The Metabolic Syndrome: Psychopharmacologists Should Weigh the Evidence for Weighing the Patient

Stephen M. Stahl, M.D., Ph.D.

Issue: *We are in the midst of a North American epidemic of obesity and type 2 diabetes. Since patients with psychiatric disorders who receive psychopharmacologic treatments may be at even greater risk than the general population for weight gain, dyslipidemia, and diabetes and their complications, psychopharmacologists now need standards for how to monitor and manage these risks.*

It is no secret that the population of the United States is getting bigger—and not just more people, but more pounds per person as well. In fact, more than 60%, or about 100 million people, are overweight, and half of these are obese,[1–3] which increases risk for diabetes, cardiovascular disease, and some cancers.[3] Furthermore, it is becoming increasingly clear that psychiatric disorders and their treatments also impact these same health factors. And the news is not good. Diabetes in particular may be even more common in patients with schizophrenia and bipolar disorder than in the general population.[4] Add to that the potential for some psychotropic drugs to increase weight and the incidence of diabetes,[5] and it seems obvious that psychopharmacologists should now be on the lookout for The Metabolic Syndrome (Table 1)[6] in their clinical practices, since they are in a powerful position to recognize and treat this syndrome as well as possibly cause or worsen it.

What is The Metabolic Syndrome and Can Psychotropic Drugs Contribute to It?

The hallmark of The Metabolic Syndrome, or Syndrome X, is the presence of insulin resistance associated with a cluster of metabolic abnormalities independent of whether the individual develops type 2 diabetes or not.[7] It is well known that an individual with a vulnerable genetic makeup and excessive caloric intake, high fat ingestion, and decreased physical activity can become obese and develop insulin resistance. Numerous psychotropic drugs are widely recognized to be factors in weight gain, and, ultimately, obesity.[5,8] What is only now being uncovered by case reports and pharmacoepidemiologic studies is the association of various atypical antipsychotics with hyperglycemia, new onset of type 2 diabetes, and occasionally ketoacidosis due to a mechanism not completely explained by weight gain.[5,8] Whether one drug or another is more likely to cause these adverse effects is greatly debated, and the field eagerly awaits the results of definitive prospective randomized studies of sufficient power to tell us the answer.

Monitoring and Managing the Risks in Psychopharmacology

In the meantime, there should be no debate that well-established risk factors have already been identified[6] (Table 2) and that the time has come for prescribers of a broad range of psychoactive drugs to begin to monitor (Table 3) and manage (Table 4) these risk factors in their practices.

The natural history of type 2 diabetes begins with the development of insulin resistance, with compensatory hyperinsulinemia, which is at first sufficient to overcome the insulin re-

BRAINSTORMS is a monthly section of The Journal of Clinical Psychiatry *aimed at providing updates of novel concepts emerging from the neurosciences that have relevance to the practicing psychiatrist.*

From the Neuroscience Education Institute in Carlsbad, Calif., and the Department of Psychiatry at the University of California San Diego.

Reprint requests to: Stephen M. Stahl, M.D., Ph.D., Editor, BRAINSTORMS, Neuroscience Education Institute, 5857 Owens Street, Ste. 102, Carlsbad, CA 92009.

Table 1. Core Features of The Metabolic Syndrome (also called Insulin Resistance Syndrome or Syndrome X)

Abdominal (central) obesity
Atherogenic dyslipidemia (ie, elevated triglycerides and reduced HDL cholesterol)
Insulin resistance
Hypertension

Table 2. Some Important Risk Factors for Diabetes and Complications

Living in North America in the 21st Century
Having a psychiatric disorder, especially schizophrenia or bipolar disorder
Taking a psychotropic drug, especially an antipsychotic
Being ≥ 45 years of age
Being an African American, Hispanic American, Native American, Asian American, Pacific Islander
Being overweight or obese (BMI ≥ 27)
Having hypertension
Having a family history of diabetes
Having low HDL cholesterol
Having high triglycerides

Abbreviation: BMI = body mass index

Table 3. "No Brainer" Monitoring Tips

Get a scale, weigh patients, and track BMI each visit for everyone
Take a history and record whether known risk factors are present or absent at baseline and monitor at regular intervals thereafter
Get a baseline fasting glucose and lipid profile for psychiatric patients who have a BMI ≥ 27 and who are treated with psychotropic drugs, then track glucose and lipid levels at regular intervals, especially if further weight gain occurs
Monitor glucose levels more frequently, including shortly after beginning a new antipsychotic agent and when treating diabetic patients

Table 4. "No Brainer" Management Tips

Refer patients with abnormal glucose or lipid levels for medical consultation
Do your best to encourage weight loss, since even modest weight loss can have health benefits
Leverage your therapeutic rapport to establish moderate exercise and discourage smoking proactively whenever possible
Be alert to the possibility of diabetic ketoacidosis, especially in diabetic patients newly begun on atypical antipsychotics
Consider discontinuing the antipsychotic, because it may resolve hyperglycemia and diabetes in some cases

sistance and maintain normal glucose tolerance. It then proceeds to a 50% loss of beta cell function, with loss of compensatory hyperinsulinemia, and then postprandial hyperglycemia. Eventually, patients may become sufficiently insulin deficient that they need exogenous insulin. This progressive metabolic disturbance is well known to be associated with increased risk for cardiovascular disease,[6] so identifying at-risk individuals and doing our best to reduce these risk factors while we are prescribing psychotropic drugs is now the state of the art for psychopharmacology practice. The interventionist psychopharmacologist should also treat or refer for treatment patients who have obesity or hyperglycemia, and should know their baseline metabolic status to assess whether adding drugs to treat psychiatric disorders will push the at-risk patient over the edge from normal weight to overweight, from overweight to obesity, or from normoglycemia to hyperglycemia and type 2 diabetes.

At minimum, psychopharmacologists should get a scale and weigh the metabolic evidence for themselves.♦

REFERENCES

1. National Heart, Lung and Blood Institute. The Practical Guide: Identification, Evaluation and Treatment of Overweight and Obesity in Adults. Available at : http://www.nhlbi.nih.gov/guidelines/obesity/practgde.pdf. Accessed August 8, 2001
2. National Heart, Lung and Blood Institute. Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults: The Evidence Report. Available at: http://www.nhlbi.nih.gov/guidelines/obesity/ob_gdlns.pdf. Accessed August 8, 2001
3. National Center for Health Statistics. Prevalence of Overweight and Obesity Among Adults: United States, 1999. Available at: http://www.cdc.gov/nchs/products/pubs/pubd/hestats/obese/obese99.htm. Accessed August 9, 2001
4. Dixon L, Weiden P, Delahanty J, et al. Prevalence and correlates of diabetes in National Schizophrenia Samples. Schizophr Bull 2000; 26:903–912
5. Henderson DC. Atypical antipsychotic-induced diabetes mellitus: how strong is the evidence? CNS Drugs 2002;16:77–89
6. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2000;23:S4–S19
7. Lebovitz HE. Insulin resistance: definition and consequences. Exp Clin Endocrinol Diabetes 2001;109(suppl 2):S135–S148
8. Wirsching DA, Boyd JA, Meng LR, et al. The effects of novel antipsychotics on glucose and lipid levels. J Clin Psychiatry 2002;63:856–865

Take-Home Points

- The weight of evidence indicates that weight gain is associated with various psychopharmacologic treatments.
- The weight of the evidence also indicates that additional risk factors for diabetes and cardiovascular disease are associated with psychiatric disorders and their treatments.
- Monitoring and managing risk factors such as weight gain, body mass index, and fasting glucose and lipids should now be incorporated into best-practice standards for psychopharmacology as they are for internal medicine and primary care.