SYNGAP1-Related Intellectual Disability

Subjects: Genetics
Submitted by: Nora Tang
(This entry belongs to Entry Collection "MedlinePlus")

Definition

SYNGAP1-related intellectual disability is a neurological disorder characterized by moderate to severe intellectual disability that is evident in early childhood.

1. Introduction

The earliest features are typically delayed development of speech and motor skills, such as sitting, standing, and walking. Many people with this condition have weak muscle tone (hypotonia), which contributes to the difficulty with motor skills. Some affected individuals lose skills they had already acquired (developmental regression). Other features of *SYNGAP1*-related intellectual disability include recurrent seizures (epilepsy), hyperactivity, and autism spectrum disorder, which is characterized by impaired communication and social interaction; almost everyone with *SYNGAP1*-related intellectual disability develops epilepsy, and about half have autism spectrum disorder.

2. Frequency

SYNGAP1-related intellectual disability is a relatively common form of cognitive impairment. It is estimated to account for 1 to 2 percent of intellectual disability cases.

3. Causes

SYNGAP1-related intellectual disability is caused by mutations in the *SYNGAP1* gene. The protein produced from this gene, called SynGAP, plays an important role in nerve cells in the brain. It is found at the junctions between nerve cells (synapses) and helps regulate changes in synapses that are critical for learning and memory. Mutations involved in this condition prevent the production of functional SynGAP protein from one copy of the gene, reducing the protein's activity in cells. Studies show that a reduction of SynGAP activity can have multiple effects in nerve cells, including pushing synapses to develop too early. The resulting abnormalities disrupt the synaptic changes in the brain that underlie learning and memory, leading to cognitive impairment and other neurological problems characteristic of *SYNGAP1*-related intellectual disability.

3.1.The Gene Associated with SYNGAP1-Related Intellectual Disability

- SYNGAP1

4. Inheritance

SYNGAP1-related intellectual disability is classified as an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Almost all cases result from new mutations in the gene and occur in people with no history of the disorder in their family. In at least one case, an affected person inherited the mutation from one affected parent.

5. Other Names for This Condition

- mental retardation, autosomal dominant 5
- MRD5

References

1. Aceti M, Creson TK, Vaissiere T, Rojas C, Huang WC, Wang YX, Petralia RS, PageDT, Miller CA, Rumbaugh G. Syngap1

haploinsufficiency damages a postnatalcritical period of pyramidal cell structural maturation linked to corticalcircuit assembly. Biol Psychiatry. 2015 May 1;77(9):805-15. doi:10.1016/j.biopsych.2014.08.001.
2. Clement JP, Aceti M, Creson TK, Ozkan ED, Shi Y, Reish NJ, Almonte AG, Miller BH, Wiltgen BJ, Miller CA, Xu X, Rumbaugh G. Pathogenic SYNGAP1 mutations impair cognitive development by disrupting maturation of dendritic spine synapses. Cell.2012 Nov 9;151(4):709-723. doi: 10.1016/j.cell.2012.08.045.
3. Clement JP, Ozkan ED, Aceti M, Miller CA, Rumbaugh G. SYNGAP1 links thematuration rate of excitatory synapses to the duration of critical-periodsynaptic plasticity. J Neurosci. 2013 Jun 19;33(25):10447-52. doi:10.1523/JNEUROSCI.0765-13.2013.
4. Mignot C, von Stülpnagel C, Nava C, Ville D, Sanlaville D, Lesca G, Rastetter A, Gachet B, Marie Y, Korenke GC, Borggraefe I, Hoffmann-Zacharska D, Szczepanik E, Rudzka-Dybała M, Yiş U, Çağlayan H, Isapof A, Marey I, Panagiotakaki E, Korff C, Rossier E, Riess A, Beck-Woedl S, Rauch A, Zweier C, Hoyer J, Reis A, Mironov M, Bobylova M, Mukhin K, Hernandez-Hernandez L, Maher B, Sisodiya S, Kuhn M,Glaeser D, Weckhuysen S, Myers CT, Mefford HC, Hörtnagel K, Biskup S;EuroEPINOMICS-RES MAE working group, Lemke JR, Héron D, Kluger G, Depienne C.Genetic and neurodevelopmental spectrum of SYNGAP1-associated intellectualdisability and epilepsy. J Med Genet. 2016 Aug;53(8):511-22. doi:10.1136/jmedgenet-2015-103451.Oct;53(10):720.
5. Ozkan ED, Creson TK, Kramár EA, Rojas C, Seese RR, Babyan AH, Shi Y, Lucero R,Xu X, Noebels JL, Miller CA, Lynch G, Rumbaugh G. Reduced cognition in Syngap1mutants is caused by isolated damage within developing forebrain excitatoryneurons. Neuron. 2014 Jun 18;82(6):1317-33. doi: 10.1016/j.neuron.2014.05.015.
6. Parker MJ, Fryer AE, Shears DJ, Lachlan KL, McKee SA, Magee AC, Mohammed S,Vasudevan PC, Park SM, Benoit V, Lederer D, Maystadt I, Study D, FitzPatrick DR. De novo, heterozygous, loss-of-function mutations in SYNGAP1 cause a syndromicform of intellectual disability. Am J Med Genet A. 2015 Oct;167A(10):2231-7. doi:10.1002/ajmg.a.37189.
7. Wang CC, Held RG, Hall BJ. SynGAP regulates protein synthesis and homeostatic synaptic plasticity in developing cortical networks. PLoS One. 2013 Dec31;8(12):e83941. doi: 10.1371/journal.pone.0083941.

Keywords

genetic conditions