Acta Neuropsychiatrica

cambridge.org/neu

Occurrence of metabolic syndrome in untreated bipolar disorders: a cross-sectional study

Qianli Liu[1,2,3,4], Lan Wang[1,2,3,4], Fengya Zhen[1,2,3,4] and Cuixia An[1,2,3,4]

[1]Mental Health Center, The First Hospital of Hebei Medical University, Shijiazhuang, China; [2]The Mental Health Institute of Hebei Medical University, Shijiazhuang, China; [3]Hebei Brain Ageing and Cognitive Neuroscience Laboratory, Shijiazhuang, China and [4]Hebei Key Laboratory of Brain Science and Psychiatric-Psychologic Disease, Shijiazhuang, China

Original Article

Cite this article: Liu Q, Wang L, Zhen F, and An C. (2024) Occurrence of metabolic syndrome in untreated bipolar disorders: a cross-sectional study. *Acta Neuropsychiatrica* **36**:357–362.
doi: 10.1017/neu.2023.47

Received: 11 January 2023
Revised: 10 July 2023
Accepted: 16 September 2023
First published online: 16 October 2023

Keywords:
Bipolar disorders; metabolic syndrome; untreated

Corresponding author:
Cuixia An; Email: acxsunny@sina.com

Abstract

Objective: This cross-sectional study aimed to observe the occurrence of metabolic syndrome in untreated individuals with bipolar disorders. *Methods:* A total of 125 untreated individuals with bipolar disorders were collected as the study group, and 201 cases from the health examination centre of our hospital were selected as the control group. The participants enrolled were assessed for general demographic data, case characteristics, and metabolic indexes including body mass index (BMI), blood pressure, triglyceride, high-density lipoprotein-cholesterol, cholesterol, low-density lipoprotein-cholesterol, and fasting plasma glucose. *Results:* The incidence of metabolic syndrome in the bipolar disorders group was higher compared to the control group (9.6% VS. 8.5%). After calibrating sex and age data, a significant difference between the two groups was observed ($P < 0.05$). Diastolic and systolic blood pressure were higher in the bipolar disorders group compared to the control group ($P < 0.01$). Men with bipolar disorders had a higher risk of developing metabolic syndrome than women (14.5% vs. 5.8%). Bipolar disorders, sex, age, and BMI were identified as independent risk factors for metabolic syndrome. No significant difference was found in terms of metabolic index and incidence of metabolic syndrome between individuals with depressive episodes ($n = 37$) and manic episodes ($n = 75$). *Conclusion:* Patients with bipolar disorders were found to have a higher risk of developing metabolic syndrome than healthy individuals. Bipolar disorders, male sex, age, and BMI may contribute to an increased risk of developing metabolic syndrome.

Significant Outcomes

- In the current study, metabolic syndrome and abnormal metabolic indexes in untreated patients with BDs were observed utilising diagnostic criteria specifically designed for the Chinese population.
- Weight management, regular monitoring, and appropriate exercise and dietary interventions were suggested for patients with BDs.
- No significant differences were found in the incidence of metabolic indexes and abnormal metabolic indexes between patients with depressive and manic episodes.

Limitations

- Considering the cross-sectional nature of the current study, the association between seizure frequency, disorder severity, and the incidence of Mets could not be evaluated.
- Lifestyle and dietary factors that may influence the prevalence of metabolic syndrome were not adequately accounted for.
- The study population primarily consisted of individuals experiencing paroxysmal episodes, limiting the generalisability of the findings.

Introduction

Bipolar disorders (BDs) are frequently linked to increased morbidity and mortality rates. A meta-analysis published in JAMA Psychiatry in 2015 showed that the mortality rate of the condition was approximately 2 to 3 times higher than that of individuals without the disorder (Walker *et al.*, 2015). Several other related studies have also indicated that individuals with BDs have a shorter life expectancy of 10 to 11 years compared to the general population (Leboyer *et al.*, 2012). This is mainly attributed to the presence of comorbid metabolic syndrome. Metabolic syndrome (Mets) is a complex metabolic disorder characterised by multiple risk factors such as obesity,

hyperglycaemia, hypertension, and dyslipidaemia. It is considered to be a significant risk factor for diabetes, cardiovascular diseases, and cerebrovascular diseases. The global prevalence of Mets among adults was reported to be around 20 to 25% (Tanner *et al.*, 2012). However, the incidence of Mets was found to be even higher in individuals with BDs. According to a meta-analysis published in World Psychiatry in 2015, the prevalence of Mets in individuals with BDs was 31.7%. After adjusting for age and sex, individuals with BDs were found to have a 1.58-fold increased risk of developing Mets compared to controls (Vancampfort *et al.*, 2015).

Based on several earlier studies conducted both domestically and internationally, the coexistence of metabolic syndrome and bipolar disorders was linked to the use of antipsychotic drugs (Bond *et al.*, 2010; Arango *et al.*, 2014). However, there is limited research available regarding the occurrence of metabolic syndrome, metabolism in various disease states, as well as risk factors among untreated individuals with BDs. Therefore, in this current study, we enrolled untreated individuals with BDs as participants with an attempt to evaluate the occurrence of metabolic syndrome and identify the associated risk factors.

Participants and methods

Participants

The current study included hospitalised patients with BDs at the Department of Psychiatry, the First Hospital of Hebei Medical University, between February 2016 and April 2017. The inclusion criteria were as follows: (1) individuals who met the diagnostic criteria of BDs according to the ICD-10 classification system; (2) aged between 18 and 65 years; (3) no history of using mood stabilisers, antipsychotics, or antidepressants. The exclusion criteria were as follows: (1) patients with metabolic disorders caused by serious somatic diseases such as endocrine diseases (e.g. hyperthyroidism or hypothyroidism), hepatitis, and digestive system diseases and (2) pregnant or lactating individuals.

The control group consisted of healthy individuals who underwent physical examinations at the First Hospital of Hebei Medical University during the same period.

Methods

Study protocol

Demographic data, metabolic data, and case characteristics of patients with BDs were collected.

Metabolic indexes

Body mass index (BMI): calculated as the ratio of weight (in Kilograms) to the square of height (in metres) (kg/m^2) (Wysokiński *et al.*, 2015).

Blood pressure: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after a 5-minute rest.

Blood lipids: triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), total cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-C).

Blood glucose: fasting plasma glucose (FPG).

Diagnostic criteria of metabolic syndrome

The diagnostic criteria of metabolic syndrome in our study were based on the criteria established by the Diabetes Branch of Chinese Medical Association (2007), specifically tailored for the Chinese population. To meet the criteria, individuals should fulfil three or more following parameters: 1) overweight or obese: BMI ≥25 kg/m^2; 2) FPG≥6.1 mmol/L, or 2-hour postprandial blood glucose ≥7.8 mmol/L, or a diagnosis of diabetes receiving treatment; 3) SBP/DBP ≥140/90 mmHg, or a diagnosis of hypertension; 4) TG levels ≥1. 7 mmol/L, or HDL-C: <0.91 mmol/L in males, <1.01mmol/L in females.

Table 1. General demographic and clinical information of two groups

	Control group ($n = 201$)	Study group ($n = 125$)	χ^2/F	P
Age (M ± SD, year)	36.75 ± 10.91	31.66 ± 11.85	1.282	<0.001**
Gender [N(%)]			0.032	0.857
Male	88(43.8)	56(44.8)		
Female	113(56.2)	69(55.2)		
Tobacco use [N(%)]	/	18(14.4)		
Alcohol misuse [N(%)]	/	17(13.6)		
Course of the disease (M[P_{25},P_{75}], month)	/	1(0.33,8)		
Hospital stay (M ± SD, day)	/	26.75 ± 16.43		

Statistical analysis

The present study applied the statistical software SPSS version 25.0 for conducting statistical analyses. The normality of continuous variables was assessed by a P-P diagram. Continuous variables were compared using *t*-test or nonparametric test, while categorical variables were compared using the Pearson chi-square test. A significance level of $P < 0.05$ was considered indicative of a statistically significant difference across the study.

Results

General demographic and clinical characteristics of the two groups

The BDs group consisted of a total of 125 patients, including 69 females (55.2%) and 56 males (44.8%), with an average age of 31.67 ± 11.85 years. Among the enrolled participants, 37 (29.6%) had depression, 75 (60%) were in a manic state, and 13 (10.4%) were in a mixed state. The median duration of the disorder was 1 month, and the average length of hospital stay was 26.75 ± 16.43 days. Notably, the average age of the control group was higher than that of the BDs group (36.75 ± 10.91 vs. 31.66 ± 11.85, $P < 0.01$, Table 1).

Comparison of metabolic parameters between the two groups

The SBP in the BDs group was found to be significantly higher compared to the control group (127.66 ± 16.21 vs. 122.67 ± 16.48, $P < 0.01$). Conversely, the HDL-C (1.13 ± 0.25 vs. 1.23 ± 0.30, $P < 0.01$) and total cholesterol (4.02 ± 0.90 vs. 4.45 ± 0.84, $P < 0.01$) in the BDs group were significantly lower than those in the control group. Nevertheless, no significant differences were observed in BMI, DBP, triglyceride, blood glucose, and LDL-C between the two groups. The incidence of Mets was

https://doi.org/10.1017/neu.2023.47 Published online by Cambridge University Press

Table 2. Comparison of the incidence of metabolic index, metabolic syndrome and abnormal metabolic indexes between the two groups

	Control group	Study group	χ^2 /F	P
BMI (M ± SD, Kg/m^2)	23.34 ± 3.54	22.69 ± 3.06	4.036	0.082
SBP (M ± SD, mmHg)	122.67 ± 16.48	127.66 ± 16.21	0.271	0.008
DBP (M ± SD, mmHg)	76.29 ± 11.36	78.76 ± 10.69	0.167	0.052
TG (M [P_{25}, P_{75}], mmol/L)	0.85(0.50,1.48)	0.89(0.59,1.16)		0.85
HDL-C (M ± SD, mmol/L)	1.23 ± 0.30	1.13 ± 0.25	3.436	0.003
FPG (M [P_{25}, P_{75}], mmol/L)	4.50(4.20,4.80)	4.40(4.02,5.11)		0.379
TC (M ± SD, mmol/L)	4.45 ± 0.84	4.02 ± 0.90	1.108	<0.001
LDL-C (M ± SD, mmol/L)	2.66 ± 0.75	2.61 ± 0.73	0.095	0.552
Abnormal BMI [N(%)]	63(28.5)	30(24)	0.825	<0.001
Abnormal SBP [N(%)]	24(11.9)	26(20.8)	4.659	0.031
Abnormal DBP [N(%)]	22(10.9)	19(15.2)	1.269	0.26
Abnormal TG [N(%)]	35(17.4)	12(10.2)	3.105	0.078
Abnormal HDL-C [N(%)]	34(16.9)	30(25.4)	3.356	0.067
Abnormal FPG [N(%)]	5(2.5)	14(11.6)	11.22	0.001
Abnormal TC [N(%)]	37(15.9)	14(11.6)	1.2	0.273
Abnormal LDL-C [N(%)]	31(15.4)	16(13.2)	0.293	0.588
Mets[N(%)]	17(8.5)	12(9.6)	0.196	0.658

Note: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; HDL-C: high-density lipoprotein-cholesterol; FPG: fasting plasma glucose; TC: total cholesterol; LDL-C: low-density lipoprotein-cholesterol; Mets: metabolic syndrome.

Table 3. Binary analysis of abnormal incidence of metabolic syndrome and metabolic indexes between the two groups by calibration gender and age data

Item	B	Wald	*P* value	*Or* value	95%*CI*
Abnormal BMI	−0.303	1.130	0.288	0.738	0.422–1.292
Abnormal SBP	−1.091	9.792	0.002	0.336	0.169–0.665
Abnormal DBP	−0.608	2.984	0.084	0.545	0.273–1.085
Abnormal TG	0.438	1.362	0.243	1.549	0.743–3.230
Abnormal HDL-C	−0.541	3.454	0.063	0.582	0.329–1.020
Abnormal FPG	−1.9	11.727	0.001	0.150	0.050–0.444
Abnormal TC	0.323	0.839	0.360	1.381	0.692–0.757
Abnormal LDL-C	−0.104	0.002	0.968	0.986	0.504–2.929
Mets	−0.926	4.007	0.045	2.525	1.019–6.253

Note: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; HDL-C: high-density lipoprotein-cholesterol; FPG: fasting plasma glucose; TC: total cholesterol; LDL-C: low-density lipoprotein-cholesterol; Mets: metabolic syndrome.

slightly higher in the BDs group compared to the control group (9.6% vs. 8.5%, $P = 0.658$), but this difference failed to reach significant statistical significance. On the other hand, the incidence of abnormal blood glucose (≥6.1 mmol/L) was associated with higher outcomes in the BDs group compared to the control group (11.6% vs. 2.5%, $P < 0.01$), whereas the incidence of abnormal BMI (BMI ≥25 kg/m^2) showed otherwise in the BDs group when comparing to the control group (24% vs. 28.5%, $P < 0.01$). After adjusting for sex and age, there were significant differences in the incidence of Mets ($P < 0.01$) and abnormal SBP (SBP ≥140 mmHg) between the two groups. However, no significant difference was seen in the incidence of abnormal BMI between the two groups ($P = 0.288$) (Tables 2 and 3).

Risk factors for metabolic syndrome in patients with BDs

The SBP (133.70 ± 13.73 vs. 122.77 ± 16.49, $p < 0.01$) and triglyceride levels (1.04 (0.62) vs. 0.75 (0.53), $P < 0.01$) were higher in males compared to females. Additionally, the level of HDL-C was significantly lower in males than in females. However, no significant differences were seen between males and females in terms of BMI, DBP, blood glucose, total cholesterol, and LDL-C. The incidence of metabolic syndrome was higher in males compared to females (14.5% vs. 5.8%, $P = 0.102$). Males also had a higher incidence of meeting at least two diagnostic criteria for Mets compared to females (33.9% vs. 17.4% $P < 0.05$). Moreover, the incidence of abnormal triglyceride levels (TG≥1.7 mmol/L) was higher in males when compared to females, but there were no

https://doi.org/10.1017/neu.2023.47 Published online by Cambridge University Press

Table 4. Comparison of metabolic indexes and metabolic abnormalities between different genders

	Male ($n = 56$)	Female ($n = 69$)	χ^2/F	P
Age (M ± SD, year)	29.61 ± 11.67	33.32 ± 11.82	0.61	0.082
BMI (M ± SD, Kg/m^2)	22.65 ± 3.25	22.72 ± 2.92	1.22	0.906
SBP(M ± SD, mmHg)	133.70 ± 13.73	122.77 ± 16.49	1.35	<0.001
DBP (M ± SD, mmHg)	79.18 ± 11.06	78.42 ± 10.45	0.03	0.697
TG (M[P_{25}, P_{75}], mmol/L)	1.04(0.62,1.26)	0.75(0.53,0.99)		0.003
HDL-C (M ± SD, mmol/L)	1.05 ± 0.21	1.21 ± 0.26	3.30	0.001
FPG (M[P_{25}, P_{75}], mmol/L)	4.38(4.07,5.14)	4.40(3.99,5.14)		0.961
TC (M ± SD, mmol/L)	3.93 ± 0.90	4.09 ± 0.90	0.10	0.353
LDL-C (M ± SD, mmol/L)	2.60 ± 0.77	2.62 ± 0.70	0.72	0.910
Mets [N(%)]	8(14.5)	4(5.8)	2.68	0.102
≥2 diagnostic criteria [N(%)]	19(33.9)	12(17.4)	4.53	0.033
Abnormal BMI [N(%)]	15(26.3)	13(19.4)	0.84	0.359
Abnormal SBP [N(%)]	16(28.6)	10(14.5)	3.72	0.054
Abnormal DBP [N(%)]	7(12.5)	12(17.4)	0.58	0.449
Abnormal TG [N(%)]	9(16.4)	3(4.8)	4.33	0.038
Abnormal HDL-C [N(%)]	12(21.8)	17(27)	0.42	0.516
Abnormal FPG [N(%)]	5(9.1)	9(13.6)	0.61	0.436
Abnormal TC [N(%)]	4(7.3)	9(13.6)	1.27	0.260
Abnormal LDL [N(%)]	7(12.7)	9(13.6)	0.02	0.883

Note: BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; HDL-C: high-density lipoprotein-cholesterol; FPG: fasting plasma glucose; TC: total cholesterol; LDL-C: low-density lipoprotein-cholesterol; Mets: metabolic syndrome.

significant differences in the incidence of abnormal metabolic indexes between the sexes (Table 4).

Discussion

In recent years, there has been an increasing focus on research related to comorbid mental diseases, particularly metabolic and endocrine disorders, including metabolic syndrome. The natural occurrence or underlying causes of metabolic syndrome are still not fully understood. In the current study, the presence of metabolic syndrome and abnormal metabolic indexes in untreated patients with BDs was examined using diagnostic criteria specifically designed for the Chinese population. The findings revealed a high incidence of metabolic syndrome in untreated patients with BDs compared to controls, which was consistent with the results reported by Anjum et al.(Anjum *et al.*, 2019) and a meta-analysis published in World Psychiatry in 2015 (Vancampfort *et al.*, 2015). However, the incidence of Mets in patients with BDs observed in our study was relatively lower than that reported in other studies, such as the study conducted by Shazia Anjum, which reported a 33.33% occurrence of Mets among BD patients (Kumar *et al.*, 2017). Additionally, a related study conducted in China reported a comorbidity rate of 25.7% for Mets, significantly higher than that in the control group (9.6%)(Xiang *et al.*, 2017). Several reasons may account for these results. First of all, the patients included in this had a relatively short duration of the disorder, with a median of 1 month, and none of them had received any psychiatric drug treatment. Secondly, the diagnostic criteria used in this study differed from those used in other studies, as most studies assess obesity based on waist circumference, whereas our study utilised BMI. Lastly, the average age of the participants in our study was relatively young (31.67 ± 11.85 years). Nevertheless, these factors (i.e. young age and short duration of the disorder) actually highlighted the susceptibility of patients with BDs to comorbid metabolic syndrome. Potential pathophysiological mechanisms contributing to this association may include hyperactivity of the hypothalamus-pituitary-adrenal axis and sympathetic medulla, increased platelet response activity, decreased heart rate variability, vascular inflammation, oxidative stress, and endothelial dysfunction (Goldstein *et al.*, 2015). Based on earlier studies, the dysregulation of cortisol in patients with BDs is crucial for the development of core manifestations of Mets, such as hyperglycaemia, obesity, and dyslipidaemia (Kim *et al.*, 2009).

According to the findings of this study, males exhibited a higher likelihood of developing metabolic syndrome compared to females. Although there was no statistical difference between the two groups, males had higher incidence of meeting at least two diagnostic criteria for metabolic syndrome. They also had higher triglyceride levels and a higher incidence of abnormal triglyceride levels compared to females. Additionally, the level of HDL-C, which plays a role in cholesterol reverse transcription, was lower in males than in females. However, a review by Anusha Baskaran demonstrated that females were more prone to developing abdominal obesity than males and controls(Baskaran *et al.*, 2014). This discrepancy may be attributed to the following factors: 1) The average age of females in this study was relatively young (33.32 ± 11.82 years), and their oestrogen levels were relatively normal, thus minimising the impact on glucose and lipids

https://doi.org/10.1017/neu.2023.47 Published online by Cambridge University Press

metabolism. Conversely, the lack of oestrogen in males may lead to increased lipid levels, inducing insulin resistance and atherosclerosis (Regitz-Zagrosek *et al*., 2007). 2) Males may tend to engage in unhealthy habits such as smoking and alcohol consumption. Moreover, females are more likely to adopt extreme measures, such as controlling their diet and increasing physical activity, in response to weight gain under social stress (Hong *et al*., 2015). Further investigation into the differences between males and females in different age groups can provide valuable insights.

The regression analysis conducted in this study revealed that age and BMI were independent risk factors responsible for Mets, which was consistent with the conclusions reported by Kumar, A. and Reda Roshdy et al.. They found that BDs patients with comorbid metabolic syndrome were older than those without comorbid metabolic syndrome, and the prevalence of Mets increased with age (Perugi *et al*., 2015; Roshdy *et al*., 2017). BMI was identified as an independent risk factor for Mets, consistent with the findings of a study conducted in China. The study reported that individuals with healthy overweight (BMI 25–29.9) and obesity (BMI >30) had a higher risk of cardiovascular disorder and mortality compared to those with abnormal metabolism but normal weight (Fan *et al*., 2013). Therefore, patients with BDs should pay also attention to changes in their weight and engage in regular weight monitoring, exercise, and maintain a balanced diet.

In terms of clinical manifestations, patients with depression are more likely to exhibit sedentary behaviour, while those experiencing manic episodes tend to be more active and energetic, leading to increased energy expenditure. It was observed that patients with depression had a higher likelihood of experiencing metabolic abnormalities compared to those with mania. However, our results did not show significant differences in the incidence of metabolic indexes and abnormal metabolic indexes between patients with depression and those with manic episodes. Hypothesis is that the comorbidity of Mets and BDs may be attributed to long-term intrinsic association between the two conditions, such as genetic associations (Lee *et al*., 2011). Additionally, there may be a subtype of metabolic-affective syndrome (Mansur *et al*., 2015), suggesting that the relationship was not solely based on emotional states. Our results revealed that patients who met more than two diagnostic criteria for metabolic syndrome had a higher proportion of individuals with depression. However, it is important to note that this did not imply that patients with depression were linked to a higher incidence of metabolic syndrome compared to those with manic episodes. It should be taken into consideration that the sample size in our study was small, and the number of patients with manic episodes was significantly higher than that of patients with depression, potentially leading to type II errors. Therefore, further research with larger sample size is needed to confirm these findings.

Conclusion

In summary, individuals with bipolar disorders were found to have a significantly increased risk of developing metabolic syndrome. Factors such as male sex, age, and BMI were identified as potential contributing factors to the development of the metabolic syndrome in these individuals.

Acknowledgements. Not applicable.

Author contribution. Conceptualisation: Qianli Liu and Cuixia An.
Methodology: Qianli Liu, Lan Wang, Fengya Zhen, Cuixia An.
Data collection: Qianli Liu, Lan Wang, Fengya Zhen.
Writing – original draft preparation: Qianli Liu.
Writing – review and editing: Lan Wang, Fengya Zhen, Cuixia An.
Project administration and funding acquisition: Cuixia An.
The author(s) read and approved the final manuscript.

Financial support. This study was funded by National Science Foundation of Hebei Province (No. H2022206544) and Hebei Medical University '14th Five-Year' Clinical Medicine Innovation Research Team Support Program (No.2022LCTD-A1).

Competing interests. The authors declare that they have no competing interests.

Ethics approval and consent to participate. This study was approved by the Ethics Committee of First Hospital of Hebei Medical University. The research had been performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects

Consent for publication. Not applicable.

References

Anjum S, Bathla M and Panchal S (2019) Prevalence and predictors of metabolic syndrome in drug naïve bipolar patients. *Diabetology and Metabolic Syndrome* **13**, 12–17.

Arango C, Gir Ldez M, N-Naranjo Merch, Baeza J, Castro-Fornieles I, Alda J, J. A, Mart Nez-Cantarero C, Moreno C, de Andr S, Cuerda P, de la Serna C, Correll E, C. U, Fraguas D and Parellada M (2014) Second-generation antipsychotic use in children and adolescents: a six-month prospective cohort study in drug-naïve patients. *Journal of the American Academy of Child & Adolescent Psychiatry* **53**, 1179–90,1190.e1-4.

Baskaran A, Cha DS, Powell AM, Jalil D and McIntyre RS (2014) Sex differences in rates of obesity in bipolar disorder: postulated mechanisms. *Bipolar Disorders* **16**(1), 83–92.

Bond DJ, Kauer-Sant'anna M, Lam RW and Yatham LN (2010) Weight gain, obesity, and metabolic indices following a first manic episode: prospective 12-month data from the Systematic Treatment Optimization Program for Early Mania (STOP-EM). *Journal of affective disorders* **124**(1-2), 108–117.

Fan J, Song Y, Chen Y, Hui R and Zhang W (2013) Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. *International Journal of Cardiology* **168**(5), 4761–4768.

Goldstein BI, Carnethon MR, Matthews KA, McIntyre RS, Miller GE, Raghuveer G, Stoney CM, Wasiak H and McCrindle BW (2015) Major depressive disorder and bipolar disorder predispose youth to accelerated atherosclerosis and early cardiovascular disease: a scientific statement from the American Heart Association. *Circulation* **132**(10), 965–986.

Hong CC, Chen CK, Yeh TC, Chu CS and Chen TY (2015) Amisulpride monotherapy may be a choice of maintenance treatment for patients with both bipolar I disorder and metabolic syndrome. *Australian & New Zealand Journal of Psychiatry* **49**(8), 757–758.

Kim B, Kim S, McIntyre RS, Park HJ, Kim SY and Joo YH (2009) Correlates of metabolic abnormalities in bipolar I disorder at initiation of acute phase treatment. *Psychiatry Investigation* **6**(2), 78–84.

Kumar A, Narayanaswamy JC, Venkatasubramanian G, Raguram R, Grover S and Aswath M (2017) Prevalence of metabolic syndrome and its clinical correlates among patients with bipolar disorder. *Asian Journal of Psychiatry* **26**, 109–114.

Leboyer M, Soreca I, Scott J, Frye M, Henry C, Tamouza R and Kupfer DJ (2012) Can bipolar disorder be viewed as a multi-system inflammatory disease? *Journal of Affective Disorders* **141**(1), 1–10.

Lee SH, Wray NR, Goddard ME and Visscher PM (2011) Estimating missing heritability for disease from genome-wide association studies. *American Journal of Human Genetics* **88**(3), 294–305.

https://doi.org/10.1017/neu.2023.47 Published online by Cambridge University Press

Mansur RB, Brietzke E and McIntyre RS (2015) Is there a "metabolic-mood syndrome"? A review of the relationship between obesity and mood disorders. *Neuroscience & Biobehavioral Reviews* **52**, 89–104.

Perugi G, Quaranta G, Belletti S, Casalini F, Mosti N, Toni C and Dell'Osso L (2015) General medical conditions in 347 bipolar disorder patients: clinical correlates of metabolic and autoimmune-allergic diseases. *Journal of Affective Disorders* **170**, 95–103.

Regitz-Zagrosek V, Lehmkuhl E and Mahmoodzadeh S (2007) Gender aspects of the role of the metabolic syndrome as a risk factor for cardiovascular disease. *Gender Medicine* **4**, S162–77.

Roshdy R, Abdelmawella SM and Bayoumy HA (2017) The prevalence of metabolic syndrome in patients with mood disorders. *Middle East Current Psychiatry* **24**, 156–160.

Tanner RM, Brown TM and Muntner P (2012) Epidemiology of obesity, the metabolic syndrome, and chronic kidney disease. *Current Hypertension Reports* **14**(2), 152–159.

Vancampfort D, Stubbs B, Mitchell AJ, de Hert M, Wampers M, Ward PB, Rosenbaum S and Correll CU (2015) Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. *World Psychiatry* **14**(3), 339–347.

Walker ER, McGee RE and Druss BG (2015) Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry* **72**(4), 334–341.

Wysokiński A, Strzelecki D and Kłoszewska I (2015) Levels of triglycerides, cholesterol, LDL, HDL and glucose in patients with schizophrenia, unipolar depression and bipolar disorder. *Diabetology & Metabolic Syndrome* **9**, 168–176.

Xiang H, Mao R and Zhao G (2017) Analysis of risk and risk factors of comorbid metabolic syndrome in patients with bipolar disorder. *Chinese Journal of Psychiatry* **50**, 107–113.

https://doi.org/10.1017/neu.2023.47 Published online by Cambridge University Press