HEIDELBERG, 18 September 2012 – The **absence** of a **specific type** of **neuron** in the **brain** can **lead** to **obesity** and **diabetes** in mice report researchers in The EMBO Journal. The outcome, however, depends on the type of diet that the animals are fed.

A lack of AgRP-neurons, brain cells known to be involved in the control of food intake, leads to obesity if mice are fed a regular carbohydrate diet. However, animals that are deficient in AgRP-neurons but which are raised on a high-fat diet are leaner and healthier. The differences are due to the influence of the AgRP-neurons on the way other tissues in the body break down and store nutrients. Mice lacking AgRP-neurons adapt poorly to a carbohydrate diet and their metabolism seems better suited for feeding on fat.

“Susceptibility to obesity and other metabolic diseases is mostly thought to be due to complex genetic interactions and the radical environmental changes that have occurred during the last century. However, it is not just a question of what you eat and your genetic makeup but also how the body manages to convert, store and use food nutrients,” commented Serge Luquet, lead author of the study and a researcher at the French Centre National de la Recherche Scientifique (CNRS) Unit of Functional and Adaptive Biology, Université Paris Diderot, Sorbonne Paris Cité.

The scientists wanted to show if a primary setting in the brain might directly affect the relative balance that exists in peripheral tissue between storage, conversion and utilization of carbohydrate and lipids. “The idea that we wanted to test in our experiments was whether the action of a specific type of brain cell known as the AgRP-neuron extended beyond its known influence on food intake. We found a new function for these cells, one that affects the communication with and activities of other tissues in the body including the liver, muscle and the pancreas,” added Luquet.

The researchers showed that mice that lacked AgRP-neurons from birth and which were fed on a regular carbohydrate diet had excessive body fat, increased amounts of the sugar-regulating hormone insulin, and normal levels of glucose in the blood. When the same animals were fed a

high fat diet they showed a reduced gain in body weight and improved glucose clearance in the blood.

“Our work shows that central circuits in the brain that control food intake also control how nutrients are used in peripheral organs of the body,” remarked Luquet. “This further role for AgRP-neurons might represent a core mechanism linking obesity and obesity-related diseases.”

The prevalence of obesity and other metabolic diseases is increasing rapidly and effective and safe treatments are urgently needed. Obesity adversely affects health, decreases life expectancy, and increases the likelihood of other diseases including heart disease and type II diabetes. “Understanding the mechanisms by which the brain controls how nutrients are metabolized and stored in peripheral organs may prove essential to achieving a clinical breakthrough for these debilitating diseases,” added Luquet.

Hypothalamic AgRP-neurons control peripheral substrate utilization and nutrient partitioning

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