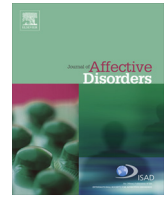




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Preliminary communication

Cognitive functions in euthymic Egyptian patients with bipolar disorder: Are they different from healthy controls?

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ABSTRACT

Background: There is marked interest to research neurocognitive functions in bipolar disorder during euthymia. Consequently we aimed to study cognitive functions in euthymic bipolar patients and factors affecting them.

Methods: It is a cross sectional case-control study of 60 euthymic bipolar patients and 30 matched healthy controls. They were subjected to: Structured Clinical Interview for DSM-IV disorders, (SCID-I) to ascertain clinical diagnosis, Young Mania Rating Scale (YMRS), Hamilton Rating Scale for Depression (HRSD) to validate euthymia. Wechsler Adult Intelligence Scale (WAIS) for general intellectual abilities, Wechsler Memory Scale-Revised (WMS-R) for memory, Wisconsin Card Sorting Test (WCST) for executive functions, Continuous Performance Test (CPT) for attention and impulsivity, and an information sheet gathering patient data.

Results: Bipolar patients had statistically significant lower mean IQ scores in all WAIS subscales ($p=0.000$), significantly lower memory abilities especially digit span and visual memory, higher impulsivity and inattention ($p=0.000$) but no significant difference in response time by CPT. They displayed significantly lower executive performance on WCST. Patients' years of education correlated positively with IQ. Hospital admission, number, type of episodes and total number of episodes affected memory functions. Hospital admission and number of hypomanic episodes correlated with attention and impulsivity. Previous hospitalization correlated with executive functions.

Conclusions: Euthymic bipolar patients exhibit cognitive deficits, which correlated with clinical variables as number, type of episodes and previous hospitalization, this knowledge could help minimize cognitive impairments for future patients.

Limitations: The small sample size, cross sectional design and lack of premorbid cognitive assessment limit generalization of findings.

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1. Introduction

There is growing interest in the research of neuro-cognition as a putative marker for subjects with bipolar disorders (BD) (Martinez et al., 2008), which is a chronic, recurrent affective disorder characterized by cyclic episodes of mania/hypomania and depression, interspersed with periods of euthymia (Torres et al., 2007). The expression of BD includes not only the core abnormality in mood regulation, but also cognitive deficits that are well established in patients during acute manic-depressive states but less established

during euthymic states (Clark and Goodwin, 2004; Martinez et al., 2010).

Evidence exists of trait-like deficits in cognitive functions of bipolar patients, and the identification of possible endophenotypes has started (Jamrozinski, 2010). Recent meta-analytic studies of cognitive performance in euthymic patients with bipolar disorder have reported impairments in patients compared to healthy controls in a range of neuropsychological domains such as attention/vigilance, processing speed, response inhibition and set shifting, as well as verbal and visual learning and memory (Bora et al., 2009; Andreoua and Bozikas, 2013).

Neuropsychological testing with standardized assessment procedures provides indirect measures of activity in brain systems. They provide the advantage of being relatively inexpensive and can be readily administered in a clinical or hospital setting (Clark and Sahakian, 2008). Various studies have used different

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neuropsychological tests as Wechsler Adult Intelligence Scale (WAIS) as an indicator of general cognitive abilities (Simonsen et al., 2008); others studied executive functioning and reported a range of discrepant findings from executive deficits (Dixon et al., 2004), the absence of executive impairments (Cavanagh et al., 2002), or marginal impairment in this domain (Torres et al., 2007).

Memory represents another frequently studied cognitive domain, which displays more uniformity in reported deficits as verbal and non-verbal episodic memory deficits relative to healthy controls (Thompson et al., 2005; Torres et al., 2007). When comparing findings of studies measuring attention many researchers report that euthymic patients exhibit deficits in tasks of sustained attention (Clark et al., 2005; Torres et al., 2007).

Due to the limited amount of Egyptian research on cognitive functions in bipolar patients and the scarcity of such research during euthymic states, the authors of this study aimed to describe the neuropsychological functioning in the euthymic phase of bipolar disorder, to evaluate the magnitude of patient-control differences in performance of the cognitive tasks assessing memory, attention, and executive functions, and, finally, to assess the effect of various demographic and clinical factors on cognitive functions in a sample of Egyptian euthymic bipolar patients.

2. Methodology

2.1. Site of the study

This is a cross-sectional, case-control study that was carried out at the outpatient clinics of the Institute of Psychiatry, Ain Shams University¹. The study was conducted in accordance with the Helsinki Declaration for medical research of 1975 and in compliance with the guidelines of the Research and Ethics committee of the Institute. The research protocol was approved by the Research and Ethics committee of Ain Shams University.

2.2. Participants in the study

2.2.1. Patient group

Sixty euthymic bipolar patients were enrolled in the study. They fulfilled the inclusion criteria of being from 18 to 50 years of age, literate and in the euthymic phase of bipolar, I or bipolar II disorder. To avoid confounding factors extreme age ranges, illiteracy, active bipolar symptoms, comorbid medical and psychiatric disorders, history of substance abuse or recent treatment with electroconvulsive therapy (ECT) within the past six months and uncontrolled medical or neurological conditions were considered as exclusion criteria for participation in the study.

Euthymic state was operationally defined to be achieved in this study when patients fulfilled the DSM-IV criteria for bipolar disorder I or II, reported being in remission/ baseline mood for the past six months, and obtained a score of < 7 on the Hamilton Depression Scale (HDRS) and < 7 on the Young Mania Rating Scale (YMRS) (Dias et al., 2009).

Control group: consisted of 30 Egyptian male and female subjects matched for age, gender, educational level and other demographic variables as far as possible. Controls who reported current, past or family history of psychiatric disorders were excluded from participation.

3. Tools applied in the study

both patients and control subjects were subjected to the following

1. *The Structured Clinical Interview for DSM-IV axis I disorder clinician version (SCID I-CV)* (First et al., 1997): to ascertain the diagnosis of bipolar disorder, determine its type and exclude other axis-I comorbid psychiatric conditions, the clinical version was used rather than the research version for its relatively easier administration and coverage of the diagnoses most commonly encountered in clinical settings.
2. *Young Mania Rating Scale (YMRS)* (Young et al., 1978): this is an 11-item clinician rated questionnaire that assesses the severity of manic symptoms and detects symptom relapse. It was used in this study to validate patients were in the euthymic phase of bipolar disorder.
3. *Hamilton Rating Scale for Depression (HRSD)* (Hamilton, 1960): This is a 21-item rating scale for assessing the severity of depressive symptoms, and monitoring treatment. In this study, it was used to validate the euthymic state of the patient group.
4. *Wechsler Adult Intelligence Scale (WAIS)* (Wechsler, 1981): For a broad assessment of general cognitive and intellectual abilities. The study used the Arabic validated version of the WAIS with Egyptian norms as a reference (Melika, 1996).
5. *Wechsler Memory Scale-Revised (WMS-R)* (Wechsler, 1987): One of the most widely used tests for evaluating memory functions in adults, the scores reflect general, verbal and visual memory, attention/concentration and delayed recall.
6. *Wisconsin Card Sorting Test, the computerized version (WCST)* (Heaton et al., 2003): For assessment of cognitive flexibility, executive functions, problem solving, working memory and set-shifting abilities. It is a measure of frontal lobe functions and provides information on problem-solving abilities.
7. *Continuous Performance Test (CPT)* (Conners, 2000): For assessment of attention/vigilance and impulsivity. The scores reflect the total number of stimuli, the number of correct targets, omission errors (the number of targets the person did not respond to), commission errors (the number of times the person responded to a non-target) and various reaction times.
8. *An information sheet* devised to collect patient data, including: gender, age, years of education, occupation, diagnosis, previous hospitalization, number of episodes, index episode, number depressive episodes, number of manic episodes, number of mixed episodes, past history of psychotic features, duration of episode (in months), duration of illness (in years), family history, medications received and physical health status.

3.1. Procedure of the study

A total of 87 patients with bipolar disorder were assessed. 5 were excluded for having had recent ECT, 6 were excluded due to incomplete resolution of symptoms, and 10 were excluded for having comorbid substance misuse and 7 patients were excluded due to having co morbid psychiatric diagnosis as an anxiety disorder or personality disorder. All participants signed an informed consent of the nature of the research, emphasizing the voluntary participation and the right to withdraw at any time without giving reasons, and this will not be followed by withdrawal of any privileges.

The assessment of each subject took 3–4 h. Therefore, was undertaken over a two-session-interview. The first session included the clinical and demographic data collection, administration of SCID-I, HAM-D and YMRS (for the patient group only). The second session was for administration of cognitive tests.

¹ The Institute of Psychiatry Ain Shams University is an academic and clinical facility representing the department of Psychiatry in the faculty of medicine of the aforementioned university that is one of the biggest universities in Egypt, located in Cairo and serves a wide catchment area of east and central Cairo.

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