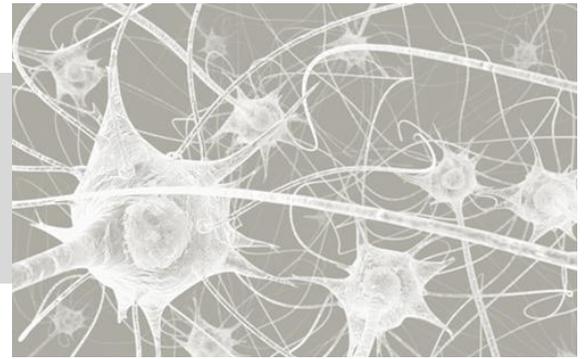


Fragile-X Syndrome



The Numbers

1/3,600 males

1/4,000-6,000 females

50% chance that a female
will inherit the mutation

1,000,000 + carriers of the
mutation

100,000 + with Fragile X
Syndrome

Physical Symptoms

- Large protruding ears
- Soft skin
- Flexible joints
- Flat feet
- Low muscle tone
- Long face
- Macroorchidism in males (large testes)

Behavioral Symptoms

- Speech/motor delay
- Hypersensitivity to environment
- Impulsiveness
- Cognitive impairment
- Poor attention span
- Poor eye contact

Quick Facts

- Most common cause of inherited mental disability
- First discovered by Martin and Bell in 1943
- X-linked recessive mutation
- Caused by a mutation in the FMR1 gene on the X-chromosome
- More severe impact on males than in females
- More common in males than in females

The FMR1 Gene/FMRP

- Also known as the “Fragile X Mental Retardation” gene
- The wildtype FMR1 gene produces the FMRP (protein) that is responsible for synaptic plasticity (and consequently learning and memory) and brain growth
- FMRP is also responsible for translation, trafficking, and targeting of mRNA in neurons
- Fragile X is caused by a repeat mutation in the FMR1 gene
- The FMR1 gene is located near the end, on the Xq27.3 band

Normal X



Fragile X



fragile
site

The CCG repeat

A normal FMR1 gene
has:

5 – 40

CCG repeats

A permuted FMR1
gene mutation has:

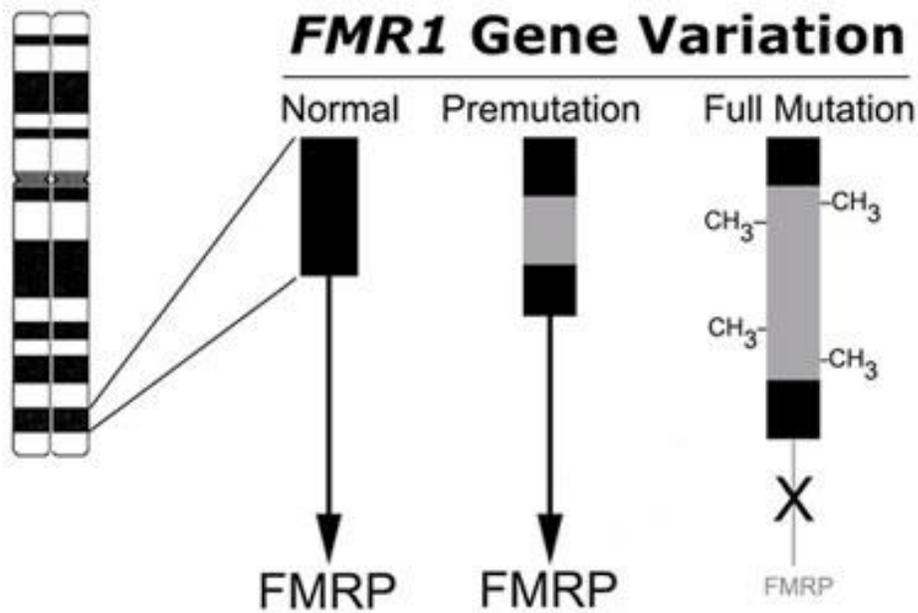
55-200

CCG repeats

A full FMR1 gene
mutation has:

200+

CCG repeats



Research – What we know

- FMRP is made in dendrites due to excitation of metabotropic glutamate receptors
- If the mGluRs are stimulated, then Long Term Depression, which reduces the effectiveness of synapses firing, occurs, causing cognitive impairment. This is called the mGluR Theory
- A mGluR receptor blocker was tested in mice with Fragile X to see if basic symptoms of Fragile X (hyperactivity and sound-induced seizures) could be alleviated and found that if the mGluR receptors are blocked, then these two symptoms are alleviated
- Lithium is being tested as a possible drug to help alleviate symptoms as well (lithium is also commonly used to treat the hyperactivity aspect of bipolar disorder, so it's not surprising it would be used to treat aspects of Fragile X) It is found to help improve speech.

http://www.fraxa.org/research_summaryfindings.aspx

Treatment and Therapy

- Speech therapy
- Language therapy
- Physical therapy (to assist with low muscle tone/muscle weakness)
- Calming techniques (to assist with hyperactivity)
- ADHD medication (to assist with hyperactivity)
- Occupational therapy (to assist with sensory integration, development of fine motor skills. and strengthen tactile weakness)



The National
Fragile X
Foundation

