



The Correlation between the Indonesian Version of Montreal Cognitive Assessment and Homocysteine Levels in Batakese Male with Schizophrenia in Prof. DR. M. Ildrem Psychiatric Hospital Medan

Yoseva Hotnauli, Bahagia Loebis^{ORCID}, M. Surya Husada*^{ORCID}, Nazli Mahdinasari Nasution^{ORCID}, Elmeida Effendy^{ORCID}

Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Abstract

Edited by: Branislav Filipović
Citation: Hotnauli Y, Loebis B, Husada MS, Nasution NM, Effendy E. The Correlation between the Indonesian Version of Montreal Cognitive Assessment and Homocysteine Levels in Batakese Male with Schizophrenia in Prof. DR. M. Ildrem Psychiatric Hospital Medan. Open Access Maced J Med Sci. 2021 Jun 13; 9(T3):135-137. <https://doi.org/10.3889/oamjms.2021.6364>
Keywords: Schizophrenia; Homocysteine; MoCA-INA; Batakese
***Correspondence:** M. Surya Husada, Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. E-mail: suryahusada03@gmail.com
Received: 08-Dec-2020
Revised: 31-May-2021
Accepted: 03-Jun-2021
Copyright: © 2021 Yoseva Hotnauli, Bahagia Loebis, M. Surya Husada, Nazli Mahdinasari Nasution, Elmeida Effendy
Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist
Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

BACKGROUND: The pathogenesis of schizophrenia and its mechanism is not convinced. Several studies indicate that schizophrenia pathogenesis can be related to changes at the cellular level. The studies show homocysteine in people with schizophrenia was significantly increased, abnormal homocysteine metabolism can lead to DNA methylation.

AIM: This study aimed to establish the correlation between the Indonesian Montreal Cognitive Assessment Version (MoCA-INA) scores and homocysteine levels in males with Batakese schizophrenia.

METHODS: This study is a numerical correlative analytic study with an approach to cross-sectional study; by evaluating the correlation between the MoCA-INA scores and the level of homocysteine in males with Batakese schizophrenia.

RESULTS: The median of the MoCA-INA score in the study subjects was 22, with a minimum score of 18 and a maximum score of 26. There was a significant correlation between the MoCA-INA scores and Homocysteine levels ($p = 0.001$).

CONCLUSION: The interpretation obtained from this study is that the higher Homocysteine level, the lower the MoCA-INA scores in Batakese men with schizophrenia is.

Introduction

Schizophrenia is a complex psychiatric condition identified by impairment, apathy social alienation, and cognitive impairment in reality testing. Many factors contribute to the development of schizophrenia [1]. Factors that contribute to schizophrenia include genetic, biological, biochemical, psychosocial, socioeconomic status, stress, and drug abuse [2].

The pathogenesis of schizophrenia and its mechanism is not convinced. Several studies show that altered DNA methylation, mitochondrial dysfunction, impaired glutamate neurotransmitters, and decreased folic acid can be associated with the pathogenesis of schizophrenia. Those studies found that homocysteine levels in people with schizophrenia were significantly increased. Abnormal homocysteine metabolism can lead to abnormal DNA methylation. Homocysteine changes are a risk factor for schizophrenia pathogenesis and high homocysteine levels can be correlated with the morbidity and cognitive impairment of schizophrenia [1].

In a study by Moustafa *et al.* in 2014 in Australia, The increase in homocysteine in schizophrenia patients and affective disorders led to their cognitive impairment. There are several mechanisms by which homocysteine may be biologically linked to psychiatric disorders. It has been found that homocysteine interacts with the receptor of N-Methyl-D-Aspartate (NMDA), initiating oxidative stress-inducing apoptosis, inducing mitochondrial dysfunction, and inducing vascular damage [3]. It has been found that homocysteine is an independent risk factor for cognitive dysfunction. Studies of individuals with a wide range of cognitive impairments have consistently shown increased plasma homocysteine and decreased enzymatic cofactors involved in methionine and homocysteine metabolism. Plasma total homocysteine also appears to be the most consistent tissue marker in the cofactor of nutrient deficiency, as well as cognitive performance in the elderly [4], [5], [6].

Deng *et al.*'s 2018 study in China, a significant increase in serum homocysteine can be used as a laboratory diagnostic tool to assess the severity of cognitive dysfunction in first-episode of schizophrenia patients. Severe cognitive impairment in schizophrenia patients is stated in this study. Previous studies have shown that 5-hydroxytryptamine and frontal lobe dopamine

biosynthesis may be affected by serum homocysteine, which later affects frontal lobe activity. Prefrontal hypofunction is associated with cognitive impairment. This is why the increase in serum homocysteine in the patients with schizophrenia correlates with cognitive function. Subjects with first-episode schizophrenia with increased serum homocysteine of more than 15 $\mu\text{mol/L}$ in this study, significantly had serum homocysteine levels and decreased cognitive function than subjects who had homocysteine levels $<15 \mu\text{mol/L}$ ($p < 0.05$) [1].

Based on the differences in previous studies, Milller *et al.* [4] stated that there was no significant relationship between homocysteine levels and cognitive impairment, while studies by Moustafa *et al.* and Deng *et al.* stated that increased homocysteine contributed to disorders of cognitive, but the same research has never been conducted in Indonesia. Thus, through this study, the authors would like to know the correlation between the Indonesian Version of the Montreal Cognitive Assessment (MoCA-I_{na}) Score and homocysteine levels in Batakese men with schizophrenia.

Methods

This research is a numerical correlative analytic study with a cross-sectional study approach which assesses the correlation between MoCA-I_{na} scores and Homocysteine levels of Batakese men with schizophrenia. The sample in this study was Batakese men with schizophrenia at the Polyclinic of RSJ, Prof. Dr. M. Ildrem Medan who met the inclusion criteria and the sampling was by means of nonprobability sampling, consecutive sampling type. The inclusion criteria in this study were Batakese men with schizophrenia who had been diagnosed based on PPDGJ III, age between 20 and 40 years, duration of illness 1–5 years, total PANSS score 60–80, understood Indonesian, were willing to be interviewed, received antipsychotic medication risperidone 4 mg/day/oral in divided doses, the latest education was at least Junior High School (SMP) or equivalent, smoking frequency ≤ 10 cigarettes/day (light smoker), whereas the in this study, the exclusion criteria were general medical conditions and/or other comorbidities, history of use of alcohol and other substances, history of use of supplements containing Vitamin B (B6, B9, B12). This research was conducted from July to September 2019, and the total sample was 49 participants.

Data analysis, before data analysis were carried out data normality test was carried out using the Shapiro-Wilk test, then checking the linearity assumption by making a scatter chart. The data were evaluated in order to obtain the correlation value (r). The data analysis was conducted using the Pearson Correlation test for data that were normally distributed. Data that were not normally distributed were analyzed using the Spearman correlation test. The collection and interpretation of data

were carried out with the assistance of the software Statistical Package for Social Sciences.

Results

In this study, demographic characteristics Table 1 were obtained based on age group, with a mean of 30.61 years with a standard deviation of 5.89, participants in the age of 20–30 years group were 24 people (48.9%), and participants in the age of 31–40 years group as many as 25 people (51.5%). Based on the level of education, junior high school grade were 18 people (36.7%), senior high school grade were 28 people (57.2%), college graduates were three people (6.1%). On marital status, participants with married status were 11 people (22.5%). Likewise with employment status, subjects who did not work were 29 people (59.2%). Based on the long sick, the median was found to be 3.00 with the minimum-maximum (1-5). The mean PANSS score was 74.82 and the standard deviation was 3.26.

Table 1: Distribution of research participants based on demographic characteristics

Demographic characteristics	Mean \pm SB Median (min–max)	n	(%)
Age			
20–30		24	(48.9)
31–40		25	(51.1)
Level of education			
Junior high school		18	(36.7)
Senior high school		28	(57.2)
University		3	(6.1)
Marriage status			
Married		11	(22.5)
Not married		38	(77.5)
Job status			
Work		20	(40.8)
Does not work		29	(59.2)
Long sick	3.00 (1–5)		
PANSS score	74.82 \pm 3.26		

The mean homocysteine levels in the participants of this study were obtained at 25.46 and the standard deviation is 9.17. The median of the MoCA-I_{na} scores in the study participants was 22, with a minimum score of 18 and a maximum score of 26. In the Table 2 the correlation between the MoCA-I_{na} scores and homocysteine levels, after normalizing the data distribution, was tested for correlation. Pearson, where previously checked the linearity assumption by making a scatter chart. From the analysis results obtained $p = 0.001$ which indicates that there is a significant correlation between the MoCA-I_{na} scores and homocysteine levels. The Pearson correlation value of -0.754 indicates a negative correlation with a strong correlation strength, this indicates that the higher the homocysteine level, the lower the MoCA-I_{na} score.

Discussion

In this study, only male participants were included in the study. This is because, in a 2002 study by

Table 2: Results of the Pearson correlation test analysis between MoCA-Ina score and Homocysteine levels in Batakese men with schizophrenia

	Homocysteine levels
MoCA-Ina score	r = -0.754 p = 0.001 n = 49

MoCA-Ina: Indonesian version of the montreal cognitive assessment.

Levine *et al.* In Israel, it was found that in younger male patients with schizophrenia, homocysteine levels were higher. It is well known that the onset of schizophrenia is earlier in male patients than in women and that the disease worsens chronically more often in younger men. In a study by Yang *et al.* in 2015 in China, it was found that the prevalence of age-related hyperhomocysteinemia in men was substantially greater than women [7], [8].

In a study by Di Lorenzo *et al.* in 2015 in Italy, it was found that in the group of people with schizophrenia, there was a significant rise in homocysteine levels with duration of illness >1 year compared to the group of people with schizophrenia with duration of illness <1 year (χ^2 test, $p = 0.02$). The study of Narayan *et al.* in India in 2014, found that there was a statistically significant relationship between homocysteine and duration of illness (Spearman's analysis test $p = 0.2866$ $p = 0.0004$; Kendall score = 940, SE = 330, $p = 0.0045$). Meanwhile, in the 2010 Mabrouk study in Tunisia, it was found that in patients with schizophrenia, homocysteine plasma levels were not associated with duration of illness ($r = -0.04$, $p = 0.78$) [9], [10], [11].

In the study conducted by Ma *et al.* 2009 in Hong Kong, it was found that there was no significant relationship between the PANSS score and serum homocysteine level ($r = 0.066$, $p = 0.303$). The same thing was found in the study of Narayan *et al.* in 2014 that the PANSS positive symptom score of schizophrenia was not significantly correlated with homocysteine levels ($r = 0.007$, $p = 0.9$), but PANSS negative scores had a significant correlation with homocysteine levels ($r = 0.7$ $p = <0.001$) [11], [12].

In this study, the correlation between the MoCA-Ina score and homocysteine levels in Batakese men with schizophrenia obtained $p = 0.001$ which indicates that the correlation between the MoCA-Ina score and homocysteine levels is significant. The Pearson correlation value of $-0,754$ indicates a negative correlation with strong correlation strength. This shows that the higher the homocysteine level, the lower the MoCA-Ina score is. The results of this study are in accordance with a study conducted by Moustafa *et al.* in 2014 in Australia which stated that increased homocysteine could also contribute to cognitive impairment. It was found that homocysteine interacted with the NMDA receptor, initiating oxidative stress-inducing apoptosis, trigger mitochondrial dysfunction, and caused vascular damage. In a study conducted by Moustafa *et al.* in 2018 in China, it was found that the first episode schizophrenic subjects had significantly increased serum homocysteine more than $15 \mu\text{mol/L}$ and lower cognitive function than participants who had homocysteine levels less than $15 \mu\text{mol/L}$ ($p < 0.05$) [1], [3].

Conclusion

The interpretation obtained from this study is that the higher Homocysteine level, the lower the MoCA-Ina scores in Batakese men with schizophrenia.

References

- Jing D, Mao X, Zhi L, Xinyuan L. Cognitive ability and the level of serum homocysteine correlations in first-episode schizophrenia subjects. *J Psychiatry Brain Sci.* 2018;3(2):1-6. <https://doi.org/10.20900/jpbs.20180003>
- Zahnia S, Sumekar DW. Epidemiological study of schizophrenia. *Majority.* 2016;5(4):160-6.
- Moustafa AA, Hewed DH, Eissa AM, Frydecka D, Misiak B. Homocysteine levels in schizophrenia and affective disorders-focus on cognition. *Front Behav Neurosci.* 2014;8(343):1-10. <https://doi.org/10.3389/fnbeh.2015.00081>
PMid:25339876
- Milller AL. The methionine-homocysteine cycle and its effects on cognitive diseases. *Altern Med Rev.* 2003;8(1):7-19.
PMid:12611557
- Teunissen CE, van Boxtel MP, Jolles J, Vente JD, Vreeling F, Verhey F, *et al.* Homocysteine in relation to cognitive performance in pathological and non-pathological conditions. *Clin Chem Lab Med.* 2005;43(10):1089-95. <https://doi.org/10.1515/cclm.2005.190>
PMid:16197303
- Sadock BJ, Sadock V, Ruiz P. In: Sadock BJ, Sadock VA, Ruiz P, editors. *Kaplan and Sadock's Comprehensive Textbook of Psychiatry.* 10th ed., Vol. 1, 2. New York: Wolters Kluwer; 2017. p. 2751. <https://doi.org/10.4067/s0717-92272002000300011>
- Levine J, Stahl Z, Sela BA, Gavendo S, Ruderman V, Belmaker RH. Elevated homocysteine levels in young male patients with schizophrenia. *Am J Psychiatry.* 2002;159(10):1790-2. <https://doi.org/10.1176/appi.ajp.159.10.1790>
PMid:12359692
- Yang B, Fan S, Zhi X, Wang Y, Wang Y, Zheng Q, *et al.* Prevalence of hyperhomocysteinemia in China: A systematic review and meta-analysis. *Nutrients.* 2015;7(1):74-90. <https://doi.org/10.3390/nu7010074>
PMid:25551247
- Mabrouka H, Doukia W, Mechrib A, Younesa MK, Omezzinec A, Bouslamac A, *et al.* Hyperhomocysteinemia and schizophrenia: Case control study. *Lencephale.* 2011;37(4):308-13.
PMid:21981892
- Di Lorenzo R, Amoretti A, Baldini S, Soli M, Landi G, Pollutri G, *et al.* Homocysteine level in schizophrenia patients newly admitted to an acute psychiatric ward. *Acta Neuropsychiatrica.* 2015;27(6):336-44. <https://doi.org/10.1017/neu.2015.30>
PMid:26017629
- Narayan SK, Verman A, Kattimani S, Ananthanarayanan PH, Adithan C. Plasma homocysteine levels in depression and schizophrenia in South Indian Tamilian population. *Indian J Psychiatry.* 2014;56(1):46-53. <https://doi.org/10.4103/0019-5545.124746>
PMid:24574558
- Ma YY, Shek CC, Wong MC, Yip KC, Ng RM, Nguyen DG, *et al.* Homocysteine level in schizophrenia patients. *Aust N Z J Psychiatry.* 2009;43(8):760-5.
PMid:19629798