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Study of Cognitive Impairment in Euthymic Bipolar Disorder Patients

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ABSTRACT

Background: researchers came to agreement on that bipolar disorder is commonly linked to impairment in cognitive functions by a remarkable degree. More and more evidence continue to support that the cognitive impairment remains persistent even within euthymic periods which in turn points to cognitive impairment as a possible characteristic of the disorder.

Aim of the Work: objective assessment of bipolar patients' cognitive deficits present during remission and holding a Comparison of these deficits with control subjects who are completely healthy.

Patients and Methods: assessing cognitive functions including executive functions, attention and memory in euthymic bipolar patients by using relevant scales, then using SPSS for comparing the results with those of a control group.

Results: when compared to healthy control subjects, euthymic bipolar patients were found to exhibit a markedly noticeable impairment in attention, executive functions and total memory score. It was also noteworthy that the association between the duration of illness demonstrated through the number of episodes and the extent of impairment in cognitive functions.

Conclusion: there is an apparent association of bipolar disorder with cognitive impairment even when patients are in euthymic state and consequently, the number of episodes increases the impairment degree.

Keywords: Bipolar, Euthymic, Cognitive

INTRODUCTION

Major characteristics of bipolar disorder are episodic pathological mood alterations which in turn can be manic, depressive or a mix of the two types [(1)] with an onset that is relatively early (in patient's twenties) and a chronic course [(2)]. There has been a consistent association of Bipolar disorder with outstanding comorbidity both medical and psychiatric, untimely death**,** high degrees of impairment of functional capacity and worsen quality of life [(3)]. There has also been a remarkable link between bipolar disorder and elevated risk of suicidal attempts and eventually going through with it [(4)] and eliciting a magnificent burden on community.

Both type I and II of bipolar disorder affect a portion of 2–3% of the worldwide population, this makes bipolar disorder even more prevalent than other fully addressed conditions as type 1 diabetes, rheumatoid arthritis, or HIV infection. To many people's shock, bipolar disorder is ranked the sixth leading cause of disability around the world. It is also known to be causing significant rates of both morbidity and mortality; to give an example, cases of death by suicide formulates a percentage of people living with bipolar disorder up to 15%. [(5)]

There has been a noticeable growth of studies directed towards monitoring cognitive dysfunction in patients with bipolar disorder. That growth is in consistence with the recent focus of NIMH together with the Research Domain Criteria (RDoC) initiative on implementing a dimensional approach towards neuropsychiatric illnesses. One of the fundamental RDoC constructs that crosses boundaries of DSM-5 and it might bring significant enhancement in our grasping the knowledge of the different brain-based illnesses, including bipolar disorder and the pathophysiology behind them. [(35)].

Recently, the most popular area of research in bipolar disorders is directed towards studying neurocognitive impairment, factors causing it and its consequences, also the production and evolving of new strategies of treatment to control or maybe prevent these deficits [(6)].

Reasons suggesting the importance of establishing cognitive impairment prevalence among people with bipolar disorder are numerous. Clinically, cognitive impairment is a huge element participating to the entire load of disability in mood disorders, it is also a core aim in therapeutic intervention. Understandable information regarding characteristics and numbers of those in need for a closer and more intense attention to clinical care and social involvement to face the hazardous and disabling effects of cognitive impairment, all of that would be of great help to service planning.

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AIM OF THE WORK

1- Objective assessment of the existence of cognitive deficits in patients living with bipolar disorder and going through remission.

2- Comparing these deficits to healthy control subjects

3- Clarifying the degree of clinical significance of these cognitive impairments in a pure neuropsychological point of view and not merely statistical.

PATIENTS AND METHODS

1- Design of the study:

This study is a cross sectional comparative study.

2- Site of the study:

Psychiatry clinic at Al-Azhar university hospitals in Cairo, Egypt. The clinic serves a catchment area of about the third of Greater Cairo. It serves both urban and rural areas, including areas around Greater Cairo as well. The Psychiatry department in AL-Azhar university hospitals provides mental health services to psychiatric patients through the inpatient department and the outpatient clinics. There are two outpatient general psychiatry clinics working 6 days per week.

3- Selection of the sample

- The sample included a group of BD patients consisted of 63 patients that were studied during remission as confirmed by Hamilton Depression Rating Scale (HDRS) and Modified Mania Rating Scales (MMRS).
- A healthy control group of 57 persons who don't have any obvious physical or neuropsychiatric morbidity. Matching was performed for their age, gender, marital status, education and residency accurately with the group of patients. The selection involved a random group of workers and employees of AL-Azhar University Hospitals.
- **Inclusion criteria:**
  - Age ranging from 18 to 65 years.
  - Diagnosis of BD-I, and BD-II according to DSM-5
  - Average IQ, at least.
  - Euthymic patients
  - Willing to participate.
- **Exclusion criteria:**
  - Comorbid psychiatric disorder.
  - Gross neurological disorder.
  - Electro-convulsive therapy in the preceding 6 months.
  - Refuse to participate.

4- Study procedures:

- **Sample preparations:**

A number of 132 Euthymic BD patients attended the clinic during the scheduled time for the study, 16 patients were excluded from the study as they suffered from comorbid neurological and other psychiatric disorder including Epilepsy and Addiction. Another 23 patients were excluded for having received ECT sessions during the last six months prior to the study, while another 13 refused to participate in the study and still another 3 patients were excluded for auditory and visual difficulties. And by applying Stanford Binet test 5th Edition 14 patient were found to have lower IQ than average so the final sample size was 63 patients.

The control group included 57 individual which were selected randomly among workers and employee of AL-Azhar University Hospitals and were cross matched as possible for Age, Gender, Education, Marital status, and residency with patients group.

- **Informed consent**

A written informed consent was signed by the subjects after discussing the aim of the study with them. The general principles that were explained for all participants in this study were:

  - Participation in this study is totally free and voluntary.
  - The patient may decide to withdraw from this study at any moment without giving any justification.
  - The results of the study could be used for scientific publication but the identity of the patient would be absolutely confidential.
- A semi structured clinical interview was conducted by the researcher and his supervisors to the patients for diagnosis of BD-I, and BD-II and exclusion of other psychiatric disorders.

- The researcher conducted Hamilton Depression Rating scale and Modified Mania Rating scale to detect patients in remission. Remission was defined by a score of less the 8 on HDRS and less than 3 on MMRS.
- The researcher also conducted Mini Mental Status Examination to exclude cognitive affection due to neurological disorders.
- **The sample of the study was grouped into 2 groups;**
  - Group I: 63 patients with single episode BD in remission.
  - Control group: 57 subjects.
- **Study tools:**

An extensive review of previous literature guided the choice of neuropsychological tests used in the present study.

Group I was examined using the following tools:

- **The Hamilton Depression Rating Scale:** Hamilton finally structured the HDRS in 1960, in response to the need for a standardized measure of the phenomenology of a depressive syndrome. Since then it has become the most commonly used rating scale of depression and has been used as a basis for the construction of other scales. The HDRS was devised only for the use on patients diagnosed as suffering from depression. The scale contains 17 variables. Some are defined in terms of a series of categories of increasing intensity, while others are defined by a number of equal valued terms.
- **Modified Mania Rating Scale:** This scale was designed by Blackburn et al in the late seventies as a modification of the original scale designed by Beigel et al. The scale was designed to be used by psychiatrist through a structured interview. It consists of 28 items; six of them are completed by the relatives and the nursing staff. The test has fair reliability and validity

Group I and control group was examined using the following tools:

- **Stanford Binet Test 5th Edition:** The Stanford-Binet test is an examination meant to gauge intelligence through five factors of cognitive ability. These five factors include fluid reasoning, knowledge, quantitative reasoning, visual-spatial processing and working memory. Both verbal and nonverbal responses are measured. Each of the five factors is given a weight and the combined score is often reduced to a ratio known commonly as the intelligence quotient, or IQ [(7)].
- **Mini Mental Status Examination:** The Mini–Mental State Examination (MMSE) or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia. It is also used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time [(8)].
- **The Wechsler Memory Scale-Revised (WMS-R)** [(9)]: The WMSR is a clinical instrument for appraising major dimensions of memory functions in adults. The scale is intended as a diagnostic and screening device for use as a part of a general neuropsychological examination. The functions assessed include memory for verbal and figural stimuli, meaningful and abstract material, and delayed as well as immediate recall.
- **The TMT Making Test Parts A & B** [(10)]: The TMT is a neuropsychological test of visual attention and task switching. The solving of the TMT requires stable focused attention, reasonable eyesight, proficiency in visual scanning and shifting stimuli during search.
- **Statistical methods:**

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done: Independent-samples t-test of significance: was used when comparing between two means, chi-square test: was used when comparing between non-parametric data, probability (P-value): P-value < 0.05 was considered significant, P-value < 0.001 was considered as highly significant, P-value > 0.05 was considered insignificant.

RESULTS

- **Sample Characteristics:**

The sample of this study consisted of 120 subjects divided into 2 groups: group I consisted of 63 euthymic bipolar patients, group II consisted of 57 matched healthy controls.

Euthymia is defined by score of less than 8 on The Hamilton Depression Rating Scale and less than 3 on the Modified Mania Rating Scale.

Group I was tested for Euthymia and the results are shown on table 1:

Table (1): Patients results on HDRS and MMRS:

Scale	Mean	±SD
HDRS	3.00	1.49
MMRS	0.62	0.79

Group I and II were cross matched for Age, Gender, and Education, Residency and Marital status as shown in table 2.

Table (2): Sociodemographic characteristics of the patients and control groups:

Sociodemographic Factor		Patients (N = 63)	Control (N = 57)	P-value
Age	mean ±SD	33.95 9.43	34.33 10.58	0.8
Sex	Male Female	48 (76.2%) 15 (23.8%)	36 (63.2%) 21 (36.8%)	0.12
Marital status	Married Unmarried	44(69.8%) 19(30.2%)	37(64.9%) 20(35.1%)	.35
Education	Collage Diploma High school	42(66.6%) 18(28.5%) 3(4.7%)	37(64.9%) 15(26.3%) 5(8.7%)	.67
Residency	Urban ruler	63(100%) 0(0%)	57(100%) 0(0%)	No P value

Table 3 shows that group I performed worse than control group and the result were highly statistically significant **(p-value < 0.001)** in all items of WMS-R except for the information item where there was no statistical significant difference **(p-value > 0.05)** between patients and control.

Table (3): Comparison between patients and control as regard Wechsler memory scale.

Variables		Patients (N = 63)	Control (N = 57)	P-value
Information (6)	Mean ±SD	5.95 0.21	6.00 0.00	0.08
Immediate recall (5)	Mean ±SD	5.48 0.59	5.00 0.00	< 0.001*
Mental control (6)	Mean ±SD	5.19 1.11	6.00 0.00	< 0.001*
Logical memory (16)	Mean ±SD	11.81 3.34	15.68 0.47	< 0.001*
Digit span (15)	Mean ±SD	8.95 1.72	14.02 0.79	< 0.001*
Visual reproduction (18)	Mean ±SD	10.10 2.83	17.04 0.98	< 0.001*
Associate learning (30)	Mean ±SD	12.05 5.75	26.11 1.67	< 0.001*

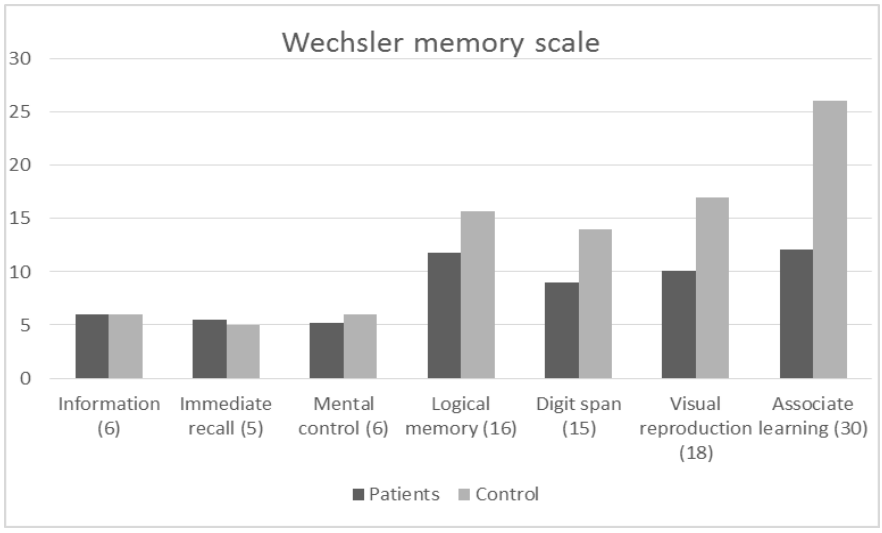

Figure (1): Comparison between patients and control as regard Wechsler memory scale.

Table 4 shows highly statistical significant difference **(p-value < 0.001)** between patients and control group as regard Trail making test (Trail A and Trial B).

Table (4): Comparison between patients and control as regard Trail making test.

Variables		Patients (N = 63)	Control (N = 57)	P-value
Trail A (29-90)	Mean ±SD	104.86 19.29	55.42 13.27	< 0.001*
Trail B (75-3min)	Mean ±SD	134.05 14.82	96.51 13.87	< 0.001*

*: p-value < 0.001 is considered highly significant.

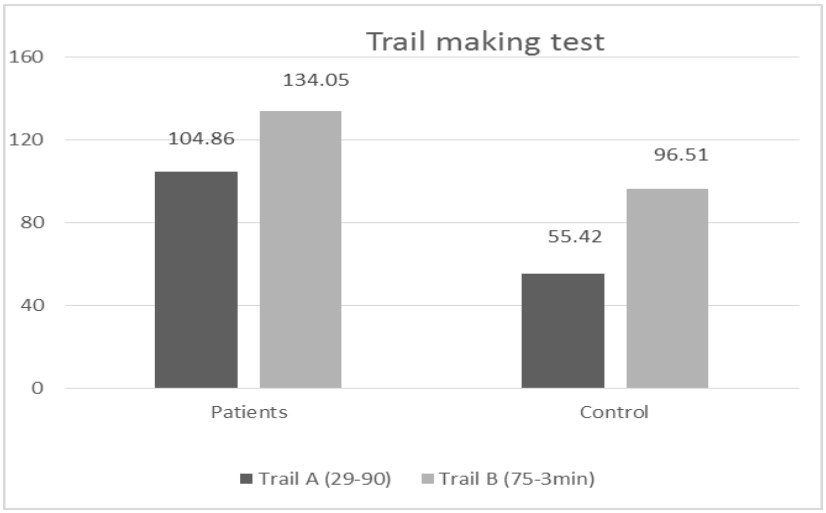

Figure (2): Comparison between patients and control as regard Trail making test.

We stratified patients according to number of episodes into 3 groups (1-4 episodes) (5-7 episodes) (8-10 episodes):

Table (5): Frequency of episodes:

Frequency of episodes	No.	%
1-4 episodes	36	57.1
5-7 episodes	24	38.1
8-10 episodes	3	4.8
Total	**63**	**100**

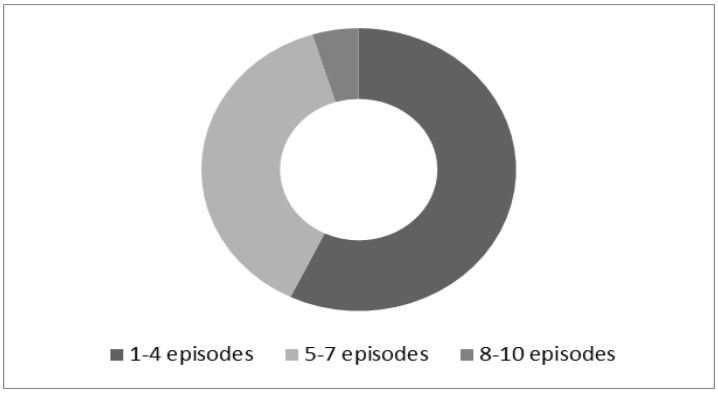

Figure (3): Frequency of episodes.

Then we made a comparison between the three groups regarding their performance in the WMS-R and TMT:

Table (6): Correlation between Wechsler memory rating scale and number of episodes:

Wechsler memory rating scale	Number of episodes			P value
	1-4 episodes	5-7 episodes	8-10 episodes	
Information	**6**	**5.8**	**6**	.07
Immediate recall	**5.58**	**5.25**	**6**	**.027**
Mental control	**5.9**	**4.3**	**3**	**.000**
Logical memory	**14**	**9.5**	**3**	**.000**
Digit span	**9.7**	**8.25**	**5**	**.000**
Visual reproduction	**11.9**	**8.2**	**3**	**.000**
Associate learning	**15.7**	**7.7**	**2**	**.000**

The previous table shows a highly statistically significant difference in the performance of the three groups in WMS-R as the first group (1-4 episodes) performed better than the other two groups with the third group i.e. the one with the greatest frequency of episodes performed worse than the other two groups.

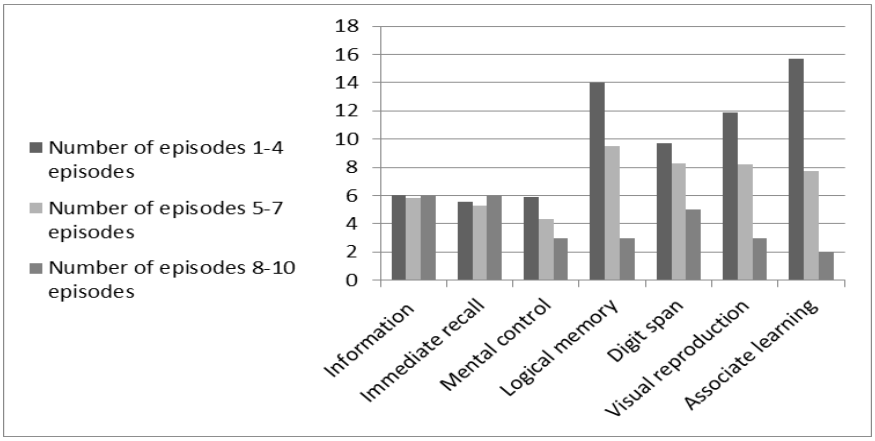

Figure (4): Correlation between Wechsler memory rating scale and number of episodes.

Table (7): Correlation between trail making test and number of episodes:

Trail making test	Number of episodes			P value
	1-4 episodes	5-7 episodes	8-10 episodes	
Trail A	**105.3**	**104.8**	**98.3**	.83
Trail B	**133.3**	**133.3**	**143.3**	.53

The previous table shows that there was no statistical difference among the three groups in the performance on the TMT.

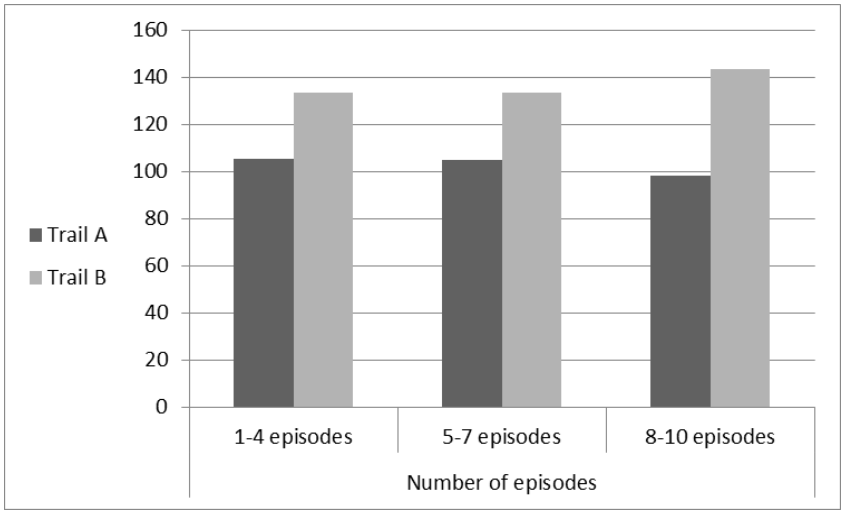

Figure (5): Correlation between trail making test and number of episodes.

We also classified the patients group according to the type of Bipolar disorder into those with BD-I, and BD-II and compared the performance of both groups on the previously mentioned tests.

Table (8): Distribution of bipolar type among patients group:

Type	No.	%
Bipolar 1	23	36.5
Bipolar 2	40	63.5
Total	63	100

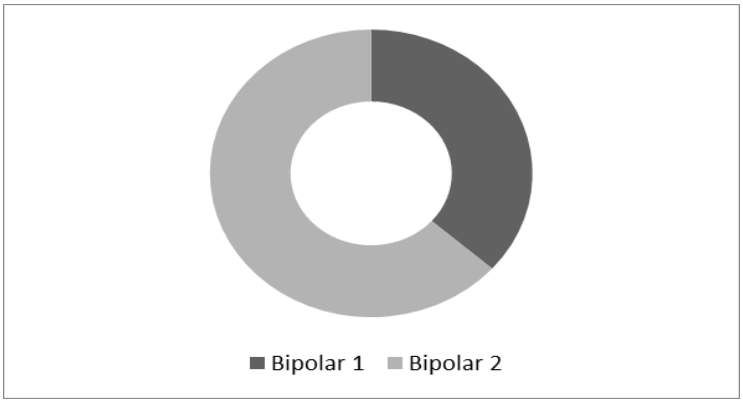

Figure (6): Distribution of bipolar type among patients group.

Table (9): Correlation between performance on Wechsler memory scale and bipolar type

Wechsler memory scale	Bipolar type		P value
	Type 1	Type 2	
Information	**5.96**	**5.93**	.68
Immediate recall	**5.5**	**5.4**	.55
Mental control	**5.57**	**4.7**	**.004**
Logical memory	**12.5**	**10.9**	**.08**
Digit span	**9.5**	**8.3**	**.009**
Visual reproduction	**10.6**	**9.3**	**.09**
Associate learning	**13.7**	**10.0**	**.01**

The previous table shows no statistical difference between both groups in their performance on the WMS-R except for mental control, digital span and associate learning where patients diagnosed with BD-II performed worse on these items.

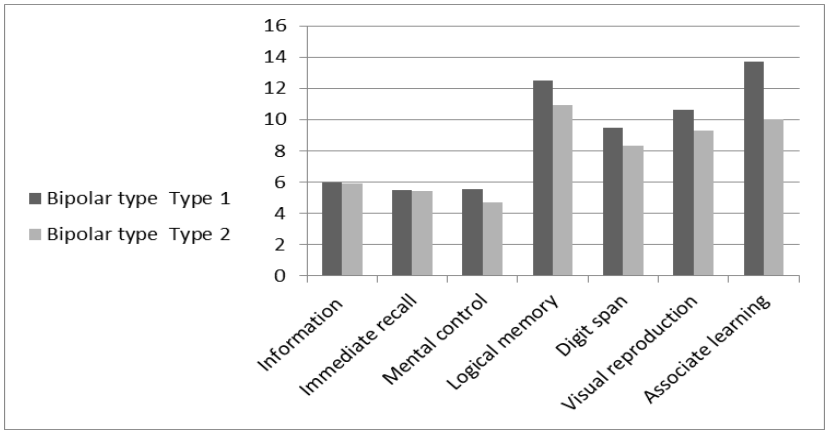

Figure (7): Correlation between performance on Wechsler memory scale and bipolar type.

Table (10): Correlation between performance trail making test and bipolar type:

Trail making test	Bipolar type		P value
	Type 1	Type 2	
Trail A	**102.8**	**106.4**	.47
Trail B	**131.1**	**135.6**	.23

The previous table shows that there is no statistically significant difference in the performance of both bipolar type patients on the trail making test.

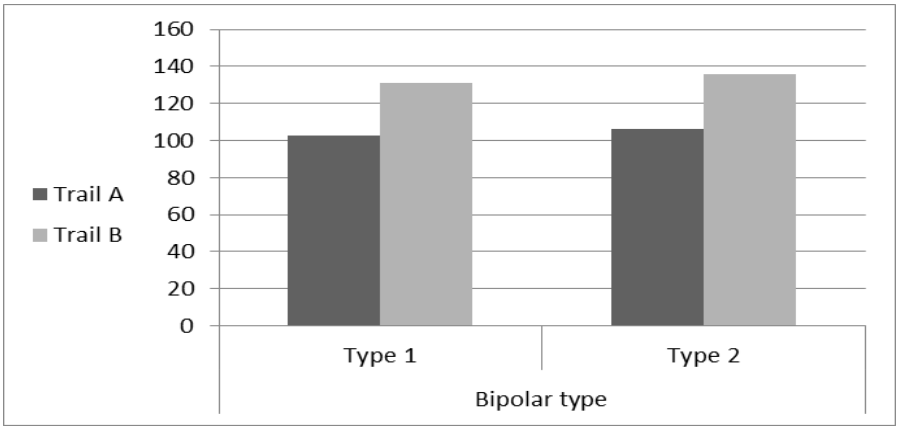

Figure (8): Correlation between performance trail making test and bipolar type.

Again we divided the patients group into three subgroups according to the predominant episode type (Manic)(Hypomanic)(Depressive) then compared between the three groups in their performance in the WMS-R and TMT.

Table (11): Distribution of different clinical episodes among patients group:

Episode	No.	%
Hypomanic	31	49.2
Manic	23	36.5
Depressive	9	14.3
Total	**63**	**100**

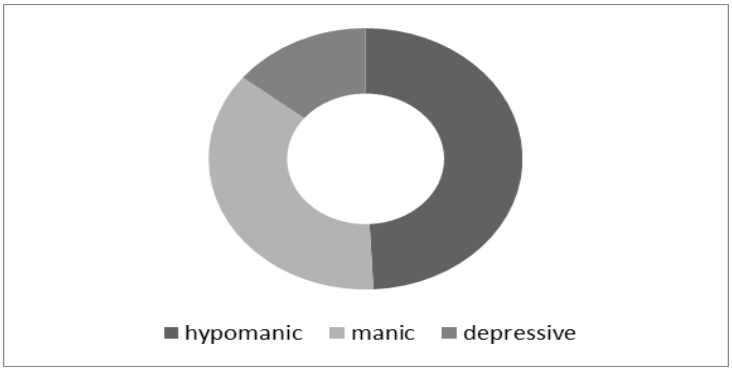

Figure (9): Distribution of different clinical episodes among patients group.

Table (12): Correlation between performance on Wechsler memory scale and episode type:

Wechsler memory rating scale	Domination			P value
	Hypomanic	Manic	Depressive	
Information	**6**	**6**	**6**	.9
Immediate recall	**5.4**	**5.6**	**5.5**	.85
Mental control	**4.8**	**5.2**	**5**	.733
Logical memory	**11.4**	**10.4**	**11.5**	**.038**
Digit span	**9**	**9.2**	**8.5**	.57
Visual reproduction	**9.6**	**9**	**10.5**	.32
Associate learning	**9.8**	**8.6**	**9.5**	.06

The previous table shows that there is no statistically significant difference between the three groups as regarding their performance on the WMS-R except for the logical memory item.

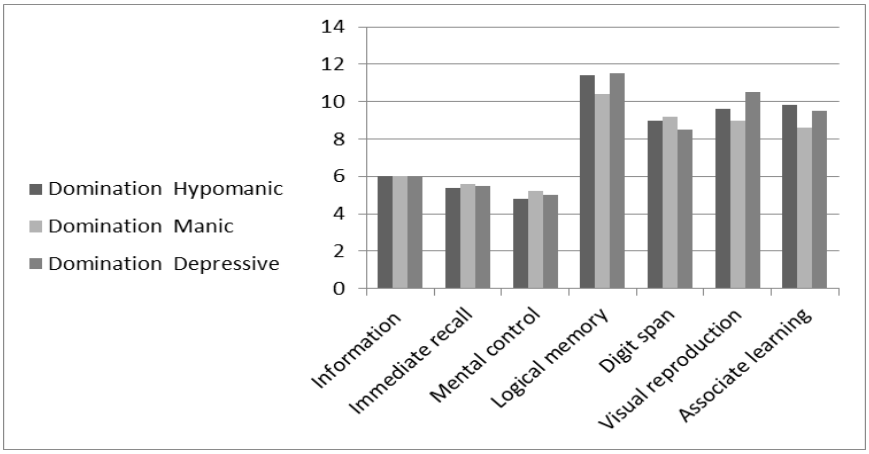

Figure (10): Correlation between performance on Wechsler memory scale and episode type.

Table (13): Correlation between performance on TMT and episode type.

Trail making test	Domination			P value
	Hypomanic	Manic	depressive	
Trail A	**104**	**108**	**110**	.9
Trail B	**136**	**140**	**130**	.8

The previous table shows that there is no statistically significant difference between the three groups on performance of the trail making test.

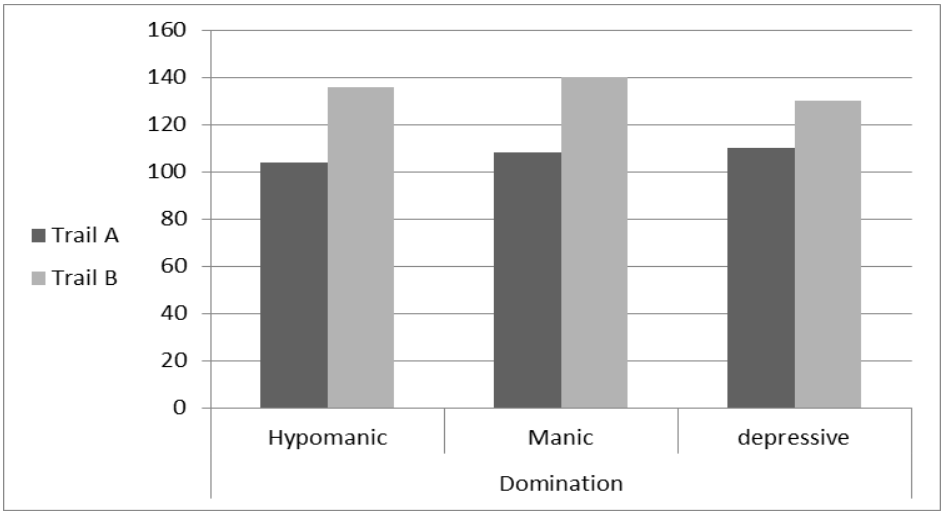

Figure (11): Correlation between performance on TMT and episode type.

DISCUSSION

There is more and more growing agreement supporting the common frequency of cognitive deficits in bipolar patients even through euthymic periods.

Specifically, the issue remains in knowing what characteristics distinguish the prodromal phase of bipolar disorder exactly, also the degree to which the cognitive manifestations of the disease manifest before or along with the first appearance of emotional signs in individuals at high risk is completely unknown. Moreover, causality direction remains unclear, mood swings may adversely affect neuropsychiatric performance, and, or, cognitive impairment may attribute to mood symptoms[12].

The approach which is considered the most direct in addressing the determination of cognitive abnormalities' path in bipolar disorder would be a longitudinal monitoring of first episode subjects with frequent evaluation of their cognitive performance. This usually is costly and quiet difficult. On the other hand, cognitive functions of patients in their first episodes can be compared with patients who have experienced multiple episodes, already. This strategy has been successfully applied in schizophrenia.

In this study in our hands, a group of euthymic BD patients were put in comparison with a control group of healthy individuals with respect to a range of cognitive areas including mainly executive functions, memory and attention, mainly using tools of cognitive assessment including Wechsler memory scale and Trail Making Test A and B.

In our present study, the performance of patients with bipolar disorder in remission than regarding attention, memory and executive function was worse those not affected.

The Trail Making Test – A was used to assess visual attention and task switching

There was 16 studies that assessed attention in euthymic bipolar patients using Trail Making Test – A

This function was impaired in all 16 studies among bipolar participants. Nevertheless, a single report exhibited that the BDI group's performance didn't show much of a difference from

that of control group, except the BDII group showcased a deficiency in same tasks [11]. Fifteen studies report dysfunction among BDI [12] and both BDI and BDII patients [11,13, 14, 15,18, 16, 17].

Attention and concentration function was assessed WMS versions of the Digit Span Test-Forward (DST-F) and Backward (DST-B).

Consistent with our study ten studies tested attention and concentration using DST-F, the majority found significant deficits among patients [11,12,14]; only one report found comparable scores between healthy controls and BDI or BDII groups [11].

Also, consistent with our study Two studies reported similar performance between patients and healthy controls in immediate and delayed recall, [14,18]. However on study demonstrated poorer performance among patients using the Wechsler Memory Scale (WMS) Logical Memory task [29].

Executive function is a broad term that refers to a collection of higher level cognitive processes, including planning, working memory, strategy deployment, inhibitory control and cognitive flexibility [20].

Executive functions were impaired among patients with BD while it remained intact in the control group.

Working memory was tested using WMS versions of Digit Span Test Backward (DST-B). consistent with our study 5 studies found impaired working memory in patients using the Digit Span Test-Backward (DST-B**)** [11,15,21], with one exception [16].

Cognitive flexibility and response inhibition are executive functions that are tested using the Trail Making Test-Part B (TMT-B).

Consistent with our study, studies that used (TMT-B) to measure cognitive flexibility and response inhibition found significant impairment among patients [12,13, 14, 15, 18, 22], with few exceptions [17].

Researches show that some medications have a neuro-protective effect especially the mood stabilizing effects of some anticonvulsants particularly those capable of inhibiting excitatory amino acids such as glutamate and other psycho-tropic medications [23]. However, in their review [24] proposed that cognitive impairments in bipolar patients are not likely to be attributed to the effect of drugs. In addition, when comparing study of euthymic patients with bipolar disorder and controls, impairment of neurocognitive function was observed in both patients receiving mood stabilizers mono-therapy and in those who were drug-free [25]. However, many patients within this study were taking several psychotropic drugs at different doses, and the effects of combined therapy were known well, especially over time.

It remains largely speculative whether neuroprotection at the cellular level confers clinical benefit for either affective symptoms or neurocognitive functioning.

Also in the current study we stratified the patients group in three subgroups according to the number of episodes and then compared the cognitive functions between the three groups using the previously mentioned scales.

In this study, patients who suffered 1-4 episodes of the disease exhibited decrease in attention, executive function and total memory score, when put into comparison with control subjects. But patients with only 1-4 episodes showed better performance than the group of patients who suffered 5-7 episodes who in turn showed better performance than those who went through 8-10 episodes.

These results are consistent with the result of a study done by Martino et al who proved that BD patients with more severe cognitive impairment are also those who suffer from more frequent episode [11].

The preceding findings are consonant with results from some cross-sectional studies [26, 27] suggesting that manic episodes have a negative impact on neurocognition and the course of BD, and supporting the concept of high heterogeneity amongst BD cohorts as regards to neurocognitive performance and functioning [28].

The existence of impairment of cognitive function in bipolar patients from the start of the first episode and their continuous existence even during remission indicate that these cognitive impairments might be trait markers for the disease [15].

Associations between illness characteristics and neuropsychological deficits may be an indication that patients with cognitive

impairments are more vulnerable to developing severe bipolar disorder [11].

In this study we classified the patients group according to the bipolar type into BD-I, and BD-II group according to DSM-5, then we compared the performance of both group on the WMS-R and the TMT.

Our main finding is that the two bipolar subgroups had somewhat different neurocognitive profiles; patients with bipolar I disorder exhibited more cognitive impairment than patients with bipolar II. Patients with bipolar I disorder had a broader pattern of cognitive impairment, showing a performance decrease on subsets of the WMS including mental control, digit span and associate learning when compared to the bipolar II group.

This is consistent with a substantial body of research reporting that patients with bipolar I disorder suffer from dysfunction in memory, attention and executive function, irrespective of affective state [29].

This is also consistent with a study conducted by ***Hsiao et al.*** [30] where he used the Digit Span and WM subtests of the WMS to compare the working memory of 50 BD1 patients and 54 BD2 patients. The results indicate worse performance by BD1s than BD2s, with small to medium differences in performance, on average (Cohen's d = -.29 and -.51, respectively).

However in a recent meta-analytical study conducted by ***Tania Dickinson*** [31] and her colleagues they found that the results of the 9 trials that compared BD1 patients and BD2 patients on attention using the WMS- Digit Span subtests were mixed. In 6 out of 9 trials, BD1 patients recalled fewer digits than BD2 patients, denoting worse performance, with the opposite results reported for the remaining three trials. Effect sizes were very small (0.07) to small (0.38) in immensity, and not of a statistical significance.

Also the current study failed to show statistically significant difference in the performance of both bipolar I and bipolar II.

This was consistent with the previously mentioned meta-analytic study conducted by Tania Dickinson and her colleagues which demonstrated that mixed results were generated by seven studies that administered the TMT-B; with the exception of one outlier [30] that demonstrated a statistically significant medium to large average difference in performance, favoring BD- II.

In addition to the commonly well received idea that BD1 is the subtype with more severity, a bigger deficit among BD1 patients was anticipated, when compared to BD2 patients. Nevertheless, this study's results, and the exploration of other studies and publications doubt that statement. To give an example, previous research has proposed that BD2 may be linked with higher morbidity and mortality, including higher episode frequency, co-morbidity, suicidality, and rapid cycling compared to BD1 [14].

We also divided the patients group into three subgroups according to the predominant episode type into:

1- Predominately Manic
2- Predominately hypomanic
3- Predominately depressive

Then we made a comparison between the three groups regarding their performance in the Wechsler memory scale and the Trail making test.

The current study failed to show statistically significant differences among the three groups as regard their performance on the WMS-R and TMT.

This is consistent with a study conducted by J. Volkert and his colleagues showed that the predominant polarity doesn't seem to have any impact on cognitive deficits [32].

In a study by ***Bonnin et al.*** [14] the degree of cognitive functioning was solely predicted by the presence of sub-depressive symptoms during euthymia.

This result might be surprising, because traditionally BD has been described as a condition that is episodic in nature. However, recent studies revealed that patients frequently suffer from persistent residual mood symptoms. In comparison to Healthy Controls, BP shows significantly higher scores in depression rating scales despite being stable for at least 6 months [33].

However one has to take into consideration when explaining these results the effect of number of episodes as recurrent hospitalization, ECT and medications as they are more pronounced in manic patients.

Because a majority of previous studies found that the predominantly depressive polarity to

be associated with higher rates of suicide attempts and number of episodes, this could explain why the patients in this study with predominant depressive polarity has close cognitive profile to patients with predominant manic and hypomanic polarity[35].

LIMITATIONS

Among the limitations of the present study is that the group sizes should have been larger in order to demonstrate significant differences more clearly. Our study was cross sectional one. A more comprehensive study was to perform a longitudinal study to assess cognitive functions in each individual prior to the onset of illness and along the course of the illness.

A more detailed study would consider the effect of medications on cognitive functions, as there is still some debate in literature about its long-term effect on cognitive functions. Further studies using brain imaging techniques are needed to investigate the findings of this study in further detail.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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