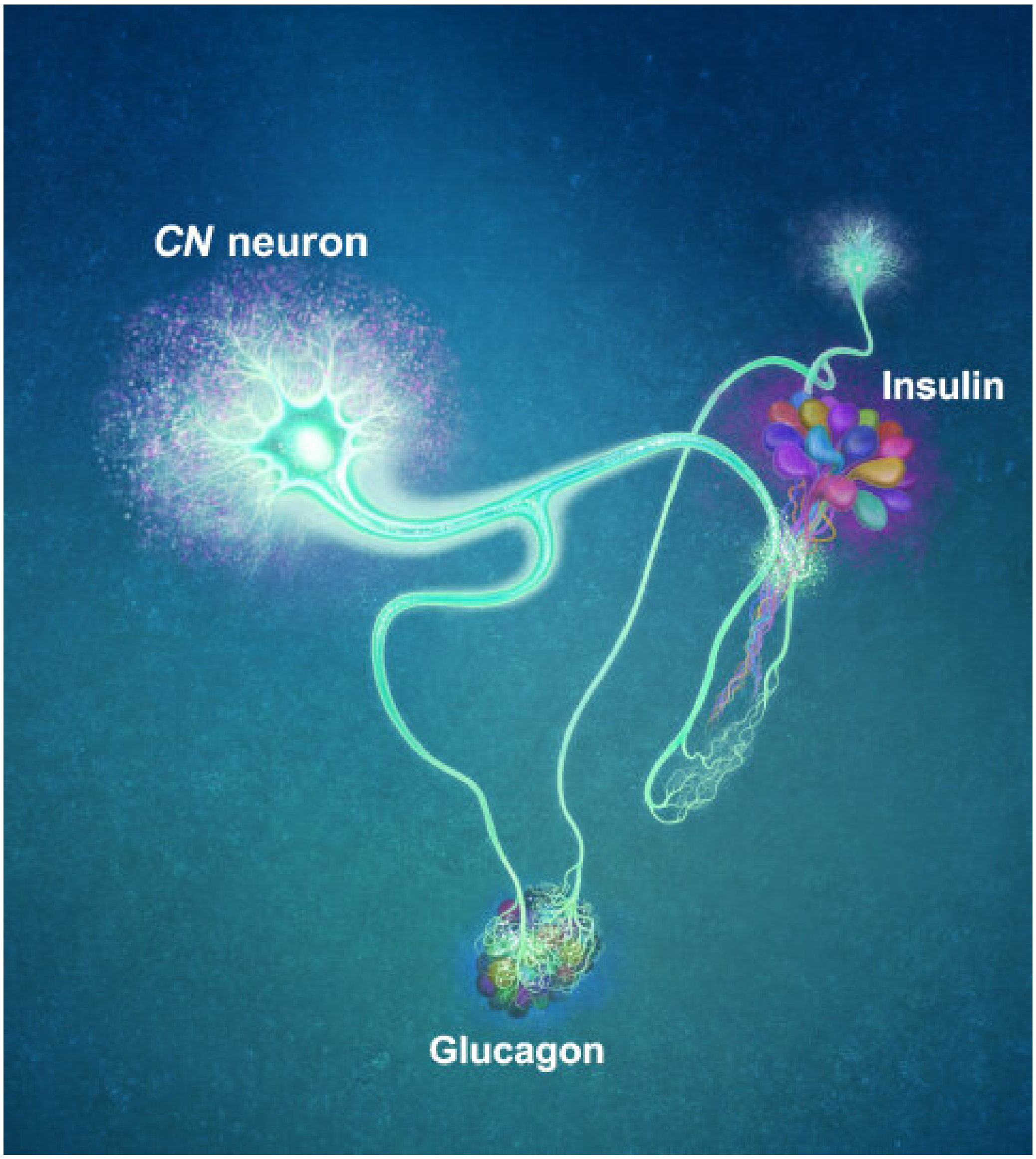
A single, master switch for sugar levels?

October 23 2019



A single glucose-excited CN neuron extends bifurcated axonal branches, one of which innervates insulin producing cells and stimulates their activity and the other axonal branch projects to glucagon producing cells and inhibits their activity. Credit: KAIST

A single neuron appears to monitor and control sugar levels in the fly body, according to research published this week in *Nature*. This new insight into the mechanisms in the fly brain that maintain a balance of two key hormones controlling glucose levels, insulin and glucagon, can provide a framework for understanding diabetes and obesity in humans.

Neurons that sense and respond to glucose were identified more than 50 years ago, but what they do in our body has remained unclear. Researchers at the Korea Advanced Institute of Science and Technology (KAIST) and New York University School of Medicine have now found a single "glucose-sensing neuron" that appears to be the master controller in Drosophila, the vinegar fly, for maintaining an ideal glucose balance, called homeostasis.

Professor Greg Seong-Bae Suh, Dr. Yangkyun Oh and colleagues identified a key neuron that is excited by glucose, which they called CN neuron. This CN neuron has a unique shape—it has an axon (which is used to transmit information to downstream cells) that is bifurcated. One branch projects to insulin-producing cells, and sends a signal triggering the secretion of the insulin equivalent in flies. The other branch projects to glucagon-producing cells and sends a signal inhibiting the secretion of the glucagon equivalent.

When flies consume food, the levels of glucose in their body increase; this excites the CN neuron, which fires the simultaneous signals to stimulate insulin and inhibit glucagon secretion, thereby maintaining the appropriate balance between the hormones and sugar in the blood. The researchers were able to see this happening in the brain in real time by using a combination of cutting-edge fluorescent calcium imaging technologies and measuring hormone and sugar levels, and applying highly sophisticated molecular genetic techniques.

When flies were not fed, however, the researchers observed a reduction in the activity of the CN neuron, a reduction in insulin secretion and an increase in glucagon secretion. These findings indicate that these key hormones are under the direct control of the glucose-sensing neuron. Furthermore, when they silenced the CN neuron—rendering dysfunctional the CN neuron in flies—these animals experienced an imbalance, resulting in hyperglycemia: high levels of sugars in the blood, similar to what is observed in diabetes in humans. This further suggests that the CN neuron is critical to maintaining glucose homeostasis in animals.

While further research is required to investigate this process in humans, Suh notes this is a significant step forward in the fields of both neurobiology and endocrinology.

"This work lays the foundation for translational research to better understand how this delicate regulatory process is affected by diabetes, obesity, excessive nutrition and diets high in sugar," Suh said.

More information: A glucose-sensing neuron pair regulates insulin and glucagon in Drosophila, *Nature* (2019). DOI: 10.1038/s41586-019-1675-4 , nature.com/articles/s41586-019-1675-4

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