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Research article

Physical Fitness and Serum Vitamin D and Cognition in Elderly Koreans

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Abstract
Poor physical fitness and low serum vitamin D are known to be modifiable risk factors for cognitive declines with normal aging. We investigated the association of physical fitness and serum vitamin D levels with global cognitive function in older adults. In this cross-sectional study, a total of 412 older Korean adults (108 men aged 74.4 ± 6.0 years and 304 women aged 73.1 ± 5.4 years) completed the Korean version of Mini-Mental State Examination (MMSE) to assess global cognitive performance and the senior fitness test to assess strength, flexibility, agility, and endurance domains of physical fitness. Body mass index, percent body fat, serum vitamin D, geriatric depression scale (GDS), level of education, smoking, and history of cardiovascular or cerebrovascular disease were also assessed as covariates. Age, sex, GDS, and body fatness were negatively associated with MMSE-based cognitive performance. Serum vitamin D and physical fitness were positively associated with MMSE-based cognitive performance. Multivariate linear regression showed that agility (partial R^2 = -0.184, p = 0.029) and endurance (partial R^2 = 0.191, p = 0.022) domains of physical fitness along with serum vitamin D (partial R^2 = 0.210, p = 0.012) were significant predictors for global cognitive performance after controlling for covariates (i.e., age, sex, education, GDS, body fatness, and comorbidity index). The current findings of the study suggest that promotion of physical fitness and vitamin D supplementation should be key components of interventions to prevent cognitive decline with normal aging.

Key words: Cognitive function, geriatrics, physical fitness, vitamin D

Introduction

With a rapidly growing older population in Korea, there is an increasing need to identify potentially modifiable risk factors for the onset of physical and mental disability and to provide evidence-based strategies for healthy and successful aging (Huh et al., 2011). Aging has adverse effects on cognitive function such as mild cognitive impairment (MCI) and dementia. Even though age-related cognitive decline is primarily associated with genetic factors, it likely also is correlated with a decrease in physical fitness (Bherer et al., 2013; Blonde et al., 2014). Indeed, common biological changes underlie decline in both age-related physical and cognitive function.

Impairments in physical performance are common age-related phenomena (Black and Ruch, 2002; Kuo et al., 2007) and are also associated with cognitive decline with normal aging. In cross-sectional studies, physical fitness was found to be positively associated with cognitive function. In older populations, those who had better mobility (Volker and Scherder, 2013), balance (Volker and Scherder, 2013), strength (Blankevoort et al., 2013), and aerobic fitness (Blankevoort et al., 2013) had better cognitive function. Prospective studies reported similar findings. Voss et al. (2010) reported that aerobic fitness was associated with better average accuracy and mean response time across all levels of a spatial memory task among older adults. Poor physical performance among older adults may also lead to more rapid cognitive decline and early onset of dementia (Sattler et al., 2011; Annweiler et al., 2011). However, due to methodological differences in the studies, there are still some gaps in the understanding of the association between cognitive function and physical fitness.

The discovery of vitamin receptors throughout the brain and the role of vitamin D in neurodevelopment have led researchers to examine this fat soluble vitamin in relation to cognition. Vitamin D deficiency is common in older adults and has been implicated in psychiatric and neurologic disorders. In a retrospective clinical chart review of 23 elderly patients (aged 79.5 ± 1.6 years) attending a monthly community-based, university-affiliated consultative clinic, Przybelski and Binkley (2007) found a significant association between serum vitamin D levels and Mini-Mental State Examination (MMSE) score-based cognitive performance. In a group of cognitively intact older adults from an Italian population-based cohort study of 1,927 elderly subjects, Toffanello et al. (2014) found that serum vitamin D levels below <75 nmol·L^{-1} at the baseline predicted cognitive decline over roughly the next 4 years, independent of other factors. In a recent review based on meta-analysis of 37 studies, Balion et al. (2012) found that lower serum vitamin D levels were associated with poorer cognitive function and a higher risk of Alzheimer's disease (AD).

In Korea, little is known about the relationships of physical fitness and serum vitamin D with cognitive function in older adults. Vitamin D deficiency in Korea has reached epidemic proportions and become a major health concern in older adults (Seo et al., 2012). Consequently, gaining insight into these relationships would contribute to the development of new or improved options for the prevention and/or treatment of age-related cognitive decline. The objectives of this study were 1) to determine the associations between a) serum vitamin D levels and cognitive function and b) physical fitness and cognitive function among community-dwelling older adults in Korea, and 2) to examine whether both physical performance and serum vitamin D levels are independent determinants of cognition in elderly Koreans.

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Methods

Subjects

A total of 467 study participants (130 men and 337 women aged ≥65 years and fluent in Korean) were recruited. Recruitment occurred from eight community healthcare centers located in the Northwestern Gyeonggi Province of South Korea between December of 2013 and December of 2014. Data was collected during three separate visits. At the first visit, demographic characteristics were gathered from 143 men (7 missing) and 335 women (15 missing), and general health status was assessed based on standardized self-administered questionnaires and interviews conducted by nurses specializing in geriatrics. One week after the first visit, participants attended a second session at which neuropsychiatric specialists conducted the MMSE, a comprehensive neuropsychological test, to assess global cognitive function. Within 2 hours of completing the cognitive function assessment, participants completed a senior fitness test (SFT) conducted by exercise specialists to assess six domains of functional fitness (Rikli and Jones, 2001). An additional 15 men and 18 women did not show up or refused to complete either the MMSE (n = 14) or the SFT (n = 19). Consequently, 412 (108 men and 304 women) out of the 467 initial participants completed all the tests, and they were included in the final data analyses (see Figure 1). The third visit involved an overnight fast, after which laboratory tests were performed to evaluate the general physical and metabolic health of the remaining 412 participants, including resting blood pressure, blood lipids, fasting glucose and fasting insulin. Common geriatric disorders were also identified. The Institutional Review Board, in accordance with the Declaration of Helsinki and the World Medical Association, approved the study protocol. All participants provided written informed consent to participate in the study.

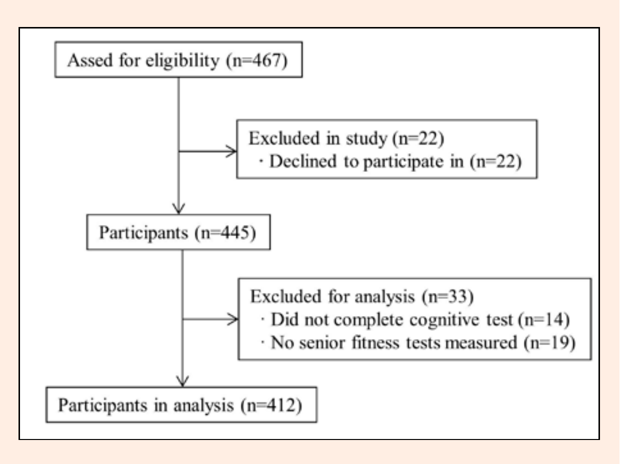

Figure 1. Flowchart of participants.

Cognitive function

Global cognitive function was assessed by trained nurses using the Korean version of the MMSE. The MMSE measures the cognitive level of elders in terms of orientation (10 points), short-term memory and recall (6 points), attention (5 points), phonic fluency (2 points), following verbal commands (4 points), judgment (2 points) and copying a double pentagon (1 point) (Folsterin et al., 1975). Scores of MMSE ranged between 0 and 30, where higher scores indicate a better cognition level. The most widely accepted and frequently used cutoff score for the MMSE is 23, with scores of 23 or lower indicating the presence of cognitive impairment. The Korean version of MMSE is the same as the MMSE described above, except instead of phonic fluency (2 points) they are rated on naming (2 points). The MMSE was validated in Korean elderly subjects (Lee et al., 2008).

Senior Fitness Test (SFT)

The SFT assesses the physiological capacity for carrying out normal daily activities independently and safely without the appearance of fatigue. Participants performed 10 minutes of warm-up as instructed by a trained fitness instructor. The test was then completed in this order: (1) Chair stand up for 30 seconds was used to assess lower-body strength, (2) Arm curl was used to assess upper-body strength, (3) Back scratch was used to assess upper-body (shoulder) flexibility, (4) Chair-sit-and-reach was used to assess the flexibility of the lower extremities, (5) Eight-foot-up-and-go was used to assess agility/dynamic balance as an index of basic mobility skills, and (6) The 6-minute walk test was used to assess aerobic capacity. Detailed procedures are available elsewhere (Rikli and Jones, 1999) and test validity has been published (Rikli and Jones, 2001).

Demographics and covariates

Height and body mass were recorded using a stadiometer attached to a scale (Jenix, Seoul, Korea). Percent body fat was assessed using bioelectrical impedance analysis following the procedures recommended by the American College of Sports Medicine (2006). Age, level of education, smoking, and history of cardiovascular or cerebrovascular disease were assessed and included as potential covariates in the analyses. Education was collected as the number of year of education, then was defined as a categorical variable for the analysis (high school education or less, vocational school or some college education, or college degree or higher). A detailed medical history, including these variables, was obtained from the participants or their informants. The comorbidity index was determined by the summation of self-reported illnesses including hypertension, heart disease, diabetes, cancer, fracture, and respiratory disease. Serum vitamin D levels were determined using the LIAISON 25(OH) Vitamin D TOTAL Assay (CLIA), which is a direct competitive chemiluminescence immunoassay for human serum intended for use on the DiaSorin LIAISON automated analyzer (Italy, DiaSorin S.P.A). The intra- and inter-assay coefficients of variation for serum vitamin D were 3% to 6% and 7% to 11%, respectively.

Statistical analyses

Descriptive analyses of the demographic characteristics of the participants were expressed as mean ± standard deviation or percentage. The Kolmogorov–Smirnov test was performed to examine the normality of data ($p > 0.05$). Pearson's correlation coefficients between physical and

Table 1. Description of the study participants.

Variables	Total (n = 412)	Men (n = 108)	Women (n = 304)	p value
Age (years)	73.4 ± 5.6	74.4 ± 6.0	73.1 ± 5.4	.038
Education (years)				
0	31 (7.5%)	4 (3.7%)	27 (8.9%)	.997
1–6	160 (38.8%)	18 (16.7%)	142 (46.7%)	.632
>7	221 (53.6%)	86 (79.6%)	135 (44.4%)	<.001
Smoking status[§]				
Never	317 (76.9%)	35 (32.4%)	282 (92.8%)	<.001
Current	53 (12.9%)	43 (39.8%)	10 (3.3%)	.032
Former	42 (10.2%)	30 (27.8%)	12 (3.9%)	.021
Prevalence of chronic disease[§]				
Hypertension	118	32	86	.093
Diabetes mellitus	47	15	32	.966
Heart	26	6	20	.293
Dyslipidemia	51	9	42	.012
Fall	45	8	37	.972
MMSE	25.8 ± 3.1	26.8 ± 2.5	25.5 ± 3.2	<.001
GDS	4.2 ± 3.8	3.9 ± 3.9	4.3 ± 3.7	.440
Body mass index ($kg \cdot m^{-2}$)	24.5 ± 3.0	23.6 ± 2.6	24.7 ± 3.1	.001
Body fat (%)	31.4 ± 6.5	23.3 ± 4.9	34.3 ± 4.2	<.001
Vitamin D ($ng \cdot mL^{-1}$)	20.1 ± 9.4	20.7 ± 8.3	29.9 ± 9.6	.702
Arm curl (no. of reps)	20.0 ± 5.3	21.9 ± 6.2	19.4 ± 4.8	<.001
Chair stand up for 30s (no. of stands)	16.1 ± 4.7	17.8 ± 5.3	15.4 ± 4.8	<.001
Back scratch (cm)	-11.3 ± 14.2	-18.4 ± 15.2	-8.8 ± 12.8	<.01
Chair-sit-and-reach (cm)	8.7 ± 12.6	7.1 ± 13.5	9.3 ± 12.2	.129
Eight-foot-up-and-go (s)	6.0 ± 1.8	5.2 ± 1.3	6.2 ± 1.8	<.001
The 6-min walk (m)	92.8 ± 27.1	97.3 ± 18.9	91.1 ± 29.3	.045

[§]Chi-square tests were used to compare sex differences. Abbreviations: MMSE, Mini-Mental State Examination; GDS, geriatric depression scale; BMI, body mass index; BF, percent body fat.

cognitive function tests were determined. Variables found to be significant using a univariate analysis at p<0.05 were analyzed using multiple hierarchical regression. Because demographics may influence cognitive or physical function, the model controlled for age, sex, race, and education level. Also, because certain medical conditions may be associated with neurocognitive or physical function, the model accounted for the comorbidity index as described above. An unstandardized coefficient was used in the regression: for every unit (score) change in the SFT as well as serum vitamin D level, cognitive function changed by X units. Physical fitness measures and serum vitamin D levels were defined as independent variables, and MMSE score was defined as the dependent variable. The number of MMSE scores that were influenced by each of the six physical fitness measure scores and serum vitamin D levels were determined. Statistical significance was accepted at $p < 0.05$.

Results

Table 1 represents the demographic and physical characteristics of the 412 subjects included in the study. The average age of the study participants was 73.4 ± 5.6 years (range 62–91 years). Compared to women, men were older (74.4 ± 6.0 vs. 73.1 ± 5.4 years, p = 0.038) and had more years of education (10.2 ± 3.3 vs. 7.2 ± 3.6 years, $p < 0.001$). Along with lower body fatness, men had higher scores on the MMSE ($p < 0.001$), higher smoking rates ($p < 0.001$) and a higher incidence of dyslipidemia (p = 0.012) than women. With respect to physical fitness, men exhibited higher performance in upper ($p < 0.001$) and lower body strength ($p < 0.001$), agility ($p < 0.001$), endurance (p = 0.045), and lower and upper body flexibility ($p < 0.001$).

Table 2. Pearson's correlation coefficients between measured variables.

Variable	MMSE
Age	-.212 **
Sex	-.187 **
Education	.559 **
GDS	-.199 **
Body mass index	-.138 **
Body fat	-.249 **
Vitamin D	.250 **
Comorbidity index	.082
Arm curl	.257 **
Chair stand up for 30 s	.152 **
Back scratch	.224 **
Chair-sit-and-reach	.262 **
Eight-foot-up-and-go	-.443 **
The 6-min walk	.255 **

MMSE: mini-mental state examination; GDS: geriatric depression scale; SFT: senior fitness test. *p<0.05; **p<0.01; p<0.001*** using Pearson correlation analyses.

Table 2 represents the correlation coefficients between the measured variables. Age, sex, GDS, and body fatness parameters were negatively associated with MMSE-based cognitive function. On the other hand, education, serum vitamin D levels, and physical fitness were positively associated with MMSE-based cognitive function.

Table 3. Influence of physical fitness and serum vitamin D levels on MMSE-based cognitive function.

Independent variables	β (95% CI)	R^2	ΔR^2
Step 1		.425 ***	.410 ***
Age	-.100 * (-.188 – -.012)		
Sex	-.358 (-1.546 – .830)		
Education	.515 *** (.388 – .642)		
GDS	-.123 * (-.247 – .001)		
Step 2		.426 ***	.403
Age	-.102 * (-.191 – -.013)		
Sex	-.833 (-3.250 – 1.583)		
Education	.519 *** (.389 – .649)		
GDS	-.127 * (-.253 – -.001)		
BMI	-.088 (-.428 – .252)		
Percent body fat	.060 (-.194 – .313)		
Step 3		.513 ***	.468 **
Age	-.021 (-.116 – .075)		
Sex	-.639 (-2.981 – 1.703)		
Education	.435 *** 0.303 – .567)		
GDS	-.065 (-.191 – .061)		
BMI	-.012 (-.351 – .327)		
Percent body fat	.044 (-.206 – .293)		
Arm curl	.010 (-.107 – .126)		
Chair stand up for 30 s	-.018 (-.178 – .141)		
Back scratch	.025 (-.010 – .061)		
Chair-sit-and-reach	-.006 (-.056 – .044)		
Eight-foot-up-and-go	-.368 * (-.697 – -.039)		
The 6-min walk	.027 * (.004 – .050)		
Vitamin D	.061 * (.014 – .108)		

* $p < 0.05$; *** $p < 0.001$ using multiple hierarchical regression. The control variables were age, sex, education level, GDS, and comorbidity index. Abbreviations: β, standardized regression coefficient; CI, confidence interval; ΔR^2, change in R^2; GDS, geriatric depression scale; MMSE, Mini-Mental State Examination.

Further analysis using a multiple hierarchical regression model was performed to examine the physical performance measures and serum vitamin D levels that seemed to be predictors of cognitive performance based on MMSE scores (Table 3). The final regression model showed that agility, as assessed using eight-foot-up-and-go (partial R^2 = -0.184, p = 0.029); endurance, as assessed using the 6 min walk test (partial R^2 = 0.191, p = 0.022); and serum vitamin D levels (partial R^2 = 0.210, p = 0.012) were significant predictors for MMSE-based cognitive function after controlling for demographics (i.e., age, sex, and education), GDS, body fatness parameters (i.e., body mass index and percent body fat), and the comorbidity index (i.e., summation of self-reported illnesses including hypertension, heart disease, diabetes, cancer, fracture, and respiratory disease).

Discussion

In this study, we investigated the relationships of physical fitness and serum vitamin D levels with cognition in elderly Koreans. We found that agility and endurance domains of physical fitness along with serum vitamin D levels were positively associated with global cognitive function based on MMSE scores.

Our results are consistent with previous studies reporting a significant association between physical performance and cognitive function in older adults (Bankevoort et al., 2013; Volkers and Scherder, 2014). Huh et al. (2011) showed that executive function based on the lexical fluency test was associated with performance-oriented mobility assessment scores and isokinetic muscle strength in a population-based sample of 629 Korean adults aged 65 or older. In the EPIDOS cohort study involving 7421 older women living in five French cities, Annweiler et al. (2011) found that, compared to their cognitively healthy counterparts, women with cognitive impairment had poor performance in dynamic balance and functional mobility, as assessed by the five-times-sit-to-stand test. Fitzpatrick et al. (2007) found a positive relationship between cognitive function and physical performance in 3035 healthy mobile participants of the Ginkgo Evaluation of Memory Study and reported that poor walking performance was significantly associated with cognitive impairment in healthy older adults. Similar to cross-sectional studies, prospective studies have also reported an association between poor physical performance (including walking, balance, chair stand, and grip strength) (Opewal et al., 2014) or neurologic gait abnormalities (Franklin et al., 2015) and the development of all-cause (Legrand et al., 2014) or vascular dementia (Bullain et al., 2013). A gait that slowed over time was significantly associated with persistent cognitive impairment (Mielke et al., 2013) as well as decline in several other geriatric outcome measures including global health, falls, and new difficulties with activities of daily living (Kolke et al., 2014).

Growing evidence suggests that structural changes of the brain in older people are related to physical performance such as gait dysfunction (Callisaya et al., 2013), postural instability (Kido et al., 2010), and lack of cardiorespiratory fitness (Vidonia et al., 2012). These results suggest that brain structure and function is associated with physical function. In a cross-sectional study involving 22 younger and 36 older women, Dupuy et al. (2015) investigated the neurophysiological changes in cerebral oxygenation associated with physical fitness level and executive functions and found that higher fit women had faster reaction times and greater cerebral oxygenation in the right inferior frontal gyrus than lower fitness women, regardless of age. Other studies reported that lower brain volume in the prefrontal areas was associated with a slower gait in high-functioning or cognitively healthy older adults (Annweiler et al., 2014). Neuroimaging studies have indicated that gait requires complex visual-sensorimotor coordination and is associated with activation of the medial frontoparietal region, including the primary sensory and motor areas, supplementary motor area, lateral premotor cortex, cingulate cortex, superior parietal lobule, precuneus, and the infratentorial region including the dorsal region (Annweiler et al., 2014; Nonekes et al., 2015).

The positive association between serum vitamin D and MMSE scores found in this study has also been supported by previous findings. Wilkins et al. (2006) found a significant positive association between low serum vitamin D levels and low scores on global cognitive performance in older adults. In a cross-sectional study, Wilkins et al. (2009) found that vitamin D deficiency was significantly associated with worse cognitive performance in older African Americans. Oudshoorn et al. (2008) reported a significant positive relationship between serum vitamin D and MMSE scores in patients with AD. In the Tromsø Study involving 5980 Norwegian inhabitants, Jorde et al. (2015) found that subjects with the highest serum 25(OH)D quartile had ~5% better performance on the cognition tests (i.e., word recall, digit-symbol coding, finger tapping, Mini Mental State Examination) than subjects with the lowest serum 25(OH)D quartile. Together, those findings suggest that vitamin D insufficiency along with poor physical fitness may be another modifiable risk factor for cognitive declines with normal aging.

Although little is known about the mechanisms by which serum vitamin D benefits cognition in older adults, experimental animal studies suggest that the active form of vitamin D has multiple biological effects on the central nervous system (CNS). For example, vitamin D functions as a neurotrophic factor by upregulating various growth factors within the CNS, including nerve growth factor (Brown et al., 2003), glial cell-derived neurotrohic factor, transforming growth factor beta 2, and neurotrophins 3 and 4 (Airavaara et al., 2003). On the other hand, vitamin D deficiency at early stages of the life cycle in rats induces structural alterations in the cortex and lateral ventricles (Harms et al., 2012) and behavioral modifications (Altemus et al., 1987). Vitamin D also protects from inflammation-induced degeneration of neurons by inhibiting the production of TNF-alpha and IL-6 (Lefebvre et al., 2003), and by preventing lipid peroxidation and apoptosis (Lin et al., 2005), decreasing reactive oxygen species generation and increasing glutathione levels (Li et al., 2008), and reversing mitochondrial dysfunction under conditions of oxidative stresses (Vos et al., 2010). Further, vitamin D may protect from glucocorticoid-induced neurodegeneration (Obradovic et al., 2006) and may prevent alterations in calcium-dependent electrophysiological functions in the hippocampus (Brewer et al., 2006).

Considering the cross-sectional nature of the current study, however, additional research is necessary to support a causal relationship between modifiable lifestyle factors such as physical fitness and serum vitamin D levels with cognitive function in the elderly. In addition, further studies are needed for a better understanding of the underlying mechanisms that mediate the protective effect of physical fitness and serum vitamin D levels on cognitive decline with normal aging. In particular, intervention studies will be very important as they have the potential to identify and verify long-term beneficial effects of physical fitness and serum vitamin D levels on brain as well as overall general health in older adults.

Conclusion

In this study, we found that the agility and endurance domains of physical fitness and serum vitamin D levels were independent predictors for MMSE scores. Thereby, the current findings of the study suggest that promotion of physical fitness and vitamin D supplementation should be key lifestyle interventions to prevent cognitive declines with normal aging.

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Key points

- Cognitive declines are associated with normal aging as well as modifiable lifestyle risk factors, and there is an increasing need to identify the modifiable risk factors for the onset of cognitive declines and to provide evidence-based strategies for healthy and successful aging.
- In Korea, little is known about the relationships of physical fitness and serum vitamin D with cognitive function in older adults, and we determined the associations between a) serum vitamin D levels and cognitive function and b) physical fitness and cognitive function among community-dwelling elderly Koreans.
- The current findings of the study suggest that agility and endurance domains of physical fitness along with serum vitamin D were significant predictors for global cognitive performance after controlling for covariates.

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