HGPPS

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Horizontal gaze palsy with progressive scoliosis (HGPPS) is a disorder that affects vision and also causes an abnormal curvature of the spine (scoliosis). People with this condition are unable to move their eyes side-to-side (horizontally). As a result, affected individuals must turn their head instead of moving their eyes to track moving objects. Up-and-down (vertical) eye movements are typically normal.

Keywords: genetic conditions

1. Introduction

In people with HGPPS, an abnormal side-to-side curvature of the spine develops in infancy or childhood. It tends to be moderate to severe and worsens over time. Because the abnormal spine position can be painful and interfere with movement, it is often treated with surgery early in life.

2. Frequency

HGPPS has been reported in several dozen families worldwide.

3. Causes

HGPPS is caused by mutations in the *ROBO3* gene. This gene provides instructions for making a protein that is important for the normal development of certain nerve pathways in the brain. These include motor nerve pathways, which transmit information about voluntary muscle movement, and sensory nerve pathways, which transmit information about sensory input (such as touch, pain, and temperature). For the brain and the body to communicate effectively, these nerve pathways must cross from one side of the body to the other in the brainstem, a region that connects the upper parts of the brain with the spinal cord.

The ROBO3 protein plays a critical role in ensuring that motor and sensory nerve pathways cross over in the brainstem. In people with HGPPS, these pathways do not cross over, but stay on the same side of the body. Researchers believe that this miswiring in the brainstem is the underlying cause of the eye movement abnormalities associated with the disorder. The cause of progressive scoliosis in HGPPS is unclear. Researchers are working to determine why the effects of *ROBO3* mutations appear to be limited to horizontal eye movement and scoliosis.

3.1. The gene associated with Horizontal gaze palsy with progressive scoliosis

- ROBO3

4. 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.

5. Other Names for This Condition

- familial horizontal gaze palsy with progressive scoliosis
- familial idiopathic scoliosis associated with congenital encephalopathy
- familial infantile scoliosis associated with bilateral paralysis of conjugate gaze
- gaze palsy, familial horizontal, with progressive scoliosis

- HGPPS
- ophthalmoplegia, progressive external, and scoliosis

References

1. Abu-Amero KK, al Dhalaan H, al Zayed Z, Hellani A, Bosley TM. Five newconsanguineous families with horizontal gaze palsy and progressive scoliosis and novel ROBO3 mutations. J Neurol Sci. 2009 Jan 15;276(1-2):22-6. doi:10.1016/j.jns.2008.08.026.
2. Bosley TM, Salih MA, Jen JC, Lin DD, Oystreck D, Abu-Amero KK, MacDonald DB,al Zayed Z, al Dhalaan H, Kansu T, Stigsby B, Baloh RW. Neurologic features ofhorizontal gaze palsy and progressive scoliosis with mutations in ROBO3.Neurology. 2005 Apr 12;64(7):1196-203.
3. Chan WM, Traboulsi EI, Arthur B, Friedman N, Andrews C, Engle EC. Horizontalgaze palsy with progressive scoliosis can result from compound heterozygousmutations in ROBO3. J Med Genet. 2006 Mar;43(3):e11.
4. Engle EC. Oculomotility disorders arising from disruptions in brainstem motor neuron development. Arch Neurol. 2007 May;64(5):633-7. Review.
5. Jen J, Coulin CJ, Bosley TM, Salih MA, Sabatti C, Nelson SF, Baloh RW.Familial horizontal gaze palsy with progressive scoliosis maps to chromosome11q23-25. Neurology. 2002 Aug 13;59(3):432-5.
6. Jen JC, Chan WM, Bosley TM, Wan J, Carr JR, Rüb U, Shattuck D, Salamon G, KudoLC, Ou J, Lin DD, Salih MA, Kansu T, Al Dhalaan H, Al Zayed Z, MacDonald DB,Stigsby B, Plaitakis A, Dretakis EK, Gottlob I, Pieh C, Traboulsi EI, Wang Q,Wang L, Andrews C, Yamada K, Demer JL, Karim S, Alger JR, Geschwind DH, Deller T,Sicotte NL, Nelson SF, Baloh RW, Engle EC. Mutations in a human ROBO gene disrupthindbrain axon pathway crossing and morphogenesis. Science. 2004 Jun4;304(5676):1509-13.
7. Jen JC. Effects of failure of development of crossing brainstem pathways onocular motor control. Prog Brain Res. 2008;171:137-41. doi:10.1016/S0079-6123(08)00618-3.
8. Sicotte NL, Salamon G, Shattuck DW, Hageman N, Rüb U, Salamon N, Drain AE,Demer JL, Engle EC, Alger JR, Baloh RW, Deller T, Jen JC. Diffusion tensor MRIshows abnormal brainstem crossing fibers associated with ROBO3 mutations.Neurology. 2006 Aug 8;67(3):519-21.