Cognitive Dysfunctions in Depressive Disorders

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Abstract

The aim of our study was to find the cognitive dysfunction in unipolar depression and depressive phase of bipolar disorder and to compare both type of depression regarding clinical and neuropsychological findings. Several domains of cognitive function were examined in 22 depressed unipolar patients and 22 depressed bipolar patients diagnosed according to ICD10 research criteria, compared with 30 healthy volunteers. History and mental state examination done, using semi-structured interview, Hamilton depression rating scale for both patients group and subtests of WMSR together with Vigil continuous performance test for both patients and control to assess various aspects of memory and attention. There were highly significant cognitive impairment in immediate, short term and visual memory together with impairment in attention in both patients group relative to the control. On the other hand, visual memory span and vigil continuous performance test were more impaired in bipolar group. Mean while, there were no significant difference regarding both patients group in most of the compared parameters except for duration of illness and number of episodes which were more in bipolar group .Although bipolar depression is distinct from unipolar depression in terms of phenomenology , clinical characteristics and management but neuropsychological distinguishing is still not well established. In the same time whether unipolar or bipolar, depression is a chronic illness with chronic disability that may need new treatment modalities is still an area that may need further and further researches.

Introduction

A long-standing scientific controversy with many clinical consequences is whether bipolar and unipolar disorder are the same or separate and distinct illnesses (*Hirschfeld, 2005)*. In the late 19th and early 20th century, Kraepelin, in Germany, emphasized the distinction between dementia precox and manic-depressive insanity (*Kraepelin and Leipzig, 1893) (Kraepelin and Leipzig, 1896)*. One source of this dichotomy was the emphasis on moods versus cognition and will. However, the major rationale for the distinction was a perceived difference in clinical course and outcome. It was not until 1966 that bipolar disorder was described as separate and distinct in articles by *Jules Angst (1966),* Carlo Perris (Perris 1966) and Winokur and colleagues (Winokur, Clayton and Reich, 1969) in the United States. These articles proposed separation between unipolar and bipolar disorders based on difference in genetics, gender, clinical course, and premorbid personality *(Murphy and Sahakian, 2001)*. Nowadays, although unipolar depression and bipolar depression are considered as distinct entities both by clinicians and researchers, it is not clear whether a pathophysiological distinction, which is the bridge between etiology and treatment, exists between these two conditions *(Lakshmi et al., 1997)*.

Unavoidable practical considerations often interfere with ideal methodologies. First, researchers often neglect to indicate whether patients are in a manic, depressed or euthymic phase at the time of assessment. This is in part owing to difficulties with monitoring what are often

rapid fluctuations in mood. Second, patients with bipolar disorder are generally receiving a combination of medications - including mood stabilizers, antidepressants, neuroleptics and benzodiazepines - that may or may not influence neuropsychological performance. Differences observed between patients and controls, or patients in different stages of bipolar illness, may be confounded by different medication regimens. *(Murphy and Shakan, 2001)*

Aiming to avoid some methodological difficulties in previous studies that search for cognitive dysfunction in depression and, or compare various types of mood disorders, our study conducted to compare unipolar depression with bipolar depression during acute episodes of depression using clinical data and neuropsychological tests.

Objectives:

1- To determine and compare the pattern of cognitive deficit in unipolar and bipolar depression
2- Compare unipolar and bipolar depression using both clinical and neuropsychological findings.

Subjects and method

44 patients between the age 18- 45 years, including 22 unipolar depression and 22 bipolar depression (during the depressive phase of bipolar disorder) as diagnosed according to ICD10-R criteria for mental illness compared with 30 healthy volunteers. The patients participating in the present study were selected from outpatient clinic or inpatients word of institute of psychiatry –Ain Shams University.

Inclusion criteria:

-Age: 18-40 years old

-Both males and females were included

- Fulfilling the criteria of diagnosis of unipolar major depression and bipolar depression according to the ICD-10 Diagnostic Criteria for Research.

- All during acute phase of the disorder

Exclusion criteria:

-Patients with below average intelligence.

-Patients below the age of 18 and above the age of 40.

-Patients with history of organic illness, head trauma, Dual diagnosis, or history of drug abuse disorder or on ECT.

Control group

The control group consisted of 30 Egyptian individuals with no apparent physical or psychiatric morbidity. They matched for age, sex, and other demographic variables as far as possible with the patient group. They have no family history of any psychiatric disorder selected from a pool of normal volunteers from the Hospital Clinics of Ain –shams university hospitals

Tools:

1. Clinical examination and history taking: Full history and examination using Ain Shams psychiatric interview sheet.
2. (ICD-10).ICD-10 Symptom Checklist of mental disorders for diagnosis: This is a semi-structured instrument for assessment of the psychiatric symptoms and syndromes in the F0-F6 categories of the ICD-10. *(Janka et al., 1994).*
3. 4- Hamilton rating scale for severity of depression: Hamilton scale is a standardized measure of the phenomenology of a depressive syndrome. Its score on 17 item ranging from 0-50, scores of 7 or less

considered normal; from 8-13 is considered mild; 14-18 is moderate; 19-22 is severe; and 23 and above is considered very severe. *Hamilton M (1960):*

4. General Health Questionnaire (Goldberg, 1983)): It is a self-administered questionnaire for the detection of mental disorders. There are 4 forms of GHQ: The scale of 28 items was used in its Arabic version

5. Neuropsychological Assessment:

The following tests were used for assessment of major areas of cognition:

a) **The Wechsler Memory Scale-Revised (WMS-R)** ***(Wechsler, 1987).***

Comprehensive set of subtests measuring attention and encoding, retrieval, and recognition of various types of verbal and visual material with both immediate recall and delayed retention; excellent age-stratified normative comparisons for adults up to age 89, with intellectual data for direct comparison. Four of the eight subtests of the WMS-R that represent good assessment of memory were chosen to the present study, as follows: (a) Verbal Paired Associates: for assessment of immediate and delayed recall, (b)Visual Paired Associates: for assessment of immediate and delayed recall, (c) Digit span: It includes digit span forward, for assessing ability to process relatively simple information and digit span backward for more complex simultaneous processing and cognitive manipulation demands, (d) Visual memory span: The two parts of the visual memory span subtest, tapping forward and tapping backward, are administered separately.(test measure visual-spatial memory)

b) Vigil continuous Performance Test:

It is the most common research paradigm in cognitive studies of sustained attention and psychopathology. The two elements distinguished are; sensitivity and the response criterion. Diminished sensitivity is a sign of decreased vigilance and results in a high miss rate (errors of omission). The response criterion can be diminished leading to a high false positive rate (errors of commission). Reaction time is variable that represents the average time from the onset of each stimulus to the initiation of each response, Vigil requires only one response to one stimulus. More than one response in the inter-stimulus interval is defined as a perseveration.

Study proper:

Our study was a case control study, which performed in the period from the February 2005 to August 2005. We include all patients presented within this period and fulfiling our inclusion criteria whether presented to Emergency room or outpatient clinic.The history and mental state examination performed using ICD10 symptom checklist by the psychiatrist using Ain Shams psychiatric interview sheet. After diagnosis, both patients group and control group gave written informed consent to participate in the study after the procedures fully explained. The Hamilton Depression Rating Scale done for both patients group to assess severity of the illness. The previously mentioned neuropsychological tests performed to both patients group and control .

Statistical methods

The results analyzed using the Stat Open, Echo Soft Corporation, USA (2001) from Apple Mac.

The following statistical procedures used in this work.

1- Logistic t test used for comparison between two mean groups.

2- Ranked Sperman Correlation Test to study the association between each two variables among each group.

3- The probability of error (p) value was used to indicate level of significance as follows:

P>0.05: non significant, this occurs when (t) value is <1.7

P<0.05: significant, this occurs when (t) value is >1.7

P<0.01: highly significant, when (t) value is >2.3

P<0.001: very highly significant, when (t) value is >3.4

Results

Table (1): Comparison between unipolar depression and bipolar depression regarding sociodemographic data

Social data		Unipolar depressed Patients n=22		Bipolar depressed patients	
		Mean	SD	Mean	SD
Age		30.77	8.59	32.25	5.44
sex		No	%	No	%
	Males	4	18.18	13	59.09
	females	18	81.81*	9	40.90
Marital status	Single	8	36.36	11	50
	Married	14	63.63*	11	50
Level of education	illiterate	1	4.54	4	18.18
	Primary & preparatory	10	45.45*	5	22.72
	Secondary	7	31.81	5	22.72
	university	4	18.18	8	36.36*

- In our sample 81.8% of unipolar depressed patients were females while in bipolar group males exceeding females about 59% were males

- Most of unipolar depressed patients were married 63.6% while in bipolar group was equal

- 50% of unipolar depressed patient were of low education or illiterate while only 41% of bipolar group were of low education or illiterate.

Table (2): Comparison between unipolar depression and bipolar depression regarding history findings:

Subscale		unipolar depressed patients		Bipolar depressed patients		T value
		Mean	SD	Mean	SD	
Age of onset		27.14	8.56	24	6.32	1.38
No of episodes		2.73	2.57	4.25	2.49	-1.99*
Duration of last episode (month)		1.98	0.76	1.69	0.26	1.69
Duration of illness (years)		3.63	3.88	8.25	4.33	-3.73***
Hamilton depression score		35	9.53	36.88	7.32	-0.73
Presence of stressor		No	%	No	%	
	+ve	19	86.36	20	90.90	-3.95***
	-ve	3	13.63	2	9.09	

-There was a significant difference regarding number of episodes in both group as it was more in bipolar depressed patients (P value <0.05).
- Also duration of illness in years were significantly more in bipolar depression (P value ,0.001)
-In addition there was significant difference regarding presence of psychosocial stressor as it was more in Bipolar group (P value <0.001)

Table (3): Comparison between Unipolar depressed patient and control group as regard Wechsler memory scale revised:

Subscale	Unipolar depressed Patient n= 22		Control n=30		T value
	Mean	SD	Mean	SD	
Visual PA (immediate)	11.23	4.17	14.00	2.33	-3.05**
Verbal PA (immediate)	16.68	2.85	19.37	2.50	-3.16***
Digit span	11.68	2.71	13.17	3.40	-1.69
Visual memory span	12.77	2.39	13.13	2.06	-0.59
Visual PA (short)	4.27	1.52	5.00	0.98	-2.10*
Verbal PA (short)	5.86	1.32	7.03	1.10	-3.49***

- There was a significant statistical differences between unipolar depressed patients and control group as regard score of visual and verbal paired associates I, II, and verbal paired associates II (short term memory), where patients had significantly lower score than control group.

Table (4): Comparison between Unipolar depressed patients and control on total results of the continuous performance test

Subscale	Unipolar depressed Patients n=30		Control n=30		T value
	Mean	SD	Mean	SD	
Total Omissions	8.14	8.11	2.77	1.92	3.51***
Total Commissions	11.14	10.33	3.27	2.66	4.01***
Average delay	501.18	53.42	522.98	39.28	-1.70

- There were very highly significant statistical differences between both groups as regard total results of continuous performance test; where patients had higher score of total omission, and total commission, than the control group.

Table (5): Comparison between Bipolar depressed patient and control group as regard Wechsler memory scale revised:

Subscale	Bipolar depressed Patient n= 22		Control n=30		T value
	Mean	SD	Mean	SD	
Visual PA (immediate)	9.63	2.97	14.00	2.33	-5.94***
Verbal PA (immediate)	15.13	3.18	19.37	2.50	-5.38***
Digit span	10.88	1.81	13.17	3.40	-2.86**
Visual memory span	11.13	1.13	13.13	2.06	-4.12***
Visual PA (short)	3.75	1.49	5.00	0.98	-3.65***
Verbal PA (short)	5.88	1.13	7.03	1.10	-3.70***

- There were highly significant statistical differences between both groups as regard score of visual and verbal paired associates I, II, and Digit span ,where patients had lower score than control group.

Table (6): Comparison between Bipolar patients and control on total results of the continuous performance test

Subscale	Bipolar depressed Patients n=30		Control n=30		T value
	Mean	SD	Mean	SD	
Total Omissions	17.63	11.45	2.77	1.92	7.00***
Total Commissions	12.5	10.38	3.27	2.66	4.68***
Average delay	537.28	52.98	522.98	39.28	1.12

- There was very highly significant statistical difference between both groups as regard total results of continuous performance test; where patients had higher score than the control group.

Table (7): Comparison between Unipolar depressed patients and Bipolar depressed Patients group as regard Wechsler memory scale revised:

Subscale	Unipolar depressed Patient n= 22		Bipolar depressed patients n=22		T value
	Mean	SD	Mean	SD	
Visual PA (immediate)	11.23	4.17	9.63	2.97	1.47
Verbal PA (immediate)	16.68	2.85	15.13	3.18	1.70
Digit span	11.68	2.71	10.88	1.81	1.15
Visual memory span	12.77	2.39	11.13	1.13	2.91*
Visual PA (short)	4.27	1.52	3.75	1.49	1.15
Verbal PA (short)	5.86	1.32	5.88	1.13	-0.05

There was highly significant statistical difference between both groups as regard score of visual memory span where bipolar depressed patients had lower score than unipolar one.

Table (8): Comparison between Unipolar depressed patients and Bipolar depressed Patients on total results of the continuous performance test

Subscale	Unipolar depressed Patients n=22		Bipolar depressed patients		T value
	Mean	SD	Mean	SD	
Total Omissions	8.14	8.11	17.63	11.45	-3.17*
Total Commissions	11.14	10.33	12.5	10.38	-0.44
Average delay	501.18	53.42	537.28	52.98	-2.25*

- There were highly significant statistical difference between both groups as regard total results of continuous performance test; where bipolar patients had higher score of total omission, and average delay, than the unipolar group.

Discussion:

There are numerous studies that compare unipolar and bipolar depression, finding the differences whether clinical, biological or both in order to explain why management should be different. In our study we try to find some of the differences using neuropsychological tests, as patients with depression frequently complain of memory difficulties, it is perhaps not surprising that these subjects demonstrate impairments on a range of memory tasks as proved by *Blaney, 1986; Johnson & Magaro, 1987; Burt et al, 1995*. Regarding socio-demographic data, there is no significant difference between both patient groups regarding age, however, since life time prevalence of unipolar depression is more among female 10–25% for women and 5–12% for men *(Blazer et al., 1994),* in fact this finding may explain why in our sample, although it is not a community sample but still most of unipolar group are female.

In addition there is statistically significant difference between both groups regarding educational level as 50% of unipolar are of low educational level or illiterate while 41% of bipolar are of low educational level or illiterate although this difference although statistically significant but clinically not significance.

On the other hand, regarding clinical characteristics of both groups, there are no significant difference between both groups regarding age of onset, duration of last episode and severity of illness as indicated by Hamilton depression rating scale. Since the age of the patients and severity of the last episode are nearly the same in both groups so any differences in cognitive function are not related to these factors which causes bias in previous studies as in the study of, *Savard et al (1980)* as patients were significantly older than those in the unipolar group, suggesting that age alone may have accounted for their findings. Additionally, *Wolfe et al (1987)* cautioned that differences between their unipolar and bipolar groups might actually reflect subtle differences in severity.

Further more there is significant difference regarding duration of illness and number of episodes which are more in bipolar group. These differences between both group may causes some bias in our results. As in the study of Philippe et al., 2004 who found that the effects of the repetition of the depressive episodes were not modulated by the subtypes of depression and may reflect sensitization to the cognitive impact of depression associated with increasing prefrontal dysfunction. Although, Philip et al., were more interested in the severity of cognitive impairment rather than the profile of cognitive impairment.

Although patients with depression have been studied using a wide range of neuropsychological tests, researchers have focused on memory and executive function, (Elliott, 1998). Deficits have been reported on tests of short-term memory, verbal and visual recognition memory, spatial working memory and immediate or delayed recall (Austin *et al*, 1992; Brown *et al*, 1994; Ilsley *et al*, 1995; Beats *et al*, 1996; Elliott *et al*, 1996). As such a broad spectrum of findings may suggest, there has been much debate over the precise nature of memory impairment, and a number of distinct formulations have been offered to explain the observed deficits (Robbins *et al*, 1992). Where as in our study comparison between unipolar depressed patients and control group revealed highly significant difference between both group as regard tests of

immediate memory, tests of short term memory and tests of sustained attention. However no difference between unipolar depressed patient and control group regarding tests of visual-spatial memory and sustained attention.

On the other-hand comparing bipolar group patient to the same control group using the same tests revealed very highly significant difference between both groups allover the whole tests as patients has significant impairment in, immediate, short term, visuo-spatial, attention and sustained attention. These differences in profile and severity of cognitive impairment in bipolar group either related to their clinical characteristics or related to the effect of bipolar illness per se or both of them. Meanwhile, when comparing both patients group on subtest of Wechsler memory scale revised and Vigil continuous performance test revealed no significant difference between both groups regarding short-term memory, immediate memory or attention. However, the main differences are in the visual-spatial memory and sustained attention as bipolar group is worse. Therefore, according to these results, we can say both differences in clinical characteristics and subtype of depression may affect pattern and severity of cognitive impairment, although clinical characteristics may have the upper hand.

These results are similar to those found by Philippe et al., 2004 who examined three group of patients, group with first episode depression , group with recurrent major depression and last group with recurrent bipolar depression comparing them with healthy control group on a verbal episodic memory task. Patients suffering from a first depressive episode did not show verbal memory impairment as compared to normal controls. Unlike first episode patients, recurrent unipolar depression and bipolar depression patients exhibited verbal memory deficits with impaired free recall and normal cued recall and recognition.

The same results found by Bearden et al 2006 who stated that despite comparable general intellectual abilities, bipolar and unipolar patients exhibited significant memory deficits relative to healthy controls. A similar deficit profile was observed in both patient groups, involving visual memory, immediate and short term memory. These impairments were not secondary to strategic processing deficits or rapid forgetting, so their results suggest qualitatively similar patterns of memory impairment in bipolar and unipolar patients, consistent with a primary encoding deficit. These impairments do not appear to be secondary to clinical state, but rather suggest a similar underlying pathophysiology involving medial temporal dysfunction.

As has been noted, the only significant differences between both patient group in our sample are regarding visual-spatial memory and sustained attention as bipolar group are worse. These results agree with the study of *Borkowska and Rybakowski (2001), as they found that, neuropsychological* frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. Again similar finding in the study *of Martinez etal, 2004*, as he found that clinical variables were associated with neuropsychological measures. As patients with a longer duration of illness showed more memory dysfunctions, more slowness or diminished attention. In-addition similarity in cognitive impairment found in our sample of unipolar and bipolar patients may agree with some

of the findings of *Bearden et al, 2006* who found that bipolar patients show declarative memory impairments, in all phases of bipolar and independent of their current state (manic versus depressive).

Thus the questions about similarities and differences between unipolar and bipolar depression is still a persistent question in our study as we found many similarities regarding pattern of neuropsychological impairment and few differences between both patients group regarding profile and severity of cognitive function as we have said these may be related to both history findings and subtype of depression , as found by of *Bearden et al, 2006, Martinez et al, 2004, Philippe et al., 2004* and *Borkowska and Rybakowski (2001).* Furthermore the differences between our study and other studies may be related to, differences in sociodemographic data, clinical characteristics of the patients group and lastly the neuropsychological tests used. Although our studies and the other studies agree on that there are cognitive deficit in depression whether unipolar or bipolar mainly in memory, attention and sustained attention these impairment may be slightly more in bipolar patients regarding some aspects of cognitive functions. Also these impairment may related to certain clinical characteristics of the patients as duration of illness and number of episode rather than related to affective state as found by of *Bearden et al, 2006 and Martinez et al, 2004.*

Opposing the researcher's predictions, although bipolar depression is distinct from unipolar depression in terms of phenomenology, clinical characteristics and management but neuropsychological distinguishing is still not well established.

Limitations:

Unavoidable practical considerations often interfere with ideal methodologies, clouding and weakening conclusions drawn from the results of clinical neuropsychological studies. (*Murphy and Sahakian.2001)*

- First although the study tried to overcome methodological difficulties in previous researches by matching both group of patients and control as much as we can, but still difficult to say, we overcome all of it as some clinical characteristics of unipolar patients group were different from that of bipolar depressed group sample such as duration of illness, number of episodes. These clinical differences affect severity of the disorder and hence may affect results of neuropsychological tests.

- Second the neuropsychological tests performed in the study are not enough to determine the whole aspects of cognitive impairment in depression.

- Lastly both patients group were on pharmaco-therapy which may affect the results of neuropsychological tests.

Clinical implications:

- Our results indicate that, whether unipolar or bipolar, depression is a chronic illness with disability, although our study could not answer the questions whether these impairment in cognitive function is a trait, state or scar marker

- The presence of such cognitive dysfunctions indicate treatment noncompliance, and poor social outcome.

- Cognitive behavioral therapy and drugs which didn't interfere with cognitive functions are recommended in both unipolar and bipolar depression in order to minimize or at least did not aggravate these cognitive deficit.

Future Directions

-More research is needed to study the difference between bipolar and unipolar depression using different neuropsychological and biological tasks.

- Further studies to determine whether these cognitive impairments are state, trait or scar marker.

- To study the effect of cognitive behavioral therapy and maintenance antidepressants on the prognosis of these cognitive deficits.

Summary:

Although many studies have demonstrated the presence of wide-ranging neuropsychological deficits in patients with major depression, but only few of them study depressive phase of bipolar. In brief, we try to study cognitive function in both unipolar and bipolar depression during acute phase of both of them. Then comparing both types of depression in order to determine similarity and differences between them as regard neuropsychological deficit. As mentioned in the previous studies, cognitive impairment were present in both types of depression, pattern of these cognitive deficits may be slightly different in both types of depression these differences either related to clinical differences in the sample or biological differences between both types of depression.

Conclusion

Depression is a chronic disorder which could affect social and cognitive function of the patients. This cognitive impairment may be related to a lesser extent to subtype of depression or phenomenology of depression but, the most important is the chronicity of the illness as shown in our study and some of the previous studies. Finally although unipolar depression is clinically distinguished from bipolar depression but yet many research needed to determine neuropsychological differences between both types.

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اضطراب الوظائف المعرفية فى مرضى الاكتئاب

إن اضطراب الوظائف المعرفيه فى مرض الاكتئاب من اهم الاعراض المرضية و لها مضاعفات كثيره وهامه وقد هدفت هذه الدراسه الي مقارنه مرضى الاكتئاب احادى القطب بمرضي الاكتئاب ثنائى القطب . شملت الدراسةاثنى وعشرون حاله من كل نوع تم اختيارهم من المرضي المترددين علي العيادات الخارجيه بمركز الطب النفسي بجامعه عين شمس. ولقد خضعت كل حاله الي اخذ التاريخ المرضي لها وتشخيصها باستخدام المقياس العالمى العاشر للامراض النفسية كما تم استخدام قائمه ملاحظه لاعراض الاضطرابات النفسيه و بعض الاختبارات من اختبار واكسلر للذكاء للكبار وقياس شده الاكتئاب باستخدام مقياس هاملتون واختبار الانتباه باستخدام اختبارفيجل للاداء المستمر. كما تم اختيار اثنان وعشرون شخصا اصحاء مطابقين للمرضي لمقارنه المرضي بهم ولقد خضع كل شخص منهم لما خضع له المرضي. ولقد نتجت الدراسات عن ان هناك اضطراب ملحوظ فى الوظائف المعرفيه فى المجموعتين و ان هناك علاقات ذات دلالات هامه احصائيه بين المجموعتين من حيث شده الاكتئاب و واختبار الانتباه باستخدام اختبارفيجل للاداء المستمر و توصي الدراسه بضروره الاخذ في الاعتبار هذه النتائج أثناء اعداد و تطبيق خطه اعاده تاهيل مرضي الاكتئاب كما توصي بعمل دراسات أخرى علي عدد أكبر من المرضي لدراسه الاختلافات بينها و بين هذه الدراسه.

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