

REFERENCES

1 Bernier R. et al., on behalf of the Simons VIP consortium. "Developmental Trajectories for Young Children With 16p11.2 Copy Number Variation." Am J Med Genet Part B. 9999. (2017): 1–14.

2 Brisset, Sophie, et al. "Inherited 1q21.1q21.2 Duplication and 16p11.2 Deletion: A Two-hit Case with More Severe Clinical Manifestations." European Journal of Medical Genetics 58.9 (2015): 497-501.

3 Zufferey, Flore, et al. "A 600kb deletion syndrome at 16p11.2 leads to energy imbalance and neuropsychiatric disorders." J. Med. Genet. 49 (2012): 660-66.

4 Li, Lin, et al. "Discordant phenotypes in monozygotic twins with 16p11.2 microdeletions including the SH2B1 gene." Am J Med Genet. 9999. (2017): 1-5.

5 Kristensson, Felipe M. et al., "Long-term effects of bariatric surgery in patients with obesity and chromosome 16p11.2 microdeletion." Surgery for Obesity and Related Diseases (2017): 1-5.

Image provided by the U.S. National Library of Medicine:

<https://ghr.nlm.nih.gov/chromosome/16>

CONTACT US

Chromosome Disorder Outreach
P.O. Box 724
Boca Raton, FL 33429-0724

Family Helpline 561.395.4252
info@chromodisorder.org

www.chromodisorder.org

YOU ARE NOT ALONE

Chromosome
Disorder Outreach

ABOUT US

Chromosome Disorder Outreach provides support and information to anyone diagnosed with a rare chromosome change, rearrangement or disorder. CDO actively promotes research and a positive community understanding of all chromosome disorders.

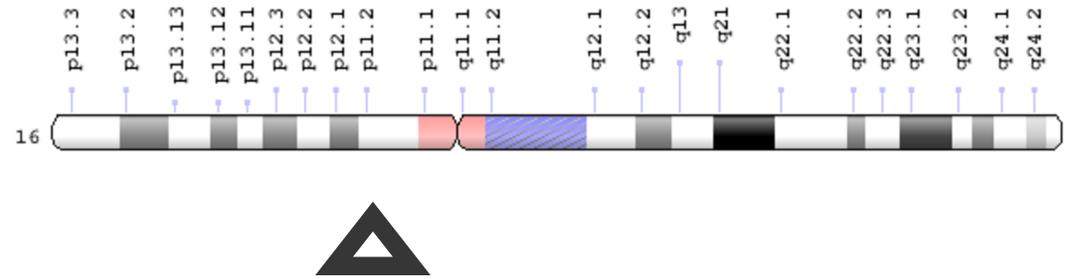
CDO is a 501c3 organization founded in 1992.

16p11.2 microdeletion

16p11.2 microdeletion

(T)he 16p11.2 region encompasses many distinct genomic structural variants; different symptomatic phenotypes are expressed depending on if this region contains a deletion or a duplication (1). Within this region, two distinct loci are described in the microdeletion syndrome: an atypical one with BP2-BP3 breakpoints, and a typical one with BP4-BP5 breakpoints (2). The typical deletion spans a region of approximately 600kb and has a prevalence in about 1 in every 2000 individuals (3).

While symptomology is variable, the 16p11.2 deletion impacts developmental and intellectual development, growth, and body mass index (3). Potential developmental and intellectual disabilities include Autism Spectrum Disorder (ASD), Attention Deficit/Hyperactivity Disorder (ADHD), speech sound disorder, developmental coordination disorder, language disorder, and intellectual disability (ID) (1). Seizures – particularly during the first three years – are also present in about a quarter of carriers (3).



The 600kb deletion contains 29 genes (3). Of these 29 genes, nine are described in detail in the literature (4). The disease-causing gene for the microdeletion in this region is thought to be SH2B14. SH2B1 encodes an adapter protein involved in leptin and insulin signaling, and is associated with many of the symptoms of the microdeletion: early-onset obesity, hyperphagia, insulin resistance, and developmental delay. More evidence is necessary to further verify this theory. The remaining eight genes include CD19, NFATC2IP, LAT (all involved in immunity), TUFM, ATXN2L (both involved in neurological disease expression), ATP2A1, RABEP2 (both associated with metabolism), and SPNS1 (unknown function) (4).

It is common for those with the 16p11.2 deletion to have syndromic obesity, obesity coupled with distinct neurological and developmental abnormalities (described above). Those with the deletion typically had higher BMI and systolic blood pressure compared to obese non-carriers (5). Bariatric surgery has been shown to be an effective treatment for obese patients with the 16p11.2 deletion, as it produces similar results in both carriers and non-carriers.

Of the potential neurological symptoms mentioned above, speech sound disorder, developmental coordination disorder, and language disorder occur at the highest frequencies, at 67%, 67%, and 54% respectively. Syndromes occurring at lower, but significant, frequencies include ASD (24%), ADHD (24%), and ID (15%). Anxiety disorders and behavioral disorders have also been found in individuals with this deletion, but at frequencies less than 10% for both (1).

Longitudinal studies give the following insights on the development of children with the 16p11.2 microdeletion (1). In terms of the development of cognitive ability, verbal IQ (VIQ) improves with age, but nonverbal IQ (NVIQ) does not. In the development of adaptive ability, aptitude in communication, socializing, motor skills and daily living skills were assessed. Development of communication and daily living skills appears to improve with age. However, motor and social skills do not increase with age, and, in some cases, even tend to deteriorate. Development of behavior was assessed by determining a child's tendency to externalize (exhibiting hyperactivity, opposition, other behavioral problems) and internalize (exhibiting anxiety, depression, withdrawal) as they grew. Externalization and internalization tendencies did not increase with age for the deletion phenotype.