Study suggests potential therapy for Huntington's disease

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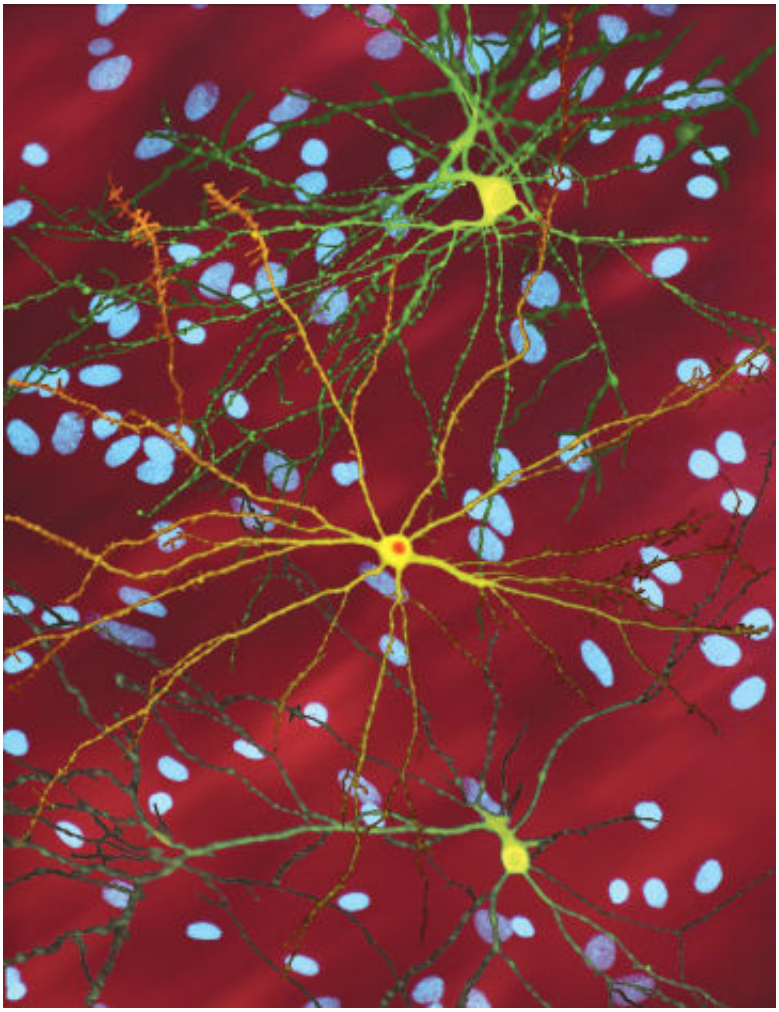

A montage of three images of single striatal neurons transfected with a disease-associated version of huntingtin, the protein that causes Huntington's disease. Nuclei of untransfected neurons are seen in the background (blue). The neuron in the center (yellow) contains an abnormal intracellular accumulation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

A new study published in the *Proceedings of the National Academy of Sciences* (*PNAS*) suggests that Huntington's disease may take effect much earlier in life than was previously believed, and that a new drug may be key in controlling the disease.

"This could be a good start to developing new promising treatments for Huntington's disease, treatments that could be administered even before signs of the illness appear," said Alexander Osmand, researcher in the Department of Biochemistry and Cellular and Molecular Biology at the University of Tennessee, Knoxville, and coauthor of the study.

The disease, which causes the progressive deterioration of both mental and physical abilities, is the result of a genetic mutation of the huntingtin gene. All humans possess this gene, and studies suggest that is necessary to healthy development. Its mutated form, however, causes the rapid decay of specific neurons, eventually resulting in death.

Usually, the effects of Huntington's disease are not apparent until an adult reaches their 30s or 40s. By studying mice, however, researchers have discovered that an array of effects may be seen much earlier.

Although these early symptoms are less clearly defined than the later, more debilitating effects, they could serve as an indicator to health care providers that further screening may be needed.

Researchers subjected several litters of mice carrying the human huntingtin gene to four different dose regiments of Panobinostat, a drug currently used in the treatment of various cancers. Researchers believe that this drug can regulate gene expression, which could be an important

step towards treating those with Huntington's disease.

The researchers also studied the mice's behavior by monitoring their vocalization, startle response, and risk-taking behavior. These behavioral abnormalities showed that symptoms of the disease were present prior to the full mutation commonly associated with Huntington's.

Although treatment with Panobinostat cannot reverse gene mutation completely, clinical trials have shown that it may prevent gene changes associated with the expression of the disease.

Until now doctors have been able to treat only some of the symptoms associated with Huntington's disease, such as depression, mood swings, and involuntary movement. While these treatments may make Huntington's easier to bear, they do nothing to combat the disease itself.

More information: Florian A. Siebzehnrübl et al. Early postnatal behavioral, cellular, and molecular changes in models of Huntington disease are reversible by HDAC inhibition, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1807962115

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