

## **A Pearl of Diabetic Wisdom**

Science has come a long way since an English doctor called Thomas Willis—one of the greatest men of medicine the world has seen—declared in the 17th century that diabetes is caused by melancholy.

Today, we know that one of the major global causes of illness and premature death is caused by high levels in the blood of a sugar called glucose, ordinarily moved from the bloodstream into muscle, fat and liver cells as a source of fuel. Diabetics cannot move this sugar into these cells. Insulin, produced by the pancreas, controls glucose levels. Diabetics produce too little insulin in their pancreas, are resistant to insulin, or both.

We know the effects of this excess glucose, stored primarily in the liver, ravage many parts of the body, leading to, among other things, eye problems, heart attacks, kidney failure and nerve damage.

We know that of more than 280 million people with diabetes worldwide, more than 50 million are Indians. No other country comes close. Doctors will tell you the disease is greater than an epidemic in emerging India. As lifestyles become more sedentary, a genetic predisposition to diabetes among Indians is massively triggered.

We know there is no cure for diabetes, and while exercise and diet help, as do many available treatments, it is always a struggle for diabetics to control sugar levels. In many patients with the most common type of diabetes, type-II, the body's glucose factory, the liver, works on overtime, wildly overproducing glucose.

We have known since the 1950s that the brain has some role to play in glucose levels, but it was not until 2002 when a group of scientists at the Albert Einstein College of Medicine in New York first showed that, in rodents, a key brain area called the hypothalamus—no larger than a pearl—seemed to be a major player regulating the sugar produced by the liver. Conventional wisdom said it was the pancreas that did this job.

Only last week did another group of scientists at the college confirm that drugs targeting the brain and the central nervous system could open a new frontier against diabetes. "This new pathway could form the basis for potential new treatments for the disease," said Preeti Kishore, assistant professor of medicine at Albert Einstein College, alumnus of a medical college in Agra, and lead author of the study published in the online edition of the *Journal of Clinical Investigation*.

Kishore and her colleagues used human subjects to address a troubling question: Might the findings in rodents not be relevant to higher mammals, especially humans? The question was especially relevant because later studies on dogs failed to replicate the results.

“This study’s goal was to resolve the controversy, by providing the first evidence in humans that signals through the brain can control how much glucose is produced by the liver,” said study leader Meredith Hawkins, an Albert Einstein College professor of medicine and director of the institute’s Global Diabetes Initiative.

It makes sense that the brain would have some say in the matter. It is the body’s only organ that needs a constant supply of glucose to survive. Without enough glucose circulating in our brains, we would lose consciousness. “This is what we observe in patients with diabetes who take too much insulin and experience a drop in the blood sugar levels,” said Hawkins.

The Einstein study involved 10 non-diabetic people. They were given oral diazoxide, a drug used to treat high blood pressure. It activated, in the hypothalamus, what are called potassium channels, which play a vital role in allowing cells to talk to each other using electric current. Simultaneously, another medication (somatostatin) given to the patients controlled hormone secretion, so that any change in sugar production would only be through the brain.

Subsequent blood tests revealed that the livers of the human subjects were producing less glucose than before, implying that the brain, specifically the hypothalamus, was a key player in regulating the production and use of glucose by the human body.

Science has suspected a link between diabetes and the hypothalamus. “It’s been known for a long time that brain injuries that involve the hypothalamus can cause weight gain and also can cause diabetes,” said Hawkins. Other research reveals growing links.

In April, for instance, researchers at the Mount Sinai School of Medicine, New York, found that insulin inside the hypothalamus is involved in controlling fat tissue, a key component in energy pathways relevant to type-II diabetes. In October 2010, a team at the Texas Southwestern Medical Centre found that the hypothalamus and special types of cells collaborate to control blood sugar levels—independent of food consumption and body fat, providing clues to female fertility and how type-II diabetes develops without obesity.

The hypothalamus has only just begun to disclose its diabetic secrets.

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