RESEARCH ARTICLE

Serum Homocysteine Levels and Its Correlation with Executive Functions in Drug Naïve Patients of Depression: A Cross-sectional Study

Mrigakshi Parasor[1], Shramana Sengupta[2]

Received on: 30 April 2024; *Accepted on:* 14 June 2024; *Published on:* 19 February 2025

Abstract

Background: Cognitive impairments, especially executive dysfunction are found to be impaired in patients with depression. Homocysteine is widely implicated in the pathophysiology of a variety of psychiatric disorders because it has a crucial role in cognitive functioning. The level of homocysteine in healthy, elderly individuals is being acknowledged as a risk factor for age-related cognitive impairments and dementia. Therefore, further research is required to understand its role in cognitive impairment, including executive dysfunction, common in depression.

Aim: To estimate the level of serum homocysteine in drug naïve patients of depression and determine the correlation with executive functions in the patients.

Materials and methods: This is a cross-sectional study done on 50 drug naïve patients diagnosed with depression as per the International Classification of Diseases, 10th revision (ICD-10) criteria. The patients were assessed using the sociodemographic and clinical proforma and their anthropometric measurements (height and weight) were taken. Assessment of the severity of depression was done using the 17-item Hamilton Depression Rating Scale (HAM-D). Stroop test was used to assess executive functioning. Blood samples were collected to assess serum homocysteine levels. The correlation between serum homocysteine levels and executive functioning was determined using appropriate statistical methods.

Results: The correlation between serum homocysteine levels and executive function in the study participants was found to be statistically insignificant.

Conclusion: The correlation between serum homocysteine levels and executive functioning in drug naïve patients of depression was not found to be significant. Hence, the role of homocysteine as a predictor and therapeutic target for the impairment in executive functioning in patients of depression remains yet unclear.

Clinical significance: Knowledge about the biological basis of executive dysfunction in depression may aid in the development of newer strategies for treatment as well as for monitoring treatment response.

Keywords: Cross-sectional study, Depression, Drug naïve, Executive functions, Homocysteine.

Indian Journal of Private Psychiatry (2025): 10.5005/jp-journals-10067-0183

Introduction

Cognitive impairments are a common component of depression, out of which the most implicated are deficits in executive functioning,[1] commonly involving domains of working memory, processing speed, learning, planning, mental flexibility, response inhibition, decision-making, and visuospatial memory.[2–6] Executive function impairments, often persist even when a patient has met the conventional criteria for remission of depressive symptoms.[7] Residual deficits in executive functioning contribute to ongoing occupational and social dysfunction and increase the risk of recurrence of depressive episodes.[8]

Recent research indicates that homocysteine plays an important role in the modulation of neurotransmitters like norepinephrine, serotonin, dopamine, and melatonin.[9] Using oxidative stress, causing mitochondrial dysfunction and neuronal apoptosis, elevated levels of homocysteine have been shown to cause neurotoxicity on dopaminergic neurons and thus, increase the risk of developing depression.[10] Hyperhomocysteinemia leads to a reduction in levels of S-adenosyl methionine (SAM),[9] which in turn is needed for methylation of serotonin. Also, serotonin and SAM are needed for the synthesis of melatonin, which too is implicated in the pathophysiology of depression.

Studies assessing homocysteine levels in healthy older adults have demonstrated the significant impact of homocysteine on behavioral and cognitive functions.[11] An increasing number of studies are identifying hyperhomocysteinemia as a risk factor for age-related cognitive decline and different forms of dementia.[12] The Rotterdam Brain Scan Study and the Framingham Offspring Study revealed that the level of plasma homocysteine had a significant correlation with performance in neuropsychological tests of psychomotor speed, executive functions, memory, and global cognitive function, which was not mediated by brain atrophy or structural changes in the white matter.[11,13]

[1,2]Department of Psychiatry, Lokopriya Gopinath Bordoloi Regional Institute of Mental Health, Tezpur, Assam, India

Corresponding Author: Mrigakshi Parasor, Department of Psychiatry, Lokopriya Gopinath Bordoloi Regional Institute of Mental Health, Tezpur, Assam, India, Phone: +91 9954780216, e-mail: mrigakshiparasor@gmail.com

How to cite this article: Parasor M, Sengupta S. Serum Homocysteine Levels and Its Correlation with Executive Functions in Drug Naïve Patients of Depression: A Cross-sectional Study. Ind J Priv Psychiatry 2025;19(1):24–29.

Source of support: Nil

Conflict of interest: None

Studies conducted on patients with various neurological and psychiatric disorders have shown that the common cognitive deficit that is observed in individuals with hyperhomocysteinemia is executive dysfunction.[14–20] The most relevant mechanism along with others for homocysteine's role in executive function appears to be demyelination, as SAM (an important metabolite in homocysteine synthesis) is a cofactor in myelin synthesis.[21]

These observations suggest that altered homocysteine level may be a potential therapeutic target and a marker to identify executive dysfunction that is commonly observed in depression. There is a dearth of research assessing the relationship between homocysteine and executive functioning in patients with depression. This study was conducted to determine whether serum homocysteine level and executive functioning in patients with depression are correlated.

Materials and Methods

The Setting

The study was conducted in a tertiary care mental health institute located in the northeastern part of India, with prior approval from the Institutional Ethics Committee. The duration of the study was 18 months (April 2021–October 2022).

Study Design

This is a cross-sectional hospital-based study.

Recruitment of Participants

In this study, drug naïve patients in the range of 18–45 years meeting the diagnostic criteria of depression as per the International Classification of Diseases, 10th Revision (ICD-10) and who provided informed consent were recruited using a convenience sampling method.

The following formula was used for the calculation of sample size in this study:

$$n = \{Z^2 p(1- p)\}/e^2$$

n = Population size; p = Population proportion; e = Margin of error; and Z = Z score.

Inclusion Criteria

- Patients fulfilling diagnostic criteria of depression as per ICD-10 (1st episode).
- Drug naïve patients of depression attending outpatient department or admitted for inpatient care.
- Range of age is 18–45 years.
- Willing to provide informed consent.

Exclusion Criteria

- Patients fulfilling criteria for depression with psychotic symptoms according to ICD-10.
- Chronic medical illness, metabolic syndrome, or any comorbid psychiatric disorders.
- History of use of any substance in dependence pattern.
- Body Mass Index (BMI) >23 kg/m^2, as obesity is an independent risk factor for Hyperhomocysteinemia.
- Hemoglobin level <13 mg/dL in males and < 12 mg/dL in females with mean corpuscular volume (MCV) > 100 fL, to exclude macrocytic anemia, which is independently associated with altered homocysteine level.
- Illiterate patients.
- Pregnant and lactating women.

Tools Used in the Study

- Hamilton Depression Rating Scale: HAM-D developed by Max Hamilton (1960) is a widely used clinician-rated scale to assess the severity of depressive symptoms. The 17-item version pertaining to symptoms of depression experienced over the past week has been used in this study. The total score can be interpreted as severity levels of depression as per the UK National Institute for Health and Clinical Excellence criteria: Not depressed 0–7; Subthreshold 8–13; Mild 14–18; Moderate 19–22; Severe > 23.[22]
- Socio-demographic and clinical proforma: It is a semi-structured proforma adopted based on various studies, describing the patient's socio-demographic information such as age, gender, residence, family type, marital status, level of education, and socioeconomic status (updated B.G. Prasad socio-economic classification for 2021)[23] as well as clinical information like age of onset, duration of illness, were recorded.
- Stroop test: It is a neuropsychological test developed by John Ridley Stroop in 1935. The Stroop test evaluates various domains of executive functioning. Mental flexibility, that is, the ability to shift between perception of one stimulus to another, and response inhibition, that is, inhibition of a habitual response for a novel response, are essential domains of executive functioning which are commonly affected in patients of depression. Other important domains of executive functioning with deficits in patients of depression are working memory, decision-making, processing speed, and planning. The Stroop test evaluates these domains of executive functioning that are commonly observed to be impaired in patients with depression.[24]

The color names green, yellow, red, and blue are printed in capital letters on a paper in 16 rows and 11 columns. The color of the print is occasionally similar to the color designated by the word. The patient is instructed to first read the words as fast as possible and the total time taken is recorded in seconds as the reading time. As a next step, the patient is asked to name the color in which the word is printed as fast as possible and the total time taken is recorded in seconds as naming time. The Stroop effect score is calculated by subtracting the reading time from the naming time. The cut-off score for executive functioning in the patients is the Stroop effect score according to the NIMHANS Neuropsychological Battery (Table 1).[25]

Procedure

Patients diagnosed with depression as per ICD-10 diagnostic criteria were assessed for fulfillment of inclusion and exclusion criteria. The socio-demographic and clinical details were obtained using the socio-demographic and clinical proforma. Anthropometric measurements for BMI (height and weight) were taken. Hamilton Depression Rating Scale was used to assess the severity of depression.

Fasting blood samples were collected in yellow-colored serum separation gel tubes coated with clot activator and gel for serum along with samples for blood hemoglobin and MCV estimation. The samples were allowed to clot at room temperature for 2 hours prior to centrifugation at approximately 2000–3000 rpm for 15 minutes. The serum was separated and stored in properly labeled aliquots at –40°C till analysis, avoiding repeated freezing/thawing.

On the day of analysis, the samples were first thawed for 45 minutes at room temperature and then pipetted onto the micro

Table 1: Cut-off score for Stroop effect score as per NIMHANS Neuropsychological Battery

	Males						*Females*					
	16–30 years		*31–50 years*		*51–65 years*		*16–30 years*		*31–50 years*		*51–65 years*	
	SE	*CE*	*SE*	*CE*	*SE*	*CE*	*SE*	*CE*	*SE*	*CE*	*SE*	*CE*
Stroop effect	226	211	259	196	283	320	200	160	204	160	192	271

CE, college educated; SE, school educated

enzyme-linked immunosorbent assay (ELISA) plate, which was pre-coated with human homocysteine antibody, and standards were prepared with dilution as instructed. The plate was incubated at 37°C for 60 minutes, covered with a new sealer, and incubated in the dark at 37°C for 10 minutes. After incubation, stop solution was added to each well to stop the ongoing reaction and the color of the solution changed to yellow. The optical density of each well was determined at 450 nm within 10 minutes of adding the stop solution which suggests the concentration of serum homocysteine in the sample.

Statistical Analysis

The collected data was tabulated and IBM SPSS version 25 for Windows was used for data analysis. The frequency and percentage of socio-demographic and clinical variables were calculated using descriptive statistics. Correlation between serum homocysteine level and executive function based on the Stroop effect score was tested using Spearman's rho and correlation *t*-test. Serum homocysteine levels were compared in groups of impaired and intact executive function groups using the paired *t*-test.

Results and Analysis

The study participants were between 18 and 44 years of age (mean age = 33.5 years, SD ± 8.34 years). Males accounted for 58% of the study participants, while 42% of the participants were females. The majority of the study participants that is, 54% were married, and 20 and 16% of the study participants were unmarried and separated, respectively. Half of the participants (50%) belonged to a rural background and the other half hailed from an urban background. The majority of the study participants (72%) were from a nuclear family, 38% of the participants were educated up to intermediate level between secondary school and graduation, and 34% of participants were educated up to secondary level of education, while the rest were graduates. The number of participants belonging to lower, lower middle, middle, upper middle, and upper socioeconomic status were 11, 14, 13, 9, and 3, respectively.

The mean age of onset of illness of study participants was 33.5 years (SD ± 8.34 years). Duration of illness ranged from 1 to 9 months. Also, 64% of participants reported insidious onset of illness and 36% of participants reported acute onset of illness. The sociodemographic and clinical details of the study sample are shown in Table 2.

The Stroop test was used to assess executive function in the 50 participants of the study. Stroop effect score ranged from 33 to 267 seconds in the participants. The mean Stroop effect score was 150.34 seconds (SD ± 69.47 seconds). It should be noted that 24 out of 50 participants (48%) had impairment in executive function and the remaining 26 (52%) participants had intact executive function (Table 3).

Table 2: Sociodemographic and clinical variables

	Sociodemographic variables	
Variable	*Frequency*	*Percentage (%)*
Gender		
Female	29	58
Male	21	42
Age group		
18–45	11	22
25–45	39	78
Marital status		
Married	27	54
Separated	8	16
Unmarried	10	20
Widowed	5	10
Level of education		
Graduate	14	28
Intermediate	19	38
Secondary	17	34
Type of family		
Joint	14	28
Nuclear	36	72
Socioeconomic status		
Upper	3	6
Upper middle	9	18
Middle	13	26
Lower middle	14	28
Lower	11	22
Residence		
Rural	25	50
Urban	25	50
Clinical variables		
Duration of illness (months)	Mean ± SD	Range
1.75 ± 0.49		1–9
Mode of onset		
Acute	18	
Insidious	32	
Age of onset (years)	Mean ± SD	Range
33.5 ± 8.34		18–44

SD, standard deviation

Serum homocysteine levels varied from 7.62 to 12.83 nmol/mL with the median at 10.21 nmol/mL in the study participants (Table 3). Mean serum homocysteine level was 10.04 nmol/mL (SD ± 1.302 nmol/mL).

As shown in Table 4, the correlation of serum homocysteine level with Stroop effect score in drug naïve patients of depression was statistically insignificant in groups of mild depression ($r = -0.362$, $p = 0.128$), moderate depression ($r = 0.018$, $p = 0.946$), and severe depression ($r = 0.121$, $p = 0.680$). On aggregate also, the correlation between the average Stroop effect score (150.34 ± 69.47 seconds) and average serum homocysteine level (10.04 ± 1.03 nmol/mL) was insignificant ($r = -0.058$, $p = 0.688$).

Paired *t*-test was used to compare mean serum homocysteine levels in the groups of intact executive functions and impaired executive functions (Table 5). The difference between serum homocysteine levels in drug naïve patients of depression with intact executive function (10.13 ± 1.30 nmol/mL) and impaired executive function (9.99 ± 1.32 nmol/mL) was statistically insignificant ($p = 0.581$).

Discussion

In this study, impairment in executive functions, as indicated by results on the Stroop test, was observed in 48% of the study participants. Many previous studies have reported deficits in executive functioning in patients with depression.[26,27] A review of 28 such studies concluded that patients of depression present with impairments in varying domains of executive functioning which further depends on the severity of depression as well as the subtype of depression (more in melancholic depression).[28] However, in the previous studies assessing executive functions in patients of depression, multiple and different assessment tools were used to evaluate functioning in different domains of executive function which contrasts with the present study.

In this study, a negative correlation between executive functions in the study participants and serum homocysteine levels was detected but was found to be statistically insignificant. There are studies conducted in patients with neurocognitive disorders such as vascular dementia and Alzheimer's disease and individuals with cognitive impairment which found no significant association between homocysteine levels and cognitive functions, including executive functions.[29–31]

Contradictory results to the current study have been found in the Framingham Offspring Study and Rotterdam Brain Scan Study, indicating a correlation between elevated homocysteine levels with poorer performance in cognitive functioning.[11,13] A prospective study showed a significant association between baseline levels of homocysteine and subsequent development of deficits in cognitive function, specifically in domains of attention, verbal learning, memory, and information processing, in dementia-free individuals.[32] However, most of these studies were conducted in the elderly population which differs from the participants recruited in the current study.

In the context of depression, a study conducted by Alexopoulos et al. to find any possible association between serum homocysteine levels and cognitive function including executive functions in patients with depression found a positive correlation

Table 3: Stroop effect score and serum homocysteine level in study participants

	Mean	*SD*	*Median*
Stroop effect score (seconds)	150.34	69.47	138.50
Serum homocysteine level (nmol/mL)	10.04	1.302	10.21

Table 4: Correlation between serum homocysteine levels and executive functions in groups of mild, moderate, and severe depression

Severity of depression	*Mean*	*SD*	*N*	*Correlation coefficient*	*p-value*
Mild					
Serum homocysteine level (nmol/mL)	10.05	1.38	19	–0.362	0.128[NS]
Stroop effect score (seconds)	149.00	67.13	19		
Moderate					
Serum homocysteine level (nmol/mL)	9.58	1.12	17	0.018 (0.946[NS])	0.946[NS]
Stroop effect score (seconds)	141.06	68.45	17		
Severe					
Serum homocysteine level (nmol/mL)	10.59	1.26	14	0.121	0.680[NS]
Stroop effect score (seconds)	163.43	76.70	14		
Total					
Serum homocysteine level (nmol/mL)	10.04	1.30	50	–0.058	0.688[NS]
Stroop effect score (seconds)	150.34	69.47	50		

NS, not significant

Table 5: Comparison of serum homocysteine level in groups with intact vs impaired executive function

Executive function	*Serum homocysteine level (nmol/mL) mean ± SD*	*Range of serum homocysteine level (nmol/mL)*	*Diff ± SE*	*t (48)*	*p-value*
Intact ($n = 26$)	10.13 ± 1.30	7.62–12.83	0.21 ± 0.37	0.56	0.581[NS]
Impaired ($n = 24$)	9.99 ± 1.32	8.04–12.65			

NS, not significant

between the two variables indicated by better performance in neuropsychological assessments by individuals with higher levels of homocysteine.[33]

These variable findings indicate that homocysteine levels may correlate with cognitive dysfunction including deficits in executive functioning in the elderly population who are at higher risk for neurostructural and neurovascular changes but the association between cognitive function impairments and homocysteine levels in drug naïve depressed adults remains yet unclear.

Conclusion

In this study, the serum homocysteine levels were reduced with increasing impairment in executive functioning in the drug naïve patients of depression, however, a significant relationship between the two variables was not observed. Hence, the role of homocysteine as a potential marker and therapeutic target for executive dysfunction in depression remains yet unclear. Future research in this context using measures to improve the methodological limitations in this study will provide further insight into this emerging area of the biological basis of executive dysfunction in depression.

Limitations

This is a study employing a cross-sectional design with a modest sample size of 50 participants, hence the results are difficult to generalize. Sociodemographic variables such as age, race, and gender influence homocysteine levels. Thus, the results obtained in this study cannot be extended to the general population, and community-based studies will provide better insight into the concept. Although the Stroop test is a reliable test for assessing functioning in several domains of executive function, it may not be as sensitive as a combination of multiple tests for executive function. Also, medical comorbidities like metabolic disorders and cardiovascular disorders which are confounding factors that influence homocysteine levels, were ruled out in this study based on history and physical examination. Factors like vitamin B12 and folic acid deficiency, which are also known to influence homocysteine levels, were ruled out based on the absence of macrocytic anemia in this study. Therefore, further research in this area with more reliable methods to rule out these factors that influence levels of serum homocysteine will provide more conclusive results.

Clinical Significance

The biological basis of cognitive dysfunction in psychiatric illnesses other than neurocognitive disorders, is relatively a new field of interest. Considering the significance of cognitive dysfunction, especially executive dysfunction, in the prognosis and functioning of patients with mood disorders, knowledge about biological markers of the same may aid in the development of newer strategies to monitor treatment response and also newer targets of therapeutic intervention.

Orcid

Mrigakshi Parasor https://orcid.org/0009-0001-7625-0570
Shramana Sengupta https://orcid.org/0009-0003-1684-0418

References

1. Atique-Ur-Rehman H, Neill JC. Cognitive dysfunction in major depression: From assessment to novel therapies. Pharmacol Ther 2019;202:53–71. DOI: 10.1016/j.pharmthera.2019.05.013.
2. Knight MJ, Air T, Baune BT. The role of cognitive impairment in psychosocial functioning in remitted depression. J Affect Disord 2018;235:129–134. DOI: 10.1016/j.jad.2018.04.051.
3. Murrough JW, Iacoviello B, Neumeister A, et al. Cognitive dysfunction in depression: Neurocircuitry and new therapeutic strategies. Neurobiol Learn Mem 2011;96(4):553–563. DOI: 10.1016/j.nlm.2011.06.006.
4. Moritz S, Birkner C, Kloss M, et al. Impact of comorbid depressive symptoms on neuropsychological performance in obsessive-compulsive disorder. J Abnorm Psychol 2001;110(4):653–657. DOI: 10.1037//0021-843x.110.4.653.
5. Elliott R, Sahakian BJ, McKay AP, et al. Neuropsychological impairments in unipolar depression: The influence of perceived failure on subsequent performance. Psychological Med 1996;26(5):975–989. DOI: 10.1017/s0033291700035303.
6. Trichard C, Martinot JL, Alagille M, et al. Time course of prefrontal lobe dysfunction in severely depressed in-patients: A longitudinal neuropsychological study. Psychological Med 1995;25(1):79–85. DOI: 10.1017/s0033291700028105.
7. Baune BT, Miller R, McAfoose J, et al. The role of cognitive impairment in general functioning in major depression. Psychiatry Res 2010;176(2–3):183–189. DOI: 10.1016/j.psychres.2008.12.001.
8. Alexopoulos GS, Meyers BS, Young RC, et al. Executive dysfunction and long-term outcomes of geriatric depression. Arch Gen Psychiatry 2000;57(3):285–290. DOI: 10.1001/archpsyc.57.3.285.
9. Fava M, Borus JS, Alpert JE, et al. Folate, vitamin B12, and homocysteine in major depressive disorder. Am J Psychiatry 1997;154(3):426–428. DOI: 10.1176/ajp.154.3.426.
10. Lee ES, Chen H, Soliman KF, et al. Effects of homocysteine on the dopaminergic system and behavior in rodents. Neurotoxicology 2005;26(3):361–371. DOI: 10.1016/j.neuro.2005.01.008.
11. Prins ND, Den Heijer T, Hofman A, et al. Homocysteine and cognitive function in the elderly: The Rotterdam Scan Study. Neurology 2002;59(9):1375–1380. DOI: 10.1212/01.wnl.0000032494.05619.93.
12. Stanger O, Fowler B, Piertzik K, et al. Homocysteine, folate and vitamin B12 in neuropsychiatric diseases: Review and treatment recommendations. Expert Rev Neurother 2009;9(9):1393–1412. DOI: 10.1586/ern.09.75.
13. Elias MF, Sullivan LM, D'Agostino RB, et al. Homocysteine and cognitive performance in the Framingham offspring study: Age is important. Am J Epidemiol 2005;162(7):644–653. DOI: 10.1093/aje/kwi259.
14. Levine J, Stahl Z, Sela BA, et al. Homocysteine-reducing strategies improve symptoms in chronic schizophrenic patients with hyperhomocysteinemia. Biol Psychiatry 2006;60(3):265–269. DOI: 10.1016/j.biopsych.2005.10.009.
15. Dittmann S, Seemuller F, Grunze HC, et al. The impact of homocysteine levels on cognition in euthymic bipolar patients: A cross-sectional study. J Clin Psychiatry 2008;69(6):899–906. DOI: 10.4088/jcp.v69n0603.
16. De Jager CA, Oulhaj A, Jacoby R, et al. Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: A randomized controlled trial. Int J Geriatr Psychiatry 2012;27(6):592–600. DOI: 10.1002/gps.2758.
17. Osher Y, Bersudsky Y, Silver H, et al. Neuropsychological correlates of homocysteine levels in euthymic bipolar patients. J Affect Disord 2008;105(1–3):229–233. DOI: 10.1016/j.jad.2007.04.005.
18. Dias VV, Brissos S, Cardoso C, et al. Serum homocysteine levels and cognitive functioning in euthymic bipolar patients. J Affect Disord 2009;113(3):285–290. DOI: 10.1016/j.jad.2008.05.011.
19. Jochemsen HM, Kloppenborg RP, de Groot LC, et al; SMART Study Group. Homocysteine, progression of ventricular enlargement, and cognitive decline: The second manifestations of ARTerial disease-magnetic resonance study. Alzheimers Dement 2013;9(3):302–309. DOI: 10.1016/j.jalz.2011.11.008.
20. Garcia AA, Haron Y, Evans LR, et al. Metabolic markers of cobalamin deficiency and cognitive function in normal older adults J Am Geriatr Soc 2004;52(1):66–71. DOI: 10.1111/j.1532-5415.2004.52012.x.

21. Boxer AL, Kramer JH, Johnston K, et al. Executive dysfunction in hyperhomocysteinemia responds to homocysteine-lowering treatment. Neurology 2005;64(8):1431–1434. DOI: 10.1212/01.WNL.0000158476.74580.A8.
22. Anderson I, Pilling S, Barnes A, et al. The NICE guideline on the treatment and management of depression in adults. National Collaborating Centre for Mental Health, National Institute for Health and Clinical Excellence. London: The British Psychological Society & The Royal College of Psychiatrists; 2010.
23. Majhi MM, Bhatnagar N. Updated BG Prasad's classification for the year 2021: Consideration for new base year 2016. J Family Med Prim Care 2021;10(11):4318–4319. DOI: 10.4103/jfmpc.jfmpc_987_21.
24. Scarpina F, Tagini S. The Stroop color and word test. Front Psychol 2017;8:557. DOI: 10.3389/fpsyg.2017.00557.
25. Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS neuropsychology battery-2004, manual. National Institute of Mental Health and Neurosciences; 2004.
26. Grant MM, Thase ME, Sweeney JA. Cognitive disturbance in outpatient depressed younger adults: Evidence of modest impairment. Biol Psychiatry 2001;50(1):35–43. DOI: 10.1016/s0006-3223(00)01072-6.
27. Paelecke-Habermann Y, Pohl J, Leplow B. Attention and executive functions in remitted major depression patients. Journal Affect Disor 2005;89(1-3):125–135. DOI: 10.1016/j.jad.2005.09.006
28. RP Alves M, Yamamoto T, Arias-Carrión O, et al. Executive function impairments in patients with depression. CNS Neuro Disord Drug Targets 2014;13(6):1026–1040. DOI: 10.2174/1871527313666140612102321.
29. Manders M, Vasse E, de Groot LC, et al. Homocysteine and cognitive function in institutionalised elderly: A cross–sectional analysis. Eur J Nutr 2006;45:70–78. DOI: 10.1007/s00394-005-0566-7.
30. Tu MC, Huang CW, Chen NC, et al. Hyperhomocysteinemia in Alzheimer dementia patients and cognitive decline after 6 months follow-up period. Acta Neurol Taiwan 2010;19(3):168–177. PMID: 20824536.
31. Siuda J, Gorzkowska A, Patalong-Ogiewa M, et al. From mild cognitive impairment to Alzheimer's disease-influence of homocysteine, vitamin B12 and folate on cognition over time: Results from one-year follow-up. Neurol Neurochir Pol 2009;43(4):321–329. PMID: 19742390.
32. Tucker KL, Qiao N, Scott T, et al. High homocysteine and low B vitamins predict cognitive decline in aging men: The Veterans Affairs Normative Aging Study. Am J Clin Nutr 2005;82(3):627–635. DOI: 10.1093/ajcn.82.3.627.
33. Alexopoulos P, Topalidis S, Irmisch G, et al. Homocysteine and cognitive function in geriatric depression. Neuropsychobiology 2010;61(2):97–104. DOI: 10.1159/000275821.