

Dentatorubral-pallidoluysian Atrophy

Subjects: Genetics & Heredity

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Dentatorubral-pallidoluysian atrophy, commonly known as DRPLA, is a progressive brain disorder that causes involuntary movements, mental and emotional problems, and a decline in thinking ability. The average age of onset of DRPLA is 30 years, but this condition can appear anytime from infancy to mid-adulthood.

Keywords: genetic conditions

1. Introduction

The signs and symptoms of DRPLA differ somewhat between affected children and adults. When DRPLA appears before age 20, it most often involves episodes of involuntary muscle jerking or twitching (myoclonus), seizures, behavioral changes, intellectual disability, and problems with balance and coordination (ataxia). When DRPLA begins after age 20, the most frequent signs and symptoms are ataxia, uncontrollable movements of the limbs (choreoathetosis), psychiatric symptoms such as delusions, and deterioration of intellectual function (dementia).

2. Frequency

DRPLA is most common in the Japanese population, where it has an estimated incidence of 2 to 7 per million people. This condition has also been seen in families from North America and Europe.

Although DRPLA is rare in the United States, it has been studied in a large African American family from the Haw River area of North Carolina. When the family was first identified, researchers named the disorder Haw River syndrome. Later, researchers determined that Haw River syndrome and DRPLA are the same condition.

3. Causes

DRPLA is caused by a mutation in the *ATN1* gene. This gene provides instructions for making a protein called atrophin 1. Although the function of atrophin 1 is unclear, it likely plays an important role in nerve cells (neurons) in many areas of the brain.

The *ATN1* mutation that underlies DRPLA involves a DNA segment known as a CAG trinucleotide repeat. This segment is made up of a series of three DNA building blocks (cytosine, adenine, and guanine) that appear multiple times in a row. Normally, this segment is repeated 6 to 35 times within the *ATN1* gene. In people with DRPLA, the CAG segment is repeated at least 48 times, and the repeat region may be two or three times its usual length. The abnormally long CAG trinucleotide repeat changes the structure of atrophin 1. This altered protein accumulates in neurons and interferes with normal cell functions. The dysfunction and eventual death of these neurons lead to uncontrolled movements, intellectual decline, and the other characteristic features of DRPLA.

3.1. The Gene Associated with Dentatorubral-pallidoluysian Atrophy

- *ATN1*

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.

As the altered *ATN1* gene is passed from one generation to the next, the size of the CAG trinucleotide repeat often increases in size. Larger repeat expansions are usually associated with an earlier onset of the disorder and more severe signs and symptoms. This phenomenon is called anticipation. Anticipation tends to be more prominent when the *ATN1*

gene is inherited from a person's father (paternal inheritance) than when it is inherited from a person's mother (maternal inheritance).

5. Other Names for This Condition

- DRPLA
- Haw River syndrome
- Myoclonic epilepsy with choreoathetosis
- Naito-Oyanagi disease
- NOD

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