Finally, we find little basis for the authors, suggestion that the actions of topiramate, a gamma-aminobutyric acidergic (GABAergic) drug, has beneficial effects independent of any possible antimanic effects. The statement that topiramate monotherapy may be similarly efficacious in treating disruptive disorders in children, gambling in adults, binge eating, and borderline personality disorder suggests a mechanism of action for topiramate that is not supported by current research.

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Drs. Barzman and DelBello Reply

TO THE EDITOR: Although the underlying biology of binge eating disorder, borderline personality disorder, pathological gambling, and disruptive behavior disorders remains largely unknown, our clinical observations, along with randomized controlled data, have shown that topiramate is effective for treating these psychiatric disorders, which are phenomenologically linked by impulse dyscontrol (1–4). Furthermore, following our case report (5), there have been two open-label studies confirming our preliminary finding that topiramate is effective for the treatment of disruptive and impulsive behavior in children and adolescents with psychiatric illnesses (6–7). Additionally, in contrast to the statement by Drs. Kruszewski and Klotz, a review of the literature reveals that the aforementioned disorders may be genotypically related. For example, the G allele of the 5H-T2A receptor gene (1438A/G polymorphism) is associated with both binge eating and borderline personality disorder (8). More strikingly, a specific gene, GABRA2, has been associated with conduct disorder and adult alcohol dependence (9). Finally, topiramate is a novel broad-spectrum anticonvulsant that inhibits glutamate activity at a subtype of glutamate receptors and augments the effects of GABA receptor subtypes ($GABA_A$) (10). Therefore, contrary to the assertion by Drs. Kruszewski and Klotz, topiramate may be effective for impulse control disorders through its effect on glutamate as well as other receptors (11).

We agree that it is important to consider both efficacy and tolerability when prescribing any medication. However, topiramate is generally well tolerated in children and adolescents. In fact, data suggest that topiramate may be better tolerated in children and adolescents than in adults (12); for example, only 14% of 56 children and adolescents experienced paresthesia, and 14% experienced somnolence in a recent double-blind placebo controlled trial of topiramate for pediatric mania (13).

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Comments on "A Note on the Partnership Between Psychiatry and Primary Care"

TO THE EDITOR: The editorial by Frank V. deGruy III, M.D., M.S.F.M., on treatment of depression by primary care physicians was eloquent and to the point (1). Most health plans are realizing that the current reimbursement system does not adequately address the most disabling and costly illnesses and that health-plan-level disease management programs that only peripherally involve the practitioner have limited value. They/we haven't figured out how to make the switch, but thanks to voices such as Dr. de Gruy's, I feel that it is heading that way. As we move to a broader acceptance of collaborative care, I feel that we need to raise the level of psychiatrist involvement in managing/monitoring chronic medical illnesses in primary care providers' patient populations.

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Olanzapine-Induced Hyperglycemia in Anorexia Nervosa

TO THE EDITOR: Recent studies on anorexia nervosa have suggested that the atypical antipsychotic agent olanzapine has favorable effects on agitation, repetitive thinking about becoming obese, and subsequent weight gain (1, 2). Although hyperglycemia is a serious adverse effect of olanzapine (3), the incidence varies from less than 1% to 10%, and to the best of our knowledge, there have been no previous reports of this effect in patients with anorexia nervosa. We present a case report of a patient with anorexia nervosa with olanzapine-induced hyperglycemia.

A 27-year-old Japanese woman with a 2-year history of anorexia nervosa (restricting type) and no personal or family history of diabetes mellitus or other metabolic or mental disorders was admitted to our hospital with agitation, general fatigue, and fear of obesity. Laboratory results revealed aspartate aminotransferase of 39 IU/l and alanine aminotransferase of 61 IU/l; results of other laboratory examinations (e.g., antiglutamic acid decarboxylase antibodies) were normal. During the first week of hospitalization (body mass index: 14.1 kg/m^2, mean value of daily energy intake: 1,043 kcal/day), we performed a corrected (1.75g-glucose/kg) oral glucose tolerance test, which showed impaired glucose tolerance (4.3 mmol/l at baseline, peak value of 9.2 mmol/l at 60 minutes, 8.6 mmol/l at 120 minutes) by World Health Organization criteria (4), with delayed insulin secretion (34.6 pmol/l at baseline, peak value of 198 pmol/l at 120 minutes).

Thereafter, we prescribed olanzapine 5 mg/day to reduce agitation and fear of obesity; we also started a multidisciplinary treatment program (4). The patient's agitation improved, and we performed another oral glucose tolerance test during the third week (body mass index: 14.2 kg/m^2, energy intake: 1,157 kcal/day). Results showed diabetes mellitus (4.2 mmol/l at baseline, peak value of 12.2 mmol/l at 120 minutes) with exaggerated insulin secretion (30.8 pmol/L at baseline, peak value of 1,210 pmol/L at 60 minutes). However, symptoms of diabetes (e.g., excessive thirst or urination) were absent. The patient's fear of obesity gradually decreased, and olanzapine therapy at 5 mg/day was carefully continued with monitoring of diabetic symptoms, weekly fasting blood glucose levels, and monthly oral glucose tolerance test examinations (3). The lack of symptoms of diabetes and weekly fasting blood glucose levels (range 4.2 to 4.8 mmol/l) remained stable over 10 weeks. Although the patient showed impaired glucose tolerance during the seventh week (body mass index: 15.2 kg/m^2, energy intake: 1,600 kcal/day), the oral glucose tolerance test results returned to normal at the time of her discharge (body mass index: 18.3 kg/m^2, energy intake: 1,800 kcal/day).

The underlying mechanism of olanzapine-induced hyperglycemia remains unclear (3, 5, 6). Theories regarding this mechanism include the induction of insulin resistance via 5-HT_{1A} antagonism or impaired insulin-signaling cascade, increased food intake via H_1 antagonism, impaired pancreatic beta cell function, induction of glucogenesis via a decrease in glycogen synthase (5), increase in glycogen phosphorylase, and upregulation of cocaine and amphetamine regulated transcripts (6). Exacerbating glucose tolerance with exaggerated insulin secretion was evident on the second oral glucose tolerance test despite no marked differences in fasting plasma glucose levels, body mass index, and energy intake compared with the first oral glucose tolerance test. These findings suggest that glucose intolerance might have been induced by *olanzapine* via insulin resistance (3, 5, 6). Moreover, hyperglycemia improved after weight restoration despite continuous use of olanzapine, which indicates that undernutrition itself might be a risk factor for olanzapine-induced hyperglycemia, particularly in patients with anorexia nervosa. Clinicians treating acute patients with anorexia nervosa should carefully monitor glucose metabolism, especially in patients being treated with olanzapine.

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