Prevalence and Consequences of Metabolic Syndrome in Bipolar Disorder

January 01, 2007 | Bipolar Disorder [1], Mood Disorders [2], Circadian Rhythm Sleep Disorders [3], Mania [4]
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Patients with bipolar disorder suffer a disproportionate burden of cardiovascular illness compared with others in the general population.\(^1\,^2\) While the pathogenesis of this excess morbidity is undetermined, biologic, behavioral, and sociodemographic factors have been implicated.\(^3\) Bipolar disorder is commonly associated with disrupted circadian rhythms,\(^4\) insomnia,\(^5\) breathing-related sleep disorders,\(^6\) immune function disorders,\(^7\) and hyperactivity of the sympathetic adrenal medullary\(^8\) or hypothalamic-pituitary-adrenal axes.\(^9\) All of these seemingly disparate phenomena are now known to have dire metabolic consequences.\(^3\) For instance, sustained hypercortisolemia is associated with visceral obesity and subsequent insulin resistance.\(^10\) Not surprisingly, several previous studies have established that the prevalence of metabolic disorders is alarmingly high among patients with bipolar disorder (Table 1).\(^11\)-\(^16\) Furthermore, medications that are commonly used in the management of bipolar disorder are now known to contribute to weight gain, dyslipidemia, and diabetes.\(^2\)

We recently conducted a study to examine the prevalence and clinical correlates of metabolic disorders in a cohort of hospitalized patients with bipolar disorder.

Methods
We recruited 41 patients with bipolar disorder, who were consecutively admitted to the psychiatric unit of a general hospital in central Michigan in a manic or mixed state during calendar years 2004 and 2005. All of the patients received the customary physical examination, laboratory tests, and comprehensive psychiatric evaluations. Following informed consent, we retrieved demographic and clinical information. Demographic data included age, sex, and ethnicity. Clinical information included height, weight, body mass index (BMI), blood pressure, fasting plasma glucose levels, and a serum lipid panel. Other clinical information included the psychiatric diagnosis, the list of discharge medications, the age of onset, and duration of psychiatric illness. We used the Young Mania Rating Scale (YMRS) scores, hospital length of stay (LOS), and number of days hospitalized in the preceding 5 years as measures of illness severity.

We used the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria to establish the diagnosis of metabolic syndrome (Table 2).\(^17\) We used a BMI value of 25 or greater as an inclusion criterion rather than the customary waist circumference value of greater than 40 inches in men and greater than 35 inches in women. Patients who met 3 or more of the diagnostic criteria were considered to have metabolic syndrome. The data were entered into a statistical software program (SYSTAT Version 11) for analysis. The mean values for age, BMI, systolic and diastolic blood pressure, high-density lipoprotein cholesterol, serum triglycerides, fasting plasma glucose, LOS, and YMRS scores were computed. The patients were then grouped according to the presence of obesity, hypertension, dyslipidemia, diabetes or prediabetes, or metabolic syndrome. The prevalence of metabolic syndrome was calculated for the entire cohort of patients and in both sex subgroups. Finally, each component of metabolic syndrome was correlated with the severity of illness assessed by the LOS and the admission YMRS score.

Results
There were 41 patients in the study: 17 men and 24 women. The mean age of the sample was 41 (SD = 11) years. The mean LOS was 16 (SD = 10) days. The mean YMRS score was 36 (SD = 9). The mean BMI was 31 (SD = 8).

Fifty-six percent of the sample met modified NCEP-ATP III criteria for metabolic syndrome, 41% were obese, 71% had dyslipidemia, 62% were hypertensive, and 48% were diabetic or prediabetic (Figure 1). The mean LOS and YMRS scores were numerically higher in patients with obesity, dyslipidemia,
diabetes or prediabetes, and metabolic syndrome than in individuals without these metabolic disorders (Figure 2 and Figure 3). However, perhaps because of the small sample size, the differences in values did not achieve statistical significance. At the time of discharge, the patients were typically maintained on combinations of mood stabilizers and antipsychotic medication, but the cross-sectional nature of this study precluded making a valid correlation between psychotropic compounds and metabolic effects.

Discussion
In the present study, the prevalence of metabolic syndrome in patients hospitalized with bipolar disorder (56%) was dramatically higher than the prevalence observed in community samples (25%). The magnitude of comorbid metabolic disorders correlated positively with the severity of the mood disorder. This suggests that patients with more severe mood disorders may be more susceptible to metabolic conditions such as visceral obesity, hypertension, dyslipidemia, and diabetes. Future studies using larger patient populations are needed to confirm this finding.

If metabolic disorders such as obesity, diabetes, dyslipidemia, and hypertension are in fact common complications of mood disorders, as they appear to be, then perhaps early and effective interventions in bipolar disorder may prevent the development of these metabolic consequences. Primary preventive measures such as regular physical exercise and dietary counseling should be routinely incorporated into the long-term treatment plan for patients.

Medications used in the treatment of bipolar disorder are commonly associated with weight gain. Antipsychotic drugs have been implicated in new-onset diabetes and in dyslipidemia. In addition, divalproex sodium is associated with polycystic ovarian syndrome. Current treatment guidelines require that psychiatrists routinely screen for the presence of obesity, dyslipidemia, hypertension, and dysglycemia. Considering the emerging recognition of the true enormity of the metabolic consequences of bipolar disorder, drugs with an advantageous metabolic profile should be considered as first-line therapy in the long-term management of this condition.

Dr D’Mello is associate professor in the department of psychiatry at Michigan State University in East Lansing. He reports that he has received speakers honoraria from Bristol-Myers Squibb, Pfizer, Janssen, and AstraZeneca and served as a consultant for Pfizer.

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