

Smith-Magenis syndrome

Description

Smith-Magenis syndrome is a developmental disorder that affects behavior, emotions, and learning processes. The major features of this condition include distinctive facial features, sleep disturbances, behavioral problems, mild to moderate intellectual disability, and delayed speech and language skills.

Most people with Smith-Magenis syndrome have a broad, square-shaped face with deep-set eyes, full cheeks, and a prominent lower jaw. The middle of the face and the bridge of the nose often appear flattened. The mouth tends to turn downward with a full, outward-curving upper lip. These facial differences can be subtle in early childhood, but they usually become more distinctive in later childhood and adulthood. Dental abnormalities are also common in affected individuals.

Disrupted sleep patterns are characteristic of Smith-Magenis syndrome, and they typically begin early in life. Affected people may have trouble falling asleep at night and awaken several times during the night and early morning. They may be very sleepy during the day.

People with Smith-Magenis syndrome typically have affectionate, engaging personalities, but most also have behavioral problems. These include frequent temper tantrums and outbursts, aggression, anxiety, impulsiveness, and difficulty paying attention. Self-injury, including biting, hitting, head banging, and skin picking, is very common. People with Smith-Magenis syndrome may have other behaviors, such as repetitive self-hugging or compulsively licking their fingers and flipping pages of books and magazines (a behavior known as "lick and flip").

Other signs and symptoms of Smith-Magenis syndrome include short stature, abnormal curvature of the spine (scoliosis), obesity, and a hoarse voice. Some people with this disorder have ear abnormalities that lead to hearing loss. Affected individuals may have eye abnormalities that cause nearsightedness (myopia) and other vision problems. Although less common, heart and kidney defects also have been reported in people with Smith-Magenis syndrome.

Frequency

Smith-Magenis syndrome affects at least 1 in 25,000 individuals worldwide. However, researchers believe that many people with this condition are not diagnosed, so the true

prevalence may be closer to 1 in 15,000 individuals.

Causes

In most people with Smith-Magenis syndrome, the condition results from the deletion of a small piece of chromosome 17 in each cell. This deletion occurs on the short (p) arm of the chromosome at a position designated p11.2. The deleted segment most often includes approximately 3.7 million DNA building blocks (base pairs), also written as 3.7 megabases (Mb). (An extra copy of this segment causes a related condition called Potocki-Lupski syndrome.) Occasionally the deletion is larger or smaller. All of the deletions affect one of the two copies of chromosome 17 in each cell.

Although the deleted region contains multiple genes, researchers believe that the loss of one particular gene, *RAI1*, underlies many of the characteristic features of Smith-Magenis syndrome. All of the deletions known to cause the condition contain this gene. The *RAI1* gene provides instructions for making a protein that helps regulate the activity (expression) of other genes. Although most of the genes regulated by the RAI1 protein have not been identified, this protein appears to control the expression of several genes involved in daily (circadian) rhythms, such as the sleep-wake cycle. Studies suggest that the deletion leads to a reduced amount of RAI1 protein in cells, which disrupts the expression of genes that influence circadian rhythms. These changes may account for the sleep disturbances that occur with Smith-Magenis syndrome. It is unclear how a loss of one copy of the *RAI1* gene leads to the other physical, mental, and behavioral problems associated with this condition.

A small percentage of people with Smith-Magenis syndrome have a variant in the *RAI1* gene instead of a chromosomal deletion. Although these individuals have many of the major features of the condition, they are less likely than people with a deletion to have short stature, hearing loss, and heart or kidney abnormalities. It is likely that, in people with a deletion, the loss of other genes in the deleted region accounts for these additional signs and symptoms; the role of these genes is under study.

[Learn more about the gene and chromosome associated with Smith-Magenis syndrome](#)

- *RAI1*
- chromosome 17

Inheritance

Smith-Magenis syndrome is usually not inherited. This condition typically results from a chromosomal deletion or an *RAI1* gene variant that occurs during the formation of reproductive cells (eggs or sperm) or in early fetal development. Most people with Smith-Magenis syndrome have no history of the condition in their family.

In a small number of cases, people with Smith-Magenis syndrome have inherited the deletion or variant from an unaffected mother who had the genetic change only in her

egg cells. This phenomenon is called germline mosaicism.

Other Names for This Condition

- 17p- syndrome
- 17p11.2 monosomy
- Chromosome 17p deletion syndrome
- Deletion 17p syndrome
- Partial monosomy 17p
- SMS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Smith-Magenis syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0795864/>)

Genetic and Rare Diseases Information Center

- Smith-Magenis syndrome (<https://rarediseases.info.nih.gov/diseases/8197/index>)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (<https://clinicaltrials.gov/search?cond=%22Smith-Magenis syndrome%22>)

Catalog of Genes and Diseases from OMIM

- SMITH-MAGENIS SYNDROME; SMS (<https://omim.org/entry/182290>)

Scientific Articles on PubMed

- PubMed ([https://pubmed.ncbi.nlm.nih.gov/?term=\(smith-magenis+syndrome%5BTIAB%5D\)+AND+english%5Bla%5D+AND+human%5Bmh%5D](https://pubmed.ncbi.nlm.nih.gov/?term=(smith-magenis+syndrome%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D))

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Last updated May 4, 2023