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Study indicates brain plays role in regulating blood sugar in humans

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Researchers at Albert Einstein College of Medicine of Yeshiva University have demonstrated for the first time that the brain is a key player in regulating glucose (sugar) metabolism in humans. The findings, published today in the online edition of the *Journal of Clinical Investigation*, suggest that drugs targeting the brain and central nervous system could be a novel approach to treating diabetes.

"The brain is the body's only organ that needs a constant supply of glucose to survive, so it makes sense that it would have some say over how much glucose is produced," said study leader Meredith Hawkins, M.D., professor of medicine and director of the Global Diabetes Initiative at Einstein. "This role for the brain was demonstrated in earlier Einstein studies in rodents, but there was considerable controversy over whether the results could be applied to humans. We hope this study helps to settle the matter."

In an earlier study in rodents, Einstein researchers showed that activation of potassium channels in the brain's hypothalamus sends signals to the liver that dampen its production of glucose. Those findings, published in Nature in 2005, challenged the conventional thinking that blood sugar production by the liver (the body's glucose factory) is regulated only by the pancreas (which makes insulin to metabolize glucose). But carefully performed studies on dogs, conducted at Vanderbilt University, failed to replicate the results, suggesting the Einstein findings in rodents might not be relevant to higher mammals, including humans.

The current Einstein study, involving people, was aimed at resolving this controversy. Ten nondiabetic subjects were given oral diazoxide, a drug that activates potassium channels in the hypothalamus. (The drug is not used to treat diabetes.) Hormone secretion by the pancreas was controlled to ensure that any change in sugar production would only have occurred through the drug's effect on the brain. After the researchers administered the drug, blood tests revealed that patients' livers were producing significantly less glucose than before.

Dr. Hawkins and her team then repeated this in rats, again giving diazoxide orally, achieving similar results. They confirmed that sufficient amounts of diazoxide crossed the blood-brain barrier to affect potassium channels in the hypothalamus. Additional experiments confirmed that diazoxide was working through the brain. Specifically, the researchers were able to completely block the effects of diazoxide by infusing a specific potassium channel blocker directly into the brain.

"This study confirms that the brain plays a significant role in regulating glucose production by the liver," said lead author Preeti Kishore, M.B.B.S., assistant professor of medicine. "We are now investigating whether this 'brain-to-liver' pathway is impaired in people with diabetes. If so, we may be able to restore normal glucose regulation by targeting potassium channels in the brain."

More information: The paper is titled "Activation of KATP channels suppresses glucose production in humans."

Provided by Albert Einstein College of Medicine