



Predictors of metabolic syndrome in first manic episode



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ABSTRACT

Objective: In the present study we aimed to investigate, whether an association between metabolic syndrome (MetS) and clinical features and affective temperaments exists or not in first manic episode of bipolar disorder (BD) and to clarify the prevalence and predictors of MetS.

Method: A total of 150 patients who were received a diagnosis of bipolar disorder type I according to DSM-IV criteria and who were experiencing their first manic episode (FME) were screened consecutively for inclusion. NCEP ATP III formulated an operational definition of MetS based on the presence of three or more of the following characteristics: abdominal obesity (waist circumference), hypertriglyceridemia, low HDL or being on an antilipidemic agent, high blood pressure or being on an antihypertensive agent, and fasting hyperglycemia or being on antiglycemic agent. The patients who had been in remission period for at least 8 weeks were evaluated with SKIP-TURK and TEMPS-A. Remission was defined as YMRS score <5.

Results: 37 (32.5%) patients had a MetS. Previous depressive episode, seasonality, negative family history and childhood trauma are determined as the predictors of MetS. Anxious and irritable temperament scores were higher in MetS (+) patients.

Conclusion: According to our results, links between MetS and BD may also have been predicted by genetic and environmental factors.

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1. Introduction

Bipolar disorder (BD) is known to be associated with premature mortality (Evans et al., 2005). Excess mortality rates due to medical disorders are between 1.5 to 3 times higher in adults with BD compared to general population. There is increasing evidence that indicates an inter-relationship between mood disorders and some physical diseases (Fagiolini and Goracci, 2009). Glucocorticoid/insulin signalling mechanisms and inflammatory effector systems are intersections pointing to pathophysiological relationships between bipolar disorder and general medical conditions that are susceptible to stress as metabolic syndrome (MetS).

MetS is more prevalent in those with bipolar disorder than in the general population (Silarova et al., 2015). A subgroup of patients with bipolar disorder has a higher risk of developing MetS based on their habits, lifestyles, genetic susceptibility, and choices of treatment (Vancampfort et al., 2016). A 35–40% prevalence of MetS has been reported in patients with bipolar disorder, and the MetS includes

obesity, diabetes, hypertension, and dyslipidemia (Vancampfort et al., 2013a, 2013b). Bipolar patients with a MetS have an adverse course and outcome, less favorable response to treatment, a greater risk for suicidality, higher rates of unemployment and thus higher cost. On the other hand, having a medical condition was associated with longer duration of untreated illness and female gender (Maina et al., 2013). In Perugi et al.'s study, length of pharmacological treatment and age at onset of first major episode were associated with the presence of comorbid MetS (Perugi et al., 2015).

Temperament originates in the brain structure, and individual differences are attributable to neural and physiological function differences and it has been suggested that temperament is associated with MetS markers, which may be partly mediated by lifestyle and socioeconomic status (Ravaja and Keltikangas-Järvinen, 1995). There aren't any studies that investigate MetS and their clinical and affective temperamental correlates in the first manic episode. In the present study we aimed to investigate, whether an association between MetS and clinical features and affective temperaments exists or not in first manic episode of BD and to clarify the prevalence and predictors of MetS.

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2. Method

2.1. Sample

A total of 150 patients who were admitted to the Erenköy Mental and Neurological Diseases Training and Research Hospital (Istanbul, Turkey) outpatient clinics or emergency services between 1 April 2011 and 1 April 2014 and received a diagnosis of bipolar disorder type I according to DSM-IV criteria and who were experiencing their first episode were screened consecutively for inclusion. Comorbid axis I disorders were excluded ($n=26$). Additional exclusion criteria were: (i) being outside the 18–45 age range, (ii) alcohol or substance use, and (iii) use of any psychotropic drugs within the last 24 h for current manic episode ($n=10$).

2.2. Assessment tools

Structured Clinical Interview for DSM-Axis I Disorders-SCID-I Turkish version (Özkürkçügil et al., 1999).

Mood Disorders Diagnosis and Following Form (SKIP-TURK) (Özerdem et al., 2004). The SKIP-TURK was used to record age at disorder onset, duration of the disorder, age at treatment initiation, physical and sexual abuse in the history, family history, academic and social functioning, age at menarche, premenstrual syndrome, stressor prior to first episode, the type of first episode, severity of the episode (Global Assessment of Functionality – GAF- score), postpartum onset, seasonality, depression subtype, psychotic episode, suicide, hospitalization, duration of the episode, the number of the episodes, dominant course pattern, acute onset and remission, chronicity and rapid cycling, switch, cigarette smoking, and alcohol and other substance use.

Young Mania Rating Scale (YMRS) (Young et al., 1978). The YMRS was used to measure the severity of manic symptoms before treatment in manic cases and to confirm the state of remission in the recovery episode. We used the Turkish version, developed by Karadağ et al., which provides equivalent reliability to the original version (Karadağ et al., 2001).

Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A). It was developed by Akiskal et al. to evaluate depressive, cyclothymic, hyperthymic, irritable and anxious temperaments (Akiskal et al., 2005). The reliability and validity study for the Turkish form was done by Vahip et al. (2005).

2.3. Procedures

Ethical permission for the study was obtained from the Local Ethical Committee of Erenköy Mental and Neurological Disease Training and Research Hospital (Istanbul, Turkey). The cost for blood level measurements was met by our hospital's Investigation Budget Fund. An informed consent form was signed by a first-degree relative of patients experiencing a manic episode, then confirmed by the patient in remission period. Information for the SKIP-TURK was collected during the remission period with the patient and at least one first-degree relative. When a clear evaluation could not be performed, information about the illness was obtained from other relatives of the patient.

Blood samples necessary for the measurement were drawn from the brachial vein after at least eight hours of fasting within the first 24 h. Use of a benzodiazepine was allowed for reasons of agitation. Simultaneous fasting blood glucose (FBG), C-reactive protein (CRP), uric acid and lipid levels (cholesterol, high and low density lipoprotein and trygliceride) were measured in the biochemistry laboratory of our hospital, using standard enzymatic procedures. Abdominal obesity was evaluated by measure of waist circumference.

The National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP ATP III) formulated an operational definition of MetS based on the presence of three or more of the following characteristics: abdominal obesity (waist circumference), hypertriglyceridemia, low HDL or being on an antilipidemic agent, high blood pressure or being on an antihypertensive agent, and fasting hyperglycemia or being on antiglycemic agent (NCEP, 2001).

The patients who had been in remission period for at least 8 weeks were evaluated with TEMPS-A. Remission for the patients was defined as YMRS score <5 .

2.4. Statistical analysis

The comparison of numerical variables was carried out using *t*-tests, and Pearson's correlation test was used for correlation analysis. The comparison of categorical variables was carried out using chi-square test. Logistic regression was performed for obtain the predictive variables. Two-tailed tests were used on all findings and a *p*-value of <0.05 was considered statistically significant.

Table 1
Comparing MS (+) and (–) patients (* $p < 0.05$ is significant).

	MetS (+) n = 37	MetS (–) n = 77	Analysis p
Age (mean ± SD)	29.1 ± 3.8	28.7 ± 3.6	0.655
Gender (female/male)	20/17	41/36	0.612
Family history (%)	24.3	53.2	0.015
Childhood trauma (%)	56.7	33.8	0.020
Previous depressive episode (%)	94.6	19.5	<0.001
Subtypes of depressive episodes (Melancholic/Atypic)	20/15	9/6	0.483
Seasonality (%)	43.2	5.2	<0.001
Psychotic symptom (%)	29.7	33.7	0.731
Suicide attempt (%)	21.6	13	0.329
Postpartum onset (%)	5.4	2.6	0.478
Premenstrual syndrome (%)	23.5	15.5	0.351
Depressive temperame nt (mean ± SD)	16.1 ± 2.4	16.2 ± 2.3	0.715
Cyclothymic temperament (mean ± SD)	13.7 ± 2.7	12.8 ± 1.6	0.424
Hyperthymic temperament (mean ± SD)	12.5 ± 3.4	14.3 ± 2.3	0.455
Irritable temperament (mean ± SD)	19.3 ± 2.2	16.8 ± 1.9	0.037
Anxious temperament (mean ± SD)	21.1 ± 2.4	17.6 ± 1.6	0.020

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