

Event related potentials in bipolar disorder with co morbid anxiety disorder

Thesis

Submitted in partial fulfillment for master degree in psychiatry
and neurology

By

Noura Samir Karawya

(M.B.B.Ch)

Faculty of medicine- Cairo University

Under supervision of

Prof. Mohamed Yousry Abd El-Mohsin

Professor of psychiatry

Faculty of medicine- Cairo University

Dr. HebaFathy Abdel Reheem

Assistant professor of psychiatry

Faculty of medicine- Cairo University

Dr. ReemAtefEl-Hadidy

Assistant Professor of neurophysiology

Faculty of medicine- Cairo University

Faculty of medicine

Cairo University, 2014

Abstract:

Objective: This study measures the suppression in P50, N100, and P200 waves in auditory evoked potential for bipolar disorder patients with and without comorbid anxiety disorder, and finding a correlation with impulsivity.

Method: 3 groups were compared in the study: 30 bipolar disorder patients, 30 bipolar disorder patients with comorbid anxiety disorder, and 30 healthy subjects as control. Auditory evoked potential was tested using the paired click paradigm; also an impulsivity score was done after full psychiatric examination.

Results: Bipolar disorder patients showed higher suppression in P50, N100, and P200 waves than bipolar disorder patients with comorbid anxiety; which is also higher than controls, and impulsivity scores were higher in bipolar disorder patients with comorbid anxiety.

Conclusion: auditory evoked potential may work as an indicative tool for measuring the severity of bipolar disorder and that anxiety disorders increase impulsivity in bipolar disorder patients.

Key Words

Bipolar disorder, Anxiety disorder comorbidity, Auditory evoked potential, Impulsivity, P50, N100, P200, sensory gating, attention.

Acknowledgment

I have the honor to present this work under the supervision of Prof. **Dr. Mohamed Yousry Abd El Mohsen**, Professor of psychiatry, Cairo University. Without his guidance and his creative thinking I could never carry on doing this work.

I feel very grateful to Prof. **Dr. Heba Fathy**, Assistant professor of psychiatry, Cairo University. Her support, patience and guidance were the corner stone for completion of this work.

I am very proud to have **Dr. Reem El Hadidy**, Assistant professor of neurophysiology, Cairo University, supervising this thesis. Without her supervision and sincere devotion this work couldn't be accomplished.

I am extremely obliged to **Dr. Mohammed Abd El Fatah**, lecturer of psychiatry, Cairo University, for his invaluable help and support.

I am very grateful to **Dr. Shaden Adel**, **Dr. Noha Adel** and **Dr. Ola Osama** for their unlimited support.

I would like to thank my colleagues and residents in Psychiatry department and Neuro-physiology department, Cairo University for their effort to help.

I would also like to thank my patients for their patience and devotion

I am also thankful for **Dr. Magdy Ibrahim Mostafa** for the help he offered in the statistical analysis.

Last but not least, I thank my **parents and family** for their invaluable care and unlimited support.

Table of content:

	Page
Introduction and aim of the work	iiv
Review	
Chapter 1: Bipolar disorder	
• Epidemiology	1
• Affective temperaments and its relation with bipolar disorder	3
• The genetic epidemiology of BPD	5
• Diagnosis	7
• Electro physiological findings of bipolar disorder	9
• Treatment	10
• Prognosis	13
• Staging of bipolar disorder	17
Chapter 2: Comorbidity	
• Introduction	24
• Comorbidity with general medical condition	25
• Comorbidity with substance use/ dependence disorder.	26

• Overlapping Pathophysiology between Bipolar Disorder, Substance Use, and General Medical Conditions	27
• Impulsiveness: A Second Common Personality Vulnerability for Substance Use and Bipolar Disorders	29
• Comorbidity with Eating disorders	31
• Axis II comorbidity	34
• Co-morbidity with Anxiety disorders	37
• History	39
• Impulsivity: in both Anxiety and Bipolar disorder	40
• Neurophysiological functions	42
• Event related potentials for bipolar patients with anxiety disorders	44
• The most common comorbid anxiety disorders.	
1. Post -traumatic stress disorder	44
2. Panic disorder.	46
3. Social anxiety disorder and Obsessive-Compulsive disorder	48
4. Generalized anxiety disorder	49
• Treatment	50
Chapter 3: Auditory evoked potential	53

• Sensory gating	55
• Sensory gating in bipolar disorder	61
• Neurotransmitters	64
• Post traumatic stress disorder	65
• Panic disorder	67
• Effect of medications	68
• Effect of psychosis	69
• Effect of anxiety disorders comorbidity	70
Subjects and methods	71
Results	79
Discussion	105
Conclusion	118
Recommendations	120
Summery	121
References	172
Appendix	176
Arabic summery	

List of tables

Table (1): Comparison of age between different groups.	80
Table (2): Comparison of gender between different groups.	80
Table (3): comparison of educational level in the three groups.	81
Table (4): shows comparison of occupational status between the three groups.	83
Table (5): Comparison of onset of illness between the patients groups.	84
Table (6): Comparison of number of depressive episode between the patients groups.	84
Table (7): Comparison of number of manic episodes between the patients groups.	85
Table (8): showing distribution of current episode among patients groups.	86
Table (9): showing the effect of the current episode.	87

Table (10): showing Distribution of psychotic features among patients groups.	88
Table (11): showing Distribution of patients taking mood stabilizers among patients groups.	89
Table (12): showing Distribution of past history of ECT treatment among patient groups.	90
Table (13): showing hospitalized patients among the patients groups.	91
Table (14): showing family history of psychosis among the patients groups.	92
Table (15): showing family history of mood disorders among the patients groups.	93
Table (16): showing family history of anxiety disorders among the patients groups.	94
Table (17): Showing Clinical type of comorbidity in the BPD with comorbid AD group.	95
Table (18): comparison of Barratt impulsiveness scale in the three groups.	96
Table (19): comparison of P50, N100 and P200 latencies and amplitudes between the three study groups.	97
Table (20): Showing P50, N100, and P200 amplitude ratio between S1 and S2 in the three groups.	100

Table (21): showing P50, N100, and P200 latency difference between S1 and S2 in the three groups.	101
Table (22): showing suppression in P50, N100, and P200.	102
Table (23): showing correlation between impulsivity and suppression	104
Table (24): showing correlation between the presence of psychotic features and suppression.	104
Table (25): showing correlation between the No. of manic episodes and suppression.	105
Table (26): showing correlation between treatment with ECT and suppression.	105
Table (27): showing correlation between family history of psychosis and suppression.	105
Table (28): showing correlation between family history of mood disorders and suppression.	106
Table (29): showing correlation between family history of anxiety disorders and suppression.	106

List of figures

Figure (1): Showing gender distribution among the three study groups.	81
Figure (2): showing educational level differences among the three study groups.	82
Figure (3): showing occupational status differences among the three study groups.	83
Figure (4): showing the current episode in the patients groups.	86
Figure (5): showing the presence of psychotic features in the patients groups.	87
Figure (6): showing distribution of patients taking mood stabilizers among patients groups.	88
Figure (7): showing no. of patients with past history of ECT therapy.	89
Figure (8): showing no. of hospitalized patients among the patients groups	90
Figure (9): showing family history of psychosis among the patients groups	91
Figure (10): showing family history of mood disorders among the patients groups.	92

Figure (11): showing family history of anxiety disorders among the patients groups.	93
Figure (12): Showing Clinical type of comorbidity in the BPD with comorbid AD group.	94
Figure (13): showing mean value of Barratt impulsiveness score between the three groups.	95

Introduction

In a recent large-scale investigation, more than half (51.2%) of patients with bipolar disorder (BD) were identified as having a co-occurring anxiety disorder at some point in their lifetime, while 30.5% were diagnosed as having a current anxiety disorder (*Simon et al., 2004*).

Anxiety disorder co morbidity in BD is associated with a number of negative sequels, including greater bipolar severity, reduced duration of euthymic episodes, elevated substance abuse, greater functional impairment, and an overall diminished quality of life (*Young et al., 1993; Cassano et al., 1999; Simon et al., 2004*).

Measuring event related potentials (ERPs) provides a valuable tool for assessing dynamic brain processes it is noninvasive and allows an exquisite temporal observation of brain signaling and cognition. In addition, the ERP is highly sensitive to sensory, cognitive, and motor aspects of information processing in the brain, and it has been shown to be of great value in studying the genetics psychiatric disorders (*Porjesz et al., 2005*).

The P50 event related potential is associated with preattentive sensory processing, and is presumed to be related to filtering of irrelevant stimuli potentially protecting higher-order functions from being overloaded (*Swann, 2010*).

Impairment in P50 gating was found regardless of treatment with antidepressants or mood stabilizers (*Olinic and Martin, 2005*).

P50, N100 and P200 gating were impaired in subjects with bipolar disorder whether or not there was a history of psychosis, though impairment was greater in subjects with than subjects without such a history (*Olincy and Martin. 2005*).

The paired-click paradigm is used to assess neuronal reactivity to redundant stimuli: a first auditory stimulus (S1) elicits a positive component at the vertex (Cz) peaking between 40 and 80 ms (P50 wave), and is attenuated in response to a second identical auditory stimulus (S2) presented within 500 ms following S1 (*Zouridakis, and Boutros. 1992, Dolu et al., 2001*).

The strength of gating is expressed either as the ratio between the P50 amplitude evoked by S2 divided by the amplitude evoked by S1 or as the absolute difference in amplitude between S1 and S2. A higher ratio and lower difference score are interpreted as weaker gating (*Lijfijt et al., 2009*).

Aim of work

- To study auditory evoked potential (P50, N100 and P200 latencies) in Bipolar disorder patients comparing it to bipolar disorder patients with comorbid anxiety disorder and controls.
- To study the correlation between P50, N100, and P200 latencies and the severity of impulsivity, the current episode, treatment with ECT, No. of manic episodes, the presence of psychotic features and the family history of psychosis, mood disorders and anxiety disorders.
- To study whether the comorbid anxiety disorder increase impulsivity or not in bipolar disorder patients.

Introduction on Bipolar Disorder.

Bipolar disorder (BPD) is a common and serious mental disorder characterized by severe mood symptoms, including episodes of mania or hypomania and depression, occurring with a typically cyclical course (*Kessler et al., 2005*).

Epidemiology:

Bipolar illness contributes to a prevalence of 2.4% of all bipolar spectrum disorders worldwide according to a study based on more than 60 000 subjects in 11 countries (*Merikangas et al., 2011*). Furthermore most recent prospective studies of adolescents estimate bipolar II prevalence rates at 3–4% (*Merikangas and Lamers, 2012*). Males and females are approximately equally at risk, and the mean age of onset is 18 years for bipolar I, and 20 years for bipolar II (*Merikangas et al., 2007*).

Bipolar disorder is still associated with a marked premature mortality, with mortality rate 2–3 times higher compared to the general population (*Muller-Oerlinghausen et al., 2002*). This increased and untimely lethality in bipolar disorder patients is in part due to accidents, medical illness and substance abuse, but the greatest part of excess lethality in bipolar patients results from suicide (*Sher et al., 2006*).

The personal and societal costs of BPD are enormous: even among adequately-treated individuals, relapse is common and the disorder can be profoundly disabling, resulting in serious economic burden (*Kessler et al., 2006*) and a lifetime risk of suicide as high as 20% (*Goldberg and Harrow, 2004*).