

Gangliosides Transmit Satiety Signal

The hypothalamus regulates – alongside other vital functions – food intake and adjusts it to energy needs. In neurons of this brain region, scientists from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now discovered a previously unknown mechanism controlling body weight in mice.

More than half a billion people worldwide have a body mass index over 30 and are considered obese. Obesity is regarded as a considerable risk factor for type 2 diabetes, cardio-vascular diseases and various cancers. The hormone leptin has been known to play an important role in fat balance. Leptin is secreted primarily by adipose tissue cells. By transmitting a satiety signal to neurons in the hypothalamus it regulates food intake. In addition, it causes the body to use up body fat for heat production.

Dr. Viola Nordström and her colleagues from DKFZ have now found so-called gangliosides to be responsible for transmitting the leptin signal in mice. Gangliosides are predominantly found in the cell membranes of neurons. “Mice whose ganglioside production in the hypothalamus had been turned off ate more than normal control animals, accumulated much more adipose tissue and gained substantially more weight,” Viola Nordström explains. “Without gangliosides, their brains could not receive a satiety signal.”

However, after six weeks at the latest, the animals changed their behavior: The ganglioside-deficient mice returned to their normal feeding behavior. Nevertheless, they did not lose weight – on the contrary: “The mice could not use their body fat as an energy source. As a result, their body temperature decreased and they continued to gain weight.”

In another experiment, the researchers proved that the obesity in the experimental mice was definitely caused by the absence of gangliosides and hence of the leptin signal. They injected a virus into ganglioside-deficient mice that had not yet returned to normal feeding behavior. The virus transmitted a gene reactivating ganglioside production. The result: “These mice gained significantly less weight than untreated mice or animals that had received the same virus without the ganglioside gene,” says Viola Nordström.

“The newly discovered mechanism will help us to understand the hypothalamus regulation of body weight,” says Professor Hermann-Josef Gröne, head of DKFZ’s Division of Cellular and Molecular Pathology. “In further experiments we will try to find out whether gangliosides influence food intake, energy use and body weight in humans, too.”

Viola Nordström, Monja Willershäuser, Silke Herzer, Jan Rozman, Oliver von Bohlen und Halbach, Sascha Meldner, Ulrike Rothermel, Sylvia Kaden, Fabian C. Roth, Clemens Waldeck, Norbert Gretz, Martin Hrabě de Angelis, Andreas Draguhn, Martin Klingenspor, Hermann-Josef Gröne, Richard Jennemann: Neuronal Expression of Glucosylceramide Synthase in Central Nervous System Regulates Body Weight and Energy Homeostasis. *PLoS Biol.* 2013. doi:10.1371/journal.pbio.1001506

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 2,500 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg, where promising

approaches from cancer research are translated into the clinic. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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