Diabetes, Depression Link Remains Muddled

BY JEFF EVANS
Senior Writer

WASHINGTON — Which comes first, diabetes or depression?

The data on this temporal relationship are mixed. Although findings from previous studies suggest that depression precedes diabetes, findings from another investigation, presented at the annual scientific sessions of the American Diabetes Association, propose that there is no time correlation between the two diagnoses.

This chicken-or-egg question is important because depression has a reported prevalence ranging from 11% to 33% in patients with diabetes, which is twice as high as it is in people without diabetes, said Dr. Lawrence S. Phillips, professor of medicine in the division of endocrinology and metabolism at Emory University, Atlanta.

Dr. Phillips and his colleagues conducted a cross-sectional study of 573 people (about half were white and half were African American) who said that they did not have diabetes. Each person received a 75-g oral glucose tolerance test after an 8-hour overnight fast, and screening for depression with a well-validated tool, the Patient Health Questionnaire.

Normal glucose tolerance (NGT) occurred in 65% of the participants, whereas 15% had impaired fasting glucose (IFG), 8% had impaired glucose tolerance (IGT), 8% had both IFG and IGT, and 4% had diabetes. Some participants had received (11%) or were currently receiving (12%) treatment for depression.

The PHQ scores rose in a statistically significant trend from being low among those who never underwent treatment for depression to being higher in people who received depression treatment in the past and highest in individuals who were currently receiving depression treatment.

But there was no relationship between the different categories of glucose tolerance and PHQ score, the prevalence of any depressive syndrome or major depressive disorder, or the severity of depression, Dr. Phillips said. In multivariate analyses, higher body mass index and current receipt of depression treatment significantly increased the risk of having any depressive syndrome, but this risk was not increased within any category of glucose tolerance.

There was no relationship between the different categories of glucose tolerance and PHQ score or the prevalence or severity of depression.

An audience member asked Dr. Phillips how he viewed the results of his study given that a poster presented at last year's ADA meeting found that patients with IGT in the Diabetes Prevention Program had a significantly increased risk for depression, suggesting depression may have preceded IGT. "It's possible that among people who are depressed, there are neuroendocrine changes that lead to diabetes. There's room in human biology for both processes," he said.

But he argued that the situation in which depression precedes the development of diabetes is unlikely given the lack of an association between depression and unrecognized IGT in his study and the fact that patients in the Diabetes Prevention Program were told that they had IGT and were at risk for diabetes, which could possibly have had a negative psychosocial effect.

Firm conclusions favoring either side of the issue, however, may have to wait for research into the dynamics of neurohormonal changes, which are believed to underlie some of the association between depression and the development of diabetes, said Dr. Sherita Hill Golden of the division of endocrinology and metabolism at Johns Hopkins University, Baltimore.

Melancholic depression increases the activation of the hypothalamic pituitary adrenal (HPA) axis, which leads to a simultaneous activation of the sympathetic nervous system, Dr. Golden said. In the tightly regulated feedback loop of the HPA axis, the hypothalamus produces corticotropin-releasing hormone (CRH) that stimulates the pituitary gland to release adrenocorticotropin hormone (ACTH), which stimulates the adrenal gland to release cortisol. Cortisol levels in turn regulate the production and release of CRH.

There is evidence to suggest that subclinical hypercortisolism, defined as having two of three abnormalities in HPA axis function (increased 24-hour urine free cortisol, failure of the dexamethasone suppression test, and decreased levels of ACTH), may contribute to the development of type 2 diabetes, Dr. Golden said.

A study of 12 patients with adrenal incidentalomas and subclinical hypercortisolism found that such patients had a higher prevalence of insulin resistance, impaired glucose tolerance, and type 2 diabetes, as well as greater central adiposity, than did 29 patients with a nonfunctioning adrenal incidentaloma and no subclinical hypercortisolism (J. Clin. Endocrinol. Metab. 2002;87:998-1003).

Dr. Golden's research has centered on determining which measures of neuroendocrine activity provide the most reliable results and on understanding how that activity correlates with metabolic parameters. Preliminary results of an extensive 3-day series of tests in 15 healthy African American women have indicated that static measures of HPA axis activity, such as salivary cortisol sampling, do not correlate well with more dynamic measurements, such as 24-hour urine-free cortisol levels. Other analyses in the patient group suggested CT scan measurements of adrenal gland volume and the results of dexamethasone suppression testing are correlated strongly with body mass index, high-density lipoprotein cholesterol, and systolic blood pressure.

The results of studies measuring the effect of neuroendocrine changes on metabolic parameters are beginning to suggest that "modification of the neurohormonal response may provide a novel approach to the primary prevention of type 2 diabetes," Dr. Golden said, adding that such an approach "would be complementary to our already established measures." ■

Metabolic Syndrome Components Differ Between African American, White Children

BY ROBERT FINN
San Francisco Bureau

ATLANTA — Although there are no formal criteria defining metabolic syndrome in children, African American and white children show important differences in some of the components, Dr. Silva A. Arslanian said at the annual meeting of the International Society on Hypertension in Blacks.

A series of studies by Dr. Arslanian of the University of Pittsburgh and her colleagues have demonstrated that black children have lower insulin sensitivity and higher insulin secretion than do their white peers. Black children are more prone to fat accretion because of lower rates of lipolysis. And they have a limited capacity to increase insulin secretion in response to decreased insulin sensitivity.

Moreover, obese black adolescents are worse off than their white peers with respect to their diabetogenic risk profile, but better off with respect to their atherogenic risk profile.

Dr. Arslanian's research strategy is to recruit black and white children, match them on the basis of various demographic and physiologic factors, and admit them overnight to the children's research center one or more times for measurement of insulin secretion, insulin sensitivity, and other factors.

In one study, she compared 22 black with 22 white 10-year-olds with matching body mass indexes, fat composition, and visceral adipose tissue. Their average BMIs were about 18 kg/m^2, putting them well within the normal range. On their first admission, the researchers used a hyperinsulinemic/euglycemic clamp to assess in vivo insulin sensitivity. Three weeks later, the children were admitted again, this time for an assessment of insulin secretion with a hyperglycemic clamp. Although these children were identical to each other in all important metabolic ways, the white children had significantly higher insulin sensitivity than the black children. One would expect that the black children would compensate for their lower insulin sensitivity by increasing insulin secretion, but that apparently did not happen.

The product of insulin sensitivity multiplied by first-phase insulin is known as the glucose disposition index (GDI), and in most populations the GDI is constant. But the black children had a significantly higher average GDI than the white children, suggesting an inherent hypersecretion of insulin. It is not clear whether this is the result of genetic differences between the populations, environmental differences, or both.

In a more recent study, Dr. Arslanian and colleagues compared adiponectin levels and body composition in 83 African American and 78 white children, aged 8-17 years, with BMIs ranging from 14 to 50 (Diabetes Care 2006;29:51-6). Adiponectin levels were lower in the African American children even after controlling for Tanner stage, sex, abdominal subcutaneous and visceral adipose tissue, and leptin levels. African American children also had lower amounts of visceral fat.

In agreement with previous studies, the African Americans had lower average insulin sensitivity than the whites, but this difference disappeared after the investigators controlled for adiponectin levels. Together these findings suggest that adiponectin level is a strong marker of insulin sensitivity, and that the lower adiponectin level in African American youth may predispose them to a greater risk of insulin resistance despite lower visceral fat. ■

Adiponectin Tied to Women's Longevity

PITTSBURGH — High levels of adiponectin are common in centenarian women and appear to be associated with a favorable metabolic profile, Dr. Agnieszka Baranowska-Bik and colleagues reported in a poster at the International Congress of Neuroendocrinology.

Adiponectin, a peptide produced and secreted in fat cells, has anti-inflammatory and atheroprotective properties. Low plasma levels of adiponectin are associated with atherogenesis, insulin resistance, and obesity.

Dr. Baranowska-Bik and colleagues in the neuroendocrinology department at the Medical Centre of Postgraduate Education in Warsaw evaluated fasting plasma levels of adiponectin, leptin, and insulin in 133 women: 25 were aged 100-102 years, 26 were aged 64-67 years, 45 were aged 20-43 years, and 37 were obese women aged 26-54 years. In the centenarian group, plasma concentrations of adiponectin were significantly higher and leptin and insulin levels were significantly lower, compared with elderly, young, and obese women. Average plasma adiponectin levels were 17 μg/mL in the centenarian group, 10 μg/mL in the elderly, 11 μg/mL in the young, and 8 μg/mL in the obese.

Adiponectin levels correlated positively with HDL levels and inversely with insulin resistance index, total cholesterol, LDL, triglycerides, blood pressure, and body mass index.

—Patrice Wendling