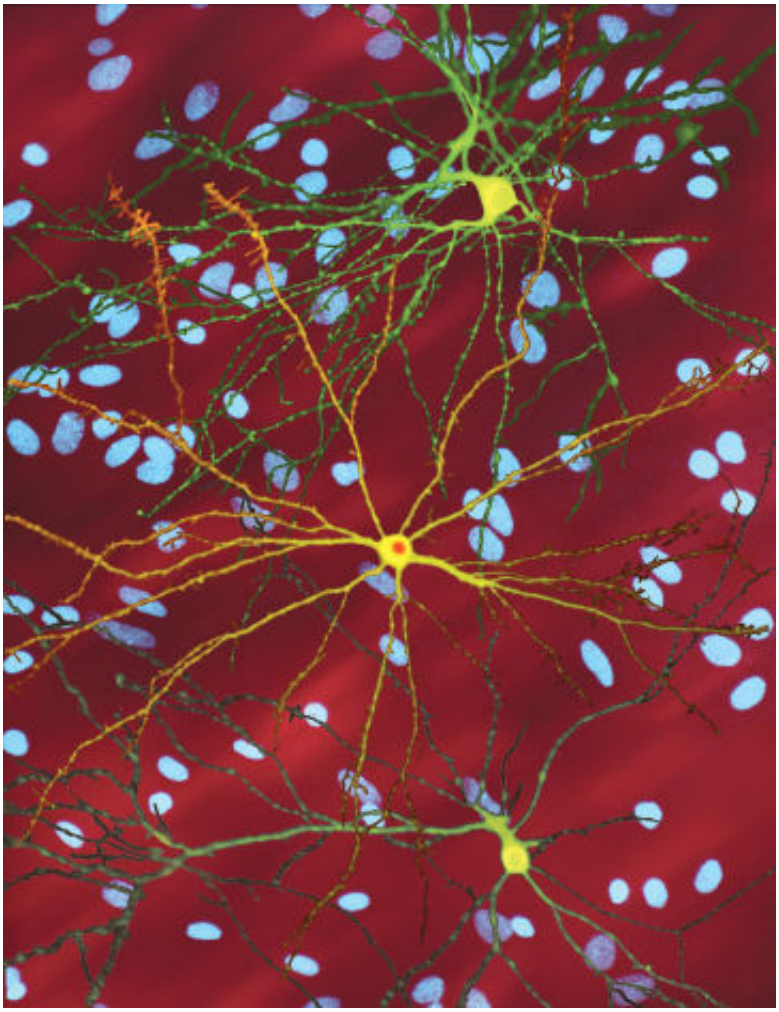
MedicalXpress

Why adults at risk for Huntington's choose not to learn if they inherited deadly gene

May 16 2019



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

As many as 90 percent of individuals who have a parent with Huntington's disease (HD) choose not to take a gene test that reveals if they will also develop the fatal disorder—and a new study details the reasons why.

Understanding the "why" matters as new clinical trials testing therapies for people who haven't yet developed symptoms of Huntington disease requires participants to be tested for the HD gene to be included in the trials.

The study, published today in *Clinical Genetics*, also suggests that individuals who have chosen not to be tested can benefit from supportive counseling, which is not usually offered.

"Health care providers really need to help individuals at risk for Huntington's disease think through their decision whether or not to participate in a clinical trial that requires testing," says the study's lead investigator, Karen E. Anderson, MD, an associate professor of psychiatry & neurology at Georgetown University Medical Center. "For someone who has not wanted genetic testing for many years, we may be leading people to do a test that has not been and still may not be in their personal interest."

She says, "For those who want testing and are ready to cope with the result, either positive or negative, it is our duty to help them get this information so they can make decisions about future care, financial planning and, possibly, study participation. For those who are not ready to be tested, or never want testing, we need also to support their choices," says Anderson, who is also director of Huntington's Disease

Care, Education & Research Center, a joint program of Georgetown University and MedStar Georgetown Hospital.

Huntington's disease is caused by an inherited defect in a single gene. Inheritance is autosomal dominant: only one copy of a mutated HD gene is needed to pass on the disorder, thus the chance of inheritance is 50 percent. (A person inherits two copies of every gene, one from each parent. A parent with a defective gene can pass on either a mutant or healthy HD gene.)

The disease produces progressive degeneration of nerve cells in the brain, which affects the ability to move and think, and often results in depression and other psychiatric disorders due to functional changes in the brain.

To date, there is no cure for the disease and no way to prevent its onset. It is always fatal. People who have the HD genetic mutation expansion will develop HD (unless they die of other causes before it develops). Anderson says there are effective treatments for the symptoms, and a "pipeline" of drugs that may alter the course of the disease are now in clinical testing. Among them are gene silencing techniques that may lower the level of abnormal protein that is produced by the HD gene.

The age at which a person with the HD genetic mutation develops the disorder depends on the number of times a coding mistake in the gene is repeated. Symptoms in adults can begin as early as age 20, or, more likely, in mid-life, (ages 30-50). Onset after age 80 has been reported. Once they begin, symptoms worsen over 10-25 years until death.

The HD gene that causes the disease was isolated in 1993 and a predictive gene test quickly followed. Studies have been conducted on why people choose to take the gene test, but only one large study has been done on why people don't—the subject of the *Clinical Genetics*

publication.

This study included 1001 potential HD mutation carriers who had chosen not to learn their HD status. These individuals agreed to participate in the Prospective Huntington At-Risk Observational Study (PHAROS), carried out between 1999 and 2008. Data from a subset of 733 of these subjects were used in the current report by Anderson and others.

The two primary reasons why participants did not want to know their risk was because they felt no effective cure or treatment exists and their inability to undo the knowledge they learned from the test.

"Our subjects were optimistic that a treatment to improve symptoms or postpone treatment would be developed with the next ten years, but they had less certainty about the prospect of preventing the disease," Anderson says.

"Back in 1993, when the genetic mutation causing HD was discovered, we anticipated that many people at risk would want to be tested, just to deal with the uncertainty, but that is not the case. Only about 10-15 percent of people who know they are at risk for HD have been tested since the test became available, and that percentage really hasn't changed much over time. This study shows there are important, relevant reasons why people don't want to be tested," she says.

As part of the PHAROS study, participants gave permission for gene analysis with the understanding that they would not be told the results.

Helping to understand why people chose not to test makes it easier for physicians and genetic counselors to broach the subject with individuals at risk, especially if they are considering a clinical trial, she says.

"We already know that clinicians have fewer conversations with people

at risk for Huntington's who chose not to test, compared with people who do seek a test, who receive evaluation and supportive counseling prior to testing. Now we know factors people cite for why they don't want to know their status," says Anderson.

"This study shows us that, as new treatments develop that will require genetic testing for clinical trial participation, we should reassess attitudes about how people at risk for disease approach this life-altering choice. It tells us that we should understand, and respect, decisions not to have that testing," she says.

Currently there are about 30,000 Americans who are symptomatic, and more than 200,000 who are at risk of developing the disease, according to the Huntington's Disease Society of America.

More information: Karen E. Anderson et al. The choice not to undergo genetic testing for Huntington disease: Results from the PHAROS study, *Clinical Genetics* (2019). DOI: 10.1111/cge.13529

Provided by Georgetown University Medical Center