Depressed From Insulin Resistance

People with prediabetes have 2-3 times the rate of developing depression

Can your blood sugar level affect your mood? Many of us have had the experience of being "hangry" and may find that a Snickers Bar (or other sugary treats) temporarily relieves our symptoms. While we can have short-term mood issues like irritability from our blood glucose, can we have long-term effects as well? Can our blood sugar levels predict our risk for depression or anxiety? Are there tests that can help to predict our risk?

This study analyzed data from over 600 participants with an average age of 41 and followed them over 9 years. Before the study, they had never had symptoms or been diagnosed with depression or anxiety. The researchers tracked the participants' blood glucose levels, waist circumference, and the ratio of triglycerides to HDL cholesterol along with regular psychiatric evaluations.

Abstract

- **Objective:** Major depressive disorder is the leading cause of disability worldwide. Yet, there remain significant challenges in predicting new cases of major depression and devising strategies to prevent the disorder. An important first step in this process is identifying risk factors for the incidence of major depression. There is accumulating biological evidence linking insulin resistance, another highly prevalent condition, and depressive disorders. The objectives of this study were to examine whether three surrogate measures of insulin resistance (high triglyceride-HDL [high-density lipoprotein] ratio; prediabetes, as indicated by fasting plasma glucose level; and high central adiposity, as measured by waist circumference) at the time of study enrollment were associated with an increased rate of incident major depressive disorder over a 9-year follow-up period and to assess whether the new onset of these surrogate measures during the first 2 years after study enrollment was predictive of incident major depressive disorder during the subsequent follow-up period.

- **Methods:** The Netherlands Study of Depression and Anxiety (NESDA) is a multisite longitudinal study of the course and consequences of depressive and anxiety disorders in adults. The study population comprised 601 NESDA participants (18–65 years old) without a lifetime history of depression or anxiety disorders. The study's outcome was incident major depressive disorder, defined using DSM-IV criteria. Exposure measures included triglyceride-HDL ratio, fasting plasma glucose level, and waist circumference.

- **Results:** Fourteen percent of the sample developed major depressive disorder during follow-up. Cox proportional hazards models indicated that higher triglyceride-HDL ratio was positively associated with an increased risk for incident major depression (hazard ratio=1.89, 95% CI=1.15, 3.11), as were higher fasting plasma glucose levels (hazard ratio=1.37, 95% CI=1.05, 1.77) and higher waist circumference (hazard ratio=1.11 95% CI=1.01, 1.21). The development of prediabetes in the 2-year period after study enrollment was positively associated with incident major depressive disorder (hazard ratio=2.66, 95% CI=1.13, 6.27). The development of high triglyceride-HDL ratio and high central adiposity (cut-point ≥100 cm) in the same period was not associated with incident major depression.

- **Conclusions:** Three surrogate measures of insulin resistance positively predicted incident major depressive disorder in a 9-year follow-up period among adults with no history of depression or anxiety disorder. In addition, the development of prediabetes between enrollment and the 2-year study visit was positively associated with incident major depressive disorder. These findings may have utility for evaluating the risk for the development of major depression among patients with insulin resistance or metabolic pathology.

More than 88 million people in the United States have prediabetes, a condition where blood sugar levels are higher than normal but not high enough to be classified as type 2 diabetes. This is an indication of insulin resistance and the majority of prediabetics will go on to develop type 2 diabetes without intervention. When your blood sugar levels are chronically high, your cells become less able to use insulin to store the glucose in your blood and use it for energy. This is insulin resistance. As this process continues, we eventually develop elevated blood glucose to a level that a diagnosis of diabetes is made.

As the participants in this study became more insulin resistant, their risk for depression increased as well. Every unit increase in the triglyceride-to-HDL ratio was linked to an 89% increased rate of depression. Triglycerides levels are strongly related to insulin resistance. Every 2-inch increase in belly fat was associated with an 11% higher rate of depression. Every increase of 18 mg/dL in fasting blood sugar levels was linked to a 37% higher rate of depression.

So why does this happen? Insulin resistance causes inflammation, and this inflammation may have effects on brain chemistry. Additionally, insulin resistance may have other effects on the way glucose is taken up in the brain. This is thought to be one mechanism of dementia (type 3 diabetes). Lifestyle commonality may also be a factor as prediabetes and depression share common risk factors of excess weight, lack of exercise, and unhealthy nutritional habits.

The strength of this study is that it was an observational study over time rather than a survey. It raises the possibility that some people may develop depressive symptoms due to their metabolism and people who are prediabetic should be monitored for the development of depressive symptoms. The good thing is that prediabetes can be reversed and by doing this we can hopefully lessen the risk for depression.

Incident Major Depressive Disorder Predicted by Three Measures of Insulin Resistance: A Dutch Cohort Study
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