

## 신장과 인지 기능

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## Height and Cognitive Function in an Older Korean Population

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**Background:** Some kind of adult anthropometry was reported as a marker of early life environment, and could be associated with cognitive impairment or dementia. This study aimed to examine whether height was associated with various cognitive domains. **Method:** A community study of 235 individuals aged 65 and over was performed in Noam-dong, Namwon city, Jeonbuk province. Cognitive function was ascertained from the Korean version of modified Mini-Mental State Examination (K-mMMSE), and cognitive domains like memory, visuoconstruction, and word fluency were derived from the previous K-mMMSE scores. Anthropometric measurement included height. **Results:** Height showed significant correlations with memory ( $r=0.41$ ), orientation ( $r=0.49$ ), word fluency ( $r=0.40$ ), and visuoconstruction ( $r=0.48$ , all  $p$  values  $<0.001$ ). Among the domains, taller stature was significantly associated with higher scores of orientation and visuoconstruction, independently of age, sex, education, and the other confounders. **Conclusion:** Taller height was associated with better cognitive performance independently of educational attainment. Height could be used as a marker of cognitive reserve capacity in our elderly population.

**Key Words:** Height, Cognitive domain, Cognitive reserve, Population

## INTRODUCTION

Structural and functional brain reserves, thought to develop in childhood and adolescence, might be crucial in determining when cognitive impairment begins[1]. Cognitive reserve is the ability of an individual to cope with advancing brain pathology so that he remained free of symptomatology[2]. Educational attainments exemplified this concept, that is, lifelong patterns of neuronal activation associated with exposure to education or occupational attainment led to an enhanced synaptic complexity, neuronal reserve, and resistance to the effects of the disease on cognition[3, 4].

In addition to education, it has been reported that some anthropometric measurements could be associated with late life cognition, and might be reflections of early life environment[5, 6]. Growth of height occurs mainly in the first growth spurt from birth to 2 years and second spurt during prepubertal period[7]. So the bone formation and growth could be largely influenced by early life environment, for example, nutritional factors or parental influences[8, 9]. The poor early life

nutritional support was known to result in small head, short stature, increased cardiovascular disease (CVD), cognitive impairment, and dementia in late life[10-12]. This finding led to adult anthropometry as a biomarker of 'early life'[13].

Even associations between anthropometric measurements and dementia or cognitive impairment have been reported, there was no study to evaluate an association between anthropometry and cognitive domains, the constituent cognitive function. The present study aimed to examine whether height was associated with various cognitive domains like memory, orientation, word fluency, and visuoconstruction.

## MATERIALS AND METHODS

### 1. Subjects

Potential participants for this study were recruited from all inhabitants of Noam-dong, Namwon, Jeonbuk, Korea, aged 65 and over in 2003, as recorded in national residents

registration lists. The area surveyed covered 8.93 km<sup>2</sup> and had an estimated population of 6,883, of whom about 7% were aged 65 or over. All participants gave informed consent, and the study was conducted in accordance with the guidelines in The Declaration of Helsinki and approved by the appropriate research ethics committee.

Among the 522 eligible subjects aged 65 and over identified from registration lists, 235 (45%) completed clinical examinations after the interview and formed the study sample for principal analysis. Of the remaining subjects, we were unable to establish contact with 162 (31%), 75 (14%) refused to participate, 18 (3%) did not complete the survey, 7 (1%) had severe pre-morbid illness including blindness and deafness, 4 (0.8%) had changed address, and 3 (0.6%) had died before the visit. The principal apparent reason for the difficulties in establishing contact was that the person was in a regular daily activity or away from home, visiting family members living elsewhere. The 18 individuals (3%) who did not complete the survey questionnaire or were not examined clinically had a mean age of  $74.9 \pm 10.3$  years; 13 (72%) were females, and 4 (22%) were educated. Of all the eligible subjects, participants and non-participants did not differ in age ( $73.5 \pm 6.8$  years vs.  $74.6 \pm 7.8$  years, respectively) or gender (female; 66% and 62%, all  $p$  values  $>0.1$ ).

## 2. Assessment and measurements

The study was conducted by sixteen graduate level research assistants. Interviewers received a seven-day training session on administering the screening instruments and were supervised throughout by the project neurologist. Interviewers carried out home-based interviews for data on cognitive function, past medical history, and demographic characteristics. Life style questions included alcohol drinking status, as estimated by frequency and duration. Smoking status was categorized into current smokers, ex-smokers and non-smokers. Blood samples were taken immediately after the interview and analyzed on the day of blood collection. Random blood glucose was measured using an enzymatic colorimetric assay with hexokinase. Blood pressure was measured on the right arm, with the subject in the sitting position, using a standard mercury manometer after at least 5 minutes of rest. First appearance (phase I) and disappearance (phase V) of Korotkoff's sounds were used to define the systolic and diastolic pressure. Readings were recorded to the nearest even number, and two readings at 5 minutes intervals were taken from each partic-

ipant. The lower of the two readings was taken as the individual's blood pressure[14]. Subjects with persistent elevation of blood pressure ( $\geq 140/90$  mmHg) or taking antihypertensive medications were classified as hypertensive[15]. Type 2 diabetes mellitus (DM) was defined as a self-reported history of being told by a physician that diabetes was present or having a random blood glucose of 200 mg/dL or greater, according to the criteria defined by the American Diabetic Association[16].

Cognitive status was classified in two stages. In the first stage, all participants were contacted for cognitive screening using the Korean version of modified Mini-Mental State Examination (K-mMMSE), which has been known as having finer discrimination of cognitive impairment or dementia[17]. K-mMMSE had 100 point in total, higher scores indicated better performance. And the participants were rated by a knowledgeable informant using the Short form of Samsung Dementia Questionnaire (S-SDQ) and the Korean Instrumental Activities of Daily Living (K-IADL)[18, 19]. At the second interview, physicians who were blinded to the cognitive scores performed a clinical examination and neuropsychiatric inventory on participants who completed the first survey questionnaire. The clinical examination verified the presence of cognitive impairment and dementia, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[20] and the guidelines of the National Institutes of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA)[21]. At both stages, home visits were repeated on at least two occasions if no contact was made.

Standing body height was measured to the nearest 0.5 cm with a commercial stadiometer without shoes and with the shoulders in a relaxed position and the arms hanging freely.

Some cognitive domains like fluency and visuoconstruction were same as the raw data from the K-mMMSE and the total score was 10 points each. The memory function summated the items of registration, immediate and delayed recall, and presidential naming for remote memory, and the total score was 26 points. The orientation summated the items for time and space, and was 20 points in total.

## 3. Statistical analysis

Results were expressed as the mean  $\pm$  SD. Categorical variables, expressed as percentages, were evaluated using chi square

( $\chi^2$ ) test. Continuous variables were analyzed with unpaired Student's t-test. The strength of cross-sectional associations was assessed by Pearson's correlation analyses. Linear regression analysis was performed using the various cognitive domains as the dependent variables and height as explanatory variable. Potential confounders added to the multivariate models were age, sex, education, smoking, alcohol drinking, hypertension, and type 2 DM. Interaction terms between independent variables were entered separately and their significance was assessed by likelihood ratio tests. All statistical analyses were conducted with Stata 8.2 for Windows package (Stata Corporation, College Station, TX, USA).

## RESULTS

Descriptive statistics were displayed in Table 1 according to gender. In total, 235 subjects aged 65 years and older were participated our survey. Formal educational attainment (y) was significantly higher in men ( $p<0.001$ ). The prevalence of smoking and alcohol drinking was each significantly higher in men ( $p<0.001$  for each). Age and prevalence of risk factors like hypertension and type 2 DM were similar in men and women. Men were taller than women. Compared to demented subjects, normal population were significantly taller ( $147.4 \pm 8.6$  cm vs.  $154.4 \pm 9.3$  cm,  $p<0.001$ ). Scores of cognitive domains were all significantly higher in men (all  $p$  values

**Table 1.** Characteristics of subjects

	Total participants (n=235)	
	Male (n=79)	Female (n=156)
Sociodemographic characteristics		
Age, years	73.0 $\pm$ 6.8	73.0 $\pm$ 7.8
Formal education, years	5.7 $\pm$ 4.6	1.9 $\pm$ 2.8*
Drinker, %	51.9	23.7*
Ever-smoker, %	87.3	19.9*
Hypertension, reported and measured, %	35.4	41.7
Type 2 DM, reported and measured, %	16.5	19.9
Height and scores of cognitive domains <sup>†</sup>		
Height, cm	163.2 $\pm$ 6.7	148.2 $\pm$ 6.4*
Memory	18.4 $\pm$ 5.3	15.0 $\pm$ 6.1*
Orientation	17.5 $\pm$ 4.0	13.7 $\pm$ 5.6*
Fluency	6.3 $\pm$ 2.3	4.7 $\pm$ 2.2*
Visuoconstruction	8.2 $\pm$ 2.1	6.0 $\pm$ 5.6*

Values are mean  $\pm$  SD unless noted otherwise. \* $p<0.001$  by chi-square test or unpaired t-test as appropriate. <sup>†</sup>Scores of each cognitive domain are derived from the K-mMMSE (Korean version of modified Mini-Mental State Examination).

$<0.001$ ), indicating better cognitive performance.

Height was significantly correlated with all the cognitive domains as in Table 2. Height showed correlation coefficients from the lowest value of 0.40 for word fluency and to the highest of 0.49 for orientation (all  $p$  values  $<0.001$ ). Between cognitive domains, the correlation coefficients were more than 0.53 and less than 0.66, suggesting modest correlations without a considerable overlapping.

Height showed significant associations with the orientation and visuoconstruction, independently of age, sex, education, smoking, alcohol drinking, hypertension, and type 2 DM as in Table 3. The orientation and visuoconstruction showed model fitness of 0.35 and 0.33 (adjusted  $r^2$  values) in the fully adjusted models, respectively. The memory showed significant associations with height, even after adjusting for educational attainment, but, after adjusting cardiovascular risk factors, the association fell to borderline significance ( $p<0.1$ ). The word fluency lost significance after an additional adjustment of education. All the interaction terms for height times sex were not significant (all  $p$  values  $>0.1$ ), adjusting for the

**Table 2.** Correlations between scores of cognitive domains and height

	Height	Memory	Orientation	Fluency	Visuoconstruction
Height	1.00				
Memory	0.41*	1.00			
Orientation	0.49*	0.66*	1.00		
Fluency	0.40*	0.57*	0.53*	1.00	
Visuoconstruction	0.48*	0.58*	0.65*	0.53*	1.00

Values are Pearson's correlation coefficients. \* $p<0.001$ .

**Table 3.** Associations between scores of cognitive domains and height

	Memory			Orientation		
	$\beta$	SE	95% CI	$\beta$	SE	95% CI
Unadjusted	0.26*	0.04	0.18, 0.33	0.28*	0.03	0.21, 0.34
Model 1	0.21 <sup>†</sup>	0.06	0.09, 0.34	0.20*	0.05	0.09, 0.30
Model 2	0.14 <sup>‡</sup>	0.06	0.02, 0.26	0.15 <sup>†</sup>	0.05	0.04, 0.25
Model 3	0.12	0.06	-0.00, 0.25	0.13 <sup>†</sup>	0.05	0.02, 0.23
	Fluency			Visuoconstruction		
	$\beta$	SE	95% CI	$\beta$	SE	95% CI
Unadjusted	0.10*	0.02	0.07, 0.13	0.14*	0.02	0.11, 0.17
Model 1	0.06 <sup>‡</sup>	0.03	0.01, 0.11	0.11*	0.03	0.05, 0.17
Model 2	0.04	0.03	-0.01, 0.09	0.07 <sup>†</sup>	0.03	0.02, 0.13
Model 3	0.04	0.03	-0.02, 0.09	0.07 <sup>†</sup>	0.03	0.01, 0.12

SE, standard errors; CI, confidence intervals. In model 1, age and sex adjusted; in model 2, age, sex, and educational years adjusted; in model 3, age, sex, educational years, smoking, alcohol drinking, hypertension, and type 2 DM adjusted with linear regression analyses.

\* $p<0.001$ , <sup>†</sup> $p<0.01$ , <sup>‡</sup> $p<0.05$

entire potential confounders.

## DISCUSSION

There were strong associations between height and cognitive domains, especially for orientation and visuoconstruction, independently of potential confounders including education. This finding supported the previous report which showed the significant associations between midlife height and late life cognitive impairment and dementia[5]. But until now, there was no report showing an association between cognitive domains and height with a cross-sectional design.

Biologic and chemical markers had important meanings to reveal the essential findings in medical fields. To define better the disease process itself, searching for new markers and understanding the characteristics of them were mandatory[22]. Cognitive reserve theory was the typical one of these explanations, as already known; there should be significant modulators of subsequent symptomatology of cognitive impairment and dementia. The unique characteristics of cognitive reserve indicators could be characterized as fixed and unmodifiable. Typical markers of cognitive reserve included an educational attainment[3] and intelligence[23].

In addition to educational attainments, anthropometric measurements were reported to be an important marker of cognitive reserve, for example, head circumference[2, 24], height[5], and arm length[6]. These anthropometric measurements were reported to represent some unique aspects of early life environment, like nutritional factors or parental influences[8, 9]. Of course, these anthropometric measurements represented the present body scheme, especially for obesity, and could be used for a research of an association between obesity and cognitive impairment[25].

Even the fact that height could be used as a marker of cognitive reserve capacity, there were some important aspects which should be clarified further. Height was closely related to the aging effect. Age or aging itself has been one of important confounders which should be carefully adjusted or stratified in research models, as reported earlier[26, 27]. Height was vulnerable to degenerative processes in older people, for example, osteoporotic kyphosis[28]. It was partially supported by a previous study showing an association between midlife height, which was not yet affected by osteoporosis or fracture, and later life cognitive function[5].

The merits, however, outnumbered demerits: the first, it

could be measured with ease and without antipathy from the examinee in clinic and epidemiologic research fields[13, 29]. The second, as the present analysis, even cognitive reserve capacity was thought as originally caused by educational attainment[1], the association between height and cognitive functions was independent of an educational attainment. That was coincide with the previous reports for limb length[6] and head circumference[30]. Conceived of the fact that a larger head size or taller height and more reserved cognitive ability were both consequences of a favourable environment during early life span, the anthropometry could be characterized as an important indicator of early life status, with some different unique meaning from education. Finally, there was no gender interactive effect for an association between height and cognitive functions in the present analysis. It meant that the strength of associations was nearly same without crossing; even the distribution of height was significantly different[data not shown].

There were some important limitations to our findings. First, the subjects who participated in this study showed very low levels of educational background, perhaps limiting its generalization. The low educational attainment, however, has been one of important characteristics of our elder population and, furthermore could be effective to show cognitive reserve because of group differential item functioning[31]. Second, author could not attain detailed information about the chronologic changes of height, even height was known to be largely influenced by vertebral or hip joint disorders. In the subsequent studies of anthropometry as for cognitive reserve, this limitation should be considered properly. Finally, although we observed no significant differences between participants and non-participants, the rate of participation in our study was somewhat low. The majority of non-participants were those with whom we could not meet on two separate visits, suggesting that individuals who refused to participate may be more intelligent or active than the participants. If this were true, however, our results would not change, and additional statistical power may be added to our analysis.

Height was strongly associated with cognitive function and could be used as an indicator of early life status, independently of an educational attainment. Further study would be needed to define the characteristics of height as a cognitive reserve capacity and to find associations between height and cognitive impairment or dementia, with community and hospital based study.

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