UNC80 deficiency

Description

UNC80 deficiency is a severe disorder characterized by nervous system and developmental problems that are apparent from birth or early infancy. The disorder does not typically get worse over time; development of intellectual function and motor skills, such as rolling over and sitting, is slow and limited, but once skills are learned, they are usually retained.

People with UNC80 deficiency have profound intellectual disability. Muscle tone is generally weak (hypotonia), but affected individuals may have increased muscle tone (hypertonia) in the arms and legs. Most people with this disorder never learn to walk. Some affected individuals have feeding difficulties because hypotonia leads to problems controlling movements of the mouth. Speech is also generally absent, although in some cases individuals have limited communication using body language, gestures, and signs. Seizures, involuntary side-to-side movements of the eyes (nystagmus), eyes that do not point in the same direction (strabismus), and a high-pitched cry can also occur in this disorder.

People with UNC80 deficiency are of normal size at birth but grow slowly during infancy and childhood. Unusual facial features typically occur in this disorder, and vary among affected individuals. These features can include a wide, short skull (brachycephaly); a triangular face shape with a prominent forehead (frontal bossing); droopy eyelids (ptosis) ; folds of skin covering the inner corners of the eyes (epicanthal folds); outside corners of the eyes that point downward (downslanting palpebral fissures); a nose with a prominent bridge and a bulbous or upturned tip; a short, smooth space between the upper lip and nose (philtrum); a mouth that remains open; and low-set ears. Other physical differences that can occur in people with UNC80 deficiency include a short neck, abnormal curvature of the spine (scoliosis), permanently bent joints (contractures), and inward- and upward-turning feet (clubfeet).

Frequency

The prevalence of UNC80 deficiency is unknown. At least 19 affected individuals have been described in the medical literature.

Causes

UNC80 deficiency, as its name suggests, is caused by mutations in the *UNC80* gene. This gene provides instructions for making a large protein that is part of the NALCN sodium channel complex (channelosome). Sodium channels transport positively charged sodium atoms (sodium ions) into cells and play a key role in a cell's ability to generate and transmit electrical signals. In particular, the NALCN channelosome is important in nerve cells (neurons), helping to regulate their activity level (excitability). In addition to forming part of the structure of the NALCN channelosome, UNC80 also helps locate and stabilize it in the cell membrane of neurons.

UNC80 gene mutations result in absence of the UNC80 protein or production of an abnormal protein. Absence of functional UNC80 protein impairs the stability and function of the NALCN channelosome. Neuron excitability is thought to be improperly regulated as a result, but it is unclear how these changes cause the specific features of UNC80 deficiency.

Learn more about the gene associated with UNC80 deficiency

- UNC80

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- IHPRF2
- Infantile hypotonia with psychomotor retardation and characteristic facies-2

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hypotonia, infantile, with psychomotor retardation and characteristic facies 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4225203/)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- HYPOTONIA, INFANTILE, WITH PSYCHOMOTOR RETARDATION AND CHARACTERISTIC FACIES 2; IHPRF2 (https://omim.org/entry/616801)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28UNC80%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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