

Cognitive Functions in First Episode Psychosis

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ABSTRACT

Introduction:	Cognitive impairment is recognized as an important feature of psychosis in its early stages and is a determinant of prognosis and management of these disorders.
Aim of the study:	To test the cognitive functions in first psychotic episode in patients with disorders of schizophrenia, schizoaffective disorder, bipolar disorder and depression with psychotic disorder and to compare them to controls.
Subjects and methods:	The study included 254 patients diagnosed according to Diagnostic and Statistical Manual of Mental disorders, 4 th edition (91 schizophrenics, 21 with schizoaffective disorder, 107 with bipolar disorder and 31 with psychotic depression) and experiencing their first psychotic episode. Seventy healthy volunteers matching as regard age and sex with patients were selected as controls. All subjects were subjected to cognitive evaluation by Trail Making Test, part B, Wisconsin Card Sorting Test 128, Benton Visual Retention Test and Wechsler Adult Intelligence Test.
Results:	All patients showed significant cognitive deterioration in all tests compared to control. On comparing patients to each other, there was no significant difference between schizophrenics and patients with bipolar disorder, but both showed marked deterioration in comparison to depressive group.
Conclusion:	Cognitive impairments are present in early stages of psychosis and need careful assessment and management.
Key words:	Cognitive functions, First episode psychosis

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INTRODUCTION

Cognitive impairments are considered a central feature of schizophrenia, mania and psychotic depression^{1,2}. However, there is still an ongoing debate about the course of cognitive functioning in these patients^{3,4}.

It has recently been suggested that cognitive impairment should be included in the diagnostic criteria of schizophrenia. One of the main arguments in support of this suggestion is that cognitive impairment may help distinguish schizophrenia from bipolar disorder (BD). However, recent evidence shows that cognitive deficits occur in BD and persist beyond euthymia. Further, mood disorders with psychotic features might be expected to manifest greater cognitive impairment, which further complicates the potential to differentiate these disorders⁵.

Several lines of investigations using cross-sectional and longitudinal methods have suggested a relative stability of cognitive functioning^{6,7,8}. Other studies suggested a process of cognitive deterioration mainly within the

first 5-10 years after onset⁹. Previous studies were criticized for insufficient monitoring of confounding variables³, for example, studies on patients treated with typical neuroleptics or other factors that differential effect cognitive performance^{1,10,11}.

Similar cognitive profiles have been reported in patients with BD and schizophrenia but the severity of impairment appears greater in schizophrenia^{12,13,14}. Although such evidence possibly supports the critics of the Kraepelinian dichotomy (who agree that similarities between these two disorders indicate they are on a continuum)¹⁵, the underlying mechanisms responsible for such deficits are not necessarily the same. Comparison of cognition among these patients' groups is problematic. Difference in illness characteristics and current symptoms are not always assessed and may confound neuropsychological test performance^{16,13,14,17}. Also, a major limitation is the different medication regimen. Patients with BD are usually receiving mood

stabilizers e.g. lithium and anticonvulsants, whereas patients with schizophrenia are often on antipsychotic medication. In addition, it is impossible to assess the degree of patients' cognitive impairment if studies fail to include a healthy control group^{18,13,17}.

A comparison of bipolar patients in depressed, manic and mixed states revealed various neuropsychological deficits in all groups as compared with control individuals but no difference between patient groups themselves. It was suggested that similar deficits in patient groups may be a consequence of small sample size¹⁹. Moreover, few studies compared cognitive functions in first episode of various psychoses.

Hypothesis of the study: Cognitive impairment is a consistent feature of schizophrenia and BD even in early stages. Heterogeneity and small sample size limited the results of many studies.

AIM OF THIS STUDY

Was to test cognitive functions in a large number of patients with various types of psychoses, presented during their first episode (to minimize the possible effect of drugs on cognitive functions), and to compare differences in cognitive functions in these disorders.

METHODOLOGY

The study was done in Tanta University Hospitals; these include Neuropsychiatry Department and Tanta University Center for Psychiatry and Neurology. Neuropsychiatry Department has 70 beds for psychiatric inpatients and 3 outpatient clinics which work 6 days/week and serve at least 60 patients per day (1500 per month, 18000 per year). Tanta University Center for Psychiatry and Neurology has 100 psychiatric beds and has 4 outpatient clinics which serve at least 25 psychiatric patients /day. These hospitals serve 4 governorates (Gharbia, Kafr El-sheikh, Menofia and Behira). Participatants were all out patients experiencing their first psychotic episode and received no treatment before or at least in the past 4 weeks.

Although, the term first episode psychosis is used variably to refer to individuals early in the course of a psychotic illness or treatment rather than individuals who are truly in the midst of a first 'episode' of illness, in this study first episode psychosis refers to patients in the midst of a first episode

The study was performed in outpatient clinics during the period from January 2009 till May 2010. Inclusion criteria included patients with age ranged between 18-50 years with DSM IV (20) criteria of schizophrenia,

schizoaffective disorder, BD and depression with psychotic features. Exclusion criteria included patients above 50 years to exclude other factors that may affect cognition, mental retardation, presence of medical or neurological disorders (by routine neurological examinations and laboratory investigations) or presence of drug abuse or dependency.

The study included 254 patients (95 schizophrenics, 21 schizoaffective, 107 bipolar [manic or mixed episode] and 31 psychotic depressions). Forty seven schizophrenia, 42 BD, 7 schizoaffective disorders and 17 psychotic depressions were drug naïve.

Seventy healthy volunteers from patients' relatives matching as regards age and sex were selected to be controls for comparison after explanations of the aim and steps of the study. Patients and controls were submitted to:

- MINI International Neuropsychiatric Interview²¹. This interview was translated and validated into Arabic²¹.

- Cognitive assessment using:

Trail Making Test B²²: a measure of visual conceptual and visual motor tracking skills focusing on divided attention, ability to shift and mental flexibility. Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1 – 25, and the patient should draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A–L); as in Part A, the patient draws lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The patient should be instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. The dependent measure is the total time (in seconds) needed by the patient to connect the "trail". If the patient makes an error, it should be pointed out immediately and the patient is allowed to correct it. Errors affect the patient's score only if the correction of errors is included in the completion time for the task. It is unnecessary to continue the test if the patient has not completed both parts after five minutes have elapsed.

Wisconsin Card Sorting Test (WCST 128)^{23,24}: a measure of prefrontal cortical function (executive functions, abstract conceptual skills, concept formation, cognitive flexibility, working memory). The task requires sorting 128 cards according to predetermined rules. There are three possible ways to sort a card, by color, number and shape of the items on the card. Feedback of accuracy is given after each trial. The criterion for correct categorization changes whenever

10 consecutive cards are sorted correctly. We used preservative errors and number of categories completed as dependent measures.

Benton Visual Retention Test (BVRT)²⁵: The BVRT assesses visual perception, visual memory and visual constructive abilities. Ten images (one showing for example a square and a rectangle of the same size and a smaller circle in the upper right part of the image) are presented to the participant one at a time for 10 seconds. After each image presentations, participants are asked to draw the image from memory. For the evaluation of the drawings, each drawing is rated as correct or incorrect (e.g. with regard to the number of objects, their relative size and alignment) and the number of errors in each incorrect drawings is assessed, whereby the results are supposed not to rely on drawing abilities. As a dependent measure, we used the number of correct drawings and the number of errors made in all incorrect drawings.

Wechsler Adult Intelligence Test (WAIS)²⁶: A comprehensive test of cognitive ability using subscales of general knowledge, similarities, picture completion and block design. I.Q score of the 4 subscales was used.

Each patient needed two sessions for cognitive assessment with no treatment in between these two sessions.

Wisconsin card sorting test was done by the authors, who were trained on the test for more than five years. Other cognitive tests were applied by expert psychologists.

Written consent was taken from all patients and controls after explanation of the all steps and aim of the study.

Statistical analysis: The collected data was organized and statistically analyzed using 15 Minitab software²⁷ statistical computer package. The mean and standard deviation was used for presentations of quantitative data. The difference as regard cognitive functions were

analyzed using multivariate analysis of variance. The student "t" test was used for comparison between two means. Chi square test was used for comparison between studied groups. The 5 % level of significance was adopted for interpretations of tests of significance.

RESULTS

The study included four groups of patients experiencing their first psychotic episode (schizophrenic group with mean age 28.22 ± 8.68 years, schizoaffective group 28.38 ± 8.15 years, bipolar group 28.06 ± 8.05 years and patients with psychotic depression 27.67 ± 8.06 years). All groups were matched regarding age and sex (mean age 28.05 ± 8.17 years, $p > 0.05$) with each other and with control group (table 1).

There were no significant differences among all groups regarding duration of illness (in months) as follows: schizophrenia 10.84 ± 2.63 , schizoaffective 10.57 ± 2.69 , bipolar 10.44 ± 3.44 and depression 9.35 ± 2.98 , or regarding level of education (in years) as follows: schizophrenics 13.92 ± 2.56 , schizoaffective 13.57 ± 2.69 , bipolar patients 13.91 ± 2.57 , psychotic depression 13.67 ± 2.62 and controls 13.90 ± 2.56 (table 1).

Cognitive assessment: Cognitive study of the studied groups (table 2) showed high statistically significant cognitive deterioration in all groups in comparison to control group in all subtests of attention/executive functions (TMT B, WCST preservative errors and WCST categories completed), memory (BVRT number of correct cards and BVRT number of errors) and intelligence (WAIS).

Comparison among schizophrenic, bipolar and depressive groups (table 3) showed no significant difference between schizophrenia and bipolar groups ($p > 0.05$) but both groups showed more cognitive deterioration than patients with depression with psychotic features in all tests except in BVRT (cards completed) where no significant differences were found.

Table (1): Demographic data of patients and controls

Variable		Schizophrenia	Schizoaffective	Bipolar	Depression with psychosis	Controls	
Number		95	21	107	31	70	
Age	Range	18-49	18-48	18-49	18-49	18-49	F=0.03
	Mean±SD	28.22±8.68	28.38±8.15	28.06±8.05	27.67±8.06	28.05±8.17	P=0.998
Sex	Males	60 (63%)	14 (66%)	67 (62%)	20 (64%)	45 (64%)	X ² =0.163
	Females	35 (37%)	7 (34%)	40 (38%)	11 (36%)	25 (36%)	P=0.997
Illness duration from onset	Range	6-15	7-15	5-16	5-14		F= 1.87
	Mean±SD	10.84±2.63	10.57±2.69	10.44±3.44	9.35±2.98		P= 0.136
Smoking	Smoker	63 (66%)	15 (71%)	73 (68%)	22 (71%)	48 (68%)	X ² =0.370
	Non-smoker	32 (34%)	6 (29%)	34 (32%)	9 (29%)	22 (32%)	P=0.985
Years of education	Range	10-18	10-18	10-18	10-18	10-18	F=0.13
	Mean±SD	13.92±2.56	13.57±2.69	13.91±2.57	13.67±2.62	13.90±2.56	P=0.969

Calculated by One Way ANOVA (F) and Chi square test (χ^2)

Table (2): Cognitive functions of studied patients and controls

Test		Schizophrenia	Schizoaffective	Bipolar	Depression with psychosis	Controls	
Number		95	21	107	70	70	
A-Attention-Executive functions							
1- TMT B (total time to complete):	Range	73-120	80-110	72-118	70-105	59-100	F=42.92
	Mean±SD	98.06±10.31	95.43±9.60	96.62±9.73	87.74±9.26	79.79±10.13	P<0.001*
2- WCST (no. of preservative errors):	Range	8-24	10-20	7-24	7-18	4-16	F=48.95
	Mean±SD	15.53±3.32	15.52±2.89	15.43±3.24	12.58±2.63	9.7±2.63	P<0.001*
3-WCST (no. of categories completed):	Range	3-9	3-8	3-9	4-9	5-10	F=33.14
	Mean±SD	5.76±1.27	5.90±1.30	5.79±1.12	6.83±1.24	7.68±1.30	P<0.001*
B- Memory							
1- BVRT (no. of correct cards) :	Range	5-9	5-8	5-8	5-9	5-10	F=10.86
	Mean±SD	6.77±0.98	6.57±0.87	6.71±0.83	7±1.06	7.61±1.19	P<0.001*
2-BVRT (no. of errors):	Range	2-7	3-6	2-7	2-6	1-6	F=17.34
	Mean±SD	4.45±1.05	4.38±0.86	4.40±1.03	3.74±1.09	3.28±1.00	P<0.001*
C- Intelligence							
WAIS:	Range	82-126	83-119	85-124	87-125	89-136	F=11.98
	Mean±SD	103.07±9.19	101.95±10.08	103.14±8.79	108.61±9.28	111.5±10.40	P<0.001*

* Significant Calculated by One way ANOVA

Table (3): Comparison of cognitive functions in patients' groups

Test		Schizophrenia	Bipolar	Depression psychosis	with
Number		95	107	70	
A-Attention-Executive functions:					
1- TMT B (total time to complete):	Range	73-120	72-118	70-105	T1 = 1.02 p= 0.308
	Mean±SD	98.06±10.31	96.62±9.73	87.74±9.26	T2 =5.24 p= 0.000* T3 =4.65 p= 0.000*
2- WCST (no. of preservative errors):	Range	8-24	7-24	7-18	T1 =0.21 p= 0.834
	Mean±SD	15.53±3.32	15.43±3.24	12.58±2.63	T2 = 5.07 P= 0.000* T3 = 5.04 p= 0.000*
3-WCST (no. of categories completed):	Range	3-9	3-9	4-9	T1= 0.15 p= 0.879
	Mean±SD	5.76±1.27	5.79±1.12	6.83±1.24	T2 = 4.14 p= 0.000* T3 = 4.21 p= 0.000*
B- Memory:					
1- BVRT (no. of correct cards)	Range	5-9	5-8	5-9	T1= 0.46 p= 0.646
	Mean±SD	6.77±0.98	6.71±0.83	7±1.06	T2= 1.02 p= 0.311 T3 = 1.35 p= 0.184
2-BVRT (no. of errors):	Range	2-7	2-7	2-6	T1 = 0.35 p= 0.730
	Mean±SD	4.45±1.05	4.40±1.03	3.74±1.09	T2 = 3.17 p= 0.003* T3 = 2.99 p= 0.004*
C- Intelligence:					
1-WAIS	Range	82-126	85-124	87-125	T1= -0.05 p= 0.985
	Mean±SD	103.07±9.19	103.14±8.79	108.61±9.28	T2 = -2.89 p= 0.006* T3 = -2.93 p= 0.005*

Significant T1 = schizophrenic group versus bipolar group, T2 = schizophrenic group versus depressive group, T3= bipolar group versus depressive group. Calculated by Two Sample T-TEST

DISCUSSION

The study showed that cognitive deficits are found in all psychotic disorders in their first episode. The cognitive deficits are the same in both schizophrenia and BD. Against these results a recent study that showed that cognitive deficits are found in all psychotic disorders but are most severe and pervasive in patients with schizophrenia and least pervasive in those with BD or mania and they found deficits in patients with BD or mania were less pervasive but evident in performance scores or verbal memory and fluency tests²⁸.

The cognitive deficits are evident in executive functions, memory and intelligence. Similar neuropsychological deficits have been reported in BD and schizophrenia. Numerous studies have reported deficits in attention, memory and executive functioning^{29,30} that are now thought to be strongly related to clinical outcome, perhaps more than positive and negative symptoms. Other studies suggest that cognitive impairment in first episode psychosis differs from that in chronic schizophrenia only in terms of

degree of severity³¹. In addition, aspects of executive functioning such as sequencing, organization and flexibility were highly impaired in first- episode psychosis compared to controls³².

In this study, the cognitive impairment is much less in psychotic depression than both schizophrenia and BD. Cognitive dysfunction are commonly reported and objectively measured by neuropsychological testing in depression and most of studies indicated that these changes are caused by neuro-anatomical changes in the fronto-subcortical and/or fronto-temporal circuits that suggest a relationship with disease duration besides other factors as age of onset and genetics^{33,34} and this may explain why cognitive dysfunctions are less in early stages of the diseases compared to schizophrenia and mania. Most of the literature before suggests that depressive symptoms and cognition play some role in determining disability at least in older or elderly persons but studies are less in early stages of the disease to detect even subtle impairments in fronto-subcortical functioning in younger or middle aged individuals.

Memory and attention deficits are common in patients with psychotic disorders and could represent the domains of cognition that are most severely disturbed our data clearly demonstrated impairment in these cognitive domains²⁸.

LIMITATIONS OF THIS STUDY

Included the difficulties to control all factors that could affect cognitive function and hence could affect results, e.g., intake of tobacco and caffeine in addition to selection of the control group from relatives of patients who may have some cognitive problems as a trait marker.

CONCLUSION AND CLINICAL IMPLICATIONS

Cognitive disability experienced by psychotic patients in their first episode needs careful assessment as it may persists after treatment of the main psychotic domain and leads to major deterioration. Cognitive dysfunctions are present in all psychotic domains and should not be ignored in BD and depression.

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