Name of Disorder: Fragile X Tremor Ataxia Syndrome (FXTAS)
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1) The X chromosome
   Women have two X chromosomes – one from each parent – while men have an X from their mothers and a Y chromosome from their fathers. Therefore mutations in genes on the X chromosome tend to cause more symptoms in men than women, as the men have not got a “spare” gene on a second X chromosome.

2) The fragile-X gene
   The fragile-X gene has a series of repeated codes within it. This series is called a “triplet repeat” because it contains the coding letters “CGG” repeated. If the series is over 200 repeats long, the gene is silenced so that not enough of the protein it codes for is made. This causes fragile-X syndrome – mental retardation, mainly in boys. However, if the series is about 55-200 repeats long, a normal amount of the protein is made but the coding message (messenger RNA) itself interferes with the functions of others genes and causes a completely different disorder: fragile-X tremor ataxia syndrome (FXTAS). A fragile-X gene with 55-200 repeats is said to have a “premutation”, because the number is unstable and can expand to cause the fragile-X mental retardation syndrome in descendants (see Section 7).

3) FXTAS
   About 1 in 800 men have 55-200 repeats in their fragile-X gene, and about one third of them develop symptoms of FXTAS. (No-one knows why the other two-thirds do not.) FXTAS typically comes on after age 50. It often starts with tremor, especially in the hands. Another common early symptom is impaired coordination, causing difficulty with balance while walking. (The incoordination is called “ataxia”).

   These two symptoms give the disorder its name. In addition, several other symptoms are quite common in FXTAS: i) “peripheral neuropathy” affecting the nerves in the limbs – especially the sensory (feeling) nerves to the feet and lower legs; ii) stiffness and slowness of movement that looks like Parkinson’s disease and that sometimes responds to Parkinson’s medications; iii) “autonomic dysfunction”, referring to problems with the small nerves that control blood pressure, sweating, the bladder, etc., and iv) problems with speed and flexibility of thought, which may ultimately become severe enough to be labelled a dementia. These three symptoms do not occur in everyone with FXTAS, but do in at least one third and probably in a majority.
4) Women and FXTAS

Women tend to get FXTAS less often and less severely than men, as they also have a normal fragile-X gene (with less than 40-45 repeats) on their other X chromosome. One particular problem that about 20% of women with 55-200 repeats develop, however, is premature menopause (before age 40).

5) Features of FXTAS on MRI scans

People with FXTAS often have features on MRI scans of their brains that help their doctors suspect the diagnosis. One of these, present in about two-thirds of FXTAS patients, is called the “MCP” sign. It consists of whiter than usual patches in the main communication pathway between the coordination part (“cerebellum”) and the stem of the brain. Your doctor may show it to you, if you have it. Other features, affecting the deep parts of the brain, are less specific.

6) Making the diagnosis

The gene test for FXTAS is fairly straightforward, and available in a number of major gene-testing centres around the country. The test requires a blood sample. This can be sent to the gene-testing centre by carrier or post – you do not have to go yourself. If you have symptoms of FXTAS, the test is to rule it in or out as the cause, and is therefore routine. If you do not have any symptoms, but are considering being tested anyway because the gene is in the family and you want to find out whether you carry it, the test is predictive. This can have implications for insurance or employment, and you should discuss your decision thoroughly with a genetic counsellor first.

7) Implications for other family members

Men with FXTAS cannot pass it on to their sons, as their sons inherit their Y chromosome, not their X chromosome. Men with FXTAS pass it on to all their daughters, but, as mentioned earlier, the daughters often show no signs of this. The daughters can then pass it to their children (a 50:50 chance). The mutation is of an unusual type, however, - the repeat number tends to get larger with each generation – such that these grandchildren (and especially the grandsons) may have more than 200 repeats and may have fragile-X syndrome with mental retardation obvious in childhood.

8) Treatment

At present there is no cure for FXTAS. It is a fairly newly discovered disease (about 20 years ago), and a number of groups of scientists here and overseas are working to try to understand it and ultimately arrest or cure it. In the meantime, the balance symptoms can be helped by, for example, physiotherapy and balance exercises; independence maintained with the aid of occupational therapists who will advise on appropriate home modifications and aids, Parkinson’s-like features with medications for Parkinson’s, and advice given on how to manage (work around) thinking problems by neuropsychologists.
References:
