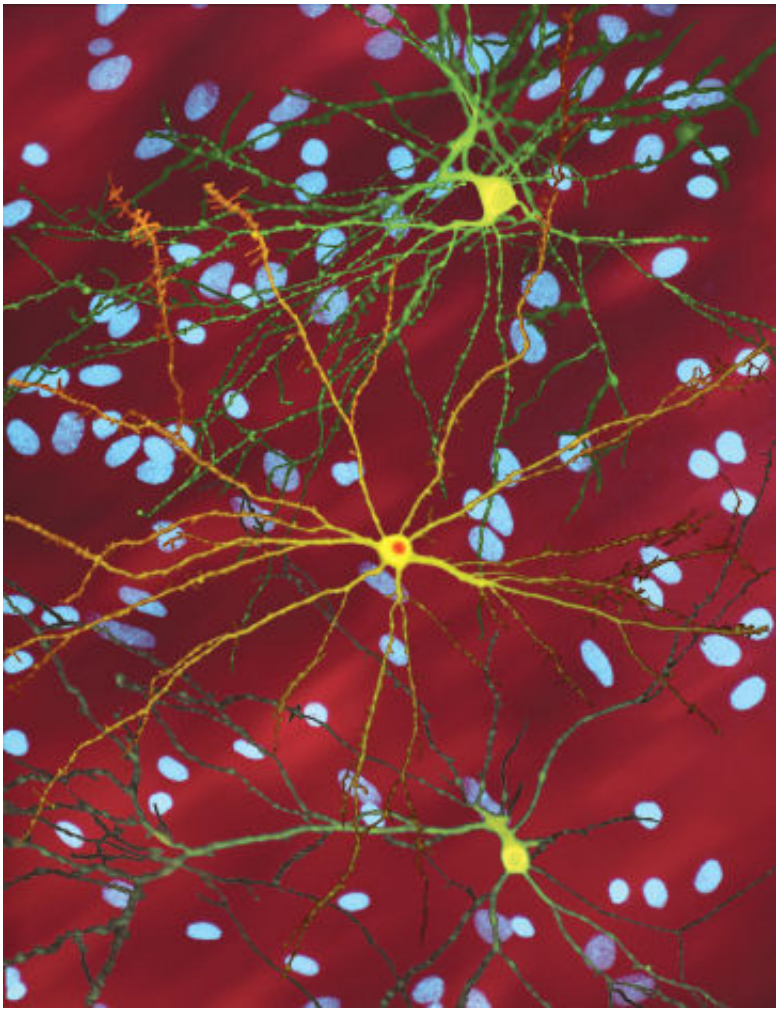
# Strict eating schedule can lower Huntington disease protein in mice

March 6 2018



A montage of three images of single striatal neurons transfected with a disease-associated version of huntingtin, the protein that causes Huntington's disease. Nuclei of untransfected neurons are seen in the background (blue). The neuron in the center (yellow) contains an abnormal intracellular accumulation of huntingtin called an inclusion body (orange). Credit: Wikipedia/ Creative

New research from the University of British Columbia suggests that following a strict eating schedule can help clear away the protein responsible for Huntington disease in mice.

Huntington disease (HD) is an inherited, progressive disorder that causes involuntary movements and psychiatric problems. Symptoms appear in adulthood and worsen over time. Children born to a parent with HD have a one in two chance of inheriting the disease, which is caused by a buildup of mutant huntingtin protein (mHTT).

In research published today, scientists stimulated autophagy—a process in which the cell cleans out debris and recycles cellular material such as proteins—by restricting access to food in mice with HD to a six-hour window each day. This led to significantly lower levels of mHTT in the brain.

"We know that specific aspects of autophagy don't work properly in patients with Huntington disease," said study lead author Dagmar Ehrnhoefer, who conducted the study while she was a researcher with the UBC Centre for Molecular Medicine and Therapeutics. "Our findings suggest that, at least in mice, when you fast, or eat at certain very regulated times without snacking in between meals, your body starts to increase an alternative, still functional, autophagy mechanism, which could help lower levels of the mutant huntingtin protein in the brain."

The researchers also uncovered a clue in the mystery of why mice expressing a modified form of the HD gene show no HD symptoms. The genetic modification prevents the mHTT protein from being cut, or cleaved, at a specific site. These mice had higher rates of autophagy than

mice with regular, cleavable mHTT, indicating that the cleavage site is important for regulating autophagy.

While current therapeutic strategies to lower mHTT are targeted at the Huntington disease gene, this new research suggests that another potential treatment approach is to stimulate autophagy, either through diet or the development of therapies that target the cleavage site.

Dale Martin, study co-author who conducted the research while he was a postdoctoral research fellow with the UBC Centre for Molecular Medicine and Therapeutics, said the findings demonstrate that seemingly small lifestyle changes could have an impact on HD.

"HD is a devastating disease with no cure available at this time," said Martin. "More studies are needed, but perhaps something as simple as a modified dietary schedule could provide some benefit for patients and could be complementary to some treatments currently in clinical trials."

The study was published in the journal *Acta Neuropathologica Communications*.

**More information:** Dagmar E. Ehrnhoefer et al, Preventing mutant huntingtin proteolysis and intermittent fasting promote autophagy in models of Huntington disease, *Acta Neuropathologica Communications* (2018). DOI: 10.1186/s40478-018-0518-0

Provided by University of British Columbia