

***PSYCHIATRIC MORBIDITY, COGNITIVE
DYSFUNCTION & NEUROLOGICAL SOFT SIGNS
IN BIPOLAR PATIENTS
&
THEIR FIRST DEGREE RELATIVES IN AN
EGYPTIAN SAMPLE***

*Thesis
Submitted for partial fulfillment of M. D.
degree in Psychiatry*

By
Menan Abd-El -Maksoud Rabi e

Under supervision of
Prof. Adel Sadek Amer
Professor of Psychiatry,
Faculty of Medicine,
Ain Shams University.

Dr. Alaa-El -Din M. Soliman
Assistant Professor of Psychiatry,
Faculty of Medicine,
Ain Shams University.

Dr. Hisham Ahmed Ramy
Assistant Professor of Psychiatry,
Faculty of Medicine,
Ain Shams University

*Faculty of Medicine,
Ain Shams University
2005*



" قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العظيم الحكيم "

صدق الله العظيم

سورة البقرة (الآية 32)

To the man who taught me how is it important to love and respect my patients and my colleagues. To the man who used to give us all without taking back.

I wish you were here to watch one of your followers showing a piece of work, which wouldn't exist without your broad minded supervision and endless support.

To my professor, Adel Sadek.

Acknowledgement

First and foremost, I would like to express my eternal gratitude to Prof. Adel Sadek the late Professor of Psychiatry and former chairman of the Institute of Psychiatry Ain Shams University, who gave me the privilege of working under his supervision, for his wisdom, trust, and support in helping me to choose this subject and to work in this interesting domain.

My ultimate thanks go to Ass. Prof. Alaa-El-Din Soliman Assistant Professor of Psychiatry Ain Shams University for his cooperation, assistance and sincere help. His generous contributions and meticulous revisions helped to realize and clarify this study.

My greatest appreciation and profound gratitude go to Ass. Prof. Hisham Ramy Assistant Professor of Psychiatry Ain Shams University for his inspiring guidance, careful advice and endless support. His creative ideas, meticulous revision and most valuable suggestions were a cornerstone without which I could not finish this work.

I ill always be grateful to Prof. Afaf Hamed Professor of Psychiatry and chair of the institute of psychiatry Ain Shams University for her kindness and generosity by allowing me to accomplish this study. Words can never describe my gratitude for her wise guidance, continuous support, valuable advice and enthusiastic encouragement.

I wish to express my deepest gratitude to Prof. Ahamed Saad Professor of Psychiatry Ain Shams University, Dr. Amira Nassib Lecturer of Psychiatry Ain Shams University and Dr. Mona Reda Fellow of the Institute of Psychiatry Ain Shams University and to my eminent professors and colleagues who gave me the opportunity to review what I have written in a comfortable and stimulating environment.

I am also grateful to Dr. Suzan-El-Kholy, Consultant of clinical Psychology, Mrs. Amany Hussein, Mrs. Ensaf Ismail, Mr. Amr Hassanein and Mrs. Hala Talaat for their help and cooperation in completing this study.

Special thanks go to the subjects of the study, the patients, their families and the workers who were the control subjects without whom this study wouldn't be possible.

Last but not least I would like to extend my sincere appreciation to my great parents, my kind brothers and lovely sister, my grateful thanks and my faithful gratitude to my little family Dr. Mohamed Amr, Adham and Seif-El-Din for their support, patience and forbearance throughout this work.

Menan

Contents

	Page
Introduction.....	1
Aim of the Work.....	8
Review of Literature:	
<u>Chapter I: Bipolar Spectrum.....</u>	9
<u>Chapter II: Cognitive Functions.....</u>	23
<u>Chapter III: Cognitive Functions in Bipolar Disorder.....</u>	35
<u>Chapter IV: Neurological Soft Signs with Bipolar Disorder.....</u>	57
Subjects and Methods.....	72
Results.....	94
Discussion.....	147
Recommendations.....	179
Summary	and 181
conclusion.....	
References.....	205
Appendix.....	245
Arabic Summary.....	247

List of Tables

		Page
Table R- 1	: <i>Lifetime prevalence of some DSM-IV-TR mood disorders.</i>	10
Table R- 2	: <i>Clinically accepted adult neuropsychological tests: cortical locations and functions hypothesized.</i>	33
Table R-3	: <i>Methodological problems of studies on cognitive dysfunctions in bipolar illness.</i>	37
Table R-4	: <i>Functional areas frequently reported as abnormal in schizophrenia, and some of the tests that can elicit disturbances in these areas.</i>	57
 Table (1)	 : <i>Demographic characteristics of the subjects:</i>	 96
Table (2)	: <i>Some clinical characteristics of the disorder with the group of patients.</i>	98
Table (3)	: <i>Different treatment modalities used for the patients</i>	99
Table (4)	: <i>Relation of the relatives to patients.</i>	100
Table (5)	: <i>Psychiatric morbidity among 1st degree relatives of bipolar patients.</i>	100
Table (6)	: <i>Prevalence of psychiatric disorders among the 1st degree relatives according to their relation to bipolar patients.</i>	101
Table (7)	: <i>Block design and similarities subtests scores of the patients, healthy relatives and control subjects.</i>	104
Table (8)	: <i>WMS-R scores of patients, healthy relatives and control subjects.</i>	105

Table (9)	: <i>WCST scores of patients, healthy relatives and control subjects.</i>	106
Table (10)	: <i>Block design and Similarities scores of the patients, and the control subjects.</i>	107
Table (11)	: <i>WMS-R scores of patients and control subjects.</i>	107
Table (12)	: <i>WCST scores of patients and control subjects.</i>	108
Table (13)	: <i>Block design and Similarities scores of the healthy relatives, and the control subjects.</i>	108
Table (14)	: <i>WMS-R scores of healthy relatives and control.</i>	109
Table (15)	: <i>WCST scores of healthy relatives and control.</i>	109
Table (16)	: <i>Block design and Similarities scores of the patients and their relatives.</i>	110
Table (17)	: <i>WMS-R scores of the patients and their relatives</i>	110
Table (18)	: <i>WCST scores of the patients and their relatives.</i>	111
Table (19)	: <i>Block design and Similarities scores of the male and the female patients.</i>	112
Table (20)	: <i>WMS-R scores of the male and female patients.</i>	113
Table (21)	: <i>WCST scores of the male and female patients.</i>	113
Table (22)	: <i>Block design and similarities subtests of WAIS in relation to the age of the patients.</i>	114
Table (23)	: <i>WMS-R scores of the patients in relation to their ages.</i>	114
Table (24)	: <i>WCST scores of the patients in relation to their ages.</i>	115
Table (25)	: <i>Block design and similarities subtests of WAIS in relation to the age at onset.</i>	115
Table (26)	: <i>WMS-R scores of the patients in relation to the age at onset of the disorder.</i>	116
Table (27)	: <i>WCST scores of the patients in relation to the age at onset of the disorder.</i>	116
Table (28)	: <i>Block design and similarities subtests of WAIS in relation to the duration of illness.</i>	117

Table (29)	: <i>WMS-R scores of the patients in relation to the duration of illness.</i>	117
Table (30)	: <i>WCST scores of the patients in relation to the duration of illness.</i>	118
Table (31)	: <i>Block design and similarities subtests of WAIS in relation to the number of admissions.</i>	118
Table (32)	: <i>WMS-R scores of the patients in relation to number of admissions.</i>	119
Table (33)	: <i>WCST scores of the patients in relation to the number of admissions.</i>	119
Table (34)	: <i>Block design and similarities subtests of WAIS in relation to the number of manic episodes.</i>	120
Table (35)	: <i>WMS-R scores of the patients in relation to the number of manic episodes.</i>	120
Table (36)	: <i>WCST scores of the patients in relation to the number of manic episodes.</i>	120
Table (37)	: <i>Block design and similarities subtests of WAIS in relation to the number of depressive episodes.</i>	121
Table (38)	: <i>WMS-R scores of the patients in relation to the number of depressive episodes.</i>	121
Table (39)	: <i>WCST scores of the patients in relation to the number of depressive episodes.</i>	122
Table (40)	: <i>Block design and Similarities scores of the male and the female healthy relatives.</i>	123
Table (41)	: <i>WMS-R scores of the male and female healthy relatives.</i>	124
Table (42)	: <i>WCST scores of the male and female healthy relatives.</i>	124
Table (43)	: <i>Block design and similarities subtests of WAIS in relation to the age of the healthy relatives</i>	125
Table (44)	: <i>WMS-R scores of the healthy relatives in relation to their ages.</i>	125
Table (45)	: <i>WCST scores of the healthy relatives in relation to their ages.</i>	126

Table (46)	:	<i>Neurological soft signs in the patients, healthy relatives and control subjects.</i>	134
Table (47)	:	<i>Neurological soft signs in the patients, and the control subjects.</i>	135
Table (48)	:	<i>Neurological soft signs in the healthy relatives and the control subjects.</i>	135
Table (49)	:	<i>Neurological soft signs in the patients, and their 1st degree healthy relatives.</i>	136
Table (50)	:	<i>Prevalence of neurological soft signs in the patients, their 1st degree healthy relatives, and the control subjects.</i>	136
Table (51)	;	<i>Neurological soft signs among male and female patients.</i>	137
Table (52)	;	<i>Neurological soft signs in relation to age of the patients.</i>	137
Table (53)	;	<i>Neurological soft signs in relation to the age at onset of the disorder.</i>	138
Table (54)	;	<i>Neurological soft signs in relation to the duration of illness.</i>	138
Table (55)	;	<i>Neurological soft signs in relation to the number of admissions.</i>	139
Table (56)	;	<i>NSS in relation to the number of manic episodes.</i>	139
Table (57)	;	<i>NSS in relation to the number of depressive episodes.</i>	140
Table (58)	;	<i>NSS among the male and female 1st degree healthy relatives.</i>	141
Table (59)	;	<i>NSS in relation to age of the 1st degree healthy relatives.</i>	142

List of Figures

	Page
<u>Figure 1:</u> Selection of patients.....	73/
<u>Figure 2:</u> Distribution of the subjects of the study: The patients, the relatives and the controls according to gender.....	97
<u>Figure 3:</u> Mean age of patients, relatives and controls.....	97
<u>Figure 4:</u> Psychiatric morbidity among the 1st degree relatives of bipolar patients.....	101
<u>Figure 5:</u> Block Design and Similarities of WAIS among the 3 groups of the study.....	104
<u>Figure 6:</u> WMS-R scores of the patients, healthy relatives and control subjects.....	105

<u>Figure 7:</u>	
WCST scores of patients, healthy relatives and controls.....	107
<u>Figure 8:</u>	
NES scores of patients, healthy relatives and controls.....	136

List of Abbreviations

5-HT	:	<i>Serotonin.</i>
ADHD	:	<i>Attention Deficit Hyperactivity Disorder.</i>
COWA	:	<i>Controlled Oral Word Association Test.</i>
CVLT	:	<i>California Verbal Learning Test- Adult Version.</i>
DM	:	<i>Diabetes Mellitus.</i>
DSM-IV	:	<i>Diagnostic and Statistical Manual of Mental Disorders. 4th edition.</i>
DSM-IV-TR	:	<i>Diagnostic and Statistical Manual of Mental Disorders. 4th edition. Text Revised.</i>
ECA	:	<i>Epidemiological Catchment Area.</i>
ECT	:	<i>Electro-Convulsive Therapy.</i>
EEG	:	<i>Electro-Encephalo-Gram.</i>
Freq	:	<i>Frequency.</i>
GHQ	:	<i>General Health Questionnaire.</i>
HS	:	<i>Highly Significant.</i>
IQ	:	<i>Intelligence Quotient.</i>
MAO	:	<i>Mono Amine Oxidase.</i>
MD	:	<i>Medical Doctorate.</i>
MDD	:	<i>Major Depressive Disorder.</i>
MRI	:	<i>Magnetic Resonance Imaging.</i>
NES	:	<i>Neurological Evaluation Scale.</i>
NS	:	<i>Non Significant.</i>
NSS	:	<i>Neurological Soft Signs</i>
S	:	<i>Significant.</i>
SCID-CV	:	<i>Structured Clinical Interview for DSM-IV Axis-I disorders. clinical Version.</i>
SCID-I/NP	:	<i>Structured Clinical Interview for DSM-IV Axis-I disorders. Research Version. Non patient edition.</i>
SCID-I/P	:	<i>Structured Clinical Interview for DSM-IV Axis-I disorders. Research Version. Patient edition.</i>

<i>SD</i>	<i>:</i>	<i>Standard Deviation.</i>
<i>SDMT</i>	<i>:</i>	<i>Symbol Digit Modalities Test.</i>
<i>SES</i>	<i>:</i>	<i>Socio-Economic Status.</i>
<i>SIG</i>	<i>:</i>	<i>Significance.</i>
<i>Stroop</i>	<i>:</i>	<i>Stroop Color and Word Test</i>
<i>TD</i>	<i>:</i>	<i>Tardive Dyskinesia.</i>
<i>TMT</i>	<i>:</i>	<i>Trail Making Test Battery.</i>
<i>TPM</i>	<i>:</i>	<i>Topiramate.</i>
<i>WAIS-III</i>	<i>:</i>	<i>Wechsler Adult Intelligence Scale. 3rd edition.</i>
<i>WAIS-III-R</i>	<i>:</i>	<i>Wechsler Adult Intelligence Scale. 3^d edition. Revised.</i>
<i>WCST</i>	<i>:</i>	<i>Wisconsin Card Sorting Test.</i>
<i>WMS-III</i>	<i>:</i>	<i>Wechsler Memory Scale. 3^d edition</i>
<i>WMS-III-R</i>	<i>:</i>	<i>Wechsler Memory Scale. 3^d edition. Revised.</i>
<i>WRAT-III</i>	<i>:</i>	<i>Wide Range Achievement Test. 3^d edition.</i>