Study provides next clue to preventing dangerous episodes of low blood sugar with diabetes

July 30 2018

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A new LSU Pennington Biomedical Research Center study reveals that a novel biomarker might give us new answers necessary to creating a

diagnostic tool for hypoglycemia-associated autonomic failure, or HAAF. No objective diagnostic tool currently exists for this condition which, if left untreated, can lead to ever-worsening and possibly life-threatening episodes of dangerously low blood sugar.

Low blood sugar, or hypoglycemia, is a major complication of type 1 and type 2 diabetes. People with diabetes can have difficulty self-administering the exact insulin dose at the correct time to keep blood sugar levels in healthy ranges. If a low blood sugar episode occurs, individuals usually begin to feel a range of symptoms such as dizziness, headaches and nausea that trigger them to seek immediate, potentially life-saving, medical care.

But when people with diabetes have too many hypoglycemic episodes, their senses may become blunted. They may stop experiencing the physical symptoms that serve as cues to seek medical attention. They may not even realize they are having one or multiple hypoglycemic episodes until it is too late. This condition is more commonly known as hypoglycemia-associated autonomic failure (HAAF).

"There is currently no objective way for a health care provider to measure whether a patient has experienced repeated episodes of low blood sugar and therefore may be suffering from HAAF," said David McDougal, Ph.D., assistant professor-research and head of Pennington Biomedical's Neurobiology of Metabolic Dysfunction Laboratory. One-third of older adults with diabetes who had experienced a severe low blood sugar episode died within three years of the incident, according to a Johns Hopkins Bloomberg School of Public Health study.

LSU Pennington Biomedical researchers set out to discover ways that biomedical imaging might be able to offer new solutions as to how to measure exposure to glucose level crashes. They decided to focus not on glucose uptake in the brain directly, but on how the brain adapts

following an episode of low glucose levels.

Blood glucose is the brain's essential metabolic fuel. If glucose isn't available because a person has hypoglycemia, the brain can adapt by increasing the rate at which it uses alternative energy sources, such as acetate.

"The results of our study suggest that this adaptation may still be present after exposure to times of low blood sugar and therefore can be used to measure how frequently a person experiences low blood sugar," Dr. McDougal said. "We believe that by measuring how well a person's brain uses acetate, we might one day be able to determine if they are suffering from HAAF or are at increased risk for developing the condition in the near future."

This would allow doctors to provide treatment for reducing this risk by changing the medication the person takes or advising them to use a continuous glucose monitoring device, Dr. McDougal said.

The research significantly advances our understanding of the scope and importance of the relationship between brain metabolism and hypoglycemia, Dr. McDougal said. However, he cautions that "more studies will have to be conducted in order to demonstrate if this biomarker can be of practical clinical use."

Dr. McDougal has filed a provisional patent application for his discovery.

More information: David Harry McDougal et al. Glial acetate metabolism is increased following a 72-h fast in metabolically healthy men and correlates with susceptibility to hypoglycemia, *Acta Diabetologica* (2018). DOI: 10.1007/s00592-018-1180-5

Provided by Louisiana State University