Body's anticipation of a meal can be a diabetes risk factor

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Alterations in our response to the taste or smell of food may be another culprit responsible for Type 2 diabetes, according to scientists at Duke University Medical Center who have identified the specific mechanism in human specimens and in mice.

When we anticipate or smell a meal, the parasympathetic nervous system triggers salivation and increases insulin production in response to the expectation that glucose will be entering the blood stream.

"We think this parasympathetic response is potentially important in type 2 diabetes," said Vann Bennett, the James B. Duke professor in the departments of cell biology, biochemistry, and neurobiology and Howard Hughes Medical Institute investigator. "Our study showed there is a novel mutation in the gene encoding ankyrin-B, which increases the risk of type 2 diabetes. This happens through an impairment of the insulin secretion that is added by the parasympathetic nervous system."

The study was released online on Tuesday, March 16 in *Science Signaling*.

Bennett was the first scientist to delineate a molecule called ankyrin and for years has been studying its roles in the heart and brain, as well as other organ systems. Bennett and colleagues discovered the importance of ankyrin-B in the insulin response and the source of a mutation that could lead to diabetes.

In earlier experiments, the group found that pancreatic beta cells that are ankyrin-B deficient display impaired insulin secretion in mice. Ankyrin-B-deficient mice had high blood sugar after eating a source of glucose, but not if the glucose bypassed the mouse's mouth. These findings indicated that ankyrin-B deficiency impaired the parasympathetic chain of events that enhance insulin secretion and had a measurable impact on blood sugar levels.

The scientists then asked whether mutations involving ankyrin-B loss of function were associated with diabetes in humans. They used the American Diabetes Association's GENNID genetic specimen collection from families with type 2 diabetes to genotype 524 people with diabetes disorders and 498 non-diabetic controls. They were searching for three ankyrin-B mutations that had previously been shown in heart muscle cells to create severe loss of function.

They found that one of these mutations of ankyrin-B (R1788W) was associated with type 2 diabetes in about 1 percent of Caucasian and Hispanic individuals. "Genomewide studies have failed to identify more than a small fraction of the genetic heritability in diabetes as well as in other complex diseases," Bennett said. "There are estimates that only 6 percent of the heritability of type 2 diabetes has been detected, by multiple genomewide studies."

Bennett said this implies there is a large reservoir of genes yet to be identified, that are risk factors in type 2 diabetes. "We are excited by our findings of a specific mutation with a known mechanism because of the potential for personalized treatment of diabetes," he said. "This particular mutation is likely to play a role in 1 percent of adults with diabetes. We hope our finding will lead to strategies to specifically benefit these individuals."

Provided by Duke University Medical Center