

((قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ))

صدق الله العظيم

سورة البقرة

الآية ٣٣

Contents

Page

• Acknowledgement.	
• List of tables.	
• List of abbreviation.	
• Introduction.....	1
• chapter I : Cognitive functions.....	7
○ Global cognitive functions	7
○ Executive functions.....	8
○ Working memory.....	12
○ Planning/Problem solving.....	15
○ Memory functions.....	17
○ Attention.....	20
○ Visuospatial functions.....	27
• chapter II : Cognitive impairment in unipolar depression	30
○ Depression and the brain.....	32
○ The vascular depression hypothesis.....	39
○ Cognitive functions during depression.....	41
○ The reciprocal relationship between depression and cognitive dysfunction.....	65
○ Factors predicting presence of cognitive dysfunction in UP patients.....	67

○ Reversibility and persistence of cognitive dysfunction after depression abates.....	72
○ Factors predicting persistence of cognitive impairment in UP.....	77
○ From depression to dementia.....	82
○ Do 1 st degree relatives of UP differ regarding cognition from general population?.....	91
● Chapter III: Cognitive impairment in BAD.....	93
○ Neuroanatomical abnormalities in BAD.....	96
○ Cognitive impairment in BAD.....	99
○ Neuropsychology and neurophysiology of BAD among the 3 phases of the disorder.....	105
○ Persistence of cognitive impairment in euthymic state of BAD.....	115
○ Factors predict persistence of cognitive impairment in bipolar patients.....	120
○ Differences between cognitive performance in BAD I and II.....	127
○ Cognitive performance in 1 st degree relatives of BAD patients.....	130
● Chapter IV: Effect of medications used in mood disorders on cognition.....	136
○ Antidepressants.....	140
○ Antiepileptic.....	144

○ Lithium.....	148
○ Antipsychotics.....	150
○ Electroconvulsive therapy.....	156
○ Repetitive transcranial magnetic resonance.....	159
● Discussion.....	162
● Recommendations.....	181
● Conclusion.....	183
● Summary.....	186
● References.....	195
● Arabic summary.	

List of abbreviation

- * **ACC:** Anterior cingulate cortex.
- * **ACT:** Auditory Consonant Trigrams.
- * **Ads:** Antidepressants.
- * **AEDs:** Antiepileptic drugs.
- * **BAD:** Bipolar affective disorder.
- * **BF:** Blood flow.
- * **BSAT:** Brixton Spatial Anticipation Test.
- * **CANTAB:** Cambridge Neuropsychological Test Automated Battery.
- * **CBF:** Cerebral blood flow.
- * **CNS:** Central nervous system.
- * **ChAT:** Choline acetyltransferase.
- * **CVLT:** California Verbal Learning Test.
- * **DBD's:** Disruptive behavior disorder.
- * **DLPFC:** Dorsolateral prefrontal cortices.
- * **DSM- IV-TR:** Diagnostic and statistical manual of mental disorders, text revision.
- * **E.C.T:** Electro-Convulsive Therapy.
- * **fMRI:** Functional magnetic resonance imaging.
- * **GABA:** Gamma amino buteric acid.
- * **HAMD:** Hamilton Depression Rating Scale.
- * **HPA axis:** Hypothalamic pituitary adrenal axis.
- * **HSCT:** The Hayling Sentence Completion.
- * **LAC:** Left anterior cingulated.
- * **LF:** Life functioning.

- * **LPC:** left posterior cingulate.
- * **LTP:** Long-term potentiation.
- * **MAOI:** Mono Amine Oxidase Inhibitor.
- * **MDD:** major depressive disorder.
- * **MDI:** Manic-depressive illness.
- * **MMSE:** Mini Mental State Examination.
- * **MRS:** Mania Rating Scale.
- * **NBM:** Nucleus basalis of Meynert.
- * **NC:** Neurocognitive.
- * **NGF:** Nerve growth factor.
- * **PDCD:** Post Depression Cognitive Decline.
- * **PFC:** Prefrontal cortex.
- * **rTMS:** Repetitive Transcranial Magnetic Stimulation.
- * **SGPFC:** Sub-genual prefrontal cortices.
- * **SNRI:** Serotonin Noradrenaline Reuptake Inhibitor.
- * **SSRI:** Selective Serotonin Reuptake Inhibitors.
- * **TCAs:** Tricyclic antidepressants.
- * **TMT:** Trail Making Test.
- * **TOL:** Tower of London.
- * **UP:** Unipolar depression.
- * **WCST:** Wisconsin Card Sorting Test.
- * **WM:** Working memory.
- * **WMH:** White matter hyperintensities .
- * **WMS-III:** Wechsler Memory Test III.
- * **5-HT:** Serotonin.

List of tables

Table Number	comment	Page
1	Comparison of unipolar depressed, bipolar depressed, frontal lobe lesion and temporal lobe lesion patients.	44
2	Cognitive impairments across mood phases in bipolar disorder.	115
3	Comparison between cognitive profile of unipolar and bipolar depression.	174

Acknowledgement

I am deeply grateful for the support and guidance of many people, who make this review possible.

I am deeply grateful to Professor **Tarek Asaad Abdo** Professor of Neuropsychiatry, Faculty of medicine, Ain Shams University, for his guidance throughout the review. His guidance and creative ideas were tremendous, without which this review would have not completed.

I am eternally grateful to Dr. **Mohamed Fekry Eissa** Assistant Professor of Neuropsychiatry, Faculty of medicine, Ain Shams University. I am obliged to him because he has willingly dispersed much of his valuable time trying to clarify any gloomy aspects in the review, guiding me with recent ideas.

I would like also to express my deep gratitude to Dr. **Hisham Ahmed Hatata** Assistant Professor of Neuropsychiatry, Faculty of medicine, Ain Shams University for his cooperation and meticulous revisions, without his ideas this work would not have seen daylight.

I wish to express my gratitude to my outstanding Professors and Colleagues who supported and guided me allthrough the period of review, especially Dr. **Mohamed Amr Sherif** Assistant Lecturer of Neuropsychiatry Ain Shams University, and Dr. **Mahmoud El-Habeby** Assistant Lecturer of Neuropsychiatry Ain Shams University for their help.

Finally, I wish to extend my thanks to my parents. Without their help and support, this work would have never been accomplished.

INTRODUCTION

Mood disorders are common conditions. Major depressive disorder has a lifetime prevalence of 5-12 % for men and 10–25 % for women. Bipolar I disorder has a lifetime incidence of about 0–2.4 %. Bipolar II disorder has a lifetime prevalence of about 0.3–4.8%. Among these disorders cognitive impairment had been described. Depressive pseudodementia and delirious mania are known descriptions (**Sadock & Sadock, 2007**).

Although depression and mania are primarily disorders of affect, but DSM IV TR report cognition as an important component of these syndromes: criterion 8 for a major depressive episode states that a depressed individual may have ‘diminished ability to think or concentrate, or indecisiveness, nearly every day’; while criteria 4 and 5 for mania put ‘flight of ideas’ and ‘distractibility’ respectively as symptoms central to mania (**Sadock & Sadock, 2007**).

A large proportion of patients fail to regain premorbid levels of functioning after the resolution of major affective symptoms (**Robinson and Ferrier, 2006**).

Patients of major depression show significant impairment of attention, visuomotor speed, immediate verbal memory, short-term retentive capacity and executive functions (strategic planning, attentional set shifting and working memory) (**Wilkinson and Goodyer, 2006; Mondal et al, 2007**).

Neurocognitive impairment persists in most depressed older people after clinical recovery. This in turn leads to increased mild cognitive impairment as well as dementia. Conversion rate from mild cognitive impairment to DSM-IV-TR dementia is about 21.9% over a period of 3 years. The occurrence of depressive symptoms may constitute a predictor for those who are more likely to progress to dementia (**Gabryelewicz et al, 2007; Thomas and O'Brien, 2008**).

Although cognitive deficits are common among unipolar depression and bipolar depression, but, unfortunately there

are only few comparisons had been taken between them regarding illness histories. So, the predictors of impairment were not well understood. Among the few researches that focused on such a comparison there were a qualitatively similar patterns of memory impairment in bipolar disorder and unipolar major depressive patients, consistent with a primary encoding deficit (**Bearden et al, 2006a**).

Cognitive impairment has been commonly found in euthymic patients with bipolar affective disorder following the first episode, showing significant attentional deficit and executive dysfunction and also poor performance on verbal and visual memory tasks (**Nehra et al, 2006; Ozdel et al, 2007**).

Meanwhile, cognitive impairment persists even during the euthymic state, and may be a contributory factor to poor psychosocial outcome (**Robinson and Ferrier, 2006**).

Moreover, cognitive deficits are more severe and pervasive in Bipolar II patients than Bipolar I patients (**Summers et al, 2006**).

The impaired neuropsychological performance was associated with duration of illness, total number of episodes per lifetime, and previous episodes with psychotic features, subclinical depressive symptoms, early onset of illness (Torrent et al, 2006; Ozdel et al, 2007).

The history of psychotic symptoms may partly account for the cognitive dysfunctions seen in euthymic bipolar patients, especially with regard to persistent verbal memory dysfunction, as well as with some executive dysfunctions. (Martinez-Aran A et al, 2008).

This review point to how mood disorders affect cognitive functions of the patients, affecting their abilities of functioning, as a step to understand and enhance the end results of mood disorders, decreasing their disabilities.

Hypothesis of the work:

In the recent few years, cognitive impairment in mood disorders has been focused of research, because it has been demonstrated that it plays a role in prognosis of patients of mood disorders, so it is hypothesized that mood disorders (major depressive disorder and bipolar disorders I, II) have a great effect on cognitive functions, which may persist even after remission of the patient.

Methodology of the study

A review of the available literature will be done, some of the data of the study will be collected from the internet. Other data will be collected from textbooks and researches in the library.

Aim of the work:

To highlight the relationship between mood disorders and cognitive impairment.

To update the information about the predictive factors of cognitive impairment in mood disorders.

To demonstrate factors leading to progression of cognitive impairment in mood disorders.

Rational of the study:

It is observed that high proportion of patients suffering from mood disorders show impairment in their cognitive functions, which may persist afterwards, affecting their lifestyles, social and occupational functioning.

Cognitive Functions

Cognition is the ability to recognize and process complex tasks adequately. It depends on the function of complex interrelated and distributed neuronal network. Neuropsychological test batteries are designed to examine various domains of cognition, such as memory, attention, vigilance, visuospatial ability, language and verbal function, concept formation, problem solving and executive functions (**Sharma and Mockler, 1998**).

Global cognitive functions:

Global cognitive functions refer to a general level of cognitive ability and are routinely assessed by intelligence tests. Different cognitive functions performed by the brain depend on one another and are affected by overall intelligence. A global assessment includes only certain aspects of cognition, it provides a baseline to assess general deterioration from premorbid level of functioning and areas of cognitive deficit and hyperfunction that may be related to brain locations, such