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The correlation of plasma Aβ42 levels, depressive symptoms, and cognitive function in the Korean elderly

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ABSTRACT

Objectives: This study aims to investigate whether plasma amyloid beta 1–42 (Aβ42) levels are associated with depressive symptoms and/or cognitive function in community dwelling elderly.
Methods: Subjects were 123 participants of a population-based project designed to screen community dwelling elderly older than 65 years old in Gangwon Province, Korea, for the early detection of depression and dementia. Symptoms of depression were assessed using the SGDS-K (Short Geriatric Depression Scale-Korean version), and the MMSE-KC (Mini-Mental State Examination-Korean version) was used to assess cognitive function. Plasma Aβ42 levels were measured with the human amyloid beta ELISA Kit.
Results: The elderly with depressive symptoms (SGDS-K score ≥ 8) had higher plasma Aβ42 levels than those without depressive symptoms (SGDS-K score < 8) ($p<0.1$). Plasma Aβ42 levels were positively correlated with SGDS-K scores ($p<0.05$). However, MMSE-KC scores were inversely associated with plasma Aβ42 levels ($p<0.01$). Plasma β42 levels were also associated with MMSE-KC ($F=8.07$, $p<0.01$) and SGDS-K ($F=4.53$, $p<0.05$) by generalized linear model (GLM) with controlling age, sex and education.
Conclusion: Plasma Aβ42 levels were associated with depressive symptoms and cognitive function in community dwelling elderly. The present study supports the possibility that plasma Aβ may be involved in the development of late onset depression.

1. Introduction

Any studies have revealed an association between cognitive impairment, dementia and depressed mood (Butters et al., 2008, Steffens et al., 2006). In a meta-analysis of case–control studies and prospective longitudinal studies of depression and dementia (Jorm, 2001), it was suggested that, when compared with non-depressed controls, depressed people have nearly twice the risk of developing dementia (Pomara et al., 2006).

Elevated plasma amyloid beta 1–42 (Aβ42) levels in cognitively-intact elderly have been linked to increased risks of Alzheimer's disease (AD) (Mayeux et al., 1999, Mayeux et al., 2003). A longitudinal study indicated that elevated plasma Aβ42 levels and greater reduction of Aβ42 levels were associated with cognitive decline (Pomara et al., 2006, Blasko et al, 2010).

Platelet activation is believed to be a major source of plasma Aβ (Chen et al., 1995, Li et al., 1994), and depressed patients exhibit exaggerated platelet reactivity (Markovitz et al., 2000, Musselman et al., 1996, Musselman et al., 2000). These findings suggest that plasma Aβ levels may be elevated in depressive patients, and these elevated plasma Aβ levels may increase susceptibility to dementia or cognitive decline.

Interestingly, recent studies reported that plasma Aβ42 levels were elevated in geriatric depression relative to controls (Pomara et al., 2006) and higher plasma Aβ42 levels independently predicts both late-onset depression and Alzheimer disease {Blasko #1863}.On the other hand, another study showed that depressive symptoms were associated with low plasma Aβ42 (Qiu et al., 2007, Sun et al., 2009). In addition, it was reported that low plasma Aβ42 levels (low Aβ42/Aβ40) was associated with increased risk of mild cognitive impairment and AD (Graff-Radford et al., 2007).

Abbreviation: Aβ42, amyloid beta 1–42; AD, Alzheimer's disease; MMSE-KC, Mini-Mental State Examination-Korean version; SGDS-K, Short Form Geriatric Depression Scale-Korean version.

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These contradictory findings and the lack of information about the relationship between plasma Aβ42 levels and elderly depression or cognitive function highlight the need for further studies to explore the possibility of using plasma Aβ42 levels as a biomarker for depression and cognition in the elderly.

This study, therefore, aims to investigate whether plasma Aβ levels are associated with depressive symptoms and/or cognition in community dwelling elderly.

2. Method

2.1. Study population and procedure

The subjects were 123 participants of a population-based project designed to screen community dwelling elderly older than 65 years old for the early detection of depression and dementia in the Hwacheon and Chulwon areas of Gangwon Province, Korea.

The participants visited local health care clinics for the assessment of their cognitive function and depressive symptoms. The 123 subjects enrolled in the present study were selected from those participants in the population-based screening project who gave approval for the taking of blood samples to measure plasma Aβ42 levels.

All participants were required to be physically able to be interviewed and to have sufficient vision and hearing to read and hear the content of screening test. All field investigators were trained in the survey methods and scales used in the study by a board-certified neuropsychiatrist, to optimize the standardization of procedures. The survey was conducted by a personalized face-to-face interview.

The study was approved by the Institutional Review Board of the Chuncheon Sacred Heart Hospital.

2.2. Measures

2.2.1. Depression

Depressive symptoms were assessed by using the Short Form Geriatric Depression Scale-Korean version (SGDS-K) (Bae and Cho, 2004), and a SGDS-K score of eight or greater was used as the cut-off point for clinical depression. This SGDS-K cut-off point had a sensitivity of 0.85 and a specificity of 0.70 for the DSM-III-R diagnosis of major depression by a board-certified psychiatrist (Bae and Cho, 2004).

2.2.2. Cognitive function

Cognitive function was assessed by the validated Korean version of Mini-Mental State Examination (MMSE-KC) which was developed as part of the Korean version of the CERAD Assessment Packet (Lee et al., 2002b). Scores ranged from 0 to 30, with higher scores indicating better cognition (Lee et al., 2002a).

2.2.3. Aβ42 measurement

Blood samples were centrifuged immediately after blood was drawn. Plasma samples were stored at −80 °C until use. The sandwich Aβ42 ELISA kit was used (BioSource, California, USA). The minimum detectable dose of Aβ42 is 10 pg/mL. The mean of the coefficient of within-assay variation was 4.0% for Aβ42. Several samples were assayed 24 times in multiple assays to determine precision between assays. The coefficient of inter-assay variation was 6.8% for Aβ42.

2.3. Statistical analysis

The Statistical Package for the Social Sciences Version 13.0 program (SPSS, Chicago, IL) was used for all data analyses. Spearman correlation and generalized linear model were used to explore the relationships between the plasma Aβ42 levels, depression and cognitive function. Differences between depressed and non-depressed participants in terms of various demographic variables (age, sex, and education), SGDS-K and MMSE-KC scores, and plasma Aβ42 levels were analyzed using Student's *t* test, chi-square test or Mann–Whitney tests.

Table 1
Demographic data of study population.

		Total subject (N = 123)
Mean age, years (SD)		76.0 (6.83)
Gender (%)	Male	91 (74.0)
	Female	32 (26.0)
Marital status (%)	Married	50 (40.7)
	Remarried	1 (0.8)
	Widowed	72 (58.5)
Medical disease (%)	Hypertension	31 (25)
	Diabetes mellitus	8 (6.5)
	Cardiovascular disease	6 (4.9)
Educational years (SD)		2.7 (3.35)
MMSE-KC (SD)		20.9 (4.26)
SGDS-K (SD)		7.2 (4.28)
Aβ42 level, pg/ml (SD)		18.9 (0.93)

Data value; mean (SD).

3. Results

The demographic characteristics of the study population are summarized in Table 1. The average MMSE-KC score, SGDS-K score, and plasma Aβ42 level for all subjects (n = 123) were 20.9 (SD = 4.26), 7.2 (SD = 4.28), 18.9 (SD = 0.93) respectively. The mean age and educational years of our study population are 76.0 (SD = 6.83) and 2.7 (SD = 3.35), respectively. MMSE-KC score 20.9 in Korean male or female (76 years old) with 2.7 educational year represents −1.0.1 Z-score (13.6%) (male; mean 24.5 ± 3.2) and −0.0 Z-score (50%) (female; mean 21.2 ± 4.1). In the age of 76.0 years with 2.7 educational year in Korean elderly, the threshold point for dementia (Z score < −2.0 or <5%) in MMSE-KC scale may be expected to be 18.0 (male) and 13.0 (female) of MMSE-KC score.

Plasma Aβ42 levels were negatively correlated with MMSE-KC scores ($r = -0.25$, $p < 0.01$), and positively correlated with SGDS-K scores ($r = 0.18$, $p < 0.05$) in spearman correlation analysis. Plasma β42 levels were also associated with MMSE-KC ($F = 8.07$, $p < 0.01$) and SGDS-K ($F = 4.53$, $p < 0.05$) by generalized linear model (GLM) with controlling age, sex and education (Table 2).

As previously suggested (Bae and Cho, 2004), study subjects were divided into depression (SGDS-K score of 8 or greater) or non-depression groups (SGDS-K score of 7 or less). The depression group showed significantly higher plasma Aβ42 levels than the non-depression group ($p < 0.1$), but there was no significant difference in MMSE-KC scores (Table 3).

4. Discussion

This study investigated the relationships between depressive symptoms, cognitive function and plasma Aβ levels in community dwelling elderly and showed that plasma Aβ42 levels were positively

Table 2
The relationship of the plasma Aβ42 level with depression and cognitive function.

Dependent variable	Independent variable	Type III sum of squares	F	P
MMSE-KC score	Age	60.42	4.79	0.03
	Sex	3.88	0.31	0.58
	Education	285.66	2.06	0.03
	Aβ42	101.75	8.07	0.005
SGDS-K score	Age	0.19	0.87	0.35
	Sex	0.82	3.79	0.05
	Education	3.16	1.32	0.22
	Aβ42	0.98	4.53	0.04

Values are from generalized linear model.