Memory Impairment and its Relation to other Cognitive Dysfunctions in a Sample of Depressed Patients

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ABSTRACT

Background: Memory is the capacity for treating experiences and reproducing them when needed. High levels of cortisol may be associated with depression and may also lead to neuronal death and cognitive decline. **Objective:** to show the effect of depression on memory, and if this effect results from the associated cognitive impairment or it occurs as a separate process. **Subjects and methods:** A sample of 50 patients diagnosed as depression according to DSM IV TR criteria. They undergo psychometric assessment of Mini-mental state examination, Beck depression Inventory, Luria Nebraska Neuropsychological Battery, Wechsler memory scale and Hamilton anxiety scale. Then memory impairment was compared by cognitive impairment in various types of depression. Some of depressive disorders affect memory beyond the level of cognitive impairment especially the major depressive type and the dysthymia. **Results:** Cognitive functions were found to be significantly impaired with the presence of melancholic and psychotic features more than memory impairment bipolar depression has a profound effect on both cognition and memory to the same degree. While in adjustment disorder and dysthymia, cognitive and memory impairment were found to be impaired than in major depression. **Conclusion:** The association of anxiety was found to affect the degree of cognitive and memory impairment.

Key words: Depression, Cognitive impairment, Anxiety, Memory impairment.

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INTRODUCTION

Memory is the capacity for treating experiences and reproducing them when needed. It is the component of information processing system that supports the encoding, storage retrieval of information over time[1]. Memory is one of the most pervasive aspects of consciousness. It helps to define identity and allows self awareness by providing a sense of continuity from our recall of past experience promotes our capacity to the present and allow us to benefit from learning and experience to prepare for the future. High levels of cortisol may be associated with depression and may also lead to neuronal death and cognitive decline. Patients with high corisol levels or other manifestation of hypothalamic- pituitary-adrenal axis dysregulation might have depressive symptoms and poor cognitive functions[2].

The treatment of depressive symptoms may not only lessen the depressive symptoms but improve cognitive function and possibly the outcomes. So, treatment of depression,

whether it is pharmacological, behavioral, or other modalities, improve cognitive function whether the treatment of depressive symptoms can delay or prevent cognitive decline, it will need further studies[3]. It is also possible that depressive symptoms, memory decline and cognitive decline are both due to an underlying genetic predisposition. For instance, the apolipoprotein E4 allele is a risk factor for Alzhiemer disease and preclinical cognitive decline.

Underlying CNS alteration may cause depressive symptoms and cognitive decline. Results from several research studies support an overlapping mechanism for dementia and depression in elderly persons. 30% of patients with vascular dementia or Alzhiemer disease have depressive symptoms[4].

Changes in the brain cortical areas have also been implicated in depression. PET and SPECT studies, have demonstrated a reduction in frontal lobe and limbic system blood flow in patients with primary and secondary depressions, including those with depression and dementia. Elderly depressed patients have more white matter and other subcortical abnormalities on brain MR[5].

Depression has such a profound effect on cognition and memory that many times depressed people are thought to have dementia. Pain also can affect cognition; particularly severe, chronic pain which causes and individual to reduce normal activities. Also sleep deprivation and medications such as used for anesthesia, sleep, pain, anxiety; sedation can cause cognitive impairment[6].

A significant low 5- hydroxy indole acetic acid (HIAA) levels was found in CSF of the depressed patients[7]. In addition, a marked loss of pigmented neurons was detected in the ventral tegmental area (VTA) in small group of depressed patients; the ventral tegmental area contains cell bodies of dopaminergic neurons that provide most of the dopaminergic inervation of the prefrontal cortex, limbic areas and nucleus accumbens.

Studies of memory function reveal that depressed patients are likely to remember emotionally negative words and negative events in their life during depressive episodes. Although studies of anxious patients has found consistent attention biases favoring attention to threat- related words, studies of attention effects in depression have yielded inconsistent results. Thus, processing and recall in depressed patients appear to be more related to emotional effects on cognition than attention biasing[8].

The attention and memory findings have suggested several theoretical frameworks that are clinically useful[9]. A schema theory of depression outlines a positive feedback loop in which negative self schemata prime persons to have negative thoughts to recall negative events in their lives, and to interpret present events with negative bias, whether as a cause or a maintaining influence, those depressogenic schemata are thought to create a series of cognitive functions that produce and maintain a depressed mood.

A network memory and emotion has been supported by research on depressed and non-depressed persons in which mood leads to a separating activation of items in memory that are congruent with the mood[10]. This emotion directly influences retrieval by a process of state dependent learning and memory. Depressed patients are likely to encode items while depressed

in a form that makes them readily accessible when retrieved in a depressed state. Depressed mood thus becomes an internal context that allows the access of depression related memories. Some patients may be prone to marked cognitive alterations because of an emotional state that may be a fundamental part of clinical presentation.

Cognitive deficits are an important component of affective illnesses like depression and are responsible for significant social and occupational morbidity. These should not merely be considered as phenomena secondary to lack of motivation. Further research in this area would make us wiser about the neuropathlogical basis of depression & also help in development of better antidepressant medication[11].

There has been a renewal of interest in testing patients with depression on a broad range of neuropsychological task in the last two decades. These deficits involve both memory and executive function. It is now commonly accepted that depression is associated with a number of deficits in episodic memory and learning. This is a consistent finding and involves both explicit verbal and visual memory in patients with endogenous as well as exogenous depression[12].

Implicit memory tasks on the other hand appear to be spared. It is well known that temporal lobe lesions typically disrupt episodic memory. As the hippocampal volume reduction is demonstrated in patients with major depression, it may be that impaired memory function is associated with dysfunction of the hippocampus in depression. The impairment in executive function seems to be selective for "set shifting task"[13].

Now an important issue, which needs to be addressed, is whether these neuro-psychological deficits are simply epiphenomena of depression or more than that patients with depression generally have difficulty with effortful (verbal recall) as compared to automatic memory (verbal recognition). Similarly dissociation between explicit (impaired) and implicit (interact) memory tasks seen in patient with depression was also a result of greater effort required for the former and more automatic performance of the latter. This "effortful-automatic" hypothesis however has been undermined by other studies[14].

Those who challenge the view that cognitive deficit are epi-phenomenon of depression put following evidences for support. Few of the studies have reported that cognitive deficits do persist even after the recovery from depression. In a controlled study of executive tasks performance in middle-aged subjects with severe depression reported improved performance on the verbal fluency task but not the stroop task upon recovery[15].

In addition, improvement in immediate memory was related to degree of recovery of depression, while performance on learning and short-term memory tasks remains impaired even after recovery[16]. Evidence is the presence of cognitive deficits even in young patients with mild depression. With advances in the field of functional and anatomical imaging of brain we are rapidly gaining insight into the functional and neuroanatomical correlates of cognitive deficits and its relation to the affective manifestations. It was also hypothesized that memory impairment in depressive disorders is a separate process rather than occurring secondary to cognitive

impairment and that each of which can be found independently.

SUBJECTS AND METHODS

Sample selection:

A sample of 50 patients with the diagnosis of mood disorder depression was taken from the outpatient clinics of Mansoura University Hospitals within the period from April to August, 2007. They were diagnosed as to have mood disorders according to DSM IVTR (functional; with exclusion of substance induced mood disorder and mood disorder due to general medical condition) depression (unipolar depression and bipolar depression), dysthymic disorder and adjustment disorder with depressed mood. The sample of major depression was further classified into depression with psychotic features, depression without psychotic features, depression with melancholic features, and depression without melancholic features.

Sample characteristics:

This is a study of 50 patients, 26 males and 24 females with the age ranges from 21-56 years. They were subdivided into:

- Dysthymic patients: 10 patients
- Adjustment disorder with depressed mood: 7 patients
- Bipolar depression: 10 patients
- Unipolar depression: 23 patients who further classified into:
- Depression with melancholia: 9 patients and with out melancholia: 14 patients
- Depression with psychotic features: 11 patients and without psychotic features12 patients.

Table (1): Sociodemographic data

	Sample character	Number	%
Sex	Male	26	52%
	Female	24	48%
Residence	Urban	23	46%
	Rural	24	54%
Occupation	Unemployed	9	30%
	student	10	20%
	H.W	10	20%
	Non sk. Lab	7	14%
	Sk.L.	5	10%
	Intermed	3	6%

Table (2): Marital status and education

	Sample character	Number	%
Marital status	Single	10	20%
	married	10	20 %
	widow	15	30 %
	divorced	15	30 %
Education	Illitera	15	20 %
	Primary	15	20 %
	Preparatory.	11	30 %
	Secondary& above	9	30 %

Psychometric assessments:

All patients were subjected to the following psychological tests:

1- *Beck depression Inventory*[17] (BID).

2- *Mini Mental State Examination*[18] (MMSE).

3- *Luria Nebraska Neuropsychological Battery*[19]: LNNB is based on the techniques of Russian neuropsychologist A.R. Luria, this battery is used to diagnose cognitive deficits, including lateralization and localization of focal brain impairments. Unlike other neuropsychological tests, which give only a global measure of cerebral dysfunction, the LNNB also detects very specific problems, as well as

mild impairment that might otherwise go unnoticed. The two forms are equivalent, although form II includes an additional scale, Intermediate memory and can only be scored by computer[20].

4- Wechsler Memory scale.

5- Hamilton Anxiety Scale[21].

RESULTS

Table (3) shows a strong correlation between duration and the degree of cognitive and memory impairment where P value was zero in both MMSE and LNNB (HS) and there was a positive correlation in LNNB (strong positive correlation) and in MMSE there was strong negative correlation. On the other hand there was no effect of duration on intelligence as P value was non-significant (NS) while r was weak positive correlation.

Table (3): Effect of duration of illness on the degree of cognitive and memory impairment.

	Luria Nebraska		Mini-mental		Wechsler memory	
Duration	**R**	**(P)**	**R**	**(p)**	**R**	**(P)**
	.8	**<0.001**	**-.8**	**<0.001**	**.06**	**NS**

The effect of number of previous episodes on cognition and memory impairment by applying Anova test we found that the history of previous episodes severely affects both cognitive and memory impairment. Where P=0 in case of MMSE, Wechsler memory and LNNB (High Significant) (HS) (table 4).

It was found in table (5) that depression with melancholic features results in more cognitive impairment, MMSE was of moderate significance (MS) (P<0.001). While in LNNB and Wechsler memory, there was no statistical significance between the effects of both depression with melancholic features and without melancholic features on the degree of memory impairment (P>0.05) (NS).

Cognitive functions were found be severely affected in Depression with psychotic features measured by MMSE where P<0.001 (HS). While it has a moderate effect on memory impairment as obtained by LNNPB and Wechslerwas moderate significant (MS) p<0.01 (table 6).

Table (7) show that bipolar depression has a profound effect on both cognition and memory to the same degree, where was P=0 in cases of bipolar disorder versus uni-polar disorder as regards both MMSE and LNNB (HS).

It was found that major depression when compared by dysthymia had a statistical Significance on memory impairment where the P<0.01 (MS) as regarding LNNB and Wechsler. While in case of MMSE the P value was (NS) (table 8).

We found that major depression when compared by adjustment disorder with depressed mood had a severe effect on cognition and memory where the P=0 (HS) in MMSE, Wechsler and LNNB (table 9).

Using the test of correlation on the two variables, the severity of depression as obtained by BID showed significant impairment of cognition and memory as p=0 (2-tailed) (HS) in both (table 10). Anxiety also had the same effect on cognition and memory like the depression severity where P=0 in cases of MMSE, Wechsler and LNNB (HS).

Table 4: Effect of number of previous episodes on the degree of cognitive and memory Impairment.

Scale	Non		1-3		More than 4		Total		Significance
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	f (P)
MMSE	26	23 (3.7)	16	14 (1.2)	8	15 (1.5)	50	19 (5.2)	59.1 (<0.001)
Luria	26	12.7 (4.4)	16	24.8 (2.4)	8	26 (4.8)	50	18.7 (7.4)	63.5 (<0.001)
Wechsler	26	12,7(403)	16	24.4 (2)	8	25(4.7)	5	1802 (7.6)	63.5 (<0.001)

Table (5): Effect of the presence of melancholic features on cognitive and memory impairment.

Scaling procedure	Depression without melancholic		Depression with melancholic		Significance
Mini-mental	n	Mean (SD)	n	Mean (SD)	t (P)
LURIA	41	41 (5.3)	9	14.9 (1.8)	2.6 (< 0.01)
Weschsler	41	17.7 (7.9)	9	22.9 (2)	1.9 (NS)
Memory	41	17.7 (7.9)	9	22.9 (2)	1.9 (NS)

Table (6): Comparison between depression with psychotic features and non-psychotic depression as regards memory and cognitive impairment.

Scales	Depression without psychotic		Depression with psychotic		Significance
	n	Mean (SD)	n	Mean (SD)	T (P)
Minimental	40	20 (5.2)	10	14.1 (1.5)	3.6 (<0.001)
LURIA	40	17.2 (7.6)	10	24.5 (1.2)	2.9 (<0.01)
Weschsler	40	17.2 (7.6)	10	24.5 (1.2)	2.9 (<0.01)

Table (7): Comparison between effects of bipolar and uni-polar depression On both memory and cognitive impairment.

Scale	Uni-polar depression		Bipolar depression		Significance
	n	Mean (SD)	n	Mean (SD)	t (P)
Minimental	40	20.1 (5.1)	10	14 (.88)	3.8 (<0.001)
LURIA	40	16.5 (6.4)	10	27.5 (3.6)	5.2 (<0.001)
Weschsler	40	16.5 (6.4)	10	27.5 (3.6)	5.2 (<0.001)

Table (8): Comparison between Dysthymia and major depression in relation to memory impairment

Scale	Dysthymia		major depression		Significance
	n	Mean (SD)	n	Mean (SD)	t (P)
Minimental	13	20.8 (3.8)	37	18.2 (5.6)	1.6 (NS)
LURIA	13	14 (4.3)	37	20.3 (7.6)	2.9 (<0.01)
Wechsler	13	14 (4.3)	37	20.3 (7.6)	. 2.9 (<0.01)

Table (9): Adjustment disorder against major depression in relation to cognitive and memory impairment.

Scale	Dysthymia		major depression		Significance
	n	Mean (SD)	n	Mean (SD)	t (P)
Minimental	7	26.9 (1.7)	43	17.5 (4.4)	5.5 (<0.001)
LURIA	7	7.9 (1.3)	43	20.4 (6.4)	5.1 (<0.001)
Wechsler	7	7.9 (1.3)	43	20.4 (6.4)	5.1 (<0.001)

Table (10): Cognition impairment against depression severity and presence of anxiety.

	Luria Nebraska		Minimental		Wechsler	
Beck scale	r	(P)	r	(p)	r	(P)
Hamilton	9	(<0.001)	- .9	(<0.001)	04	(NS)
anxiety scale	7	(<0.001)	.7	(<0.001)	-.03	(NS)

DISCUSSION

In the current study both cognitive and memory was observed to be globally impaired in depressive disorders of high significance (HS) statistical value and this is similar toprevious reports[22].

In the current study, cognitive and memory impairment were studied in depression with melancholic features against depression without melancholic features. Cognitive function was found to be significantly impaired with the presence of melancholic features with moderate significance (MS). So that, melancholic features had the effect on cognition that it causes more cognitive decline than depression itself can cause. This is concordant with that the fact that melancholia associating major depressive episode is characterized by marked cognitive impairment, he also added that psychomotor agitation and retardation occur in depression, producing states of over activity and under activity respectively[23]. Agitation and retardation can lead to

impaired cognition, judgment, reason, and decision making, which often further isolates depressed people and prolongs symptoms. Psychomotor agitation can also lead to generalized restlessness.

In the present work, it was found also that both cognition and memory are impaired in depression with psychotic features (HS for cognition & MS for memory), this coincides with Kevin et al. who compared the outcome of psychotic depression (depression with delusion or hallucinations or both), he found that patients with psychotic depression have lower rates of recovery, more chronic symptoms, higher rates of relapse and recurrence and more cognitive impairment[24]. Mood-incongruent psychotic features unlike the mood congruent psychotic features are psychotic symptoms which do not involve typical depressive themes, for example, persecutory delusions, delusions of reference, and thought insertion. These have clinical implications that mood-incongruent delusions are said to be infrequent and imply poor treatment response, more cognitive impairment and a bad prognosis.

Also thought disorder is associated with and may result from semantic processing abnormalities. In particular, patients with severe thought disorder may have difficulties accessing semantic systems and to a more limited degree, may lack a semantic or conceptual knowledge base[25]. In addition, major depression is endocrinally different from non-psychotic depression and produces cognitive changes distinct from those seen in non genuine major depression (reactive depression)[26].

Bipolar depression found to have a stronger impact on cognition and memory (HS) than the unipolar depression and patients with bipolar disorders show greater deterioration in memory[27].

In adjustment disorder and dysthymia, it is found to be less cognitive and memory impairment than in major depression where the specific test for memory was (MS) in case of dysthymia & both tests of cognition and memory was found impaired (HS) in adjustment disorder when compared with major depression. This may be due to the less severity of depressive illness such as the slight lowering in depressed mood, insomnia, anhydonia, and worthlessness.

The association of anxiety was found to worsen the degree of cognitive and memory impairment (HS). This is agreed with the report that in anxiety, the unconscious activity provoked by the anxiogenic words is observed leading to selective distractibility that produces the cognitive vulnerability in anxious persons but not trait anxiety induces working memory performance deficit, and that the generated information processing in anxiety leads to better performance in simple tasks by recruiting motivational capacities but not in high content tasks[28].

Residence and age were found to be statistically non-significantly linked to both cognitive and memory impairment. This may be due to most of age groups limited between 40s-50s (33 cases) this narrow range of age might contribute to the low significance in cognition and memory performance scores. Although, depression is more sever in late life and elderly patients with cognitive impairment may experience cognitive improvement with antidepressants but they may not reach the base line of performance, particularly in memory and executive functions. This group of late life depression is more liable to develop progressive dementia[29].

Education was not of statistical significance opposing the observation that, having more than 8 years of formal education was associated with less cognitive decline[30]. However beyond 9 years, additional education was not associated with a further reduction in cognitive decline. This suggests that a minimal amount of education during early critical periods might confer protection against cognitive decline. This may be due to the low number of highly educated patients attending the university outpatients, but most of them are farmers and illiterate

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