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My46 Trait Profile

Huntington Disease

Huntington disease is a genetic brain disorder that affects a person's ability to move, think, and talk. It is caused by mutations in the HTT gene which makes a protein called huntingtin.

Characteristics of Huntington Disease

Huntington disease (HD) is an inherited condition that causes progressive degeneration or decline of specific areas of the brain. This leads to difficulties with coordination and balance, involuntary movements called "chorea", and problems with memory, thinking and judgment. Mood disorders (e.g., personality changes, mood swings, impulsiveness, irritability) and psychiatric problems (e.g., depression) often occur in individuals with HD. The average age of onset of symptoms is around age 40, although onset can occur earlier (i.e., in childhood) or later (i.e., after the age of 65 years). Symptoms typically progress over a period of 15-20 years until a person is no longer able to walk, talk or swallow.

Diagnosis/Testing

Changes or mutations in a gene called HTT cause HD. This gene makes a protein called the huntingtin protein that is thought to play an important role in normal brain development. The HTT gene contains a three-letter code, CAG, that is repeated over and again, and thus it is known as a "CAG repeat." The number of CAG repeats can be different from one person to another. Individuals who do not have HD usually have less than 26 CAG repeats. However, individuals with HD usually have over 40 CAG repeats. This causes the huntingtin protein made by the HTT gene to not function normally. It is not yet known exactly how the changed HTT protein leads to dysfunction of specific areas of the brain.

Management/Surveillance

There is no treatment or cure for HD, however medications can help treat symptoms. Some medications can reduce chorea, and others can treat psychiatric symptoms. Care of the person with HD is supportive and focused on physical safety, obtaining disability benefits, fall prevention, and ensuring dietary intake is sufficient. Physical and occupational therapy can be beneficial for maximizing independence and function at each stage of symptom progression.

Mode of inheritance

HD is inherited in an autosomal dominant pattern. This means that having only one copy of the HTT gene with 40 or more CAG repeats is enough for an individual to develop symptoms of HD. Most individuals with HD have an affected parent.

The number of HTT CAG repeats that an individual has falls into one of four categories (see table below).

Category of HTT CAG repeat size	Number of HTT CAG repeats
Normal	Less than 26
Intermediate	27-35

Reduced penetrance	36-39
Full penetrance	Over 40

Individuals with 27 to 35 CAG repeats (i.e., the intermediate range) are not at risk of HD. However, there is a small chance that number of CAG repeats that are passed on by a parent with CAG repeats in this range may increase in the next generation (e.g., a father with 35 CAG repeats may have a child with over 40 CAG repeats). Individuals with 36 to 39 CAG repeats (i.e., the reduced penetrance range) may or may not develop symptoms during a normal lifespan. Individuals with 40 or more CAG repeats will develop symptoms of HD at some point in his or her lifetime. It is important to know that the repeat size does not provide exact information about the age of symptom onset, or which symptoms a person will manifest.

Risk to family members

Children of a person with HD have a 50% chance of inheriting the condition. The number of CAG repeats can change in size when passed from parent to child. Usually it stays about the same size, but it can increase or decrease. If the size increases when passed on, this can lead to earlier onset of symptoms in a child, a phenomenon called anticipation. Rarely, symptoms occur before the age of 21; this is called juvenile HD.

Special considerations

The decision to have predictive genetic testing (i.e., genetic testing for the condition before onset of symptoms) for HD requires careful thought and consideration. It is recommended that individuals considering such testing have genetic counseling prior to undergoing testing.

Resources

Huntington Disease Society of America
http://www.hdsa.org/
Genetics Home Reference: Huntington disease
http://ghr.nlm.nih.gov/condition/huntington-disease
Testing for Huntington Disease: Making an Informed Choice
http://depts.washington.edu/neurogen/downloads/hungtinton.pdf
Predictive Testing for Huntington Disease
http://predictivetestingforhd.com

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