Published in final edited form as:

JAMA. 2008 November 12; 300(18): 2115–2116. doi:10.1001/jama.2008.565.

Depressive Symptoms and Diabetes

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To the Editor: In their longitudinal cohort study, Dr Golden and colleagues¹ reported an inverse association between impaired fasting glucose and depressive symptoms; a positive association was identified between treated type 2 diabetes and the development of depressive symptoms. A complementary analysis showed a significantly higher incidence of type 2 diabetes among participants with elevated depressive symptoms. However, the authors did not report whether there was an association between baseline depressive symptoms and the incidence of impaired fasting glucose. This is important because early identification of prediabetes and subsequent intervention with lifestyle modifications or pharmacotherapy (eg, metformin) may reduce the onset of type 2 diabetes.²

In addition, the findings related to impaired fasting glucose must be interpreted in light of it being a component of the metabolic syndrome, a constellation of factors that increase the risk for developing cardiovascular disease and type 2 diabetes. Men and women with metabolic syndrome develop elevated depressive symptoms twice as frequently as those without metabolic syndrome.³ Neurobiological mechanisms that might explain the link between depression and prediabetic states include cytokine-mediated inflammation, allostatic load, insulin-mediated sympathetic stimulation, and activation of the hypothalamic-pituitary-adrenal axis.⁴

Although the authors acknowledge limitations of the self-reported Center for Epidemiologic Studies Depression Scale, an additional shortcoming is the inability of the instrument to distinguish between depression resulting from unipolar major depressive disorder vs bipolar disorder. Approximately one-fifth of unipolar depressed patients in primary care settings show evidence of bipolarity after careful screening.⁵ Given the differences in etiology, pathogenesis, longitudinal course, and treatment response in unipolar and bipolar depression, glucose metabolism may not be similarly affected in these 2 heterogeneous populations. An inadvertent inclusion of patients with bipolar depression could partly account for the unexpected association between impaired fasting glucose and lower risk of depressive symptoms.

Given the complex relationships between mood and metabolic disorders, we believe that studies in this area should discriminate between depressive disorders using structured diagnostic assessments, quantify insulin sensitivity through frequently sampled glucose tolerance tests or glucose clamps, and include clinical trials to test whether interventions targeting aberrant metabolic networks constitute a disease-modifying avenue for treating depressive disorders.

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