Inheritance and Testing

- Both males and females can be FMR1 carriers and can pass the premutation on to their children.
- Male premutation carriers will pass the premutation on to all their daughters and none of their sons.
- Female premutation carriers have a 50 percent chance in each pregnancy of passing the premutation to their children of either gender.
- Only premutations carried by women can expand to the full mutations that cause fragile X syndrome.
- Many adult males with FXTAS have been diagnosed after a grandchild or other relative was diagnosed with fragile X syndrome or found to be an FMR1 carrier.

Anyone with a family history of a Fragile X full mutation or premutation should consider FMR1 DNA testing. The test can be arranged by your GP/family doctor, any physician or genetic counsellor.

For more information about testing, visit www.fragilex.org.uk and then click on "testing".

www.fragilex.org.uk

About the Fragile X Society

The Fragile X Society was founded in 1990 to provide support and information to fragile X families, to raise awareness of fragile X and to encourage research into all aspects of fragile X. The Society offers support and information through its family support workers, website, bi-monthly newsletters and other publications. It also organises annual conferences and supports research through the participation of its family members in fragile X studies.

For more information on FXTAS and other topics related to Fragile X, email: info@fragilex.org.uk
or telephone 01371 875100

Special thanks for assistance on this leaflet to:
The National Fragile X Foundation

Photography by kind permission of the fragile X families whose photographs appear.

Additional copies of this leaflet available free of charge.

The Fragile X Society
helping fragile x families

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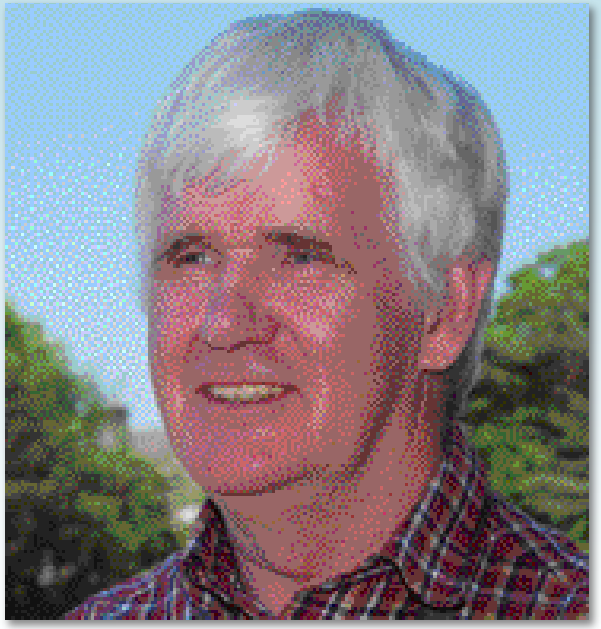
FXTAS

Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS)

An Introduction for Individuals, Families and Healthcare Providers



The Fragile X Society
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A Fragile X Overview

Fragile X is associated with changes in the Fragile X gene. The gene (also known by its scientific name of "FMR1") can be normal, but it can also exhibit a "premutation" or a "full mutation". When a premutation or full mutation is present, it can result in a Fragile X condition. These include:

- **Fragile X syndrome (FXS):**

  An inherited condition affecting intellectual, behavioural, language and social development. It occurs in both males and females who have a full mutation of the FMR1 gene.

- **Fragile X-associated tremor/ataxia syndrome (FXTAS):**

  An adult onset (over 50 years of age) neurological condition, more common and more severe among males, that causes tremor, memory difficulties and balance problems in those with a premutation of the FMR1 gene. (Both males and females who have a premutation are also referred to as "carriers".)

- **Fragile X-associated primary ovarian insufficiency (FXPOI):**

  A condition affecting ovarian function that can lead to infertility and early menopause. It occurs in some female carriers, who have a premutation of the FMR1 gene.

The FMR1 Gene

The FMR1 gene can undergo changes which cause these fragile X conditions. These changes affect a pattern of DNA called CGG repeats. Typically, the FMR1 gene has up to about 54 CGG repeats. A premutation in the FMR1 gene results in approximately 60–200 CGG repeats, and a full mutation in more than 200 CGG repeats.

www.fragilex.org.uk

FXTAS Symptoms and Diagnosis

FXTAS usually develops between the ages of 50–80. Symptoms that family members may notice (but often attribute to simple aging) include:

- "Intention" tremors – shaking that occurs during intended/purposeful movement such as reaching for or pouring something, or writing
- Balance problems (ataxia) that cause falling or instability while walking
- Numbness in the extremities (neuropathy)
- Mood instability, irritability, and other changes in personality
- Short-term memory loss and gradual intellectual decline

Diagnosis of FXTAS is based on:

1. Neurological examination with signs of FXTAS as described above
2. Positive carrier testing for the FMR1 premutation
3. Magnetic resonance imaging (MRI) findings consistent with FXTAS, such as specific white matter lesions in the brain or generalized brain atrophy (shrinkage)

Individuals with FXTAS are often misdiagnosed with other conditions including Parkinson's, Alzheimer's, dementia, stroke and peripheral neuropathy. Anyone experiencing any of the symptoms described above should contact their GP/family doctor and request a referral to a neurologist. Some doctors and neurologists may not yet be aware of this newly described (in 2001) syndrome, but they can find out more at www.fxtas.org.

Progression and Risk Concerns

FXTAS is a progressive condition, often beginning with mild symptoms and becoming more severe over time. Disease progression can vary greatly, however, among individuals. Many individuals function well for years or even decades, until carrying out many daily living tasks and walking without assistance become difficult. Some individuals exhibit only tremor and/or ataxia and never develop psychiatric or cognitive problems.

Fragile X premutation carriers over 50 years of age are at risk for FXTAS. The condition has not been reported in individuals with a full mutation. It occurs more frequently and more severely in male carriers. Experts think at least one-third of male carriers will develop symptoms, though research is ongoing in this area.

There is no cure for FXTAS at this time, but symptoms can be treated with the goal of lessening its severity and progression.

Medications may be prescribed to treat tremors, psychiatric and physical symptoms. Occupational, physical therapy and psychotherapy may also be beneficial.