PPM-X syndrome

Description

PPM-X syndrome is a condition characterized by psychotic disorders (most commonly bipolar disorder), a pattern of movement abnormalities known as parkinsonism, and mild to severe intellectual disability with impaired language development. Other symptoms may include muscle stiffness (spasticity), exaggerated reflexes, and an abnormally small head (microcephaly). Affected males may have enlarged testes (macro-orchidism). Not all affected individuals have all these symptoms, but most have intellectual disability. Males with this condition are typically more severely affected than females, who usually have only mild intellectual disability or learning disabilities.

Frequency

PPM-X syndrome is thought to be a very rare condition, although its prevalence is unknown.

Causes

Mutations in the *MECP2* gene cause PPM-X syndrome. The *MECP2* gene provides instructions for making a protein called MeCP2 that is critical for normal brain function. Researchers believe that this protein has several functions, including regulating other genes in the brain by switching them off when they are not needed. The MeCP2 protein likely plays a role in maintaining connections (synapses) between nerve cells. The MeCP2 protein may also control the production of different versions of certain proteins in nerve cells. Although mutations in the *MECP2* gene disrupt the normal function of nerve cells, it is unclear how these mutations lead to the signs and symptoms of PPM-X syndrome.

Some *MECP2* gene mutations that cause PPM-X syndrome disrupt attachment (binding) of the MeCP2 protein to DNA, and other mutations alter the 3-dimensional shape of the protein. These mutations lead to the production of an MeCP2 protein that cannot properly interact with DNA or other proteins and so cannot control the expression of genes. It is unclear how *MECP2* gene mutations lead to the signs and symptoms of PPM-X syndrome, but misregulation of genes in the brain likely plays a role.

Learn more about the gene associated with PPM-X syndrome

- MECP2

Inheritance

More than 99 percent of PPM-X syndrome cases occur in people with no history of the disorder in their family. Many of these cases result from new mutations in the *MECP2* gene.

A few families with more than one affected family member have been described. These cases helped researchers determine that PPM-X syndrome has an X-linked pattern of inheritance. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males, who have only one X chromosome, a mutation in the only copy of the gene in each cell is sufficient to cause the condition. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell can lead to less severe features of the condition or may cause no signs or symptoms at all. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- MRXS13
- PPMX
- X-linked mental retardation, syndromic 13

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Rett syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0035372/)

Genetic and Rare Diseases Information Center

- X-linked intellectual disability-psychosis-macroorchidism syndrome (https://rarediseases.info.nih.gov/diseases/3506/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- INTELLECTUAL DEVELOPMENTAL DISORDER, X-LINKED, SYNDROMIC 13; MRXS13 (https://omim.org/entry/300055)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ppm-x+syndrome%29+OR+%28X-linked+mental+retardation,+syndromic+13%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated January 1, 2018