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A COMPARATIVE STUDY OF NEUROCOGNITIVE IMPAIRMENT IN MAJOR DEPRESSIVE DISORDER AND BIPOLAR AFFECTIVE DISORDER TYPE 1(MAJOR DEPRESSIVE EPISODE).

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ABSTRACT ***BACKGROUND -*** *Cognition includes attention, memory, language, orientation, praxis, executive function, judgment and problem solving. Cognitive deficits are also found in mood disorders. We planned this study to asses and compare neurocognitive deficits among (BAD-I and MDD).*

MATERIAL &METHODS: - *It was a cross sectional study. Patients of BAD-I (n = 60) and MDD (n = 120) group (HAMD> 14), and 60 demographically matched healthy controls were assessed on various neurocognitive tests. Sociodemographic data and clinical parameters between groups were analysed by ANOVA, chi square and independent t-test. Cognitive deficits among all groups were analysed by ANOVA and further group differences by Tukey HSD post-hoc analysis.*

RESULTS: - *Most of the subjects were married, educated upto middle to secondary level with monthly income of the family above Rs. 15,000, from urban background and were Hindu. Patients with BAD-I and MDD performed poor on all the neurocognitive tests in comparison to control. Longer time than usual was required to complete the TRAIL part A and B was due to impairment in processing speed and executive functions respectively. Patients with UD performed significantly better in TMT-B, Stroop Color Test and COWA than BD-I group. Bipolar depressive patients were more significantly impaired only on the domains of executive functioning and verbal fluency in comparison to MDD patients.*

CONCLUSIONS: *Patients with BAD-I displayed more widespread cognitive impairment than the MDD group and performed significantly worse than subjects with MDD on measures of executive functioning and verbal fluency.*

KEYWORDS : Cognitive deficits, bipolar depression, unipolar depression

INTRODUCTION:-

Cognition is a comprehensive term used to describe higher mental functions and includes attention, memory, language, orientation, praxis, executive function, judgment and problem solving. Any degree of impairment in these processes, results in cognitive deficit. Cognitive deficits are also found in mood disorders, including bipolar disorder (BAD) and major depressive disorder (MDD).

Cognitive impairments in BAD are consistently observed during mood episodes [1,2] as well as during euthymia. [1,3] The presence of cognitive disturbances during depressive phase of bipolar affective disorder is observed mainly in domains namely executive functions, working memory, verbal learning and verbal fluency. [1,2,4,5]

Studies done in past few decades, reported that cognitive deficits are unavoidable component of MDD, though there was differences both in the sample size as well as in the assessment tools used to assess cognitive impairment. Nevertheless, several recent meta-analyses suggest that there were several cognitive domains that appear to be consistently affected in MDD. Most consistent neurocognitive deficits that have been reported were psychomotor speed, [6] memory, [7] sustained attention, [8] and executive functioning especially in domains including working memory and complex problem solving. [9]

Multiple researches have been conducted, to differentiate bipolar affective disorder (major depressive episode) from major depressive disorder on the basis of neurocognitive tests. They directly compared cognitive profiles of bipolar affective disorder (major depressive episode) with MDD patients, but the results were inconsistent. [5,10,11,12,13]

Some studies were in favour that, cognitive deficits in BAD and MDD patients differed in pattern and magnitudes, [5, 10] while others found no difference. [11,12] Though, most of these studies recruited patients of both Bipolar I and II disorder [11,12] and it was found in many studies that there is difference in performance on cognitive tests in both the groups. [14,15]

Thus, the only consistent finding in previous studies was in the domain of executive functioning which is significantly impaired in bipolar depressed patients (BAD I) as compared to MDD patients. [5,15]

There were very few studies comparing differences in neurocognition in major depressive disorder and bipolar affective disorder type 1 (major depressive episode) patients with inconsistent and contrary results. Therefore, we planned a study to test, both groups of depressed patients (BAD I and MDD) and healthy controls on a battery of neurocognitive tests in a tertiary care hospital setting.

MATERIAL &METHOD:-

After getting approval from Ethics Committee, a cross sectional study was planned among patients attending OPD/IPD with diagnosis of Bipolar affective disorder type 1 (major depressive episode) and major depressive disorder. The diagnosis was confirmed by any of two psychiatrist as per DSM-5.

Those fulfilling the inclusion criteria were recruited in study. Healthy controls were also recruited as per inclusion criteria. Aims objective and methods adopted were explained to all the patients and healthy controls. After getting written consent from bipolar affective disorder type 1(major depressive episode) (n=60), major depressive disorder (n=120) and healthy controls (n=60) their sociodemographic details were noted.

For the assessment of neurocognitive functions various tools (Digit span, Trail Making Test (TMT A and B), Verbal Learning & Memory Test (VLMT), Stroop Color Test, Visuospatial working memory matrix (VWWM), Controlled oral word association (COWA) test) were applied. It took approximately 1.5 to 2 hours to complete the tests in either one or two settings, depending upon subject's compliance.

INCLUSION CRITERIA FOR CASES:-

Those fulfilling the diagnostic criteria as per DSM-5 of major depressive disorder and bipolar affective disorder type 1 (major depressive episode) [Moderate to severe category, Score on HAM-D > 14] were recruited in study. They were literate enough to understand the nature of tests, gave written informed consent and of either gender between 18-50 years of age.

EXCLUSION CRITERIA FOR CASE:-

Those fulfilling the diagnostic criteria as per DSM-5 of major depressive disorder and bipolar affective disorder type 1 (major depressive episode) but were not giving consent, unwilling and uncooperative, substance dependent except tobacco with comorbid significant physical or neurological illness and Color blindness and had undergone ECTs during last 6 months were excluded.

Selection criteria for healthy control group:-

Those who were willing and cooperative, literate enough to understand the nature of tests, not taking any medication and substance except tobacco in last one month after their consent irrespective of their gender with age in between 18-50 years were recruited as healthy control.

Exclusion criteria for healthy control group:-

Those who were not giving consent, unwilling and uncooperative, color blind subjects with substance dependence except tobacco and the immediate relatives of mood disorder patients were excluded.

Neurocognitive tests:–

1. **Digit span test -** It has two parts - digit forward test and Digit backward test. In digit forward test, the subject is asked to repeat the digits called by examiner. It measures short term memory. In digit backward test, the subject is asked to repeat the digits read out by the examiner backward. It measure verbal working memory (Gong 1982). Total score for the Digit Span Test is the sum of the scores on digit forward and digit backward test. The maximum score that can be achieved on the test is 17. [16]

2.Trail Making Test (TMT A and B) - In Trail A – on a sheet of paper containing an irregular array of numbered circles, participant draws line connecting them in sequence. In Trail B, participants alternately connect numbers and letters in order (e.g. 1 to A to 2 to B).This construct encompasses many neuropsychological abilities, such as visual attention, planning and sequential behavior, initiating and choosing behavior, and cognitive flexibility. Total time taken to finish the task will be the score of the individual in both Trail A and B. [17]

3. Verbal Learning & Memory Test (VLMT) - In this test, subject is asked to pay attention to the story that is being read by Examiner. The passage containing 23 bits of information is read out to the subject 4 times. After each trial the subject is asked to recall the passage immediately. In fourth trial the subject is asked to recall after 10 minutes. The total numbers of correct responses on each trial are noted qualitatively, confabulatory responses, perseverance, poor logical memory are elicited on this test. [18]

4. Stroop Color Test- It measures the executive function. Susceptibility to interference and inability to inhibit inappropriate automatic responses are assessed more specifically by tasks that provoke competing responses, such as Stroop procedure. [19]

5. Visuospatial working memory matrix (VWWM) - Two different components are critical to visuospatial working memory: passive store and active imagery operation. Both are mutually independent, and can be examined by this test. [20]

Controlled oral word association (COWA) test - Also known as word fluency test, FAS fluency, letter fluency, and category fluency test. It is also a sensitive measure of executive functions, because it requires the subject to generate its own strategy. For phonemic fluency the subject is asked to produce as many words as possible beginning with a given letter in a limited period (one minute). [21]

Medications Used In Present Episode		Bipolar affective disorder type 1(major depressive episode)	Major depressive disorder
Mood stabilisers	Sodium valproate	4	0
	Lithium	6	12
Antidepressants	Fluoxetine	12	13
	Escitalopram	3	11
	Sertraline	0	6
Antipsychotics	Olanzapine	6	7
	Risperidone	2	3
	Aripiprazole	1	0
Benzodiazepines	Clonazepam	4	10
	Diazepam	1	2
	Lorazepam	0	2

36 patients of bipolar affective disorder type 1 (major depressive episode) and 90 patients of major depressive disorder were not taking any medicines in current episode.

Only 2 patients of bipolar affective disorder type 1 (major depressive episode) were taking anticholinergics [THP- Trihexyphenidyl].

STATISTICAL ANALYSIS:-

Statistical analysis was done by using SPSS version 20. Group comparison was done with the help of 'independent t-test' and chi squire test. For the group comparison of age, one way ANOVA was applied. Group comparisons for neurocognitive tests were done with the help of ANOVA. Further group differences were obtained with the help of Tukey HSD Post Hoc Analysis.

RESULTS:-

Table no. 1 shows the sociodemographic details of participants. No significant difference in socio-demographic details like sex, marital status, occupation, education, monthly income, religion, locality and family type among groups was found. Most of the subjects were Hindu, Married, educated upto middle to secondary level with monthly income of the family above Rs. 15,000, residing in urban locality.

Table 1: Socio-demographic details of BAD, MDD and control group

Socio-demographic details		BAD	MDD	CONTROL
Mean Age ± SD		31.83(3.05)	32.1(3.12)	32.4(2.9)
Sex	Male	33	50	31
	Female	27	70	29
Marital status	Married	46	94	45
	Unmarried	14	26	15
Occupation	Govt service	6	12	7
	House Wife	18	44	19
	Student	12	22	14
	Unemployed	4	2	0
	Businessmen	5	16	19
	Semi or unskilled Worker (Farmer)	15	24	11
Education	Upto Senior	45	92	44
	Graduates or PG	15	28	16
Monthly income of family	<6000	2	6	2
	6001-15000	10	26	6
	>15000	48	88	52
Family type	Nuclear	17	42	22
	Nuclear extended	11	18	9
	Joint	32	60	29
Locality	Urban	42	84	43
	Rural	18	36	17

Abbreviations: BAD- Bipolar Affective Disorder (depressive phase), UD- Unipolar Depression, p- probability value, X- test statistics, df- degree of freedom; SD- standard deviation.

Table no 2 shows the clinical variables of the patients. Mean age of onset of illness in BAD and MDD group was 23.85 and 26.15 years respectively. Mean duration of illness for patients with BAD and MDD was 7.98 and 5.95 years respectively. Number of episodes in BAD and MDD group were 4.03 and 2.42 respectively. Number of manic and depressive episodes in BAD patients were 1.71 and 2.32 respectively. Number of hospitalization in BAD and MDD group was 1.97 and 1.58 respectively. Family history of similar illness was seen in 28 (46.7%) BAD and 46 (38.3%) MDD patients. Mean HAM-D score in BAD and MDD patients was 22.00 and 23.02 respectively. Thirty six (60%) BAD and 90 (75%) MDD patients were not taking any medicines in current episode. Rest of the patients in both the groups was taking medicines like Mood stabilisers, Antidepressants, Antipsychotics, Benzodiazepines and Anticholinergics. No significant difference was seen in both the groups in terms of current medication. Statistically significant difference was found on t-test in clinical characteristics like age of onset, duration of illness, number of episodes and number of hospitalization.

Table 2: Clinical characteristics of patients

Clinical Characteristics	BAD(SD)	MDD (SD)	t-test value	p-value
Age of onset	23.85(5.69)	26.15(6.02)	-2.151	.034
Duration of illness (years)	7.98(3.09)	5.95(3.40)	3.428	.001
No. of episodes	4.03(1.49)	2.42(1.08)	6.793	.001
No. of manic/ depressive episodes	7.9(3.9)	2.42(1.08)	6.793	.001
No. of hospitalisation	1.97(1.07)	1.58(0.96)	2.061	.042
Family History	28	46	2.67	.10
Mean HAMD score	22.00(3.94)	23.02(3.21)	-1.550	.124
Current Medication None Medication	36	90	1.2	0.13
Mood Stabiliser	10	12		
Anti-depressant	15	30		
Antipsychotic	9	10		
Benzodiazepine	5	14		
Anticholinergic	2	0		

Abbreviations: BAD- Bipolar Affective Disorder t- t value, df- degree of freedom, p-Sig. (2-tailed); 0.05

Table no 3 shows the comparison of cognitive function of participants. Patients with bipolar affective disorder (major depressive episode) performed poor on all the neurocognitive tests in comparison to patients with major depressive disorder, although, the results were significant only in executive functioning and verbal fluency.

Table 3- Comparison of cognitive functions in all three groups

TEST	BAD (SD)	MDD (SD)	CONTROL (SD)	ANNOVA, F	Posthoc (Tukey test) P value
TMT-A	69.53 (4.19)	68.58 (4.75)	45.08 (4041)	622.21	BAD-MDD 0.382 BAD-CONT 0.00 MDD-CONT 0.00
TMT-B	165.02 (10.8)	140.3 (4.374)	79.92(4.34)	2744.90	**BAD- MDD 0.01** BAD-CONT 0.01 MDD-CONT 0.001
COWA-1	3.90 (1.6)	5.50 (1.9)	7.85(1.83)	73.58	**BAD-MDD 0.001** BAD-CONT 0.01 MDD-CONT 0.01
COWA-2	6.38 (1.8)	8.07 (1.9)	10.87(1.9)	86.19	**BAD-MDD 0.01** BAD-CONT 0.001 MDD-CONT 0.01
VWMM	2.97 (1.23)	3.38 (1.8)	4.55(1.35)	17.00	BAD-MDD 0.22 BAD-CONT 0.01 MDD-CONT 0.001
SCT-1	37.12 (3.4)	34.08 (4.05)	25.77(3.4)	153.18	**BAD-MDD 0.01** BAD-CONT 0.01 MDD-CONT 0.001
SCT-2	42.23 (3.01)	38.90 (4.7)	29.08(2.9)	190.49	**BAD-MDD 0.01** BAD-CONT 0.01 MDD-CONT 0.001
SCT-3	51.70 (4.8)	42.85 (3.7)	31.48(3.24)	405.99	**BAD-MDD 0.01** BAD-CONT 0.01 MDD-CONT 0.001
SCT Total Error	6.07 (2.1)	4.05 (1.8)	2.27(1.25)	70.52	**BAD-MDD 0.01** BAD-CONT 0.01 MDD-CONT 0.001
SCT Total Time	131.87 (10.9)	115.80 (12.3)	86.23(8.11)	267.43	**BAD-MDD 0.001** BAD-CONT 0.01 MDD-CONT 0.01
VLMT	10.88 (2.5)	11.40 (2.6)	15.53(1.7)	72.59	BAD-MDD 0.36 BAD-CONT 0.01 MDD-CONT 0.01
FDST	5.27 (1.7)	5.62 (1.5)	6.28(1.7)	6.36	BAD-MDD 0.35 BAD-CONT 0.002 MDD-CONT 0.02
BDST	3.97 (0.96)	4.17 (0.81)	4.97(0.7)	26.13	BAD-MDD 0.28 BAD-CONT 0.001 MDD-CONT 0.01

Abbreviations: TMT-A=Trail Making Test-A, TMT-B=Trail Making Test-B, SCT-1=Stroop Color Test-1, SCT-2 = Stroop Color Test-2, SCT-3 = Stroop Color Test-3, VLMT=Verbal Learning & Memory Test, VWMT=Visuospatial Working Memory Test, COWA-1 = Controlled Oral Word Association Test-1, COWA-2= Controlled Oral Word Association Test-2, FDST=Forward Digit Span Test, BDST=Backward Digit Span Test

DISCUSSION:-

The purpose of the present study was to assess neurocognitive performance in patients with bipolar affective disorder (major depressive episode) and major depressive disorder in comparison to healthy control. There was no significant difference in distribution of age, sex, marital status, occupation, and education, monthly income of the family, religion, family type and locality.

Mean age of onset of illness in BAD and MDD group was 23.85 and 26.15 years respectively. The onset of illness was significantly earlier in BAD as compare to MDD which was in line with the previous study. [22] Mean duration of illness for patients with BAD and MDD was 7.98 and 5.95 years respectively. Number of episodes in BAD and MDD group are 4.03 and 2.42 respectively. Number of manic and depressive episodes in BAD patients was 1.71 and 2.32 respectively. Number of hospitalization in BAD and MDD group were 1.97 and 1.58 respectively. There was significant difference on t- test in clinical characteristics like duration of illness, number of episodes and number of hospitalization. The results were similar to the study [13] where duration of illness, number of episodes and number of hospitalisations were more in BAD group. As family members were more worried about manic symptoms so BAD group tends to have more hospitalisations. Family history of similar illness was seen in 28 (46.7%) bipolar affective disorder (major depressive episode) and 46 (38.3%) MDD patients. Though, it was more in bipolar group in our study but difference was non-significant.

Mean HAM-D score in BAD and MDD patients was 22.00 and 23.02 respectively which is non-significant (p =.124). Thus, both the groups were comparable in respect of their current depressive status.

Pattern of cognitive impairment in patients with BAD and MDD-

Patients of BAD and MDD were showing significant impairment on all the neurocognitive domains like attention, psychomotor speed, executive functions, verbal fluency, verbal learning and memory, visuospatial working memory, short term memory and verbal working memory as compared to controls that was in line with previous studies. [1,2,4,6,8,9]

From the previous studies, it was evident that pattern of neurocognitive impairment between bipolar affective disorder type 1(major depressive episode) and major depressive disorder was inconsistent. We found that patients with bipolar affective disorder type 1(major depressive episode) performed poor on all the neurocognitive tests as compared to patients with major depressive disorder, though the results were significant only in tests like TMT B, COWA 1, COWA 2, and Stroop Color Test. This shows that bipolar depressive patients were more significantly impaired only on the domains of executive functioning and verbal fluency as compared to major depressive disorder.

On neurocognitive tests like TMT A, digit span forward, digit span backward, VWMM, VLMT; both group of patients performed poor as compared to controls, but no statistically significant difference among the groups was noted. This shows that both the group of patients were similarly impaired in various domains like attention, psychomotor speed, verbal learning and memory, visuospatial working memory, short term memory and verbal working memory with slightly more impairment among bipolar affective disorder. A study done by Xu G et al. 2012 [15] noted that bipolar depressed patients (BAD I) performed significantly poor in the domains of executive functioning and verbal fluency as compared to MDD patients. In domains like processing speed, verbal and visuospatial working memory; no significant difference was found among the groups, though, the bipolar group performed poor as compared to unipolar group which was also supported by previous studies. [5, 10, 22] Borkowska et al. 2001 [5] also found that the patients in the BAD group achieved significantly lower levels of performance in the non-verbal part of WAIS-R, in both parts of the Stroop test, in the verbal fluency test and also showed a tendency to achieve poorer results in TMT-B in comparison to MDD group. Bipolar depressed patients also produced significantly poorer results with the WCST as they made twice as many perseverative errors and only completed half of the correct categories compared with the MDD patients. The results of the TMT-A tests, which measure psychomotor slowness, were similar in BAD and MDD patients.

Cotrena C et al. 2016 [22] in his study found that, patients with MDD showed poor selective and sustained attention, and exhibited impairments in timed tasks, suggesting low efficiency of executive processing. The depressed patients with BAD displayed more widespread cognitive impairment than the remaining groups, and performed worse than subjects with MDD on measures of sustained attention and inhibitory control.

On the TMT part A and B, patients (BAD1 and MDD) performed significantly poor as compared to controls. More time to complete TMT part A, may due to impairment in processing speed whereas a significantly longer time of complete part B, may be the result of impairment in executive functions. These deficits indicate disorders in functioning of the dorsolateral part of the prefrontal cerebral cortex.

On Stroop test, patients with depression scored significantly worse than healthy controls. This showed that impairment in executive functions was responsible for suppressing well-learned reactions (reading) and following instructions which demand an untypical reaction (naming the colour of the print). It reported dysfunction in the supraorbital part of the prefrontal area of the brain.

Results obtained on COWA test among depressed patients were significantly worse as compared to control group, which indicates impairment in verbal fluency. Completing the tasks on COWA test was dependent on the supervisory control of executive functions, as fluency demands effective word recall according to a given criterion, suppressing words that are not related to the criterion, and also self-monitoring the process (remembering words which have been already listed). An effective working of verbal fluency is related to the functioning of the prefrontal areas of the brain.

The qualitatively similar pattern of memory impairment was seen in BAD and MDD patients. These impairments did not appear secondary to clinical state, but rather suggest a similar underlying pathophysiology involving medial temporal dysfunction.

Mahmoud et al. 2005 [13] found that bipolar depressed patients performed significantly poor in comparison to unipolar depressed patients on visuospatial working memory which was contrary to our results. In our study, bipolar patients performed poor on visuospatial working memory in comparison to unipolar patients, though the result were not significant. The contrary result could be due to small sample size or different methodology. The inconsistent results seen in previous studies could be due to the reason that most studies [11, 12] included both bipolar I and bipolar II patients. Previous studies also suggested that the two subtypes of BAD differ in neurocognitive tests. [14, 15] A study done by Xu G et al., 2012 [15] suggested that bipolar I depressed patients had a similar pattern of cognitive dysfunction compared with bipolar II depressed patients, but had a greater magnitude on all measures of executive function (measured by TMT-B,WSCT-Mand TOH), visual memory and verbal fluency. The other reasons of different result could be the small sample size, differences in sociodemographic data, clinical characteristics of the patients group and lastly, the neurocognitive tests used.

The following factors were not adequate to explain the differences of neurocognitive performance in both the depressed group of patients. Firstly, depressive symptoms and psychomotor speed could not explain the difference as all the patients satisfied the criteria of major depressive episode. Moreover, depressive symptoms and psychomotor speed impairment were similar in both the patient groups. Secondly, bipolar patients have an earlier age of onset than UD patients, so bipolar patients are more likely to suffer more episodes and have more hospitalizations. These differences are consistent with epidemiologic data of the differences between BAD and UD patients [24] so we consider them as the inherent characteristics of the disorder rather than the confounding factors. Thus, the difference in performance on neurocognitive tests could be attributed to the different subtypes of depression.

Effect of medication on cognition:-

Undoubtedly, drugs interfere cognitive functioning of patients receiving medicines, especially when comparing with healthy controls. But the previous studies did not gave convincing results about the impact of drugs on neurocognitive impairment. Previous studies which compared the cognitive performance of euthymic medication free bipolar subjects with those taking mood stabilisers, found no statistically significant differences [25] and minimal impact of lithium on cognitive function. [26] This indicates that the use of mood stabilisers is not wholly responsible for the observed deficits. The contribution of antipsychotics to cognitive impairment in BAD is also controversial with evidence of negative [27] as well as beneficial effects [28] on measures of executive function. The effect of SSRIs to neurocognition in depression is also controversial with evidence of negative [29] neutral [30] as well as beneficial. [31]

CONCLUSION:-

There was a marked neurocognitive impairment in patients (BAD and MDD), on all the domains like attention, psychomotor speed, executive functions, verbal fluency and learning, visuospatial working memory, short term memory and verbal working memory in comparison to controls. Patients with bipolar depression reported more impairment mainly on tests like TMT B, COWA 1, COWA 2 and Stroop Color Test means on domains of executive functioning and verbal fluency in comparison to patients with major depressive disorder.

Limitations:-

It was a cross sectional study.

Sample size was small and highly selective.

Patients were not medication free so effects of medications cannot denied.

Future Directions:-

A longitudinal study could be planned with larger sample size to reduce the confounding factors to a very less extent. Ideally, patients should be medication free because medication may alter the results.

Declaration of Conflicting interests- No conflict of interest'.

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REFERENCES

1. Malhi, G. S., Ivanovski, B., Hadzi.Pavlovic, D., Mitchell, P. B., Vieta, E., & Sachdev, P. (2007). Neuropsychological deficits and functional impairment in bipolar depression, hypomania and euthymia. Bipolar disorders, 9(1.2), 114-125.
2. Martínez-Arán, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sánchez-Moreno, J., & Salamero, M. (2004). Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. American Journal of Psychiatry, 161(2), 262-270.
3. Bora, E., Yücel, M., Pantelis, C., & Berk, M. (2011). Meta.analytic review of neurocognition in bipolar II disorder. Acta psychiatrica scandinavica, 123(3), 165-174.
4. Dixon, T., Kravariti, E., Frith, C., Murray, R. M., & McGuire, P. K. (2004). Effect of symptoms on executive function in bipolar illness. Psychological medicine, 34(5), 811-821.
5. Borkowska, A., & Rybakowski, J. K. (2001). Neuropsychological frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. Bipolar Disorders, 3(2), 88-94.
6. Lee, R. S., Hermens, D. F., Porter, M. A., & Redoblado-Hodge, M. A. (2012). A meta-analysis of cognitive deficits in first-episode major depressive disorder. Journal of affective disorders, 140(2), 113-124.
7. MacQueen, G. M., Galway, T. M., Hay, J., Young, L. T., & Joffe, R. T. (2002). Recollection memory deficits in patients with major depressive disorder predicted by past depressions but not current mood state or treatment status. Psychological Medicine, 32(2), 251-258.
8. Landrø, N. I., Stiles, T. C., & Sletvold, H. (2001). Neuropsychological function in nonpsychotic unipolar major depression. Cognitive and Behavioral Neurology, 14(4), 233-240.
9. Trivedi, M. H., & Greer, T. L. (2014). Cognitive dysfunction in unipolar depression: implications for treatment. Journal of affective disorders, 152, 19-27.
10. Bearden, C. E., Glahn, D. C., Monkul, E. S., Barrett, J., Najt, P., Villarreal, V., & Soares, J. C. (2006). Patterns of memory impairment in bipolar disorder and unipolar major depression. Psychiatry research, 142(2-3), 139-150.
11. Hermens, D. F., Naismith, S. L., Redoblado Hodge, M. A., Scott, E. M., & Hickie, I. B. (2010). Impaired verbal memory in young adults with unipolar and bipolar depression. Early intervention in psychiatry, 4(3), 227-233.
12. Tavares, J. V. T., Clark, L., Cannon, D. M., Erickson, K., Drevets, W. C., & Sahakian, B. J. (2007). Distinct profiles of neurocognitive function in unmedicated unipolar depression and bipolar II depression. Biological psychiatry, 62(8), 917-924.
13. Mahmoud A, Abelrazek G, AbdelSamee A, Azzam H. (2006) Cognitive Dysfunctions in Depressive Disorders. Current Psychiatry; 13(2):281-293.
14. Harkavy-Friedman, J. M., Keilp, J. G., Grunebaum, M. F., Sher, L., Printz, D., Burke, A. K., & Oquendo, M. (2006). Are BPI and BPII suicide attempters distinct neuropsychologically?. Journal of affective disorders, 94(1-3), 255-259.
15. Xu, G., Lin, K., Rao, D., Dang, Y., Ouyang, H., Guo, Y., & Chen, J. (2012). Neuropsychological performance in bipolar I, bipolar II and unipolar depression patients: a longitudinal, naturalistic study. Journal of affective disorders, 136(3), 328-339.
16. Wechsler, D., & De Lemos, M. M. (1981). Wechsler adult intelligence scale-revised.
17. Army US. Army individual test battery. Manual of directions and scoring. 1944.
18. Rao SL, Mukundan CR, Jamuna N, Das BS, Sastry KV, Hegde T, Reddy MV. (1997) Patterns of association between symptoms and neuropsychological deficits in post-traumatic syndrome. NIMHANS JOURNAL.; 15:157-168.
19. Stroop, J. R. (1992). Studies of interference in serial verbal reactions. Journal of Experimental Psychology: General, 121(1), 15.
20. Vecchi, T., Monticellai, M. L., & Cornoldi, C. (1995). Visuo-spatial working memory: Structures and variables affecting a capacity measure. Neuropsychologia, 33(11), 1549-1564.
21. Spreen, O. (1977). Neurosensory center comprehensive examination for aphasia. Neuropsychological Laboratory.
22. Cai, Y., Kuang, W., Guo, T., Yan, L., Zhu, J., & Chen, H. (2012). Clinical characteristics

and cognitive function of unipolar and bipolar depression. Zhong nan da xue xue bao. Yi xue ban= Journal of Central South University. Medical Sciences, 37(11), 1152-1155.
23. Cotrena, C., Branco, L. D., Shansis, F. M., & Fonseca, R. P. (2016). Executive function impairments in depression and bipolar disorder: association with functional impairment and quality of life. Journal of affective disorders, 190, 744-753.
24. Winokur, G., Coryell, W., Endicott, J., & Akiskal, H. (1993). Further distinctions between manic-depressive illness (bipolar disorder) and primary depressive disorder (unipolar depression). American Journal of Psychiatry, 150, 1176-1176.
25. Joffe, R. T., MacDONALD, C. A. T. H. E. R. I. N. E., & Kutcher, S. P. (1988). Lack of differential cognitive effects of lithium and carbamazepine in bipolar affective disorder. Journal of Clinical Psychopharmacology.
26. Goswami, U., Gulrajani, C., Moore, P. B., Varma, A., Young, A. H., Khastgir, U., & Ferrier, I. N. (2002, September). Neurocognitive decline in bipolar mood disorder role of mood stabilizers. In Journal of Psychopharmacology (Vol. 16, No. 3, pp. A45-A45). 6 BONHILL STREET, LONDON EC2A 4PU, ENGLAND: SAGE PUBLICATIONS LTD.
27. Landau, S., Raymont, V., & Frangou, S. (2003). The Maudsley Bipolar Disorder Project: the effect of medication, family history, and duration of illness on IQ and memory in bipolar I disorder. Journal of Clinical Psychiatry, 64, 86-93.
28. MacQueen, G., & Young, T. (2003). Cognitive effects of atypical antipsychotics: focus on bipolar spectrum disorders. Bipolar disorders, 5, 53-61.
29. Gorenstein, C., De Carvalho, S. C., Artes, R., Moreno, R. A., & Marcourakis, T. (2006). Cognitive performance in depressed patients after chronic use of antidepressants. Psychopharmacology, 185(1), 84-92.
30. Wadsworth, E. J., Moss, S. C., Simpson, S. A., & Smith, A. P. (2005). SSRIs and cognitive performance in a working sample. Human Psychopharmacology: Clinical and Experimental, 20(8), 561-572.
31. Alves, T. C., Rays, J., Telles, R. M., Júnior, R. F., Wajngarten, M., Romano, B. W., & Busatto, G. F. (2007). Effects of antidepressant treatment on cognitive performance in elderly subjects with heart failure and comorbid major depression: an exploratory study. Psychosomatics, 48(1), 22-30.