Original Research Article

Assessment of cognitive dysfunctions in patients with major depressive disorders

Ananda Reddy Endreddy[1], Lakshmi Rajesh Ch[2*], Subhani Shaik[3], Sandeep S[4]

[1,2,3,4]Department of Psychiatry, Narayana Medical College and Hospital, Nellore, Andhra Pradesh.
Email: anandendreddy@gmail.com

Abstract

Background: Impaired cognitive functioning is a common, but frequently underestimated phenomenon in patients with depression. A large majority of patients with depression present to physicians with complaints of medically unexplained somatic symptoms, or masked depression, hence an attempt is made to study the cognitive dysfunctions in depression patients. **Aims and Objectives:** To evaluate Cognitive Dysfunctions in people with Depression and to investigate the relationship between Cognitive Dysfunction and Severity of Depression. **Materials and Methods:** 120 People who are being diagnosed depression by ICD 10 and also scoring ≥ 20 on Becks Depression Inventory (BDI – II) scale are taken as cases. Then the cognitive functions of depression patients were assessed using Standardized mini mental status examination (SMMSE) Digit Symbol Substitution Test (DSST), Trial Making Test - A and Trail Making Test – B. Later BDI – II score (ie severity of depression) was correlated SMMSE, DSST, TMT - A and TMT– B. **Results:** The mean Beck Depression Inventory (BDI – II) scores among the cases was 32.37 with a standard deviation of 7.915. the mean Standardized Mini Mental Status Examination (SMMSE) score among the cases was 18.87 (± 4.353) ,the mean (± SD) of Digit Symbol Substitution Test (DSST) scores among the cases was 62.1 (± 19), the mean Trail making – A (TMT _A) scores among the cases was 39.07 (± 20.63), the mean Trail making – B (TMT – B)scoresamongthecaseswas160.43(±90.29). **Summary And Conclusions:** Depressive patients poorly performed on Standardized mini mental status examination, gave less correct responses on Digit Symbol Substitution Test took longer time in completion of both Trail making tests A and B. Comparison is statistically significant between BDI – II score and SMMSE,DSST,TMT – B and statistically not significant with TMT – A, TMT – A Error and B Error.
Key Words: Depression, Cognitive dysfunction, BDI, SMMSE, TMT-A,TMT-B.

[*]**Address for Correspondence:**
Dr. Lakshmirajesh.ch, Associate Professor, Department of Psychiatry, Narayana Medical College and Hospital, Nellore-524003, Andhra Pradesh, INDIA.
Email:anandendreddy@gmail.com
Received Date: 02/06/2019 Revised Date: 28/06/2019 Accepted Date: 11/08/2019
DOI: https://doi.org/10.26611/1071124

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 16 August 2019

INTRODUCTION

Depression is a common, treatable disorder which continues to remain leading cause of global disease burden, accounting for 4.3% of total disability adjusted life years.[1-4] Depression will become leading cause of psychiatric morbidity by 2030, if the same trend continues.[5-6] Cognitive symptoms appear to represent one of the core features of depressive disorders with an impact on many functional outcomes.[7-8]Contemporary neuroimaging research links "cold" cognition to structural changes in dorsolateral prefrontal cortex (DLPFC), while "hot" cognition is typically associated with structural abnormalities in orbitofrontal cortex (OFC) and the hippocampus.[9,10] The cognitive dysfunction symptoms, including slowing, impairment of executive functions and working memory significantly contribute to the patients deteriorated functioning and may prolong their malaise even after the resolution of typical depressive symptoms.[11] Cognitive dysfunctions also play an important role in diminishing the capacity to perform the activities of daily living, thus hindering psychosocial activity and negatively affecting patients everyday functioning.[12] In depression, most affected domains of

How to cite this article: Ananda Reddy Endreddy, Lakshmi Rajesh Ch, Subhani Shaik, Sandeep S. Assessment of cognitive dysfunctions in patients with major depressive disorders. *MedPulse – International Journal of Psychology.* August 2019; 11(2): 33-39.
http://www.medpulse.in

cognitive function are attention, working memory and learning, processing speed and executive function.[13] The results from the morphometric studies pronounced alterations in the hippocampus and prefrontal cortex during the first depressive episode suggest that the functional correlate of morphological changes in structures implicated in the modulation of the cognitive processes.[11]the cognitive deficits occur early in the course of the depression and may progress with recurring depression episodes.[9]Positive Co-Relation is established between serotonergic dysfunction and cognitive symptoms of depression.[14] Acute tryptophan depletion leads not only to low mood in vulnerable subjects, but also cognitive dysfunction in Depression. [15]Antidepressants may exert a beneficial effect on cognitive impairment in individuals with depression, converging evidence indicates that the cognitive deficits are often optimally treated with conventional psychopharmacological treatments. [16,17]

MATERIALS AND METHODS

Source of data

Participants were recruited from outpatient department of Psychiatry, Narayana Medical College and Hospital, Nellore, Andhra Pradesh. This study included Depressive Patients.

Duration of study

Data has been collected from January 2017 to January 2018.

Sample of the study

The sample of the study comprised of 120 participants who attended the department of psychiatry, OP at Narayana Medical College and Hospital, Nellore. 120 participants who are being diagnosed Depression by ICD 10 and also scoring ≥ 20 on Becks Depression Inventory (BDI – II) are taken as cases.

Type of sampling

Purposive sampling.

Inclusion criteria

1. Age between 18 to 60 years of both sexes.
2.Grade 5 or above.
3.Diagnosed depression by ICD – 10.
4.BDI-II SCORE ≥ 20.
5.Patients who are willing to give consent to participate in the study.
6.Patients present with first episode of Depression

Exclusion criteria:

1. Patients with any history of Neurocognitive or Neurological Disorders or Head injuries.
2. Patients diagnosed with any other Psychiatric disorders, Mental retardation and any Substance dependence or ECT treatment within 6 months prior to the study.
3. Patients with any history of Endocrinological problems or other Physical Comorbidities.

Instrumemts used

1. Becks Depression Inventory – II (BDI – II)
2. Standardized mini mental status examinantion (SMMSE).
4. Digit Symbol Substitution Test (DSST).
5. Trial Making Test - A.
6. Trail Making Test – B.

Method of data collection

People who are being diagnosed depression by ICD 10 in psychiatry OP in Narayana Medical College and Hospital and also scoring ≥ 20 on Becks Depression Inventory (BDI – II)[18]scale are taken as cases. Institutional ethical committee approval was taken. The patients fulfilling the selection criteria were approached and explained about the purpose of the study. Informed consent were obtained from all the participants. 120 Cases were selected by using Becks depression inventory – II and scoring ≥ 20. Then the cognitive functions of cases were assessed using Standardized mini mental status examination (SMMSE)[19], Digit Symbol Substitution Test (DSST)[20], Trial Making Test - A and Trail Making Test – B[21]. Later BDI – II score (ie severity of depression) was correlated with SMMSE, BCRS, DSST, TMT - A and TMT – B.

Statistical analysis

The data has been entered into MS-Excel and statistical analysis has been done by using IBM SPSS Version 20.0. To test association between the groups chi-square test was used. For estimation of continuous nature of numbers shown as mean and standard deviation. To estimate the difference between two groups student's t-test (Independent/Paired) was used. To test the correlation between the scores, Spearman's rank correlation was used. The p value less than 0.05 are considered as statistical significant.

RESULTS

Table 1: Socio-Demographic Variables of Depressive Patients (Cases)

Socio-Demographic Variable	Cases N (%)
Age Group	
21 – 30 Years	12 (10.0)
31 – 40 Years	56 (46.7)
41 – 50 Years	40 (33.3)
> 50 Years	12 (10.0)
Sex	
Male	48 (40.0)
Female	72 (60.0)
Domicile	
Rural	64 (53.3)
Urban	56 (46.7)
Marital Status	
Single	44 (36.7)
Married	68 (56.7)
Separated	4(3.3)
Divorced	4 (3.3)
Education	
Primary School	48 (40.0)
Middle School	44 (36.7)
High School	20(16.7)
Posthigh School/ Intermediate	4(3.3)
Graduate/ Pg	4 (3.3)
Occupation	
Unskilled Worker	60 (50.0)
Semi Skilled Worker	28(23.3)
Skilled Worker	12 (10.0)
Clerical / Shop Owner	4(3.3)
Semi Profession	8 (6.7)
Profession	8 (6.7)

Table 1. shows the socio-demographic variables of Depressive patients (cases) From the table it is clear that Majority of the subjects belongs to 31 – 40 years /41 – 50 years age group, females more than males, coming from rural areas than urban, educated up to primary school/middle school, unskilled workers, married and belonging to nuclear family.

Table 2: The Mean values of Duration of depression and BDI-II Scores in Cases (Depressive patients)

	Mean ± SD
Duration of depression	44.5 ± 3.25
BDI – II	32.37 ± 7.915

Table 2:shows the duration of depressive episodes and mean Becks Depression Inventory (BDI – II) scores of the Depressive patients (cases). The mean duration of depression among the cases was 44.5 days with a standard deviation of 3.25 days and the mean BDI – II scores among the cases was 32.37 with a standard deviation of 7.915.

Table 3: Distribution of the study group according to SMMSE scores

SMMSE	Cases	T value	P value, Sig
Mean ± SD	18.87 ± 4.353	10.9	<0.001, HS

Table 3. shows the comparision of SMMSE scores between Depressive patients (cases).The mean (± SD) SMMSE score among the cases was 18.87 (± 4.353).This mean difference was statistically significant in the cases with a p – value <0.001.

Table 4: Distribution of the study groups according to DSST scores

DDST	Cases	T value	P value, Sig
Mean ± SD	62.1 ± 19.0	5.362	< 0.0001, HS

Table 4. shows the comparison of correct responses of digit symbol substitution test between Depressive patients (cases) The mean (± SD) of DSST scores among the cases was 62.1 (± 19) and it was statistically significant with a p – value < 0.0001. This shows Depressive group are doing less correct responses.

Table 5: Distribution of the study group according to TMT _ A and TMT _ B scores

	Cases	T value	P value, Sig
TMT _ A Mean ± SD	39.07 ± 20.63	3.827	< 0.0001, HS
TMT _ B Mean ± SD	160.43 ± 90.29	4.03	< 0.0001, HS

Table 5. shows the comparison of time taken for completion of TMT_A and TMT _ B between depressive patients (cases).This shows Depressive group are taking more time to complete the tasks and this was statistically significant at a p – value < 0.0001.

Table 6: Correlation of Severity of Depression (BDI – II score) with SMMSE, DSST, TMT – A, TMT – A errors, TMT – B, TMT – B errors.

BDI-II score	SMMSE	DSST	TMT – A	TMT – A errors	TMT – B	TMT – B
Correlation coefficient (r)	-0.676	0.431	0.252	0.176	0.345	0.221
P value	0.000	0.001	0.052	0.178	0.007	0.09

The correlation between BDI – II scores (ie severity of depression) and SMMSE, DSST, TMT-A, TMT-B, and its errors had shown that :

1. The correlation was negative and significant between SMMSE and DSST.
2. Positive and significant for TMT – B
3. Positive and non significant for TMT – A, TMT – A Error and TMT - B Error.

DISCUSSION

The Becks Depression Inventory scores of the depressive patients:

The mean Becks Depression Inventory(BDI – II) scores among the cases was 32.37 with a standard deviation of 7.915 in the present study suggesting that most of the cases were with Moderate depression (score : 21-30) and Severe depression (score : 31-40). But the inclusion criteria for the cases group was patients with BDI – II >20 in the present study. In a study done by Grant L. Iverson and colleagues, 62 participants with depression were considered, average age was 41.1 years (SD = 12.5) and 71% were women. Their average score on the BDI-II was 24.1 (SD = 11.2).[22] our study findings are in accordance with the above studies.

Standardized Mini Mental Status Examination (SMMSE) scores of the Depressive patients.

In the present study, the mean Standardized Mini Mental Status Examination (SMMSE) score among the cases was 18.87 (± 4.353) .This was statistically significant with p – value < 0.001. When compared to previous studies, the present study had low Standardized Mini Mental Status Examination (SMMSE) scores among the depressive patients. In a study done by Ping Yao and Can Meng, comprising of 3050 patients, the mean CES-D (Center for Epidemiologic Studies Depression Scale score) the mean was 24.69±4.70.[23] In a study done by Ling Han, Two hundred eighty-one medical inpatients were followed up with the Becks Depression Inventory(BDI – II) and standardized Mini-Mental State Examination (SMMSE) they had a mean standardized Mini Mental Status Examination (SMMSE) score of 25.8 (standard deviation = 3.5) with 26.0% below 24.[24]

Correct responses of Digit Symbol Substitution Test in Depressive patients

In the present study, the mean (± SD) of Digit Symbol Substitution Test (DSST) scores among the cases was 62.1 (± 19). This is statistically significant at a p value < 0.0001. It reflects that Depressive patients performed poorer in giving the correct responses with in a time period of 120 seconds on Digit symbol substitution test (DSST). The present study results were similar with previous studies in relation to DSST scores among the depressed patients. In a Meta-analysis done by Lim J and colleagues, a total of 22 trials involving 955 MDD patients and 7,664 healthy participants were considered. Major Depressive Disorder patients showed significantly impaired results compared with healthy participants on the Digit Span and Continuous Performance Test in the attention domain.[25] In a study done by Mark D. Sullivan and colleagues, Participants with scores indicative of depression (PHQ-9 > 10) showed greater cognitive decline during 40-months follow-up on tests, with the following differences in estimated means: DSST (Digit Symbol Substitution Test) 0.72 (95%CI 0.25, 1.19, p=0.0029).[26] In the Austin *et al* study subjects with endogenous/melancholic depression were impaired on working memory (digits backwards) as well as on tasks heavily reliant on set-shifting (Trails B, and Digit Symbol Substitution Test).[27]

Trail making – A and Trail making – B tests and its errors in Depressive patients. In the present study, the mean Trail making – A (TMT _A) scores among the cases was 39.07 (± 20.63). This was statistically significant with p – value < 0.0001. These show Depressive patients are taking more time in performing

the task. In the present study, the mean Trail making – A (TMT – A) errors was 1.47 (± 1.04) among the cases. But this was not statistically significant with a p – value > 0.05. The present study results were similar to the previous studies in relation to trail making tests. In a study by Switalska *et al*, the mean Trail making – A (TMT A) was 54.83 secs in the cases.[28] Talarowska *et al* have observed that the mean Trail making – A (TMT A) time was 36.08 secs among the patients with first episode of depression and recurrent episodes of depression was 52,78 secs.[29] Airaksinen reported that the mean scores for Trail Making – A test among the cases was 23.5 and controls was 23.5 unlike the results of this study.[30] The present study, the mean Trail making – B (TMT – B) scores among the cases was 160.43 (± 90.29) This was statistically significant with a p – value < 0.0001. This show depressive patients are taking more time to complete the task. In the present study, the mean Trail making – B (TMT – B) errors was 7.2 (± 4.2) among the cases. This was statistically significant with a p – value < 0.05.

In a study done by Switalska *et al*, the mean Trail making – B (TMT B) scores was 152.07 among the cases and 84.67 secs among the controls. The mean score for errors was 1.04 in the study group and 0.23 in the control group. In TMT test part A and B, patients with depression received almost twice as long execution time as healthy controls, suggesting a distinct disturbances in the visuo-spatial working memory. These patients also committed significantly more errors in Part B of the test, based on reacting in accordance with established patterns (making a trail in numerical or alphabetical order), On this basis, it can be concluded that in these patients, there are attention disorders involving difficulties in searching the perceptual field and in switching attention. Difficulties in execution of part A can also be related to impairment in sustained attention, and can also be the result of a general psychomotor slow down.[28] Talarowska *et al* have observed that the mean Trail making – B(TMT B) time was 82.78 secs among the patients with first episode of depression and 110.98 among the patients with recurrent episodes of depression.[29] Two studies conducted by Martinez-Aran *et al* , patients with depression obtained significantly worse results in both parts of the test Trail making (TMT) than healthy controls. The execution times obtained in those studies, 51.2 seconds for Part A and 151.2 seconds for Part B. These results are consistent with previous reports of Martinez-Aran *et al*, in which patients with depression received prolonged execution times of part A (55.2 sec.) and Part B (154.3 sec.).[8] In a study by Basso's *et al*, patients with depression obtained in the test (Trail making test) TMT A and B significantly worse results than healthy individuals. [31]

Correlation between Becks Depression Inventory(BDI – II) scores (ie severity of depression) with SMMSE, DSST, trail making A and B and its errors among the Depressive patients.

In the present study, Comparison between Becks Depression Inventory (BDI – II) scores and SMMSE, DSST, trail making A and B of Depressive patients shows that, the correlation was negative and significant between SMMSE and DSST, positive and significant for TMT – B, positive and non significant for TMT – A, TMT – A Error and TMT - B Error. In the present study, when Becks Depression Inventory (BDI – II) scores were compared with Standardized Mini Mental Status Examination (SSMSE) scores, the correlation was negative and statistically significant with a p – value <0.000. This shows with an increase in severity of Depression (ie increase in BDI – II score) the SMMSE score is decreasing, which ensures that deficits in Attention, Orientation, Registration, Recall, Language, Construction abilities are increasing. In the present study, when Becks Depression Inventory (BDI – II) scores were compared with Digit Symbol Substitution Test(DSST) scores, the correlation was negative and statistically significant. This study shows higher BDI – II score is associated with lesser number of correct responses on Digit Symbol Substitution Test (DSST) .i.e., BDI - II score is inversly related to the number of correct responses in Digit Symbol Substitution Test (DSST). As the severity of depression is increasing, the number of correct responses on Digit Symbol Substitution Test (DSST) are decreasing. In the present study, when Becks Depression Inventory (BDI – II) scores were compared with Trail making A test scores, the correlation was positive, but statistically not significant. This study shows that higher the Becks Depression Inventory(BDI – II) score (ie with increase in severity of depression), more time is taken to complete the Trail making test– A (TMT_A). It signifies that Depressive patients with higher BDI - II score have significant deficits in visual attention, task switching, visual search speed, scanning ,speed of processing, cognitive flexibility and executive functions which results in more time to complete the Trail making test – A (TMT_A) i.e., BDI – II score is directly related to time taken for the completion of Trail making test – A(TMT_A), but was not statistically significant. In the present study, when Becks Depression Inventory (BDI – II) scores were compared with Trail making B test scores, the correlation was positive, and statistically significant. This study shows that higher the Becks Depression Inventory (BDI – II) score (ie with increase in severity of depression), more time is taken to complete the Trail making test – B (TMT_B).It signifies that Depressive patients with higher BDI – II score have

significant deficits in visual attention, task switching, visual search speed ,scanning ,speed of processing ,cognitive flexibility and executive functions which results in more time to complete the Trail making test – B (TMT_B) .i.e. BDI - II score is directly related to time taken for the completion the TMT_B . In the present study, the correlation between trail making test _A errors and Becks Depression Inventory (BDI – II) score was positive, but not statistically significant and correlation between trail making test _B errors and Becks Depression Inventory (BDI – II) score was positive, but not statistically significant. In a study done by Sabrina Paterniti and colleagues, participants with high levels of depressive symptoms showed a greater decrease in SMMSE score at baseline and at 4-year follow-up assessments. High levels of depressive symptoms were also associated with a higher risk of a 3-point decrease in SMMSE score and with a higher risk of low cognitive functioning at follow-up. These results were similar to the present study results.[32] In a study done by Ling Han and colleagues, after adjusting for age, cardiovascular risk, illness severity, baseline physical and cognitive function, and other covariates, a one-point increase in Hamilton Depression Rating Scale (HAMD) score (baseline mean ± standard deviation: 14.4 ± 7.4) was associated with a lower SMMSE score, this is similar with the present study results.[24]Han and colleagues, showed that increase in Hamilton Depression Rating Scale (HAMD) scale scores were linked with poorer performance on the Standardised Mini-Mental State Examination (SMMSE) scale, similar to the present study results.[24] The meta-analysis of Snyder showed that performance in some neuropsychological measures of Executive Functions is sensitive to symptom severity, revealed by the existence of a positive relation between both measurements.[4]In the meta-analysis of McDermott and Ebmeier 14studies were included. These works assessed the relationship between severity of the depressive episode according to Hamilton Depression Rating Scale (HAMD) or MADRS (Montgomery-Asberg Depression Scale) scores and performance on different neuropsychological tests. Significant negative correlations were observed between symptom severity and episodic memory (g=0.31), Executive function tasks(g=0.32) and processing speed (g=0.16).[33] Chaves'*et al* study, shows the deterioration of verbal fluency along with intensification of depressive symptoms.[34] In a study done by Switalska *et al*, that depressive patients performed poorly in Trail making – A and Trail making – B tests, but when compared with the severity of Depresion, the correlation coefficient was 0.23 with TMT A, -0.14 with the TMT A errors, 0.01 with TMT B and -0.07 with the TMT B errors unlike the results of this study.[28]

LIMITATIONS OF THE STUDY

a. The sample size was relatively small. Thus comparing variables with such small sample size will reduce the effect size of the results.

b. The study samples have been taken from our department. Since it is general hospital psychiatry setting the results could not be extrapolated to community samples.

c. In this study illiterates are not taken. So the cognitive deficits in them were not assessed.

d. It was not possible to correlate duration and number of episodes of depression with severity of cognitive dysfunctions.

CONCLUSION

The results clearly indicate that Cognitive Dysfunctions are present in Depression. As the Severity of Depression increases measured by Beck Depression Inventory (BDI – II) has significant cognitive dysfunctions.

REFERENCES

1. Trivedi MH, Greer TL, Cognitive Dysfunction in Unipolar Depression: Implications for Treatment. Journal of Affective Disorders. 2014; 152 (4): 19–27.
2. Snyder, H.R. Major Depressive Disorder is associated with Broad Impairments on Neuropsychological Measures of Executive function: A Meta-analysis and Review. Psychological Bulletin. 2013; 139(1): 81-132.
3. Hasselbalch BJ, Knorr U, Kessing LV, Cognitive Impairment in the Remitted State of Unipolar Depressive Disorder: A Systematic Review. Journal of Affective Disorders 2011; 134(1-3): 20–31.
4. Porter RJ, Gallagher P, Thompson JM, Young AH, Neurocognitive Impairment in Drug-free Patients with Major Depressive Disorder. The British Journal of Psychiatry 2003; 182(3): 214–220
5. Üstün TB, Ayuso-Mateos JL, Chatterji s, Mathers C, Murray CJL. Global Burden of Depressive Disorders in the year 2000. British Journal of Psychiatry 2004;184(5): 386-392.
6. Thirunavukarasu M, Thirunavukarasu P. Training and National Deficit of Psychiatrists in India - A critical analysis. Indian J Psychiatry 2010; 52(7): 83.
7. Atre-Vaidya N *et al*. Cognitive Deficits, Psychopathology and Psychosocial Functioning in Bipolar Mood Disorder. Neuropsychiatry, Neuropsychology, and Behavioral Neurology 1998; 11(5): 120-126.
8. Martinez-Aran A Vieta E, Reinares M, Colom F, Torrent C, Sanchez-Moreno J, Benabarre A, Goikolea JM, Comes M, Salamero M, Cognitive Functions Across Manic or Hypomanic, Depressed, and Euthymic states in Bipolar Disorder. The American Journal of Psychiatry. 2004; 161(2): 262-270.
9. Erickson K, Drevets WC, Clark L, Cannon DM, Bain EE. Mood-Congruent Bias in Affective go/no-go performance of unmedicated patients with Major Depressive Disorder.

American Journal of Psychiatry 2005; 162(11): 2171–2173.
10. Roiser JP, Sahakian B. Hot and Cold Cognition in Depression. CNS Spectrums. 2013; 18(3): 139–149.
11. MacQueen GM, Campbell S, McEwen BS. Course of illness, Hippocampal Function, and Hippocampal Volume in Major Depression. Proceedings of the National Academy of Sciences. 2003; 100(3): 1387-1392.
12. Greer TL, Sunderajan P, Grannemann BD, Kurian BT, Trivedi MH. Does duloxetine improve cognitive function independently of its antidepressant effect in patients with major depressive disorder and subjective reports of cognitive dysfunction. Depression Research and Treatment. 2014; 14(2): 1-17.
13. Lee RS, Hermens DF, Porter MA, Redoblado-Hodge MA. A Metaanalysis of Cognitive Deficits in First-Episode Major Depressive Disorder. Journal of Affective Disorders 2012; 140(2): 113-124.
14. Sobczak S, Riedel WJ, Booij I. Cognition following Acute Tryptophan Depletion: difference between Firstdegree relatives of Bipolar Disorder patients and matched Healthy Control Volunteers. Psychological Medicine 2002; 32(3):503–515.
15. Bortolato B, Carvalho AF, McIntyre RS, Cognitive Dysfunction in Major Depressive Disorder: A state of the Art Clinical Review, CNS and Neurological disorders – Drug targets, 2015: 13(10): 1804 – 1818.
16. Jaeger J, Berns S, Uzelac S, Davis-Conway S. Neurocognitive Deficits and Disability in Major Depressive Disorder. Psychiatry Research. 2006; 145(1): 39-48.
17. Etkin A, Gyurak A, O'Hara R. A Neurobiological Approach to the Cognitive Deficits of Psychiatric Disorders. Dialogues in Clinical Neuroscience. 2013;15(1): 419–429.
18. Beck, A.T., Steer, R.A., and Brown, G.K. (1996). Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation.
19. Molloy DW, Alemayehu E, Roberts R. Reliability of a standardized Mini-Mental State Examination compared with the traditional Mini-Mental state Examination. American Journal of Psychiatry, Vol. 14, 1991a, pp.102-105
20. Alan S. Kaufman Test Review: Wechsler, D. Manual for the Wechsler Adult Intelligence Scale, Revised. New York: Psychological Corporation, 1981 *Journal* of Psychoeducational Assessment. (1983) *;* 1, (3): 309 – 313.
21. McKinlay A. (2011) Trail Making Test. In: Goldstein S., Naglieri J.A. (eds) Encyclopedia of Child Behavior and Development. Springer, Boston, MA.
22. Iverson GL, Lam RW. Rapid Screening for Perceived Cognitive Impairment in Major Depressive Disorder. Annals of Clinical Psychiatry 2013; 25(2): 135–140.
23. Yao P, Meng C, Longitudinal Causal Inference of Cognitive Function and Depressive Symptoms in Elderly People, Epidemiology Biostatistics and Public Health: 2015: 12(3) 54.
24. Han L, McCusker J, Abrahamowicz M, Cole M, Capek R, The Temporal Relationship Between Depression Symptoms and Cognitive Functioning in Older Medical Patients—Prospective or Concurrent?, Journals of Gerontology Series A: Biological Sciences and Medical Sciences (2006) 61 (12): 1319-1323.
25. Lim J, Oh IK, Han C, Huh YJ, Jung IK, Patkar AA, Steffens DC, Jang BH. Sensitivity of Cognitive Tests in Four Cognitive domains in Discriminating MDD patients from Healthy controls: A Meta-analysis, International Psychogeriatrics: 2013; 25(9):1543-1557.
26. Sullivan MD, Katon WJ, Lovato LC, Miller ME, Murray AM, M.D.,Horowitz KR *et al*, Depression is associated with accelerated cognitive decline among patients with Type 2 diabetes in the ACCORD-MIND trial, JAMA psychiatry. 2013; 70(10): 1041 – 1047.
27. Austin MP, Mitchell P, Goodwin GM. Cognitive deficits in depression. The British Journal of Psychiatry. 2001;178(3): 200-206.
28. Switalska J, Borkoswa A, Cognitive functioning in a depressive period of bipolar disorder, Archives of Psychiatry and Psychotherapy: 2014. 16(4): 27 – 37.
29. Talarowska M, Zajączkowska M, Gałecki P. Cognitive Functions in First-episode Depression and Recurrent depressive disorder, Psychiatria Danubina, 2015; 27(1): 38–43.
30. Airaksinen E, Wahlin Å, Larsson M, Forsell Y. Cognitive and Social Functioning in Recovery from Depression: results from a population-based three-year follow-up. Journal of AffectiveDisorders. 2006; 96(1-2):107-110.
31. Basso M, Neel J, Bornstein RA, Lowery N, Purdie R, Neuropsychological Impairment among Manic, Depressed, and Mixed-epizode inpatients with Bipolar Disorder. Neuropsychology. 2002; 16(1): 84-91.
32. Paterniti S, Taillefer MV, Dufouil C, Pérovitch A . Depressive symptoms and Cognitive decline in Elderly people Longitudinal study, The British Journal of Psychiatry. 2002; 181 (5) 406 – 410.
33. McDermott LM, Ebmeier KP. A Meta-analysis of Depression Severity and Cognitive function. Journal of Affective Disorders. 2009;119(1- 3):1-8.
34. Chaves OC, Lombardo LE, Bearden CE, Woolsey MD, Martinez DM, Barrett JA, Miller AL, Velligan DI, Glahn DC. Associationof clinical symptoms and Neurocognitive Performancein Bipolar Disorder: a longitudinal study. Bipolar Disorders: 2011; 13(1): 118-123.

Source of Support: None Declared
Conflict of Interest: None Declared