluency.

Introduction

Obesity is a growing public health concern and a well-recognized risk factor for cerebrovascular disorders and overall mortality[1]. However, an increasing body of evidence suggests that obesity is associated with favorable functional outcomes, lower mortality, and lower risk of stroke progression after stroke. [2–4]. Referred to as the ‘obesity paradox’, this paradoxical phenomenon has been observed in association with cerebrovascular disorders, cardiovascular diseases[5], peripheral arterial disease[6], diabetes mellitus[7], malignancy[8], and dementia[9,10].

This paradox has also been reported in the correlation between body mass index (BMI) and cognitive function in the general population. A higher BMI in middle-to-late life predicts a lower risk of developing dementia[10], whereas being underweight (BMI, < 20kg/m^2) is associated with an increased risk of dementia[9]. However, these reports did not explore the independent association between BMI and post-stroke cognition. One Swedish study reported that BMI did not influence cognitive impairment at 20

months after stroke in a sample of 149 stroke survivors[11]. However, that study used only the Mini-Mental Status Examination (MMSE) to assess cognition, which cannot be considered appropriate given the higher incidence of frontal dysfunction among stroke survivors[12]. To date, few studies have used detailed neuropsychological evaluations to determine how obesity affects post-stroke cognitive impairment. Considering that a lesion's localization and pathogenesis can be estimated through the pattern of domain-specific cognitive impairment, it would likely be of clinical significance to determine whether obesity affects particular domains of cognitive function after stroke.

In this context, we aimed to investigate the differential effects of BMI on domain-specific and global cognitive function at 3 months post-ischemic stroke using the Korean Vascular Cognitive Impairment Harmonization Standards-Neuropsychological Protocol(K-VCIHS-NP), a comprehensive neuropsychological test developed for post-stroke survivors. We hypothesized that BMI might have distinct roles in each neural substrate associated with each cognitive domain, as previous studies have shown that high BMI is associated with executive dysfunction and frontal lobe atrophy in a generally healthy population [13–15].

Methods

Study participants

Participants were enrolled from the Korean Vascular Cognitive Impairment Harmonization Standards (K-VCIHS) study, which has been previously described in detail[16]. The K-VCIHS cohort enrolled patients with ischemic stroke who had been consecutively admitted to 12 university hospitals from October 2007 to August 2008. Inclusion criteria for our study comprised the following: (i) a diagnosis of acute ischemic stroke with neurological deficits persisting for ≥ 24 hours, (ii) a relevant ischemic lesion observed on magnetic resonance imaging, (iii) admission within 7 days after symptom onset, and (iv) available data on admission concerning BMI and the results of K-VCIHS-NP performed at 3 months post-ischemic stroke. In total, 335 participants from the K-VCIHS cohort who fulfilled the inclusion criteria were finally analyzed. We collected clinical variables and the results of K-VCIHS-NP with the consent of the principal investigator of the K-VCIHS-NP study group and the Institutional Review Board of Hallym University Sacred Heart Hospital. BMI was calculated as a participant's weight (kg) divided by their height (m) squared, measured at the first day of admission according to the institutional protocol with an automatic weight and height machine. Body weight and height were measured to the nearest 0.1kg and 0.1cm respectively using BSM-330(InBody, South Korea). Those who were not able to stand were weighed using an electronic bed scale, SCB330-7(SOHWA Inc, South Korea), in the supine position. The participants were then stratified into BMI quartiles[17], namely, Q1, < 21.87kg/m^2; Q2, 21.88–23.87 kg/m^2; Q3, 23.88–25.96 kg/m^2, and; Q4, > 25.97 kg/m^2. From the cohort registry data, we collected clinical data concerning age, sex, and stroke subtype according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification[18]. Moreover, initial stroke severity represented as the National Institute of Health Stroke Scale and vascular risk factors were also collected. Hallym University Sacred Heart Hospital Institutional

Review Board approved the study and waived the requirement for patient consent because of the retrospective nature of this study as well as the minimal risk that it posed to participants. The study protocols conformed to the guidelines of the Declaration of Helsinki.

Cognitive function assessment

Participants completed the Korean Mini-Mental Status Examination (K-MMSE) and a 60-minute neuropsychological test as described in the K-VCIHS study protocol[19]. The K-VCIHS assesses four cognitive domains: (i) executive/activation function, using the Korean version of the controlled oral word association test (COWAT) for phonemic and semantic fluency, digit symbol coding, and trail making tests A and B; (ii) language, using the Korean-Boston naming test; (iii) visuospatial, using the Rey complex figure test (copy), and; (iv) memory, using delayed recall scores from the Seoul verbal learning test. The K-VCIHS study protocol also included the Informant Questionnaire of Cognitive Decline in the Elderly (IQCODE) for the premorbid history of cognitive dysfunctions. The specific tests and scales which comprises the K-VCIHS protocol and relevant references are described in Supplemental Table I. We obtained standardized Z-scores for each domain and for the K-MMSE after adjustment for age, sex, and educational level to directly compare groups according to BMI quartiles.

Brain imaging

All participants underwent brain magnetic resonance imaging (MRI), performed using a 3T whole-body MRI system. Diffusion-weighted imaging was used to obtain the apparent diffusion coefficient and assess acute cerebral infarction. The location and number of acute ischemic stroke lesions were rated and quantified. We subdivided the stroke lesions as follows: (i) cortical vs. subcortical-only, (ii) left-sided vs. right-sided, and; (iii) single vs. multiple[2].

Statistical analysis

In order to detect an effect $\eta^2p=0.04$ with 80% power in a between-subjects ANCOVA(four groups, numerator df = 3, alpha = 0.05), a priori power calculation of G*Power 3.1.9.4 [20] suggested that we would need 67 subjects in each group(n = 266). Pearson's chi-square test and an analysis of variance (ANOVA) were used, as appropriate, to compare demographic characteristics between the groups according to BMI quartiles. For the univariate analysis, an ANOVA was used to compare the Z-scores of each cognitive domain between the groups. The Levene's test and Kolmogorov-Smirnov tests were performed to check for equality of variances and normality of dependent variables, respectively. An analysis of covariance (ANCOVA) was performed adjusting for the covariates which had a p-value less than 0.10 in the univariate analysis. Age, sex, and education levels were considered in the z-score transformation process and were not included as covariates. The effect size of BMI quartiles on dependent variables in the ANCOVA were presented with partial eta squared (η^2p). Two-sided p-values < 0.05 were considered to indicate statistical significance. All analyses were performed using IBM SPSS, version 26.

Results

The mean age of the participants was 64.8 ± 12.4 years, and women comprised 38.9% of the study population. The median "BMI was 23.89 ± 3.10 kg/m^2 (range, 15.82–32.93 kg/m^2). The BMI quartile groups did not differ in terms of age, sex, years of education, previous stroke history, or pre-stroke cognitive decline. There were no significant differences in initial stroke severity, stroke etiology according to the TOAST classification, or the number and location of ischemic lesions. However, the prevalence of hypertension was higher in the Q4 BMI group (the highest) than in the Q1 BMI group (the lowest). The prevalence of other vascular risk factors did not differ significantly between the groups (Table 1).

The Z-scores of the K-MMSE differed significantly between the quartile groups at 3 months post-ischemic stroke onset after adjustment for hypertension and hyperlipidemia, showing a p-value < 0.1 in univariate analysis ($p = 0.003$, $\eta^2p=0.042$, ANCOVA). A multiple comparison analysis indicated that stroke survivors in the Q1 BMI group showed significantly lower global cognitive functions (K-MMSE Z-score, -2.1 ± 3.4) than those in the Q2 and Q4 BMI groups (K-MMSE Z-score, Q2: -0.71 ± 1.95; Q4: -1.21 ± 1.65). The Z-scores of the COWAT also significantly differed between the quartile groups. A multiple comparison analysis of the COWAT results indicated that participants in the Q4 BMI group had significantly lower phonemic and semantic word fluencies than their counterparts in the Q2 BMI group, despite similar levels of global cognitive function after adjustment for a history of hypertension and hyperlipidemia ($p = 0.012$, $\eta^2p=0.035$ and $p = 0.012$, $\eta^2p=0.034$ respectively; ANCOVA). Other neuropsychological test findings relating to frontal lobe functions, including processing speed and mental set-shifting, and other cognitive domains, did not differ significantly between the groups (Table 2).

Discussion

In this study, we assessed the association between obesity phenotypes defined using BMI quartiles at admission and cognitive function at 3 months post-ischemic stroke onset. To our knowledge, this study is the first to evaluate BMI and domain-specific cognitive outcomes using a comprehensive, standardized, neuropsychological protocol in relation to a multicenter cohort of stroke patients[16]. Our data analysis indicated that a lower BMI at admission was associated with a higher risk of global cognitive deterioration, while a higher BMI was associated with significantly worse frontal dysfunction post-ischemic stroke. These findings suggest that BMI has differential effects on various cognitive domains following an ischemic stroke.

Previous epidemiologic studies concerning the relationship between BMI and cognitive impairment have yielded controversial findings. The relationship between obesity and long-term cognitive outcomes has alternately been identified as direct, inverse, U-shaped, or even absent[21,22]. However, as previous studies only performed the MMSE to assess cognition, they might have overlooked the influence of BMI on frontal/executive function, given that the MMSE is not sensitive to evaluating frontal lobe function[23]. Our results are in line with previous studies showing that a low BMI was significantly associated with a high risk of cognitive decline[9].

Despite uncertainly concerning the precise mechanism underlying post-stroke worsening of cognitive function, decreased body weight has been identified as an early indication of declining health and even neurodegeneration[24]. Moreover, several studies have proposed that leptin, an adipokine produced by adipose tissue, exerts neuroprotective effects through anti-oxidative activity and its promotion of hippocampal progenitor cell proliferation. As underweight patients may have decreased levels of leptin, a lower BMI may result in less neuroprotection after neurological insult[25].

Our results also showed that a higher BMI was significantly associated with worse frontal/executive function, specifically in phonemic and semantic fluencies. This finding is in agreement with those of previous studies that have linked obesity to temporal atrophy[13]. Moreover, one study that used high-resolution 3D MRI scans reported that obese individuals had a significantly lower density of gray matter in the frontal lobe, post-central gyrus, and middle frontal gyrus than control group participants[14]. Obesity has also been reportedly related to executive dysfunction with other cognitive functions preserved, even in neurologically healthy adults without cognitive impairment[15]. Specifically, obese adults perform worse on executive function tests, especially those testing verbal interference, than their counterparts with a lower BMI. These findings may indicate vulnerability of the frontotemporal lobe in obese patients to acute stroke, regardless of lesion location.

Our study had some limitations. First, only participants' height and weight measurements were used to determine the BMI. Other adiposity data, such as abdominal circumference or waist-hip ratio, were unavailable; therefore, we could not address possible differences between leanness and being underweight and their relationships with long-term cognitive outcomes[26]. Future studies should consider replicating the approach of studies that have investigated the relationship between obesity and Alzheimer's disease through using the waist-to-hip ratio and waist circumference at multiple sites as a measure of central obesity. Second, we were unable to determine any causal relationships between BMI and cognition because this study spanned a relatively short observational period. Third, restrictions were inevitable concerning the number of participants studied and some of the explanatory variables because this study was the result of a secondary analysis of a multicenter study that aimed to investigate the prevalence of cognitive disorders post-stroke. Consequently, we did not include several image variables such as cerebral atrophy or white matter hyperintensities, which may have affected cognitive function post-stroke. Furthermore, we did not assess temporal changes in BMI from stroke onset. Nonetheless, the main strength of our study is that it is by far the first study to investigate the effects of BMI on each cognitive domain after stroke. These findings may provide additional evidence for pathophysiological aspects of BMI on each neural substrate after ischemic stroke.

Conclusions

Our research suggests that BMI may interact variably with cognitive domains post-ischemic stroke. Although being underweight might negatively affect global cognition post-stroke, obesity might also induce frontal lobe dysfunctions, specifically in terms of phonemic and semantic word fluency. Though

exact pathomechanisms being unclear, these findings may be attributed to the distinct roles of BMI on neural substrates, specifically the frontal lobe area. A large prospective cohort study with a focus on neural substrates evaluated with brain imaging is necessary to elucidate further relationships between BMI and post-stroke cognitive outcomes and to validate our findings.

Declarations

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Author contributions statements

ML, JSL and KHY made substantial contributions to the conception and design of the work; MSO, SJ, JHL, CHK, MUJ, YEK, HJB,BC made contributions to the acquisition, analysis and interpretation of data; JP and YK contributed to the interpretation of data. ML, JSL, and KHY have drafted and revised the manuscript.

Competing interests

The author(s) declare no competing interests.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Kernan, W. N., Inzucchi, S. E., Sawan, C., Macko, R. F. & Furie, K. L. Obesity: a stubbornly obvious target for stroke prevention. *Stroke* **44**, 278-286, doi:10.1161/STROKEAHA.111.639922 (2013).
2. Kim, B. J. *et al.* Dynamics of obesity paradox after stroke, related to time from onset, age, and causes of death. *Neurology* **79**, 856-863, doi:10.1212/WNL.0b013e318266fad1 (2012).
3. Kim, Y., Kim, C. K., Jung, S., Yoon, B. W. & Lee, S. H. Obesity-stroke paradox and initial neurological severity. *J Neurol Neurosurg Psychiatry* **86**, 743-747, doi:10.1136/jnnp-2014-308664 (2015).
4. Ryu, W. S., Lee, S. H., Kim, C. K., Kim, B. J. & Yoon, B. W. Body mass index, initial neurological severity and long-term mortality in ischemic stroke. *Cerebrovasc Dis* **32**, 170-176, doi:10.1159/000328250 (2011).

5. Elagizi, A. *et al.* An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. *Prog Cardiovasc Dis* **61**, 142-150, doi:10.1016/j.pcad.2018.07.003 (2018).
6. Ludhwani, D. & Wu, J. Obesity Paradox in Peripheral Arterial Disease: Results of a Propensity Match Analysis from the National Inpatient Sample. *Cureus* **11**, e4704, doi:10.7759/cureus.4704 (2019).
7. Han, S. J. & Boyko, E. J. The Evidence for an Obesity Paradox in Type 2 Diabetes Mellitus. *Diabetes Metab J* **42**, 179-187, doi:10.4093/dmj.2018.0055 (2018).
8. Lee, D. H. & Giovannucci, E. L. The Obesity Paradox in Cancer: Epidemiologic Insights and Perspectives. *Curr Nutr Rep* **8**, 175-181, doi:10.1007/s13668-019-00280-6 (2019).
9. Fitzpatrick, A. L. *et al.* Midlife and late-life obesity and the risk of dementia: cardiovascular health study. *Archives of neurology* **66**, 336-342, doi:10.1001/archneurol.2008.582 (2009).
10. Suemoto, C. K., Gilsanz, P., Mayeda, E. R. & Glymour, M. M. Body mass index and cognitive function: the potential for reverse causation. *International journal of obesity* **39**, 1383-1389, doi:10.1038/ijo.2015.83 (2015).
11. Pascoe, M., Ski, C. F., Thompson, D. R. & Linden, T. Serum cholesterol, body mass index and smoking status do not predict long-term cognitive impairment in elderly stroke patients. *Journal of the neurological sciences* **406**, 116476, doi:10.1016/j.jns.2019.116476 (2019).
12. Stephens, S. *et al.* Neuropsychological characteristics of mild vascular cognitive impairment and dementia after stroke. *International journal of geriatric psychiatry* **19**, 1053-1057, doi:10.1002/gps.1209 (2004).
13. Gustafson, D., Lissner, L., Bengtsson, C., Bjorkelund, C. & Skoog, I. A 24-year follow-up of body mass index and cerebral atrophy. *Neurology* **63**, 1876-1881, doi:10.1212/01.wnl.0000141850.47773.5f (2004).
14. Pannacciulli, N. *et al.* Brain abnormalities in human obesity: a voxel-based morphometric study. *Neuroimage* **31**, 1419-1425, doi:10.1016/j.neuroimage.2006.01.047 (2006).
15. Gunstad, J. *et al.* Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Compr Psychiatry* **48**, 57-61, doi:10.1016/j.comppsych.2006.05.001 (2007).
16. Yu, K. H. *et al.* Cognitive impairment evaluated with Vascular Cognitive Impairment Harmonization Standards in a multicenter prospective stroke cohort in Korea. *Stroke* **44**, 786-788, doi:10.1161/STROKEAHA.112.668343 (2013).
17. Tanne, D., Medalie, J. H. & Goldbourt, U. Body fat distribution and long-term risk of stroke mortality. *Stroke* **36**, 1021-1025, doi:10.1161/01.STR.0000162584.39366.1c (2005).
18. Adams, H. P., Jr. *et al.* Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* **24**, 35-41, doi:10.1161/01.str.24.1.35 (1993).
19. Hachinski, V. *et al.* National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards. *Stroke* **37**, 2220-2241, doi:10.1161/01.STR.0000237236.88823.47 (2006).

20. Faul, F., Erdfelder, E., Lang, A. G. & Buchner, A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* **39**, 175-191, doi:10.3758/bf03193146 (2007).
21. Beydoun, M. A., Beydoun, H. A. & Wang, Y. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. *Obes Rev* **9**, 204-218, doi:10.1111/j.1467-789X.2008.00473.x (2008).
22. Singh-Manoux, A. *et al.* Obesity phenotypes in midlife and cognition in early old age: the Whitehall II cohort study. *Neurology* **79**, 755-762, doi:10.1212/WNL.0b013e3182661f63 (2012).
23. Fu, C. *et al.* Comparison of the Mini-Mental State Examination and Montreal Cognitive Assessment executive subtests in detecting post-stroke cognitive impairment. *Geriatr Gerontol Int* **17**, 2329-2335, doi:10.1111/ggi.13069 (2017).
24. Lee, E. B. Obesity, leptin, and Alzheimer's disease. *Ann N Y Acad Sci* **1243**, 15-29, doi:10.1111/j.1749-6632.2011.06274.x (2011).
25. Tang, B. L. Leptin as a neuroprotective agent. *Biochemical and biophysical research communications* **368**, 181-185, doi:10.1016/j.bbrc.2008.01.063 (2008).
26. Sakakura, K. *et al.* Association of body mass index with cognitive function in elderly hypertensive Japanese. *Am J Hypertens* **21**, 627-632, doi:10.1038/ajh.2008.157 (2008).

Tables

Table 1
Clinical Characteristics according to the quartiles of body mass index

	Q 1 (< 21.87, n = 84)	Q 2 (21.88–23.87, n = 84)	Q 3 (23.88–25.96, n = 84)	Q 4 (> 25.97, n = 83)	P values
Age, mean ± SD	66.2 ± 14.6	65.8 ± 12.8	63.8 ± 11.1	63.3 ± 10.9	0.329
Women, %(N)	46.4(39)	42.9 (36)	27.4 (23)	39.8 (33)	0.064
Vascular Risk Factors					
Hypertension, %(N)	54.8 (46)	63.1 (53)	58.3 (49)	74.7 (62)	0.045
Diabetes, %(N)	31.0 (26)	23.8 (20)	33.3 (28)	39.8 (33)	0.172
Dyslipidemia, %(N)	31.0 (26)	23.8 (20)	33.3 (28)	39.8 (33)	0.085
History of Stroke, %(N)	23.8 (20)	14.3 (12)	20.2 (17)	27.4 (23)	0.194
Smoking, %(N)	44.0 (37)	42.9 (36)	50.0 (42)	43.4 (36)	0.772
Atrial fibrillation, %(N)	13.1 (11)	16.7 (14)	16.7 (14)	14.5 (12)	0.896
Education					0.148
Illiterate, %(N)	9.5 (8)	6.0 (5)	1.2 (1)	6.0 (5)	
0–6 years, %(N)	31.0(26)	48.8(41)	38.1(32)	28.9(24)	
7–12 years, %(N)	39.2 (33)	31.0(26)	38.1(32)	47.0(39)	
13 years and more, %(N)	20.2 (17)	14.3 (12)	22.6 (19)	18.1 (15)	
Prestroke Cognitive Impairment[a], %(N)	8.3 (7)	3.6 (3)	7.1 (6)	8.4 (7)	0.565
NIHSS score, median [IQR]	2.5[1.0;5.5]	3.0[2.0;5.0]	3.0[1.5;6.0]	3.0[1.0;5.0]	0.942
Ischemic stroke subtype					0.813
Large artery atherosclerosis, **%**(N)	39.3 (33)	34.5 (29)	42.9 (36)	47.0 (39)	
Small vessel occlusion, %(N)	26.2 (22)	33.3 (28)	25.0 (21)	26.5 (22)	

[a] Pre-stroke cognitive impairment was evaluated with the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)

Abbreviations: NIHSS; National Institute of Health Stroke Scales, SD; Standard deviation, IQR; Interquartile range, MRI: Magnetic Resonance Image

	Q 1 (< 21.87, n = 84)	Q 2 (21.88–23.87, n = 84)	Q 3 (23.88–25.96, n = 84)	Q 4 (> 25.97, n = 83)	P values
Cardioembolism, % (N)	14.3 (12)	15.5 (13)	19.0 (16)	12.0 (10)	
Other determined causes, %(N)	2.4 (2)	2.4 (2)	1.2 (1)	0.0 (0)	
undetermined causes, %(N)	17.9 (15)	14.3 (12)	11.9 (10)	14.5 (12)	
Brain MRI findings					
Left/Right/Both, %	52.4/40.5/7.1	40.5/53.6/6.0	41.7/51.2/7.1	53.0/42.2/4.8	0.624
Cortical/Subcortical only, %	46.4/53.6	39.3/60.7	45.2/54.8	47.0/53.0	0.734
Single/Multiple, %	51.2/48.8	58.3/41.7	53.6/46.4	49.4/50.6	0.680

[a] Pre-stroke cognitive impairment was evaluated with the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)

Abbreviations: NIHSS; National Institute of Health Stroke Scales, SD; Standard deviation, IQR; Interquartile range, MRI: Magnetic Resonance Image

Table 2
Comparison of Z scores of cognitive tests according to the quartiles of body mass index

	Q 1 (< 21.87, n = 84)	Q 2 (21.88–23.87, n = 84)	Q 3 (23.88–25.96, n = 84)	Q 4 (> 25.97, n = 83)	Unadjusted P values	Adjusted P values*
K-MMSE, Z score	-2.1 ± 3.4	-0.71 ± 1.95	-1.68 ± 3.03	-1.21 ± 1.65	0.007	0.003
raw score	22.99 ± 6.7	25.23 ± 5.21	24.89 ± 5.32	24.56 ± 5.52	0.025	0.008
COWAT semantic	-0.87 ± 1.41	-0.58 ± 1.18	-1.03 ± 1.24	-1.14 ± 1.00	0.019	0.012
COWAT phonemic	-0.88 ± 1.30	-0.47 ± 1.57	-0.96 ± 1.44	-1.18 ± 1.16	0.012	0.012
DSC	-1.06 ± 1.22	-0.70 ± 1.06	-1.05 ± 1.37	-1.11 ± 0.96	0.112	0.074
TMT-A	-1.44 ± 3.41	-1.03 ± 2.29	-1.36 ± 2.84	-0.62 ± 1.50	0.205	0.072
TMT-B	-1.13 ± 2.32	-0.89 ± 1.96	-1.06 ± 2.09	-1.09 ± 2.20	0.920	0.807
K-BNT	-0.95 ± 2.12	-0.69 ± 1.98	-1.33 ± 2.76	-0.67 ± 1.58	0.181	0.121
RCFT Copy	-1.53 ± 2.44	-0.88 ± 1.48	-1.63 ± 2.51	-1.35 ± 2.06	0.128	0.075
SVLT-E	-0.83 ± 1.11	-0.89 ± 1.14	-1.08 ± 1.29	-0.95 ± 1.19	0.557	0.546

*Adjusted for the history of hypertension and hyperlipidemia.

Abbreviations: K-MMSE, Korean Mini-Mental Status Examination; COWAT, Controlled Oral Word Association Test; DSC, Digit Symbol Coding; TMT, Trail Making Test. K-BNT, Korean version-Boston Naming Test; RCFT, Rey Complex Figure Test; SVLT-E, Seoul Verbal Learning Test-Elderly's version

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