Check for updates

Association of head circumference with cognitive decline and symptoms of depression in elderly: a 3-year prospective study

Oh Dae Kwon[1], So-Young Choi[1], Jisuk Bae[2]

Departments of [1]Neurology and [2]Preventive Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea

Background: Brain volume is associated with dementia and depression in the elderly. An easy way to predict relative brain volume is to measure head circumference. In this study, we investigated the relationship between head circumference and cognition as well as depression in a non-demented elderly community.

Methods: Baseline and follow-up surveys were conducted in 2007 and 2010. At baseline, community residents aged 65 years or over (n=382) within a rural area of South Korea were screened for dementia and symptoms of depression and were followed using the same screening battery after 3 years (n=279). Data from anthropometric measurements (head circumference, height, and body weight), demographics, and blood tests were gathered. Neuropsychological tests, including the Korean version of mini-mental state examination (K-MMSE), clinical dementia rating (CDR) including the CDR-sum of boxes, the Korean version of instrumental activities of daily living, and geriatric depression scale (GDS), were performed. None of the 279 subjects followed were demented.

Results: Baseline performance on the K-MMSE and GDS was poorer for participants with smaller head circumferences. Follow-up performance on the MMSE was also poorer for participants with smaller head circumferences. Interestingly, participants with smaller head circumference showed worse GDS scores at baseline but on follow-up examination, participants with larger head circumference showed rapid worsening than those with smaller head circumference with marginal significance by ANOVA test. In regression coefficient analysis, GDS decline showed significant difference.

Conclusion: Head circumference was not associated with cognitive change but was associated with symptoms of depression in non-demented community residents.

Keywords: Clinical dementia rating; Cognition; Geriatric depression scale; Head circumference; Mini mental state examination

INTRODUCTION

There is evidence that a beneficial developmental environment correlates positively with a higher brain weight [1] and a

thicker cerebral cortex [2]. Brain atrophy in the elderly is frequently seen and especially common in the hippocampus and temporal, parietal, and frontal lobes. Positive correlation between brain atrophy and cognitive decline in Alzheimer's disease has been reported [3]. Neuroimaging studies in normally cognitive elderly have also shown that people with lower education have a reduced glucose metabolism compared with those with a higher education [4]. Therefore, brain volume as well as environmental enrichment, such as higher education, seems to have some association with a positive cognitive reserve [5-7].

Until now, the effect of brain volume, as estimated by head circumference, and the level of cognitive function in normal elderly as well as in patients with Alzheimer's disease, has been discussed controversially. Evidence supporting a cognitive reserve resulting from large brain volume showed that lower brain volume is correlated with cognitive impairment and the onset of Alzheimer's disease [8-11]. However, there are studies that do not support this theory [12-14]. Depression may advance cognitive dysfunction while cognitive dysfunction commonly accompanies symptoms of depression. Aging can cause frontal lobe atrophy which may, in turn, result in the development of depression [15,16]. Therefore, it is important to evaluate depressive symptoms as well as cognitive symptoms in studies of dementia.

We observed methodological weaknesses in some studies in community dwelling elderly. The participants of those studies were tested with limited cognitive tests and only a few were longitudinal cohort studies. Furthermore, thorough assessments of symptoms of depression, which may indicate a degree of frontal degeneration [17,18], were not performed. We estimated that smaller head circumference may have a negative effect on cognition and symptoms of depression in the elderly.

In the current, prospective study, we investigated whether head circumference affects cognitive decline and depressive symptoms in a non-demented elderly community cohort.

MATERIALS AND METHODS

1. Study population

The population for this study included inhabitants aged 65 years or over that were recorded in the National Residents Registration Lists within one defined rural geographic area of Koryung province, South Korea in 2007. Participants were recruited by community survey. All participants gave their written informed consent before participating in this study. The data collection protocol was approved by the Institutional Review Board of Daegu Catholic University Medical Center in Daegu, Korea (DCUMC IRB approval number: CR-10-096-ETC-01-R).

2. Assessment and measurements

Details of study procedures and findings have been pub-

lished elsewhere [19]. Head circumference was measured by passing a plastic tape around the head above the eyebrows and over the most posterior protuberance of the occiput [20].

3. Cognitive assessment and dementia diagnosis

Cognitive function was assessed using the Korean version of the mini-mental state examination (K-MMSE) [21], and clinical dementia rating (CDR) scale [22]. The Korean version of instrumental activities of daily living (K-IADL) [23] and a short form of geriatric depression scale (GDS-S) were also performed [24]. An informant interview for dementia diagnosis and subtype was also administered [25]. A physical examination included blood pressure examination and a neurological examination. Using the above information, consensus diagnosis of dementia and dementia subtypes were made by two neurologists.

4. Statistical analysis

One-way ANOVA and post-hoc analysis (Tukey's studentized range test) were conducted to compare the mean differences among head circumference quartile groups. Mantel-Haenszel chi-square test for trend was used to assess the differences in proportions among head circumference quartile groups. Multiple regression models were also used. Statistical significance was evaluated with a two-sided significance level of 0.05. All statistical analyses were performed by the IBM SPSS version 19.0 (IBM Co., Armonk, NY, USA).

RESULTS

1. Recruitment

In 2007, 388 subjects (68% of total residents) participated in first interviews, blood tests, and neurological examinations. Six of them were excluded due to poor compliance during psychological examination. Of the 382 people included, 279 underwent the second survey in 2010.

2. Comparison of men and women

Men who completed follow-up were better educated ($p<0.001$), were less illiterate ($p<0.001$), had a higher rate of current alcohol consumption ($p<0.001$), lower total choles-

terol ($p<0.001$) and LDL levels ($p<0.001$), were taller ($p<0.001$), and heavier ($p<0.001$), and had a larger head circumference than women ($p<0.001$). They also showed higher baseline cognitive scores in K-MMSE ($p<0.001$) and were less depressive ($p<0.001$) in initial tests.

Table 1. Baseline characteristics of the study participants according to head circumference quartile group (among total participants, n=279)

Scoring system	Head circumference quartile group				p-value[a]	Post-hoc analysis[a]
	Q1	Q2	Q3	Q4		
Age (yr)	73.43±5.47	71.74±4.67	70.96±5.00	71.46±5.84	0.04	Q1>Q3
Year of education	1.72±2.61	3.30±3.49	2.45±3.15	2.83±3.01	0.04	Q1<Q2
Literate	37 (66.07)	42 (79.25)	72 (80.00)	64 (80.00)	0.08	
Female	44 (78.57)	29 (54.72)	60 (66.67)	54 (67.50)	0.48	
Current alcohol drinking	21 (37.50)	27 (50.94)	44 (48.89)	47 (58.75)	0.05	
Current smoking	10 (17.86)	11 (20.75)	19 (21.11)	15 (18.75)	0.92	
Family history of stroke	11 (19.64)	9 (16.81)	17 (18.89)	18 (22.50)	0.60	
Hypertension	17 (30.36)	13 (24.53)	26 (28.89)	32 (40.00)	0.16	
Diabetes mellitus	6 (10.71)	3 (5.66)	17 (18.89)	10 (12.50)	0.33	

Data were expressed as mean±SD for continuous variables and number (%) for categorical variables.
[a] Calculated by one-way ANOVA (Tukey's studentized range tests were used for post hoc analysis) for continuous variables and Mantel-Haenszel chi-square test for trend for categorical variables.

Table 2. Baseline and 3-year follow-up (FU) scores of K-MMSE, K-IADL, CDR-G, CDR-SB, and GDS-S (mean±SD) according to head circumference quartile group (among total participants, n=279)

Scoring system	Head circumference quartile group				p-value[a]	Post-hoc analysis[a]
	Q1	Q2	Q3	Q4		
K-MMSE						
Baseline [a]	22.20±4.94	22.88±4.10	24.14±4.19	24.43±4.33	0.01	Q1<Q4
3-year FU [b]	21.67±5.02	22.33±4.28	23.30±4.63	24.05±4.51	0.01	Q1<Q4
Difference [a]-[b]	0.53±3.67	0.55±2.56	0.84±2.81	0.38±3.00	0.67	
K-IADL						
Baseline [a]	0.05±0.10	0.08±0.14	0.06±0.12	0.07±0.18	0.59	
3-year FU [b]	0.18±0.37	0.13±0.22	0.27±0.54	0.14±0.32	0.10	
Difference [a]-[b]	-0.13±0.36	-0.05±0.22	-0.21±0.52	-0.07±0.33	0.05	
CDR-G						
Baseline [a]	0.15±0.23	0.18±0.24	0.13±0.22	0.16±0.26	0.59	
3-year FU [b]	0.29±0.29	0.23±0.25	0.26±0.35	0.22±0.26	0.47	
Difference [a]-[b]	-0.13±0.36	-0.05±0.30	-0.13±0.38	-0.06±0.31	0.17	
CDR-SB						
Baseline [a]	0.23±0.36	0.32±0.50	0.17±0.32	0.33±0.78	0.23	
3-year FU [b]	0.60±0.86	0.41±0.54	0.64±0.95	0.50±0.89	0.45	
Difference [a]-[b]	-0.37±0.91	-0.09±0.58	-0.47±0.91	-0.17±1.10	0.06	
GDS-S						
Baseline [a]	6.80±4.70	5.65±4.23	5.23±4.07	4.40±3.49	0.007	Q1>Q4
3-year FU [b]	6.49±4.11	5.35±4.34	6.26±4.16	5.56±4.01	0.37	
Difference [a]-[b]	0.31±4.03	0.30±3.88	-1.03±3.66	-1.16±3.73	0.05	

K-MMSE, Korean version of mini-mental Sstatus examination; K-IADL, Korean version of instrumental activities of daily living; CDR-G, clinical dementia rating-global; CDR-SB, clinical dementia rating-sum of Boxes; GDS, geriatric depression scale-short form.
[a] Calculated by one-way ANOVA (Tukey's studentized range tests were used for post hoc analysis).

3. Anthropometric measures and cognitive decline

When we carried out partial correlation analysis between each anthropometric measure and the amount of cognitive decline, there was no significant correlation among measures of cognition; however, differences in GDS-S were apparent (p=0.010).

4. Head circumference and changes of cognition and depressive symptoms

The study participants were grouped into quartiles according to head circumference. In males, the lower quartile was 54.0 cm, the median quartile was 55.0 cm, and the upper quartile was 57.0 cm. In females, the lower quartile was 53.0 cm, the median quartile was 53.5 cm, and the upper quartile was 54.5 cm. In the total of all participants, the ANOVA test showed that people in the lowest quartile were older (p=0.01) and less educated (p=0.01) (Table 1). When we compared baseline and 3-year follow-up scores, baseline and follow-up K-MMSE scores and baseline GDS scores were worse in the lowest head circumference group (p=0.05) (Table 2). We divided the group by gender and analyzed males and females separately. In males (n=92), K-MMSE scores were higher in groups with larger head circumferences in baseline (p=0.01) and follow-up (p=0.01) tests. No differences were seen in scores between baseline and follow-up tests in each of the four quartile groups. The group with the smallest head circumference showed severe depressive symptoms in baseline (p=0.01) tests but there was no difference in follow-up tests or in the difference between baseline and follow-up tests (Table 3). In females (n=187), there was no significant difference between cognitive scores at baseline and follow-up, nor was there a difference between baseline and follow-up tests among the four quartile groups (Table 4). In a crude model of regression analysis, dif-

Table 3. Baseline and 3-year follow-up (FU) scores of K-MMSE, K-IADL, CDR-G, CDR-SB, and GDS-S (mean±SD) according to head circumference quartile group (among male participants, n=92)

Scoring system	Head circumference quartile group				p-value[a]	Post-hoc analysis[a]
	Q1	Q2	Q3	Q4		
K-MMSE						
Baseline [a]	26.92±2.54	26.25±2.82	25.79±3.77	26.31±3.33	0.47	
3-year FU [b]	25.75±3.55	25.33±4.19	25.52±4.00	25.31±4.07	0.99	
Difference [a]-[b]	1.17±1.85	0.92±2.50	0.27±2.28	1.00±2.24	0.56	
K-IADL						
Baseline [a]	0.01±0.03	0.05±0.12	0.05±0.13	0.07±0.22	0.75	
3-year FU [b]	0.05±0.12	0.19±0.39	0.10±0.22	0.10±0.24	0.50	
Difference [a]-[b]	-0.04±0.09	-0.14±0.39	-0.05±0.25	-0.03±0.33	0.67	
CDR-G						
Baseline [a]	0.08±0.19	0.11±0.21	0.16±0.27	0.08±0.23	0.63	
3-year FU [b]	0.17±0.25	0.17±0.28	0.24±0.25	0.17±0.28	0.70	
Difference [a]-[b]	-0.09±0.29	-0.06±0.31	-0.08±0.26	-0.09±0.32	0.98	
CDR-SB						
Baseline [a]	0.13±0.23	0.15±0.38	0.31±0.86	0.25±0.98	0.84	
3-year FU [b]	0.29±0.40	0.52±1.12	0.48±0.90	0.42±0.89	0.91	
Difference [a]-[b]	-0.16±0.39	-0.37±1.00	-0.17±1.11	-0.17±1.32	0.85	
GDS-S						
Baseline [a]	2.50±3.71	3.61±3.87	3.96±2.83	4.04±3.40	0.59	
3-year FU [b]	3.42±4.19	5.21±4.09	5.21±4.33	4.85±3.17	0.57	
Difference [a]-[b]	-0.92±2.84	-1.60±4.04	-1.25±3.32	-0.81±3.43	0.95	

K-MMSE, Korean version of mini-mental status examination; K-IADL, Korean version of instrumental activities of daily living; CDR-G, clinical dementia rating-global; CDR-SB, clinical dementia rating-sum of boxes; GDS, geriatric depression scale-short form.
[a]Calculated by one-way ANOVA (Tukey's studentized range tests were used for post hoc analysis).

Table 4. Baseline and 3-year follow-up (FU) scores of K-MMSE, K-IADL, CDR-G, CDR-SB, and GDS-S (mean±SD) according to head circumference quartile group (among female participants, n=187)

Scoring system	Head circumference quartile group				p-value[a]	Post-hoc analysis[a]
	Q1	Q2	Q3	Q4		
K-MMSE						
Baseline [a]	21.45±4.79	21.86±4.37	23.18±4.09	22.42±4.37	0.23	
3-year FU [b]	21.02±4.92	21.48±4.65	22.37±4.25	22.33±4.49	0.40	
Difference [a]-[b]	0.43±3.90	0.38±2.23	0.81±3.11	0.09±3.48	0.72	
K-IADL						
Baseline [a]	0.06±0.10	0.09±0.16	0.07±0.13	0.09±0.17	0.60	
3-year FU [b]	0.21±0.40	0.09±0.13	0.26±0.42	0.21±0.54	0.36	
Difference [a]-[b]	-0.15±0.38	0.00±0.16	-0.19±0.42	-0.12±0.51	0.21	
CDR-G						
Baseline [a]	0.16±0.24	0.19±0.25	0.18±0.24	0.19±0.25	0.91	
3-year FU [b]	0.31±0.29	0.26±0.25	0.28±0.27	0.25±0.35	0.81	
Difference [a]-[b]	-0.15±0.37	-0.07±0.35	-0.10±0.30	-0.06±0.42	0.66	
CDR-SB						
Baseline [a]	0.25±0.38	0.31±0.47	0.26±0.43	0.34±0.52	0.74	
3-year FU [b]	0.63±0.91	0.43±0.58	0.63±0.75	0.55±0.89	0.69	
Difference [a]-[b]	-0.38±0.97	-0.12±0.70	-0.37±0.78	-0.21±0.95	0.47	
GDS-S						
Baseline [a]	7.61±4.54	5.28±4.02	6.44±3.95	4.92±3.95	0.009	Q1>Q4
3-year FU [b]	7.00±4.02	5.28±4.29	6.36±4.05	6.45±4.35	0.40	
Difference [a]-[b]	0.61±4.09	0.00±3.92	0.08±3.56	-1.53±4.29	0.10	

K-MMSE, Korean version of mini-mental status examination; K-IADL, Korean version of instrumental activities of daily living; CDR-G, clinical dementia rating-global; CDR-SB, clinical dementia rating-sum of boxes; GDS, geriatric depression scale-short form.
[a]Calculated by one-way ANOVA (Tukey's studentized range tests were used for post hoc analysis).

ferences in K-MMSE at baseline (p=0.002) and follow-up (p=0.005) showed significance. However, no significance was noted after adjusting for age and education. In the crude model of regression analysis, GDS-S at baseline (p=0.002) and the differences between baseline and follow-up (p=0.002) tests were significant among the four quartile groups. Here, significance was noted after adjustment for age and education at baseline (p=0.02) and in differences between baseline and follow-up tests (p=0.006) (Table 5).

DISCUSSION

The aim of this study was to investigate whether cognitive decline during aging is less severe in persons with larger head circumferences among non-demented community dwelling elderly. There was no evidence of a more rapid decline of K-MMSE in the smaller head circumference group. People with larger head circumferences showed lower depressive scores at baseline. However, they showed a rapid worsening of depressive symptoms during the 3-year interval between measurements. Head circumference did not affect K-MMSE scores, but GDS-S scores seemed to be affected in the female group.

Smaller head size has been known to be associated with the prevalence [26] and incidence of dementia [27], as well as with age at onset [28], severity [29], and progression [30] of Alzheimer's disease, and with lower cognitive function in non-demented older populations [9,31]. People with larger brains and better cognitive reserves may learn easier than people with smaller brains and less cognitive reserves. However, not all studies have found associations between head size and dementia [32,33].

Measuring brain volume by neuroimaging methods is costly and complex. Head circumference is a reliable surrogate marker of brain volume; easy to check and with good correlation to intracranial volume [34,35]. Therefore, head circumference can be used as a marker for brain volume.

Table 5. Regression coefficients between head circumference and scores of K-MMSE, K-IADL, CDR-G, CDR-SB, and GDS-S (among total participants, n=279)

Scoring system	Crude model		Adjusted model[a)]	
	β	p-value	β	p-value
K-MMSE				
Baseline [a]	0.38	0.002	-0.06	0.61
3-year follow-up [b]	0.37	0.005	0.04	0.67
Difference [a]-[b]	0.01	0.87	-0.10	0.30
K-IADL				
Baseline [a]	0.001	0.73	0.003	0.41
3-year follow-up [b]	-0.005	0.67	0.003	0.77
Difference [a]-[b]	0.006	0.57	0.0006	0.96
CDR-G				
Baseline [a]	-0.004	0.55	-0.0008	0.90
3-year follow-up [b]	-0.006	0.49	0.001	0.88
Difference [a]-[b]	0.001	0.88	-0.002	0.85
CDR-SB				
Baseline [a]	0.004	0.81	0.01	0.56
3-year follow-up [b]	-0.008	0.74	0.02	0.52
Difference [a]-[b]	0.01	0.65	-0.007	0.84
GDS-S				
Baseline [a]	-0.37	0.002	-0.27	0.02
3-year follow-up [b]	-0.009	0.94	0.06	0.65
Difference [a]-[b]	-0.34	0.002	-0.32	0.006

K-MMSE, Korean version of mini-mental status examination; K-IADL, Korean version of Instrumental activities of daily living; CDR-G, clinical dementia rating-global; CDR-SB, clinical dementia rating-sum of boxes; GDS, geriatric depression scale-short form.
[a)]Multiple regression models were used after adjusting for age and education.

We thought that larger head circumference may be beneficial, protecting against cognitive decline and the worsening of symptoms of depression. However, association analysis did not show any significant correlation between head circumference and any decline of cognitive scales during the 3 years of follow-up but did show a correlation with marginal significance in worsening GDS-S scores. An interesting result of the current study was that participants with larger head circumferences showed a tendency to more rapid worsening of GDS scores than those with smaller head circumferences. Regression coefficient analysis also supported rapid GDS worsening in participants with larger head circumference. CDR and the sum of box values of CDR, which showed better significance in assessing cognitive change [36,37], were included along with K-MMSE in our cognitive assessment methods

but did not show any significant changes during the 3-year interval. Scoring activities of daily living (ADL), especially instrumental IADL, also may be an important diagnostic tool for cognitive decline but did not show any evidence of changes during this period [38].

The reason why there was no correlation between head circumference and cognitive decline may be explained as follows: first, the follow-up period was too short to show significant differences. We expected K-MMSE would show a negative correlation and CDR and IADL would show a positive correlation. Though the study showed a modest tendency towards the results we expected, they were not statistically significant. Secondly, the population enrolled in the study were community dwellers who managed to live on their own. Several previous studies suggest that the course of cognitive changes in non-demented people are not the same as those in demented patients [12,14]. These studies suggested that head circumference does not affect the age associated deterioration of cognition in non-demented persons. In participants that did have dementia, the results may have shown the outcomes we had expected.

GDS represents the severity of depressive mood in an elderly population [39]. However, depressive mood can arise from frontal lobe degeneration that itself may cause cognitive decline [15,16]. We found significant correlation between head circumference and worsening of depression scores, especially in females. Women in this study had smaller head circumferences than men and GDS-S scores in both the initial and follow-up studies were significantly higher in women. Interestingly, GDS scores in females with smaller head circumferences were higher at baseline but decreased in the follow-up study. In contrast, GDS scores in females with larger head circumferences were lower at baseline but increased over the 3 years.

These results do not have a clear explanation that we can put forward. The first possible reason for smaller head circumferences in females may be gender difference. The other reason could be the poorer socioeconomic circumstances in South Korea at the time when the participants were young. In addition, the Confucius culture of this period prohibited females from getting an education and enough nutrition.

The poor socioeconomic state during the main developmental period of participants could also have affected their symptoms of depression [40]. Changes of depressive mood in

elderly may reflect cognitive changes more sensitively than cognitive indicators. However, there was no report showing rapid decline of depressive symptoms in subjects with larger head circumferences. A larger amount of frontal gray matter and the effect of female sexual hormones may play a role in the symptoms of depression [41,42], but this could only be investigated in a longer prospective study.

The current study had several advantages. First, participants were quite unique in their homogeneity. All of them lived in the same socio-cultural environment for decades. This may have provided more robust results. Second, we used reliable cognitive measures. Previous studies usually used the MMSE score only in epidemiological studies. In our study, we used not only the K-MMSE but also CDR and IADL. Third, our study was a prospective longitudinal study. Many previous studies were cross-sectional or anecdotal.

There are also limitations to the current study. First, the size of this study may not have been large enough to support the hypothesis. Second, a 3-year follow-up was not enough to uncover cognitive changes in community dwelling elderly. More people and a longer period of study is needed.

In conclusion, there was no relationship between cognitive decline and head circumference in an elderly community. However, there seemed to be some relationship between symptoms of depression and head circumference, especially in females. Studies in larger populations and with long term periods of follow-up are needed.

ACKNOWLEDGEMENT

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article were reported.

ORCID

Oh Dae Kwon, https://orcid.org/0000-0002-7465-2904
So-Young Choi, https://orcid.org/0000-0003-0624-8405
Jisuk Bae, https://orcid.org/0000-0002-5809-5394

REFERENCES

1. Krech D, Rosenzweig MR, Bennett EL. Effects of environmental complexity and training on brain chemistry. J Comp Physiol Psychol 1960;53:509-19.
2. Diamond MC. Enriching heredity: the impact of the environment on the anatomy of the brain. New York: Free Press; London: Collier Macmillan; 1988.
3. Duarte A, Hayasaka S, Du A, Schuff N, Jahng GH, Kramer J, et al. Volumetric correlates of memory and executive function in normal elderly, mild cognitive impairment and Alzheimer's disease. Neurosci Lett 2006;406:60-5.
4. Kwon OD, Cho SS, Seo SW, Na DL. Effect of illiteracy on neuropsychological tests and glucose metabolism of brain in later life. J Neuroimaging 2012;22:292-8.
5. Bennett DA, Schneider JA, Wilson RS, Bienias JL, Arnold SE. Education modifies the association of amyloid but not tangles with cognitive function. Neurology 2005;65:953-5.
6. Zhang MY, Katzman R, Salmon D, Jin H, Cai GJ, Wang ZY, et al. The prevalence of dementia and Alzheimer's disease in Shanghai, China: impact of age, gender, and education. Ann Neurol 1990;27:428-37.
7. Katzman R, Terry R, DeTeresa R, Brown T, Davies P, Fuld P, et al. Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques. Ann Neurol 1988;23:138-44.
8. Perneczky R, Wagenpfeil S, Lunetta KL, Cupples LA, Green RC, Decarli C, et al. Head circumference, atrophy, and cognition: implications for brain reserve in Alzheimer disease. Neurology 2010;75:137-42.
9. Reynolds MD, Johnston JM, Dodge HH, DeKosky ST, Ganguli M. Small head size is related to low Mini-Mental State Examination scores in a community sample of nondemented older adults. Neurology 1999;53:228-9.
10. Gale CR, Walton S, Martyn CN. Foetal and postnatal head growth and risk of cognitive decline in old age. Brain 2003; 126:2273-8.
11. Wolf H, Julin P, Gertz HJ, Winblad B, Wahlund LO. Intracranial volume in mild cognitive impairment, Alzheimer's disease and vascular dementia: evidence for brain reserve? Int J Geriatr Psychiatry 2004;19:995-1007.
12. Espinosa PS, Kryscio RJ, Mendiondo MS, Schmitt FA, Wekstein DR, Markesbery WR, et al. Alzheimer's disease and head circumference. J Alzheimers Dis 2006;9:77-80.
13. Jenkins R, Fox NC, Rossor AM, Harvey RJ, Rossor MN. Intracranial volume and Alzheimer disease: evidence against the cerebral reserve hypothesis. Arch Neurol 2000;57:220-4.
14. Christensen H, Batterham PJ, Mackinnon AJ, Anstey KJ, Wen W, Sachdev PS. Education, atrophy, and cognitive change in an epidemiological sample in early old age. Am J Geriatr Psychiatry 2009;17:218-26.
15. Elderkin-Thompson V, Boone KB, Hwang S, Kumar A. Neurocognitive profiles in elderly patients with frontotemporal degeneration or major depressive disorder. J Int Neuropsychol Soc 2004;10:753-71.
16. Sözeri-Varma G, Kalkan-Oğuzhanoglu N, Efe M, Kıroglu Y,

Duman T. Neurochemical metabolites in prefrontal cortex in patients with mild/moderate levels in first-episode depression. Neuropsychiatr Dis Treat 2013;9:1053-9.

17. Hu X, Meiberth D, Newport B, Jessen F. Anatomical correlates of the neuropsychiatric symptoms in Alzheimer's disease. Curr Alzheimer Res 2015;12:266-77.

18. Brommelhoff JA, Sultzer DL. Brain structure and function related to depression in Alzheimer's disease: contributions from neuroimaging research. J Alzheimers Dis 2015;45:689-703.

19. Kim YH, Kwon OD. Clinical correlates of Hachinski ischemic score and vascular factors in cognitive function of elderly. Biomed Res Int 2014;2014:852784.

20. Perneczky R, Alexopoulos P, Wagenpfeil S, Bickel H, Kurz A. Head circumference, apolipoprotein E genotype and cognition in the Bavarian School Sisters Study. Eur Psychiatry 2012;27:219-22.

21. Kang Y, Na DL, Hahn S. A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients. J Korean Neurol Assoc 1997;15:300-8. Korean.

22. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. Br J Psychiatry 1982;140:566-72.

23. Kang SJ, Choi SH, Lee BH, Kwon JC, Na DL, Han SH, et al. The reliability and validity of the Korean instrumental activities of daily living (K-IADL). J Korean Neurol Assoc 2002; 20:8-14. Korean.

24. Burke WJ, Roccaforte WH, Wengel SP. The short form of the Geriatric Depression Scale: a comparison with the 30-item form. J Geriatr Psychiatry Neurol 1991;4:173-8.

25. Dewey ME, Copeland JR. Diagnosis of dementia from the history and aetiology schedule. Int J Geriatr Psychiatry 2001; 16:912-7.

26. Schofield PW, Logroscino G, Andrews HF, Albert S, Stern Y. An association between head circumference and Alzheimer's disease in a population-based study of aging and dementia. Neurology 1997;49:30-7.

27. Borenstein Graves A, Mortimer JA, Bowen JD, McCormick WC, McCurry SM, Schellenberg GD, et al. Head circumference and incident Alzheimer's disease: modification by apolipoprotein E. Neurology 2001;57:1453-60.

28. Schofield PW, Mosesson RE, Stern Y, Mayeux R. The age at onset of Alzheimer's disease and an intracranial area measurement. A relationship. Arch Neurol 1995;52:95-8.

29. Graves AB, Mortimer JA, Larson EB, Wenzlow A, Bowen JD, McCormick WC. Head circumference as a measure of cognitive reserve. Association with severity of impairment in

Alzheimer's disease. Br J Psychiatry 1996;169:86-92.

30. Mori E, Hirono N, Yamashita H, Imamura T, Ikejiri Y, Ikeda M, et al. Premorbid brain size as a determinant of reserve capacity against intellectual decline in Alzheimer's disease. Am J Psychiatry 1997;154:18-24.

31. Tisserand DJ, Bosma H, Van Boxtel MP, Jolles J. Head size and cognitive ability in nondemented older adults are related. Neurology 2001;56:969-71.

32. Edland SD, Xu Y, Plevak M, O'Brien P, Tangalos EG, Petersen RC, et al. Total intracranial volume: normative values and lack of association with Alzheimer's disease. Neurology 2002; 59:272-4.

33. Mortimer JA, Snowdon DA, Markesbery WR. Head circumference, education and risk of dementia: findings from the Nun Study. J Clin Exp Neuropsychol 2003;25:671-9.

34. Wolf H, Kruggel F, Hensel A, Wahlund LO, Arendt T, Gertz HJ. The relationship between head size and intracranial volume in elderly subjects. Brain Res 2003;973:74-80.

35. Tramo MJ, Loftus WC, Stukel TA, Green RL, Weaver JB, Gazzaniga MS. Brain size, head size, and intelligence quotient in monozygotic twins. Neurology 1998;50:1246-52.

36. Lowe DA, Balsis S, Miller TM, Benge JF, Doody RS. Greater precision when measuring dementia severity: establishing item parameters for the Clinical Dementia Rating Scale. Dement Geriatr Cogn Disord 2012;34:128-34.

37. O'Bryant SE, Waring SC, Cullum CM, Hall J, Lacritz L, Massman PJ, et al. Staging dementia using Clinical Dementia Rating Scale Sum of Boxes scores: a Texas Alzheimer's research consortium study. Arch Neurol 2008;65:1091-5.

38. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. Md State Med J 1965;14:61-5.

39. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1983;17: 37-49.

40. Melchior M, Moffitt TE, Milne BJ, Poulton R, Caspi A. Why do children from socioeconomically disadvantaged families suffer from poor health when they reach adulthood? A life-course study. Am J Epidemiol 2007;166:966-74.

41. Steingard RJ, Renshaw PF, Hennen J, Lenox M, Cintron CB, Young AD, et al. Smaller frontal lobe white matter volumes in depressed adolescents. Biol Psychiatry 2002;52:413-7.

42. Shanmugan S, Epperson CN. Estrogen and the prefrontal cortex: towards a new understanding of estrogen's effects on executive functions in the menopause transition. Hum Brain Mapp 2014;35:847-65.