

Correlation between brain-derived neurotrophic factor and cognitive function in older adults

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ABSTRACT

Aim Brain-derived neurotrophic factor (BDNF) plays a crucial role in supporting neuronal survival, promoting neurogenesis, and enhancing synaptic plasticity, all of which are vital for cognitive health. The aim of this study was to investigate the relationship between BDNF levels and cognitive impairment in the elderly population.

Methods This was a cross-sectional study involving older adults at a social service care. Cognitive function was assessed using the Montreal Cognitive Assessment-Indonesian Version (MoCA-INA). BDNF levels were measured in peripheral blood samples using the enzyme-linked immunosorbent assay.

Results Of 88 participants (50 females 38 males) with a median age of 69.5 years, 71 (80.7%) had cognitive impairment. The median MoCA-INA score was 15.0. The most affected cognitive domain was abstraction, in 87 (98.9%) patients. The mean BDNF level was 1.55 (± 0.62) ng/mL with 50 (56.8%) patients having normal level. A weak positive correlation was found between BDNF level and performance in the visuospatial-executive ($r = 0.232$; $p = 0.029$) and abstraction domains ($r = 0.249$; $p = 0.019$). BDNF levels were significantly lower in those with cognitive impairment compared to those with normal cognitive function ($p = 0.029$).

Conclusion A correlation between BDNF levels and cognitive function, particularly in the visuospatial-executive and abstraction domains, highlighting the potential role of BDNF in cognitive decline in aging.

Keywords: aging, biomarkers, cognition, memory, nerve growth factors

INTRODUCTION

Aging is associated with various physiological changes, including a decline in brain function due to neuronal atrophy, which can lead to degenerative diseases, particularly those that impair cognitive function (1). As cognitive abilities decline, daily activities become increasingly challenging, diminishing the quality of life for older adults (2). Neural aging is a complex process influenced by genetic and environmental factors, including health, life experiences, diet, and physical activity (3). As neurons age, they lose regenerative capacity, leading to cognitive decline in areas such as learning, memory, and decision-making. This is accompanied by structural changes, such as atrophy of the gyri and expansion of the sulci and ventricles (4). The cerebral cortex, responsible for higher cognitive functions, is particularly vulnerable to neuronal loss during aging (5).

A key protein involved in maintaining brain health during aging is brain-derived neurotrophic factor (BDNF) (6). BDNF supports the differentiation, survival, and maturation of neurons, offering neuroprotective effects. It also plays a crucial

role in regulating energy balance. BDNF is found in several areas of the brain, including the olfactory bulb, cortex, hippocampus, basal forebrain, hypothalamus, and brainstem (7). Importantly, peripheral BDNF levels mirror those in the central nervous system, and reductions in BDNF have been linked to several age-related neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, as well as conditions like diabetes, depression, and schizophrenia (8).

BDNF is particularly important for brain plasticity in the hippocampus and cortex - regions critical for learning and memory (7). Research shows that BDNF levels can be influenced by activities such as learning and physical exercise, both of which stimulate its production and may help mitigate cognitive decline (9). However, as cognitive abilities naturally decline with aging, particularly in memory and learning, exploring the relationship between BDNF levels and cognitive function in normal aging is essential (10). Understanding this connection could provide valuable insights into potential interventions to maintain cognitive health in older adults.

While existing research has highlighted the neuroprotective role of BDNF and its potential to mitigate cognitive decline (6,7,8,10), there remains a gap in understanding how fluctuations in BDNF levels correspond to specific cognitive abilities in older adults. The aim of this study was to investigate the correlation between BDNF level and cognitive function in older adults.

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PARTICIPANTS AND METHODS

Participants and study design

This was a cross-sectional study conducted at the Older Adult Social Service in Binjai, North Sumatra, Indonesia from February to July 2024. All older adults presented in the service aged ≥ 60 years with a consent to participate were included. Exclusion criteria were subjects with uncorrected visual and/or hearing impairments that could impair the cognitive assessment, subjects with history of stroke, dementia or other degenerative diseases such as Parkinson's disease.

All participants provided informed consent before taking part in the study.

The research was carried out following ethical guidelines and received an approval from the Ethics Committee of the Faculty of Medicine at Universitas Sumatera Utara (No. 380/KEPK/USU/2024).

Methods

Cognitive function was assessed using the MoCA-Ina (Montreal Cognitive Assessment – Indonesian version), a widely used screening tool for detecting cognitive impairment in older adults. Scores range from 0 to 30 was used, with higher scores indicating better cognitive performance (11).

The BDNF levels were measured in peripheral blood samples using the enzyme-linked immunosorbent assay (ELISA), a highly sensitive method for detecting and quantifying specific proteins. Blood samples were collected from each participant, processed to obtain serum, and the BDNF concentration was quantified using a commercially available human BDNF ELISA kit (Elabscience, Wuhan/China). BDNF levels were expressed in ng/mL and were then compared with the MoCA-Ina scores to explore the potential relationship between BDNF levels and cognitive function.

Statistical analysis

Descriptive statistics were used to summarize participant characteristics and BDNF levels. To assess the relationship between BDNF levels and cognitive function, a comparative test (e.g., independent t-test or Mann-Whitney U test) was performed. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 88 older adult participants were included in the study. The median age was 69.5 years (range 61–92). Of the participants, 38 (43.2%) were males, and 50 (56.8%) were females. The participants mostly had at least some formal education, with 20 (22.7%) having completed elementary school and another 20 (22.7%) completing junior high school. A smaller proportion had senior high school education, 25 (28.4%), and only six (6.8%) had attended college. Regarding health status, only three (3.4%) participants reported having diabetes, and four (4.5%) had hypertension, while the remaining participants were free from these conditions (Table 1).

Cognitive function, as assessed by the MoCA-Ina revealed that 71 (80.7%) participants exhibited abnormal cognitive function, while only 17 (19.3%) had normal cognitive function. The total MoCA-Ina scores had a wide range, with a median score of 15.0 (range: 2–28). When broken down by cognitive domains,

Table 1. Demographic characteristics of 88 older adults

Characteristic	No (%) of participants	
	Normal	Abnormal
Median age (Min - Max) years	69.5 (61 – 92)	
Gender		
Male	38 (43.2)	
Female	50 (56.8)	
Education		
Non-Formal	17 (19.3)	
Elementary School	20 (22.7)	
Junior High School	20 (22.7)	
Senior High School	25 (28.4)	
College	6 (6.8)	
Marital status		
Not married	15 (17)	
Married	63 (71.6)	
Divorced	10 (11.4)	
Diabetes		
YES	3 (3.4)	
NO	85 (96.6)	
Hypertension		
YES	4 (4.5)	
No	84 (95.5)	

Min, Minimal; Max, Maximum;

the **Visuospatial-Executive domain** showed significant impairment, with 81 (92%) participants scoring abnormally (median score = 2, range: 0–5). Similarly, the **attention domain** and **language domain** were also predominantly abnormal, affecting 83 (94.3%) and 81 (92%) participants, respectively, with median scores of 2 (range: 0–6) and 1 (range: 0–3). In the **memory domain**, 80 (90.9%) participants scored abnormally, with a median score of 0.5 (range: 0–5). The **abstraction domain** showed the least impairment, with 87 (98.9%) participants scoring abnormally, though the median score was 0 (range: 0–2). Lastly, the **orientation domain** had a median score of 4.0 (range: 0–6), with 63 (71.6%) participants showing abnormal performance (Table 2).

Table 2. Characteristics of cognitive function in 88 older adults

Variable	No (%) of participants		
	Normal	Abnormal	Median (Min-Max)
MoCA-Ina Total Score	17 (19.3)	71 (80.7)	15.0 (2-28)
Visuospatial-Executive Domain	7 (8)	81 (92)	2.0 (0-5)
Domain Naming	56 (63.6)	32 (36.4)	3.0 (0-3)
Attention Domain	5 (5.7)	83 (94.3)	2.0 (0-6)
Language Domain	7 (8)	81 (92)	1.0 (0-3)
Domain of Abstraction	1 (1.1)	87 (98.9)	0 (0-2)
Memory Domain	8 (9.1)	80 (90.9)	0.5 (0-5)
Orientation Domain	25 (28.4)	63 (71.6)	4.0 (0-6)

Min, Minimal; Max, Maximum; MoCA-Ina, Montreal Cognitive Assessment-Indonesian Version

The analysis of BDNF levels based on age, gender, ethnicity, diabetes, and hypertension revealed no significant differences (p ranged from 0.198 to 0.973). For instance, participants < 70

years of age had a mean BDNF level of 1.61 ng/mL (SD=0.68), while those aged ≥ 70 had a mean BDNF level of 1.49 ng/mL (SD=0.56) ($p=0.359$). Similarly, BDNF levels did not differ significantly between males (mean=1.58 ng/mL, SD=0.69) and females (mean=1.53 ng/mL, SD=0.54 ($p=0.692$)). However, a significant difference in BDNF levels was observed between those with normal and abnormal cognitive function as assessed by the MoCA-Ina. Participants with normal cognitive function (median=1.86 ng/mL, range 0.59 – 2.68) had higher BDNF level compared to those with abnormal cognitive function (mean=1.47 ng/mL, SD=0.60) ($p=0.029$) (Table 3).

Table 3. Characteristics of brain-derived neurotrophic factor (BDNF) level in older adults

Variable	No (%) of participants	BDNF (ng/mL)	p
		Mean (SD)	
Age (years)			
<70	44 (50)	1.61 (± 0.68)	0.359
≥ 70	44 (50)	1.49 (± 0.56)	
Gender			
Male	38 (43.2)	1.58 (± 0.69)	0.692
Female	50 (56.8)	1.53 (± 0.54)	
		Median (Min - Max)	Mean (SD)
Diabetes			
Yes	3 (3.4)	1.74 (1.12 – 2.28)	0.621
No	85 (96.6)	1.54 (± 0.62)	
Hypertension			
Yes	4 (4.5)	1.73 (0.82 – 2.41)	0.681
No	84 (95.5)	1.54 (± 0.62)	
Cognitive Function, MoCA-Ina			
Normal	17 (19.3)	1.86 (0.59 – 2.6)	0.029
Abnormal	71 (80.7)	1.47 (± 0.60)	

SD, Standard deviation; Min, Minimal; Max, Maximum; MoCA-Ina, Montreal Cognitive Assessment-Indonesian Version

Table 4 examines the relationship between BDNF levels (categorized as <1.59 ng/mL and ≥ 1.59 ng/mL) and cognitive function. Of the 88 participants, 37 (42%) had BDNF levels below 1.59 ng/mL, while 51 (58%) had levels above this threshold. Among those with BDNF levels below 1.59 ng/mL, 28 (75.7%) participants had abnormal cognitive function, while 24.3% (nine participants) had normal cognitive function. In contrast, 43 (84.3%) participants with BDNF levels ≥ 1.59 ng/mL exhibited abnormal cognitive function, while eight (15.7%) had normal cognitive function. Despite these trends, the difference between the two groups was not statistically significant ($p = 0.311$) (Table 4).

Table 4. Brain-derived neurotrophic factor (BDNF) level and cognitive function

BDNF level*	No (%) of participants with cognitive function			p
	Normal	Abnormal	Total	
<1.59 ng/mL	9 (24.3)	28 (75.7)	37 (100)	0.311
≥ 1.59 ng/mL	8 (15.7)	43 (84.3)	51 (100)	
Total	17 (19.3)	71 (80.7)	88 (100)	

*Limit: <1.59 ng/mL

Spearman’s correlation test was conducted to assess the relationship between BDNF level and MoCA-Ina scores. The analysis revealed a weak positive correlation between BDNF level and cognitive function, but this was not statistically significant ($r=0.149$, $p=0.166$). This suggested that, while there was a trend toward higher BDNF level in participants with better cognitive performance, the correlation was not strong enough to draw definitive conclusions.

The ROC curve was used to evaluate the diagnostic ability of BDNF level in distinguishing between normal and abnormal cognitive function. The area under the curve (AUC) and other diagnostic parameters from the ROC analysis will help further assess the potential of BDNF as a biomarker for cognitive impairment in the older adults. Laboratory analysis showed a mean BDNF concentration of 1.55 ± 0.62 ng/mL. A cut off value of 1.59 ng/mL was used to categorize BDNF level as low (<1.59 ng/mL) or normal/high (≥ 1.59 ng/mL). Of the 88 participants, 51 (58%) had BDNF levels ≥ 1.59 ng/mL. Statistical analysis revealed a significant difference in BDNF levels between participants with normal cognitive function and those with impaired cognitive function ($p=0.029$). The sensitivity and specificity of using a BDNF threshold of 1.59 ng/mL for identifying impaired cognitive function were 60.6% and 64.7%, respectively (Figure 1).

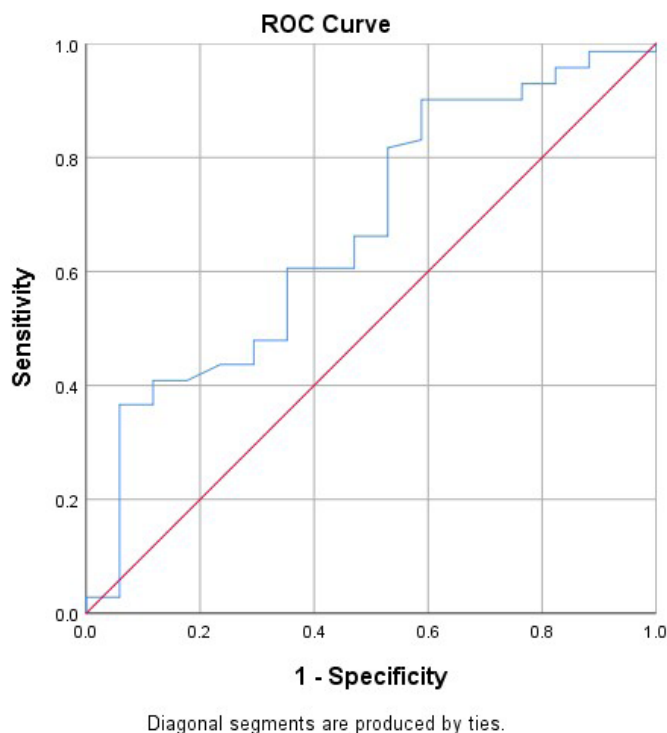


Figure 1. Receiver operating characteristic (ROC) curve for brain-derived neurotrophic factor level (BDNF)

DISCUSSION

This study provides valuable insights into the demographic characteristics, cognitive function, and the potential relationship between BDNF level and cognitive performance in the older adult population. The results highlight the complex interplay between age, health status, cognitive impairment, and biomarkers such as BDNF.

The demographic profile of the study participants reflects a typical older adult population in terms of age, gender, education, and employment. The median age of 69.5 years is consistent with the aging population in Indonesia, where a significant

proportion of people are approaching or have surpassed the age of 60 (12). A majority of participants were females (56.8%), which aligns with global trends showing that females generally outlive males in most populations (13). Regarding education, the sample represented varying levels of formal education, with the highest proportion having completed elementary or junior high school (45.4%). This educational distribution may influence cognitive function, as lower educational attainment is often associated with higher risks of cognitive decline in later life (14). Our results showed that a high proportion of older adult individuals are self-employed (73.9%), which might reflect a form of continued engagement in mental and physical activities that could impact brain health (4,9).

The cognitive function data from the MoCA-Ina (Montreal Cognitive Assessment - Indonesian version) revealed a striking prevalence of cognitive impairment, with 80.7% of participants showing abnormal cognitive function. This is consistent with previous research that suggests cognitive decline affects a large proportion of the older adult population, especially as they age (15,16). The data indicate significant impairments across most cognitive domains, particularly visuospatial-executive, attention, and language, which are commonly affected in neurodegenerative conditions such as Alzheimer's disease and other dementias (17). These findings reinforce the need for effective early screening tools like MoCA-Ina to detect cognitive deficits in older adults.

While the demographic data provided some insights into the characteristics of the participants, the primary objective was to explore the relationship between BDNF level and cognitive function. The analysis of BDNF level showed that there were no significant differences based on most demographic factors such as age, gender, or health status (diabetes or hypertension), which is in line with some studies suggesting that BDNF level can be relatively stable across these variables in older adults (18,19). However, a significant difference was observed in cognitive function. Participants with normal cognitive function had higher BDNF levels compared to those with abnormal cognitive function, consistent with previous studies (20,21). Despite this difference, the relationship between BDNF level and cognitive function was not straightforward. Our results suggest that while BDNF may play a role in cognitive health, its ability to predict cognitive function in the older adults is not definitive. This could be due to the multifactorial nature of cognitive decline, where genetics, lifestyle factors, and other biomarkers may also contribute to the observed deficits (22). Spearman's correlation test further explored the relationship between BDNF levels and MoCA-Ina scores, revealing a weak positive correlation ($r = 0.149$, $p = 0.166$). This finding indicates that, while higher BDNF levels might be slightly associated with better cognitive performance, the relationship is not strong enough to support BDNF as a reliable predictor of cognitive function on its own. Other factors, such as inflammation, vascular health, or additional neurotrophic factors, may play a more substantial role in cognitive decline (23).

The Receiver Operating Characteristic curve analysis provided an opportunity to evaluate the diagnostic ability of BDNF levels in identifying normal versus abnormal cognitive function. The ROC curve is particularly useful for determining the threshold at which BDNF level may serve as an effective biomarker for cognitive decline. Although the results indicated

trends in BDNF levels and cognitive function, the lack of a strong correlation between BDNF and MoCA-Ina scores suggests that BDNF may not be a sufficient standalone marker for diagnosing cognitive impairment in this population. It is possible that BDNF could be more valuable in conjunction with other biomarkers or neuroimaging techniques to improve the accuracy of early diagnosis.

This study has several limitations that should be considered when interpreting the findings. First, the **cross-sectional design** limits the ability to establish causal relationships between BDNF levels and cognitive function. Longitudinal studies are needed to assess changes in BDNF and cognitive performance over time. Second, BDNF levels were measured **only in serum**, which may not accurately reflect central nervous system activity; cerebrospinal fluid levels or neuroimaging markers might provide a more direct measure of brain health. Third, the study did not examine **potential confounding factors** such as physical activity, nutritional status, sleep quality, or psychosocial stress—all of which can influence both BDNF expression and cognitive performance. Finally, the use of a **single cognitive screening tool (MoCA-Ina)**, while practical, may not fully capture the complexity of cognitive function across different domains.

Further studies should aim to clarify the role of BDNF in the context of other neurodegenerative markers, such as tau, amyloid-beta, or inflammatory cytokines, which may work synergistically with BDNF to influence cognitive function. Longitudinal studies examining changes in BDNF level over time and their relationship with the progression of cognitive decline could also provide more robust evidence on the utility of BDNF as a predictive biomarker for conditions like Alzheimer's disease and other forms of dementia.

In conclusion, this study underscores the high prevalence of cognitive impairment among the older adults and suggests that BDNF levels may be weakly associated with cognitive function.

AUTHOR CONTRIBUTIONS

Conceptualization, ERNS and FIF.; Methodology, ERN, FIF, TA.; Supervision, ASR; Data curation, ERNS and FIF; Writing – original draft preparation, ERNS and FIF; Investigation, ERNS and FIF; Writing – review & editing, FIF; Formal analysis, ERNS and TA. All authors have read and agreed to the published version of the manuscript.

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