

Correlation Between Serum BDNF Levels and Specific Cognitive Domains of MoCA-Ina in the Elderly with Mild Cognitive Impairment: An Exploratory Study

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Abstract

Brain-Derived Neurotrophic Factor (BDNF) decline is closely linked to Mild Cognitive Impairment (MCI) in the elderly. However, sociodemographic variables frequently confound this neurobiological relationship. This study evaluates the correlation between baseline serum BDNF levels and specific MoCA-Ina cognitive domains in MCI patients, adjusting for age and educational background. This exploratory cross-sectional study included 30 MCI subjects (≥ 60 years) at Dr. Mohammad Hoesin General Hospital. Serum BDNF was quantified via ELISA. Cognitive performance was measured across seven MoCA-Ina domains. Data were analyzed using Spearman's rank and non-parametric partial correlations. The initial unadjusted analysis showed no significant correlation between BDNF and total MoCA-Ina scores ($r = 0.282$, $p = 0.131$). However, statistically controlling for age and education revealed a significant moderate positive correlation ($r = 0.428$, 95% CI 0.07–0.69, $p = 0.023$). Domain-specific analysis demonstrated a significant positive correlation exclusively in the Abstraction domain ($r = 0.392$, 95% CI 0.02–0.67, $p = 0.039$). Adjusting for age and cognitive reserve unmasks a significant positive correlation between baseline serum BDNF, global cognition, and abstraction performance in MCI. Peripheral BDNF represents a potential biomarker for prefrontal cognitive dynamics when sociodemographic confounders are properly integrated.

Keywords: BDNF, Mild Cognitive Impairment, MoCA-Ina, Cognitive Domains, Elderly

1. Introduction

The physiological aging process naturally correlates with a gradual deterioration in functional and cognitive capacities.^{1,2} Within this spectrum, Mild Cognitive Impairment (MCI) acts as a vital intermediary stage, carrying an estimated 10-15% yearly probability of advancing to clinical dementia. The global prevalence of MCI exhibits substantial heterogeneity, with estimates spanning from 1.2% to 87%, heavily influenced by advanced age and diagnostic criteria in various clinical settings.^{3,4} Although elderly patients with MCI retain the ability to perform daily routines autonomously, the underlying cognitive deficits significantly elevate the risk of psychological distress and diminished overall well-being.⁵ Based on Indonesian internal medicine guidelines, comprehensive geriatric assessment is

paramount in addressing these transitional cognitive declines.⁶

The neurobiological underpinnings of cognitive deterioration in older adults are intrinsically linked to the depletion of essential neurotrophic factors. Brain-Derived Neurotrophic Factor (BDNF) acts as a pivotal protein that safeguards neuronal integrity, enhances synaptic plasticity, and supports broad intrinsic capacity, encompassing both cognitive and physical functionalities.⁷ Contemporary prospective evaluations confirm that diminishing baseline systemic BDNF concentrations directly precipitate accelerated cognitive decline and heighten the likelihood of transitioning into MCI.⁸ Furthermore, physiological aging inevitably provokes a gradual reduction in circulating BDNF, rendering the aging neural network

particularly susceptible to oxidative stress and functional vulnerability.^{7,9}

Human cognition comprises multiple interconnected domains, such as memory, attention, language, and executive problem-solving.¹⁰ In geriatric clinical practice, the Montreal Cognitive Assessment (MoCA) serves as a primary screening instrument to evaluate these diverse domains. Specifically, the adapted Indonesian version, the MoCA-Ina, exhibits high sensitivity and specificity in detecting MCI among the elderly population in Indonesia, making it a reliable diagnostic tool in various local clinical settings.^{11,12} By evaluating specific cognitive facets, this tool provides a comprehensive clinical profile essential for targeted neurobiological analysis.

From a neurobiological perspective, analyzing specific cognitive domains is clinically meaningful because BDNF expression and the brain's vulnerability to aging are highly regionalized. BDNF is known to be heavily concentrated in the hippocampus, a region critical for synaptic plasticity and memory consolidation, which corresponds to the delayed recall domain in clinical assessments. Furthermore, BDNF modulates neuronal development and dynamics in the prefrontal cortex, which governs executive functions and attention. Strengthening the rationale for domain-level analysis allows for a more granular understanding of how neurotrophic decline targets specific functional networks, which may be obscured when only global cognitive scores are evaluated.⁹

While previous research has established the association between BDNF and global cognitive decline, there is limited evidence detailing which specific cognitive domains are most strongly correlated with serum BDNF levels in the Indonesian elderly population. Therefore, this exploratory study aims to evaluate the correlation between baseline

serum BDNF levels and specific cognitive domains of the MoCA-Ina in elderly patients with MCI at Dr. Mohammad Hoesin General Hospital, Palembang.

2. Method

This study utilized a cross-sectional design, analyzing the baseline, pre-intervention data of elderly patients from a broader clinical trial evaluating the effect of Vitamin D supplementation on BDNF levels and cognitive function. The study was conducted at the Geriatric Outpatient Clinic of Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia, from August 2025 to January 2026. Because this was a sub-analysis utilizing pre-existing baseline data, the sample size ($n = 30$) was strictly constrained by the parent study's enrollment, rendering this an exploratory analysis. The study population consisted of 30 elderly subjects who fulfilled the inclusion criteria, including being aged ≥ 60 years and diagnosed with Mild Cognitive Impairment (MCI). Subjects were excluded if they were illiterate or had aphasia, Alzheimer's disease, Parkinson's disease, severe depression (Geriatric Depression Scale score >4), malignancies, or severe renal or hepatic impairment. Ethical approval was granted by the Health Research Ethics Committee of Dr. Mohammad Hoesin General Hospital (No. DP.04.03/D.XVIII.06.08/ETIK/182/2025), and written informed consent was obtained from all participants prior to their involvement in the study.

Peripheral venous blood samples (3 cc) were collected in the morning (08:00–10:00 AM) to determine serum BDNF levels. The serum BDNF concentration was quantitatively measured using the Enzyme-Linked Immunosorbent Assay (ELISA) method at the Laboratory of the Faculty of Medicine, Universitas Sriwijaya. Cognitive function was evaluated using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina).

For the purpose of this analysis, the total MoCA-Ina score was categorized into seven specific cognitive domains: visuospatial/executive, naming, attention, language, abstraction, delayed recall, and orientation.

Data processing and analysis were conducted using SPSS version 26.0 for Windows. The normality of the data distribution was assessed using the Shapiro-Wilk test. Normally distributed data (such as serum BDNF levels) were presented as mean $\pm$ standard deviation, while non-normally distributed or ordinal data (such as MoCA-Ina scores) were presented as medians with minimum and maximum values. Because the MoCA-Ina scores represent ordinal data and were not normally distributed, an initial unadjusted correlation analysis was performed using Spearman's rank correlation. To rigorously address the potential confounding effects of age and educational level highlighted in geriatric populations, a non-parametric partial correlation analysis was subsequently conducted. Age and educational level were selected as the primary control variables to represent the sociodemographic influence on cognitive reserve while maintaining sufficient degrees of freedom for the exploratory sample size. Other potential confounders, such as severe depression and major systemic comorbidities, were effectively addressed through strict exclusion criteria during participant recruitment. This was achieved by first transforming the continuous and ordinal variables into fractional ranks, followed by a partial correlation of the ranked variables. A p -value of <0.05 was considered statistically significant.

3. Result

This sub-analysis included the baseline data of 30 elderly subjects diagnosed with Mild Cognitive Impairment (MCI). To provide a comprehensive understanding of the study

population, the sociodemographic and clinical characteristics of the subjects are presented in Table 1.

As shown in Table 1, the majority of the subjects were female (66.7%) and aged between 60 and 74 years (66.7%). Most participants had a higher educational background (56.7%). To further understand the specific cognitive deficits within this MCI cohort, a detailed descriptive analysis of the Montreal Cognitive Assessment Indonesian version (MoCA-Ina) scores was conducted. The distribution of scores across the total assessment and its specific domains is detailed in Table 2.

The descriptive analysis (Table 2) reveals the baseline cognitive performance of the subjects across various domains. The lowest performance relative to the maximum possible score was observed in the Delayed Recall and Abstraction domains.

To determine the relationship between peripheral neurotrophic factors and cognitive performance, an initial Spearman's rank correlation analysis was performed. Subsequently, to address potential confounding effects prominent in geriatric populations, a non-parametric partial correlation analysis was conducted, controlling for age and educational level. The results are summarized in Table 3.

As shown in Table 3, the initial unadjusted analysis revealed no statistically significant correlation between baseline serum BDNF levels and the total MoCA-Ina score ($r = 0.282$, $p = 0.131$), nor with any of the specific domains.

However, after statistically adjusting for age and educational level, a moderate, statistically significant positive correlation emerged between baseline serum BDNF levels and the total MoCA-Ina score ($r = 0.428$, 95% CI [0.07, 0.69], $p = 0.023$). Furthermore, upon evaluating the specific cognitive domains in the adjusted model, a statistically significant

positive correlation was identified specifically in the Abstraction domain ($r = 0.392$, 95% CI [0.02, 0.67], $p = 0.039$). The Delayed Recall

domain showed a moderate positive correlation coefficient ($r = 0.262$) but did not reach statistical significance ($p = 0.178$).

Table 1. Baseline Characteristics of the Study Population (N = 30)

Characteristics	Frequency, n (%) / Median (Min-Max)
Gender	
Male	10 (33.3%)
Female	20 (66.7%)
Age Category	
60–74 Years	20 (66.7%)
≥ 75 Years	10 (33.3%)
Educational Level	
Basic (Elementary/Junior High)	6 (20.0%)
Middle (Senior High)	7 (23.3%)
Higher (Diploma/Bachelor/Master)	17 (56.7%)
Clinical Profile	
Serum BDNF Level (pg/mL)	2688.2 ± 38.72*
Total MoCA-Ina Score	23 (18–25)

*(Note: Data presented as Mean ± Standard Deviation).

Table 2. Profile of MoCA-Ina Total and Specific Domain Scores

Cognitive Domain	Maximum Possible Score	Median (Minimum - Maximum)
Total MoCA-Ina Score	30	23 (18–25)
Visuospatial / Executive	5	4.0 (1.0–5.0)
Naming	3	3.0 (2.0–3.0)
Attention	6	5.0 (3.0–6.0)
Language	3	2.0 (0.0–3.0)
Abstraction	2	1.5 (0.0–2.0)
Delayed Recall	5	1.0 (0.0–4.0)
Orientation	6	6.0 (4.0–6.0)

Table 3. Unadjusted and Adjusted (Non-Parametric Partial) Correlation between Baseline Serum BDNF Levels and MoCA-Ina Scores (N=30)

Variables	Unadjusted (Spearman)		Adjusted (Partial Rank)*		
	Correlation (r)	p-value	Correlation (r)	95% CI	p-value
Total MoCA-Ina Score	0.282	0.131	0.428	[0.07, 0.69]	0.023
Specific Cognitive Domains					
Visuospatial / Executive	-0.095	0.619	-0.034	[-0.40, 0.34]	0.865
Naming	-0.015	0.935	-0.041	[-0.41, 0.33]	0.835
Attention	0.072	0.704	0.138	[-0.24, 0.48]	0.484
Language	-0.192	0.309	-0.116	[-0.47, 0.26]	0.556
Abstraction	0.304	0.103	0.392	[0.02, 0.67]	0.039
Delayed Recall	0.198	0.295	0.262	[-0.11, 0.57]	0.178
Orientation	-0.026	0.890	0.076	[-0.30, 0.43]	0.701

*(Note: Adjusted partial correlation was conducted using ranked variables to statistically control for the confounding effects of age and educational level).

These findings indicate that adjusting for sociodemographic confounders unmasks the underlying biological association, demonstrating that baseline peripheral serum BDNF levels directly correlate with the global cognition score and specific prefrontal-mediated abstraction performance in this cohort of elderly patients with MCI.

4. Discussion

The present study explored the biological association between baseline peripheral BDNF concentrations and granular cognitive domains evaluated by the MoCA-Ina among elderly individuals diagnosed with MCI. Our primary findings underscore a prominent suppressor effect driven by sociodemographic characteristics on the neurotrophins-cognition axis. While the initial unadjusted bivariate analysis did not yield a statistically significant relationship, the application of non-parametric partial correlation, controlling for age and educational attainment, unmasked a significant moderate positive correlation. Specifically, this adjusted relationship was observed for both the overall MoCA-Ina score ($r = 0.428$, $p = 0.023$) and the distinct Abstraction domain ($r = 0.392$, $p = 0.039$).

The initial masking of this biological correlation strongly emphasizes the clinical relevance of the "Cognitive Reserve" (CR) hypothesis among the aging adult demographic in Indonesia.¹¹ In our evaluated cohort, a substantial proportion of participants (56.7%) held higher educational degrees, which serves as a robust proxy for CR. Elevated CR is theorized to cultivate greater synaptic density and more efficient neural compensatory networks, thereby safeguarding global cognitive performance and mitigating dysfunctional cognitive beliefs despite underlying neurodegeneration.^{13,14} This enhanced neural resilience likely empowered subjects to sustain relatively

stable MoCA-Ina outcomes, effectively obscuring the linear biological association with peripheral BDNF until sociodemographic confounders were statistically isolated.^{3,13} Furthermore, alterations in peripheral BDNF dynamics may reflect a systemic compensatory effort where the body attempts to upregulate neurotrophin expression to counteract the early neuropathological burdens of MCI before significant cognitive collapse occurs.¹⁵

The specific correlation identified in the Abstraction domain is particularly relevant from a neurobiological perspective. Abstraction and executive functions are primarily modulated by the prefrontal cortex, a region characterized by high plastic vulnerability and a dense concentration of BDNF receptors.^{9,10} BDNF is known to be a crucial protein for maintaining the dendritic complexity and synaptic integrity of these prefrontal networks. The results suggest that in patients with MCI, declining peripheral BDNF may specifically mirror the depletion of neurotrophic support in frontal-mediated circuits before a more generalized cognitive collapse occurs.⁹ This is consistent with recent evidence suggesting that BDNF signaling is a key determinant of resilience and functional maintenance in the aging brain.^{2,9}

However, the interpretation of peripheral BDNF as a proxy for central nervous system activity remains complex. Serum BDNF levels can be influenced by various systemic factors, including platelet activation and chronic low-grade neuroinflammation, often referred to as "inflammaging".⁹ In this study, where 33.3% of subjects were over 75 years old and presented with various comorbidities (Table 1), systemic factors may act as confounders that complicate the direct translation of serum levels to central hippocampal or cortical dynamics.^{1,9} Furthermore, standard serum measurements do not distinguish

between mature BDNF and its precursor, pro-BDNF, which are known to exert opposing effects on neuronal survival and synaptic plasticity.⁹

Several methodological limitations should be considered. First, the small sample size ($n=30$) was constrained by the recruitment of the parent clinical trial, rendering this an exploratory sub-analysis. While a significant correlation was uncovered, the limited power may have prevented the detection of more subtle associations in other domains, such as Delayed Recall ($r = 0.262$, $p = 0.178$). Second, the cross-sectional nature of this baseline analysis precludes definitive causal inferences regarding the direction of the relationship between BDNF and cognitive decline. Finally, although age and education were controlled, other potential confounders, such as physical activity and specific metabolic profiles, were not included in the multivariate model. Future longitudinal research with larger cohorts and the differentiation of BDNF isoforms is warranted to further validate these exploratory findings.

5. Conclusion

In conclusion, after statistically adjusting for the confounding effects of age and cognitive reserve, baseline serum BDNF levels demonstrate a statistically significant positive correlation with global cognitive function and the specific domain of Abstraction in elderly patients with Mild Cognitive Impairment (MCI). These findings highlight that peripheral BDNF levels may serve as a meaningful biological marker for prefrontal-mediated cognitive dynamics, particularly abstraction performance, in the early stages of cognitive decline. However, the initial masking of these associations underscores the critical necessity of integrating sociodemographic factors, such as educational background, into the clinical interpretation of neurotrophic biomarkers.

Further longitudinal studies with larger cohorts are warranted to evaluate the predictive value of baseline BDNF levels in determining the trajectory of cognitive deterioration in the elderly.

6. Acknowledgment

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