16p11.2 Deletion Syndrome Guidebook

SIMONS SEARCHLIGHT

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16p11.2 Deletion Syndrome Guidebook

This guidebook was developed by the Simons Searchlight study team to help you learn important information about people with a 16p11.2 deletion syndrome.

Inside, you will find a review of everything from basic genetics and features of 16p11.2 deletion syndrome to clinical care and management considerations.

– Simons Searchlight

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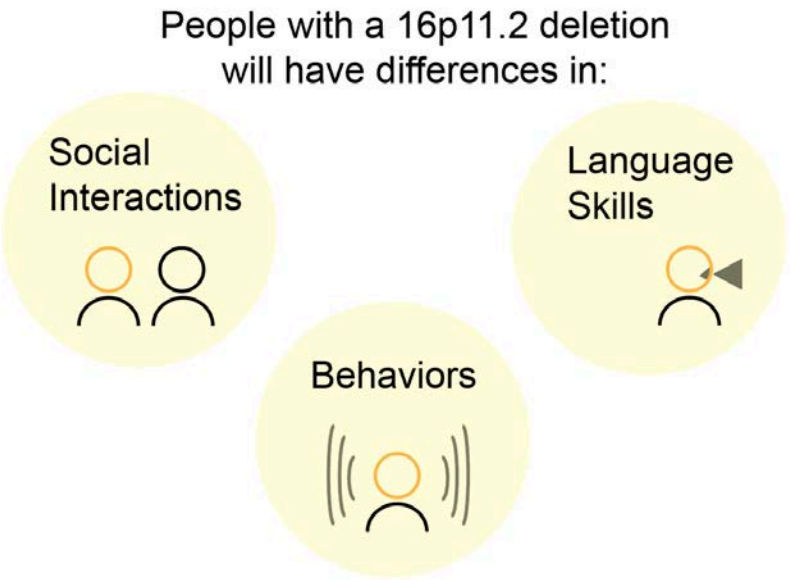
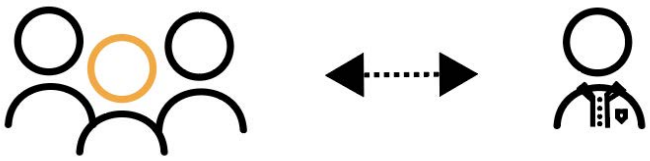
How Did We Collect All of This Information?

Simons Searchlight is a research project aimed at characterizing specific genetic changes that have been associated with autism and other neurodevelopmental conditions, such as differences in social interactions, behaviors and, speech and language development.



Thanks to the many 16p11.2 deletion families who have participated in Simons Searchlight (formerly Simons Variation in Individuals Project), we have learned a wealth of information about 16p11.2 deletion syndrome. This guidebook provides an in-depth summary of findings from the ongoing Simons Searchlight study. We are glad we can share this information with you and other newly diagnosed families. Simons Searchlight research has helped us to better understand what to expect for children and young adults with 16p11.2 deletion syndrome. The success of this project can be attributed to the close partnership between families and researchers.



What Is Simons Searchlight?

In 2010, the Simons Foundation began working to build a collaborative relationship between families and researchers to advance our understanding of 16p11.2 deletion syndrome. Families shared their medical histories and participated in tests, and researchers compiled this information and published what they had learned in medical journals. When families and researchers partner together like this, we are able to answer questions quickly and give back to the 16p11.2 community. Families involved in Simons Searchlight not only receive useful feedback by participating in research, but they also are helping other families now and in the future.

Simons Searchlight has been an important resource for connecting and supporting families who once felt alone after receiving a genetic diagnosis such as 16p11.2 deletion. Now, the online community at Simons Searchlight extends from our website to other social networks, like Facebook, where families from all over the globe support each other by sharing their stories and advice.

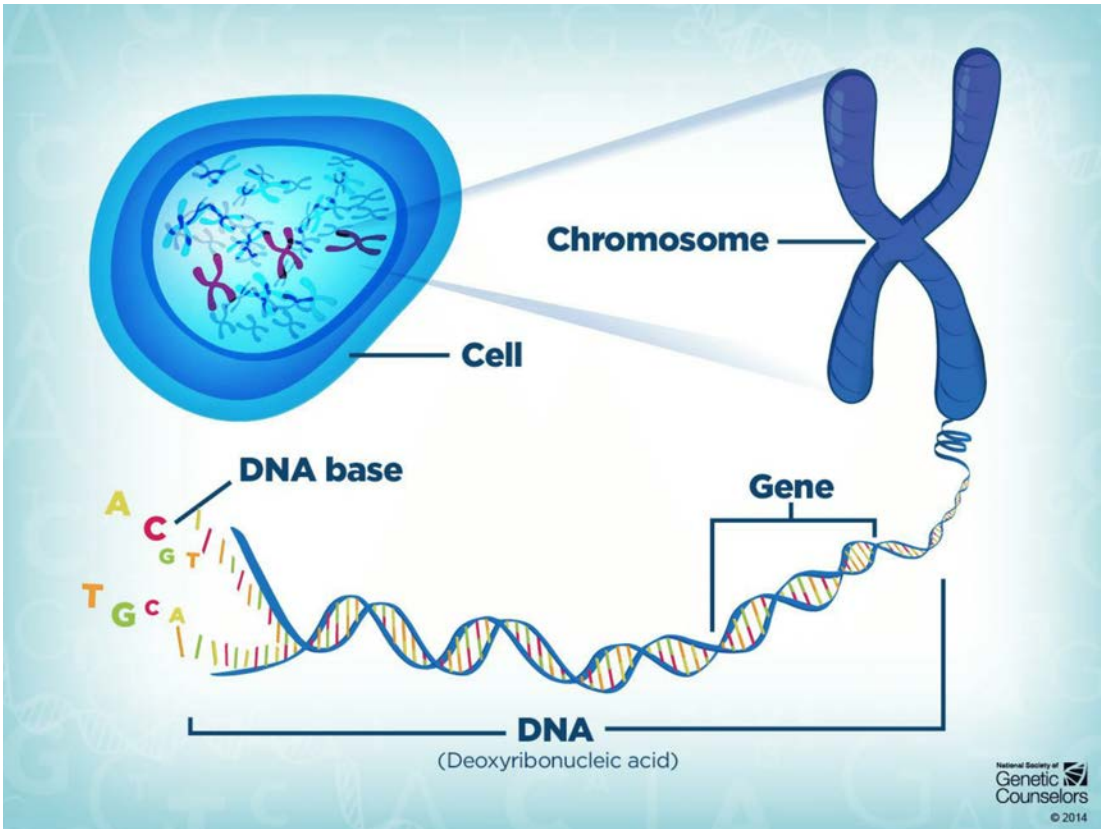
If you are not already a part of Searchlight's online community, please visit our website at www.simonssearchlight.org/. There you can learn more about 16p11.2 deletion syndrome by watching informational webinars, participating in research, or asking an expert any questions that this guidebook hasn't answered.

Simons Searchlight Research

In the Simons Searchlight study, families partner with researchers to share information and learn about the behavioral, psychological, physical, and medical features associated with certain genetic changes. In particular, Simons Searchlight is interested in genetic changes known to cause autism and other neurodevelopmental conditions. Sharing information with Simons Searchlight helps researchers build a vast repository of data, including de-identified medical information from you or your child. This advances our knowledge about genetic causes of these conditions. Our resource is used by researchers across multiple medical disciplines.

Definition of a 16p11.2 Deletion

The human body is made up of millions of cells. In every cell there is a copy of our DNA, which contains all of our genetic information. DNA is written in a code consisting of four base “letters” — A, C, T, G — that the body reads like sentences. The “spelling,” or order, of these letters is important to give the instructions for everything our body needs to function. Our DNA sentences are very long, so the DNA needs to be coiled up into packages, or structures we call chromosomes.



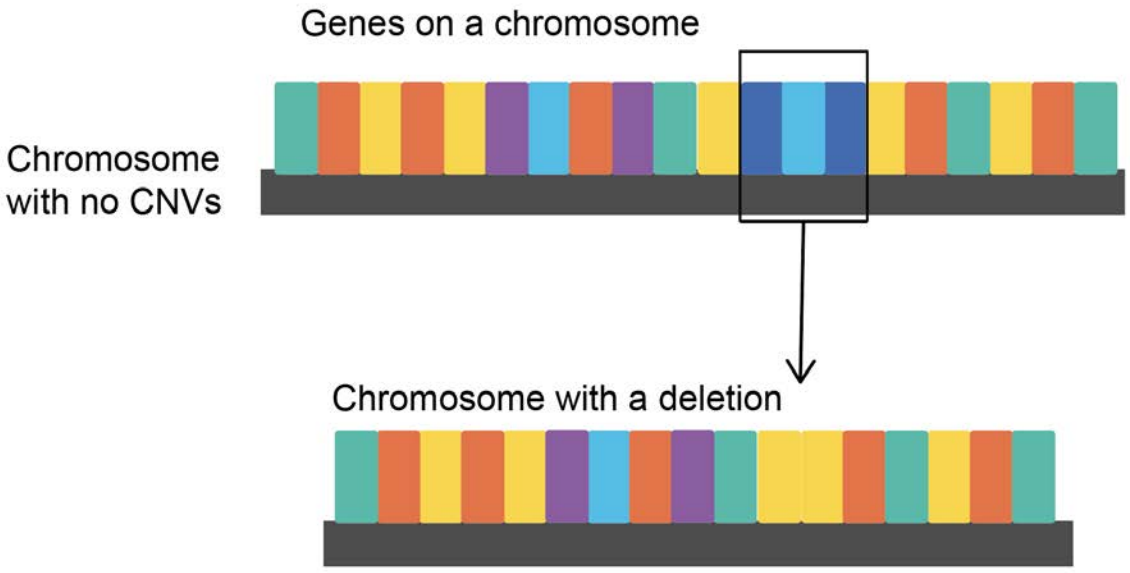
Humans have 46 chromosomes: 23 chromosomes from mom and 23 chromosomes from dad, this is why most of us look like both our parents. We label the pairs of chromosomes 1 through 22, with the last pair being the sex chromosomes. These are made up of either two X chromosomes (female) or one X and one Y chromosome (male).

Humans have more than 20,000 genes. Each chromosome has a few hundred to thousands of genes. Each gene provides a set of instructions to make the building blocks of the human body.

When a person has a 16p11.2 deletion, typically we find that a group of about 29 genes (~600,000 letters of DNA code) is missing, or deleted. This means that one of the pairs of chromosomes has the expected number of genes, while the other chromosome is missing information. Researchers now know that this section of chromosome 16 contains genes that play an important role in health, development, and brain function.

What Is a Copy Number Variant (CNV)?

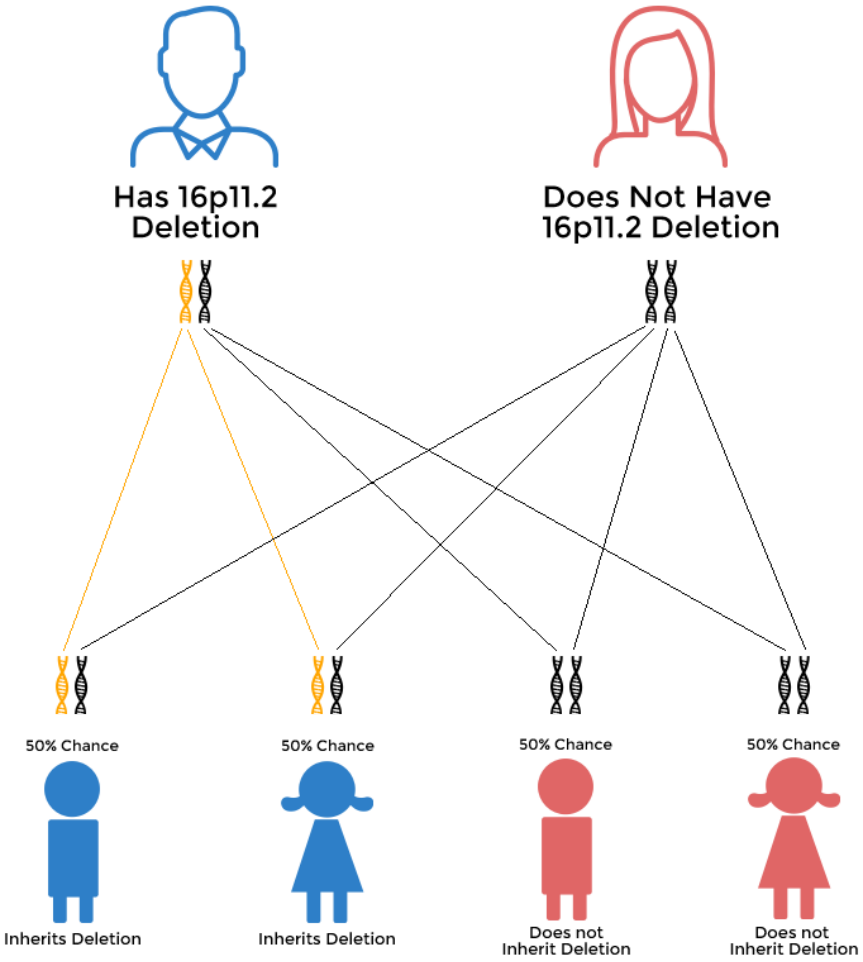
The 16p11.2 deletion is also often referred to as a copy number variant, or **CNV**. A CNV is a difference in the amount of genetic material. Since most people have two copies of their genetic material (one copy from mom and one copy from dad), a **deletion** of genetic material (a missing section of a chromosome) is considered a CNV.



The picture above shows different genes in blocks of colors along **one** chromosome. The deletion is shown here as a missing set of colored blocks. Someone with a 16p11.2 deletion will have one chromosome with a deletion and one chromosome without a deleted section.

Inheritance

The 16p11.2 deletion can happen in either of two ways. It can be brand new in the family, in which case it is called a *de novo* change. Most often, 16p11.2 deletions are *de novo*. Studies have found that close to three out of four (75%) of children with a 16p11.2 deletion did not inherit it from mom or dad. In some families, the deletion is inherited. That is, either mom or dad also has the 16p11.2 deletion and passed it on to their child.



When a child is found to have a 16p11.2 deletion, their parents are often offered genetic testing.

If a parent is found to have a deletion, it means that any of their children have a 50% chance of inheriting it.

In the example at left, dad is shown to have a 16p11.2 deletion (shown in yellow). Of his four children, one son and one daughter inherited the deletion, and his other son and daughter did not inherit it.

If one of the parents has the deletion, it is possible that other family members, including aunts, uncles, and grandparents, have the deletion as well. There are tests that can be done during, or after pregnancy with the next child to find out if this child will have the 16p11.2 deletion that the parent carries. Talk to your genetic counselor about these testing options.

How Is a 16p11.2 Deletion Found?

Children diagnosed with 16p11.2 deletion syndrome have had genetic testing. There are different types of genetic tests, and the ones we talk about here are able to detect a typical 16p11.2 deletion.

Genetic testing has improved over the past 20 years, and we are now able to identify many different types of genetic changes. Genetic tests now include a **chromosome microarray test**, which looks for copy number variants across a person's chromosomes and can look for many different copy number changes at the same time. A chromosome microarray test is often the first test ordered when a health care provider suspects that there may be a genetic reason for a child's issues.

Another test, **called fluorescence in situ hybridization** (FISH*)*, can also detect a 16p11.2 deletion. The FISH test is only used once a specific chromosomal condition is suspected or identified. Currently, it is used primarily to determine if other relatives also carry the genetic change that was identified in the family.

How Common Are 16p11.2 CNVs?

A loss of material from 16p11.2 is one of the most common chromosome conditions. Several research studies indicate that about one in 2,300 people in the general population have a 16p11.2 deletion.

About 1 in 200 people with autism has a 16p11.2 deletion. However, it is important to remember that not all children with 16p11.2 deletion will have autism. Many people with the deletion are neurotypical.

Different Deletions, Different Groups

Not everyone with a 16p11.2 deletion is the same. Different 16p11.2 deletions have different names, according to the location and the amount of genetic material deleted.

Group 1 has the "typical," or most common, 16p11.2 deletion (shown in dark red below). This guidebook is tailored to individuals with a group 1 deletion.

Group 2 has deletions that do not overlap with group 1 and are found closer to the end of chromosome 16, which is called the distal 16p11.2 region. Group 2 distal 16p11.2 deletions are further grouped by size and location. Group 2a is a larger deletion (indicated in blue), and group 2b is a smaller deletion on the distal edge of the group 2 region (shown in bright red).

Group 3 (shown in green) is a larger deletion that include all of the genetic material missing in group 1 and group 2.

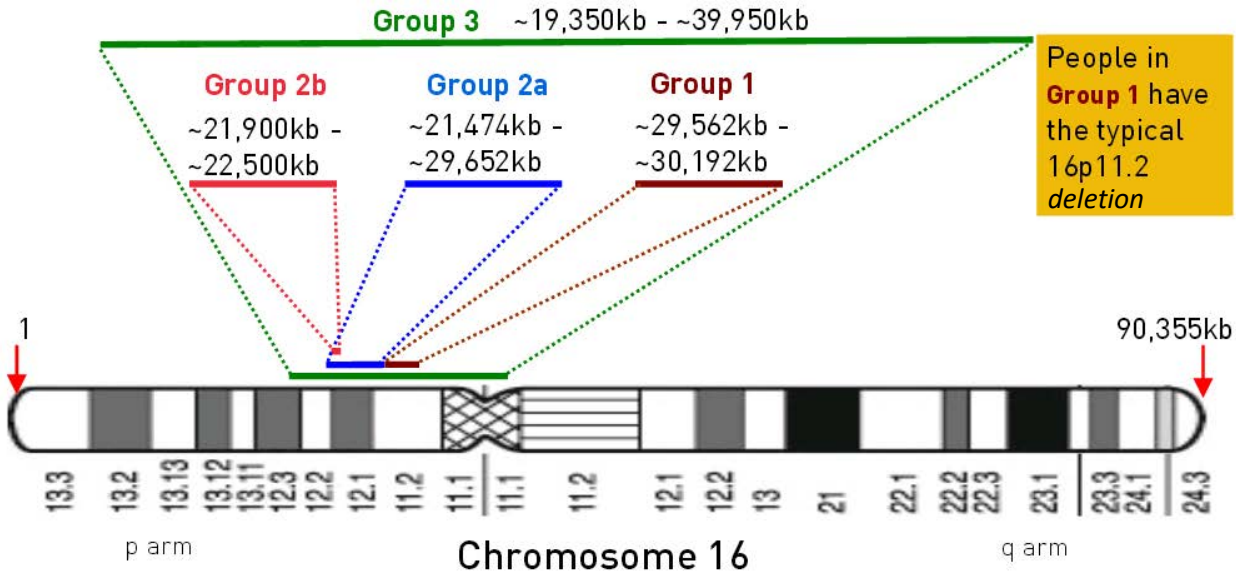


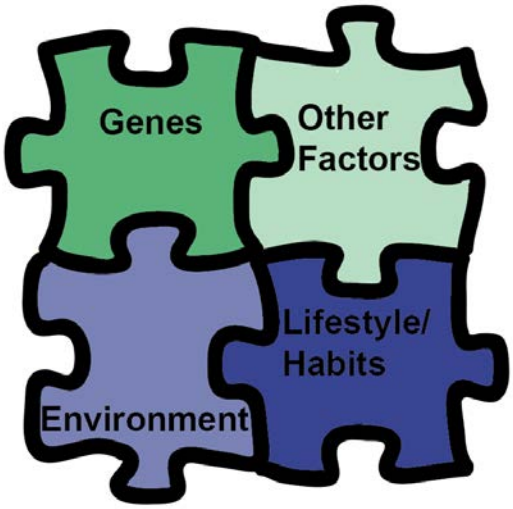
Image courtesy of Unique. More information on deletion groups 2 and 3 may be found in Unique's microdeletion guidebook.

Common Features of 16p11.2 Deletion Syndrome

What Makes Something a "Syndrome"?

A syndrome is a recognizable pattern of features, signs and symptoms (such as medical, developmental, and behavioral concerns or characteristic physical findings) that are due to the same underlying cause. The characteristics of 16p11.2 deletion syndrome include a wide range of developmental and behavioral concerns, as well as some specific medical conditions. Importantly, the syndrome can be quite variable from one person to the next, and not everyone with the deletion will have the same abilities or challenges.

Some people with a 16p11.2 deletion have few reported problems, apart from a mild learning disability in school, for example. Other people with a deletion may have more significant learning and behavioral issues or medical problems. The reasons for the variation among individuals with the same (or a similar) deletion are still being studied. At this point, we know that several factors contribute to how a person is affected by a 16p11.2 deletion, such as other genes in the body and environmental factors.



While it is possible for someone with a 16p11.2 deletion to have no noticeable health or behavioral problems, this is not usual. *The majority of people with 16p11.2 deletion syndrome have at least some of the features described below.*

For young children, it is helpful to know the range of medical, learning, and behavioral issues that can occur in 16p11.2 deletion syndrome, so that you can help your child receive the right supports and care. The most common features fall into the categories of developmental delay, behavior, growth patterns, and other medical issues, which we discuss below.

Differences in Development

Thinking and Learning Skills (Cognition)

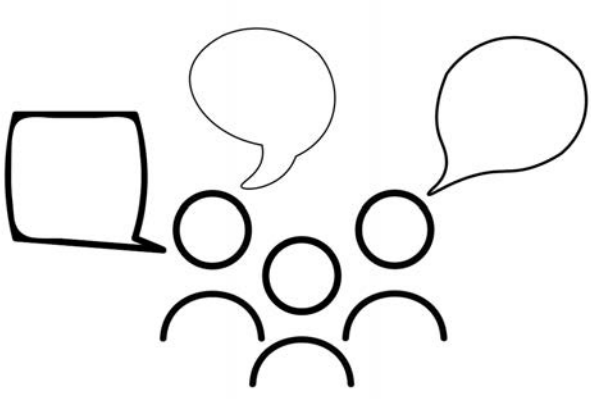
Many children with 16p11.2 deletion syndrome have difficulties with learning.

Measures of cognitive ability are often lower in children with the deletion than in their other family members without the deletion. About 25% do not outgrow their learning delays. If learning delays are present across several areas of functioning and the child does not catch up at elementary school age, they may receive a diagnosis of intellectual disability and require special education classes and supports for daily living. In most cases, though, it is language-based learning that is most impaired.

Speech and Language

Speech and language problems are the most common features seen in 16p11.2 deletion syndrome. The majority (71%) of people with the syndrome have a confirmed speech or language disorder.

Language delay may be one of the first signs of 16p11.2 deletion that parents notice in their child. Most children go on to be diagnosed with a speech sound disorder or language disorder, or both, without intellectual disability. Children with a speech sound disorder do not use all of the speech sounds expected for their age group or may have trouble combining speech sounds. For example, the word “spoon” may be pronounced as “soon,” and the child may be difficult to understand. A language disorder is a significant difficulty with expressive language, including learning new words or making sentences, and/or with receptive language, including understanding others. Most children with 16p11.2 deletion syndrome have more trouble with expressive language than receptive language. Families have told us that using sign language and communication devices can help with early communication skills.



As the child grows, it is important for school providers to also monitor for learning disabilities in reading and writing. These commonly follow language impairment and require special education services and targeted approaches to teaching reading.

Motor Skills

Many children with a 16p11.2 deletion have trouble with motor skills development.

Children in Simons Searchlight showed significantly impaired motor coordination in testing, and 58% were diagnosed with developmental coordination disorder. Neurological differences in people with 16p11.2 deletion syndrome are thought to cause problems with coordination. Parents often describe their children as clumsy. Interestingly, many more people with 16p11.2 deletion syndrome are either left-handed or able to use right and left hands equally, as compared with the general population. Scientists believe that this is probably due to differences in the way their brains developed. Low muscle tone (hypotonia) is also frequently seen in infancy.

Behavior

Autism Spectrum Disorder

About one in five individuals with the 16p11.2 deletion have a clinical diagnosis of autism.

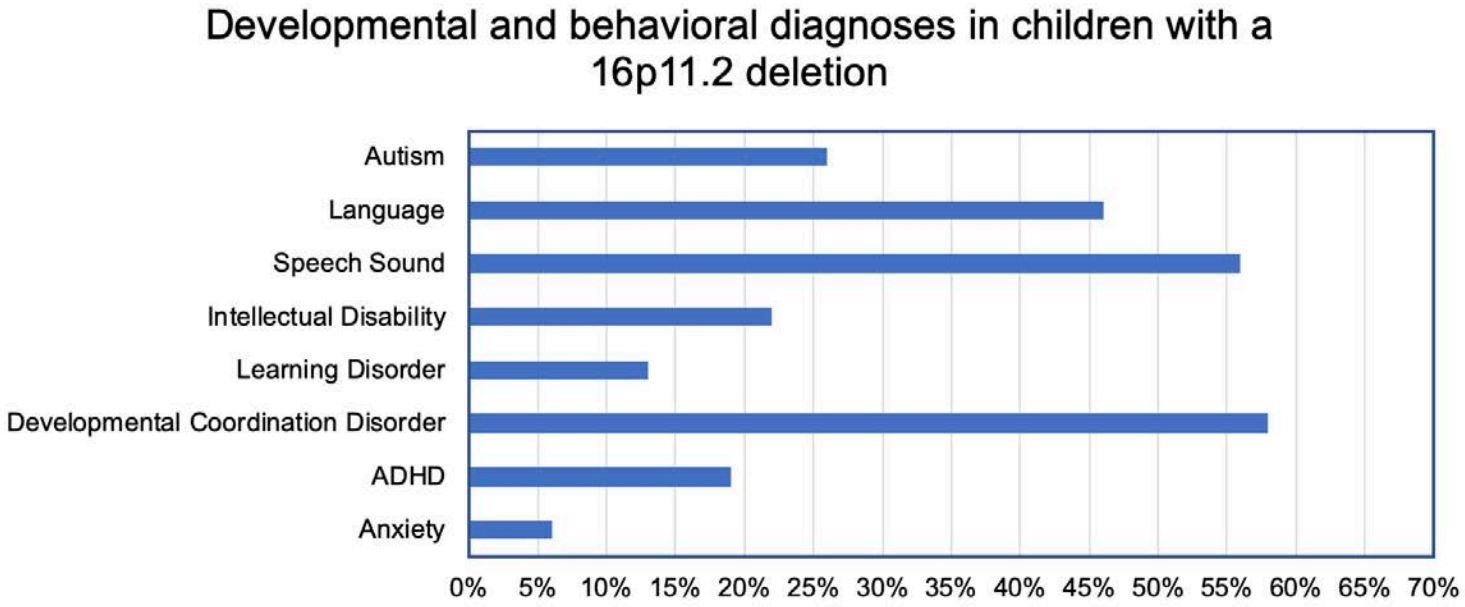
16p11.2 deletions are often found in people diagnosed with autism; but not everyone with 16p11.2 deletion syndrome will be diagnosed with autism. In fact, even though autism is probably one of the best-known features of 16p11.2 deletion syndrome, it is not the most common.

More commonly, a child with the deletion will have some behaviors that are similar to those seen in autism, such as restricted and repetitive behaviors. For example, the child may feel most comfortable doing certain activities over and over or may be intensely interested in one television show or activity. Many children with the deletion are described as less mature socially, but they do not have the unusual or disengaged quality of interactions that children with autism do. The types of language difficulties seen in children with 16p11.2 deletion are usually also different than those seen in autism. If a parent wonders whether their child has autism, testing as early as possible is recommended, to make sure the child receives therapies and school services that are a good fit for them.

Other Behavior Issues

The second most common behavior issue in children with 16p11.2 deletion is attention deficit hyperactivity disorder (ADHD), affecting about one in five children. It is also estimated that one in five children is taking medication for mood, attention, or behavior.

The graph below is a summary of clinical diagnoses in 78 children with a 16p11.2 deletion in the Simons Searchlight study.

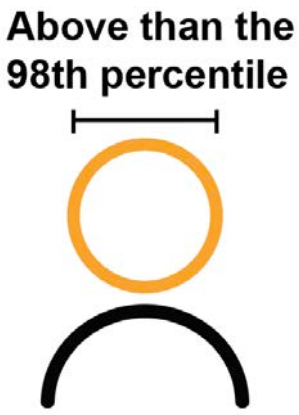


Growth Patterns

Increased Head Size

A larger head is common in people who have the 16p11.2 deletion.

In many cases, a larger-than-average head does not directly cause neurological problems. But researchers are trying to understand how having a larger head may affect brain structure and function.



Feeding Difficulties

Trouble with feeding has been reported by some parents for their child's first few weeks or months.

While some children feed without any issues, others have trouble latching, sucking, and swallowing. These feeding problems can make it difficult for infants to gain weight early in life. To help with this issue, some babies have used a modified nipple on the baby bottle that is designed to help smaller babies get more milk. In extreme cases, feeding tubes are used to make sure an infant gets the necessary nutrition.

BMI (Body Mass Index)

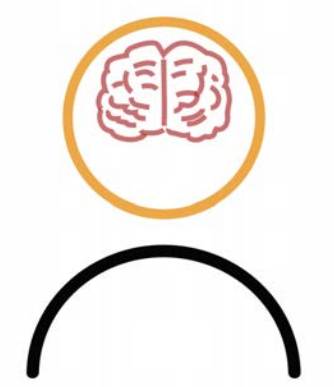
$$\text{BMI} = \frac{\text{Your Weight}}{(\text{Your Height})^2}$$

Although some children with a 16p11.2 deletion may start out having trouble gaining weight, becoming overweight can be an issue as they get older.

BMI is a measure of a person's weight (kilograms) relative to their height (meters). As children with a 16p11.2 deletion get older, their BMI tends to be above average. You may find it helpful to consult with a dietitian about how to support your child in maintaining a healthy weight.

Neurological Issues

Neurological Exam Findings



In neurological exams performed in clinic in Simons Searchlight, the most common findings in individuals with a 16p11.2 deletion included low muscle tone and overactive reflexes, or nerve impulses. These problems mean that it's important for a child to have occupational and physical therapy evaluations.

Brain Structure and Function

As part of the initial Simons Searchlight study, people with a 16p11.2 deletion had magnetic resonance imaging (MRI) scans to study brain structure and function. People with a deletion tend to have larger brain size or volume than their family members and others who do not have the deletion. They may have other differences in brain structure as well. Most of these brain differences do not require any treatment.

Seizures

About 29% of people with a 16p11.2 deletion have seizures.

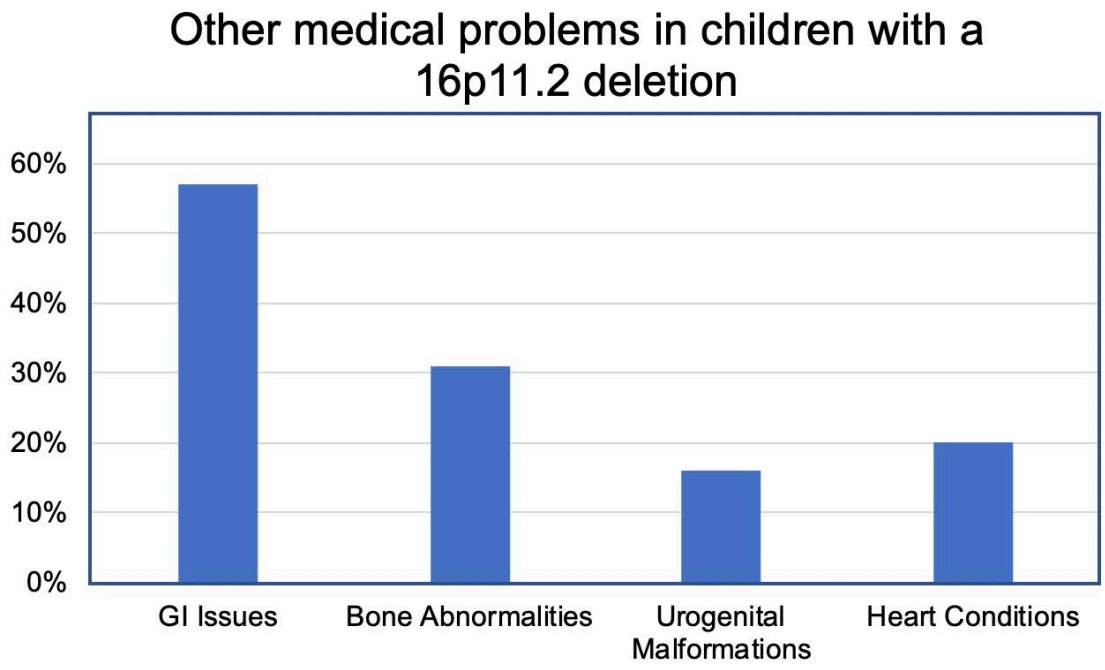
The kinds of seizures most commonly seen in people with a deletion are grand mal (generalized tonic-clonic, whole body convulsions) and focal seizures. All seizures are caused by abnormal electrical activity in the brain. Generalized seizures involve both sides of the brain. Focal, or partial, seizures occur when the electrical activity occurs in a limited area of the brain. A person may have more than one type of seizure. Some seizures, such as absence seizures, can be subtle and not easily recognized. In some children, an absence seizure may look like the child is "zoning out" or daydreaming. If you suspect your child is having seizures, ask your health care provider whether they should be evaluated by a neurologist or given an electroencephalogram (EEG) test. Some families find it useful to take pictures or videos of their child during seizure-like activity. These recordings may help the neurologist understand and diagnose what your child is experiencing.

Other Medical Problems

Other medical issues that are found are shown are summarized in the table and graph below.

This data was gathered from 215 individuals with a 16p11.2 deletion in Simons Searchlight. The most frequent problems reported were gastrointestinal problems (such as heartburn) and scoliosis (a curved spine), which should be monitored by the doctor as they grow. Also, children with the deletion may be prone to ear infections and respiratory infections. In addition to epilepsy, a smaller number of individuals with the deletion are reported to have paroxysmal dyskinesia syndrome (repeated, brief involuntary movements triggered by sudden voluntary movements).

Other medical problems	How common is it in a person with a 16p11.2 deletion?	Description of health issue
Gastrointestinal (GI) problems	57%	GI problems include constipation, gastro-esophageal reflux disease (GERD), and diarrhea during childhood.
Bone abnormalities	31%	Scoliosis, the most common abnormality, is curvature of the spine that develops over time, often in adolescence. Other abnormalities may be seen in fingers, feet, or the chest.
Urogenital malformations	16%	Differences in the growth/development of the male or female genitalia, kidneys, or urinary system.
Heart conditions	20%	Including atrial septal defects, ventricular septal defects, Shone's complex, and tetralogy of Fallot. Heart conditions are seen in 1% of all babies at birth, but they are more common in babies who have a 16p11.2 deletion.



Adult-Onset Conditions

The most common difficulties experienced by adults with 16p11.2 deletion are obesity, emotional issues, and side effects of medications used to treat these conditions. One very small study showed that adults had continuing difficulties with speech. More research is needed in adults, but very few adults with 16p11.2 deletion have been identified.

Evaluations After Initial Diagnosis[1]

There are not now any published guidelines for what evaluations should be done immediately after diagnosis. What tests should be ordered mainly depends on the child's symptoms. These are suggestions based on symptoms of individuals with 16p11.2 deletion. The recommendations below are based on symptoms common in people with a 16p11.2 deletion.

1. Regular check-ins with pediatrician
    a. Measure height and weight at every visit with the pediatrician to monitor growth and BMI
2. Routine clinical exam and broad review of all organ systems
    a. Consultation with a geneticist and/or genetic counselor is recommended
3. Cognitive and behavioral testing to assess development
4. Consider consultation with a neurologist
    a. If the history suggests the possibility of seizures, consider EEG testing
    b. If there's a history of severe headaches, neck pain, and/or trouble with swallowing, consider a brain MRI
5. If a physical exam shows scoliosis, X-ray of the spine
6. If a heart murmur is found, consider evaluation and echocardiogram by a cardiologist
7. Consider a hearing evaluation
8. In patients who are overweight or obese, screening for hypertension and diabetes

[1] Miller DT, Chung W, Nasir R, *et al.* 16p11.2 Microdeletion. 2009 Sep 22 [Updated 2015 Dec 10]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK11167/

Ongoing Follow-Up and Management[2]

Different people with a 16p11.2 deletion, even members of the same family, may have different symptoms. Each person's treatment should be targeted to findings identified by a physician. The physician will make referrals to other medical specialists based on specific symptoms. Specialists may include a developmental/behavioral pediatrician, pediatric neurologist, and a medical geneticist.

Early intervention can lead to improved outcomes.

Routine Management

1. Monitoring of height, weight, and BMI.
2. Monitoring for abnormal movements, staring spells, or other events of concern for possible seizures.
3. Monitoring for headache (especially at the back of the head), neck pain, and other symptoms such as gait abnormalities, scoliosis, and trouble swallowing. If your child has these symptoms, consider a consultation by a neurologist.
4. Annual clinical screening for scoliosis until about the age of 20, when your physician believes your child's development is complete.
5. Annual evaluation and monitoring of hearing in first three years of life.
6. Periodic reevaluation by a medical geneticist to inform the family about new developments and/or recommendations.

[2] Miller DT, Nasir R, Sobeih MM, et al. 16p11.2 Microdeletion. 2009 Sep 22 [Updated 2015 Dec 10]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK11167/

Symptom-Based Management

1. Many children with a 16p11.2 deletion have neurodevelopmental disabilities. So referral to a clinical psychologist or developmental pediatrician is suggested. Children under age 6 should have psychological and neuropsychological assessments every year. Children aged 6 and older should have a psychological evaluation every three years and at major transition points during childhood. They may benefit from speech and language therapy, occupational therapy, and physical therapy. Because expressive language delays are common, speech therapy and augmentative and assistive means of communication should be considered early.
2. Children with a 16p11.2 deletion, including those with autism, may also benefit from behavioral, social, and educational interventions. Guidelines for ongoing care for children with autism are available from the American Academy of Pediatrics.
3. Weight management and nutrition counseling are an important part of care for people with a 16p11.2 deletion
4. Brain and spine MRIs should be considered if there are symptoms that suggest a Chiari I malformation or spinal cord dysfunction. These symptoms include gait abnormalities, scoliosis, and trouble swallowing.
5. A pediatrician should screen for and monitor scoliosis annually.
6. If the child has repeated ear infections (three or more in one year), ear tubes should be considered.
7. People with 16p11.2 deletion have more frequent infections. Rarely, the 16p11.2 deletion has been associated with severe combined immunodeficiency (SCID). If a child has more than six infections in a year, talk with the pediatrician about an evaluation by an immunologist.

Living with 16p11.2 Deletion Syndrome

Growing Up

Over time, you may feel as if there is a gap between your child with a 16p11.2 deletion and your other children, or that your child isn't able to keep up with peers. The gap in academic skills between a child and their typical peers tends to widen as they grow up. Children with the deletion often still learn and achieve goals at school, but it may be at their own pace. It's important to talk with your child's teacher about developing an Individualized Education Program (IEP) that meets your child's learning style and needs, but also challenges them.

Services

Most children with 16p11.2 deletion syndrome receive services from several kinds of professionals. The services needed depend on your child's symptoms. You are going to play an important role in directing, organizing, and advocating for your child's care. One or more of the following professionals may help you care for your child:

Genetic counselors **and** ***geneticists*** work with families with many different genetic diagnoses. Genetic counselors can educate families about the 16p11.2 deletion and discuss how the diagnosis affects their family. They can also coordinate genetic testing for family members and identify appropriate support resources. To locate a genetic counselor near you, visit www.nsgc.org and click on "Find a Genetic Counselor."

A geneticist may help with the initial diagnosis, medical assessment, and coordination of appropriate referrals based on what is known about a child's medical concerns related to the diagnosis.

Pediatric neurologists will be involved if there are concerns that seizures are occurring or if other neurological issues are present. If your child is having seizures, a neurologist can monitor and manage them.

Occupational therapists work with people to help improve their ability to perform everyday tasks. They can evaluate the impact of the 16p11.2 deletion on daily activities at home, school, or work. For example, many children have trouble with their fine motor skills. Children with a 16p11.2 deletion may struggle with handwriting, using scissors, turning pages, or using a computer. An occupational therapist can work with your child to improve their skills in areas like these.

Physical therapists can evaluate and provide therapy to improve motor skills and coordination. Therapy can include stretches, exercises, and body movements that increase a person's motor abilities and coordination.

Nutritionists can help children manage their weight. Having 16p11.2 deletion syndrome does not mean the person will definitely be overweight, but it may take more work for them to control their weight. A nutritionist can help a family develop the right eating and weight management plan, including appropriate portion sizes, for a child with a 16p11.2 deletion.

Developmental pediatricians are physicians who specialize in developmental and behavioral disorders in children, including autism, developmental delay, and intellectual disability. They can recommend medical treatments and behavioral interventions, and they can provide information about school and intervention services in your local area.

Psychiatrists are experts in the diagnosis and treatment of ADHD, obsessive compulsive disorder, schizophrenia, and other mental health conditions. While there is no cure for these disorders, psychiatrists can prescribe and monitor medications to treat psychiatric symptoms.

Psychologists and neuropsychologists can assess, diagnose and treat a wide range of cognitive, learning, emotional, and behavioral problems.

Social workers help families to coordinate care and can provide supportive counseling.

Primary care providers (**PCPs**) serve as the "quarterbacks" for a child's overall medical care. A child with a 16p11.2 deletion should still go for a wellness check-up every year, just like any other child. In addition, a PCP can coordinate specialty referrals and make sure that any necessary lab tests are done.

Applied behavior analysis (ABA) psychologists focus on understanding behavior and how it is affected by a child's environment, including interactions with other people. ABA-based techniques are used to teach academic, social, communication, motor, and adaptive skills. Research shows that ABA is helpful for children with autism, and for teaching language and other skills to children with developmental delay/intellectual disability.

Speech-language pathologists (SLPs) Many people with 16p11.2 deletion syndrome work with a SLP. SLPs help children and adults with a variety of communication, reading, and swallowing problems. The speech and language diagnoses that are common among children with a 16p11.2 deletion are listed below (from the American Speech Language Hearing Association).

Speech Disorders

- Speech sound disorders (articulation)
- Control of the muscles of the face and mouth (orofacial myofunctional disorders, dysarthria)
- Difficulty planning and coordinating the movements needed to make speech sounds (apraxia)
- Stuttering
- Voice disorders

Language Disorders

- Difficulty understanding language (receptive language)
- Difficulty using language (expressive language)
- Social communication disorder (pragmatic language)

Other Disorders Treated by Speech-Language Pathologists

- Deafness and hearing loss. Therapy includes developing lip-reading and speech skills, and/or using alternative communication systems
- Oral-motor disorders: weak tongue and/or lip muscles
- Swallowing/feeding disorders

If you are concerned about your child's communication skills, you may wish to consult an SLP. Your school/school district should have a certified SLP who can observe and/or test your child for speech and language difficulties. Your local children's hospital will also have certified SLPs on staff. You will find them in departments such as the department of hearing and speech, clinic for communication disorders, or developmental clinic. Your child's primary care provider can also recommend an SLP. A search engine from the American Speech-Language-Hearing Association can help you find a certified SLP in your area: http://www.asha.org/findpro/.

If a child has been diagnosed with a speech or motor delay, he or she may be eligible to receive early intervention services. The American Academy of Pediatrics says that "early intensive behavioral and educational intervention can make a significant positive impact on long-term outcomes." Early intervention can include many different types of therapies.

What to Tell Teachers

Children with special learning and behavioral needs often receive an Individualized Education Program (IEP) through their school to help them reach their full learning potential. While not all children with a 16p11.2 deletion have autism, most will have language disorders, developmental delay, intellectual disability, or learning disability and will need an IEP at school. It's important to inform your child's teachers about your child's needs. It may be helpful to give them a copy of this guidebook so they can better understand 16p11.2 deletion syndrome.

A request for the school district to conduct a comprehensive psychoeducational assessment and tests to identify strengths/weaknesses is a good starting point. If you would like your child's school to complete this assessment, you must submit your request in writing. The school should monitor your child's progress, and your child should receive an IEP and/or curricular modifications. Outside school, many children benefit from additional help from a tutor or aide to encourage and reinforce skills.

Since the vast majority of children with 16p11.2 deletion have language impairments, reading disabilities are also common, and special education services and targeted interventions for reading and writing are often necessary.

Some children participate in a general education classroom and may receive supplemental learning services. Other children may benefit most from participation in a special education classroom. Picking the right school setting for your child is an important decision that should involve you, your child's teachers, administrators, and therapists.

Some children with 16p11.2 deletion syndrome may not have significant learning problems but may still benefit from receiving accommodations such as receiving extra time on tests or taking tests in a quiet or private space. These children often receive these services through a 504 plan. The school system can provide a 504 plan.

Adaptive Technologies

There are numerous technologies that can aid a child with 16p11.2 deletion syndrome with learning and language skills. To find out what adaptive technologies may help your child most, request an assistive technology (AT) or augmentative and alternative communication (AAC) evaluation from a skilled clinician.

When selecting a speech device, take the following points into account:

- The child's interest in and comfort level with the technology
- The child's ease in learning about and using the technology
- The degree to which the technology relates to the child's strengths
- The extent to which the child is able to use the technology independently and troubleshoot as necessary
- The effectiveness of the technology in compensating for specific difficulties as compared with alternative strategies

(Information adapted from Assistive Technology: A Parent's Guide.)

Learn more about these devices here.

Tablets and iPads can now be used in assistive technology. While Simons Searchlight researchers and clinicians do not endorse any specific assistive devices, you may wish to watch our webinar on AAC and on selecting an iPad.

In this webinar, Kelly A. Johnson, Ph.D., of the University of Washington Autism Center discusses how to choose a tablet and applications (apps) for your child to use as a communication device. For example, it's important to consider what size tablet will best fit your child's needs. For example, a child with poor hearing will benefit from having a larger device with larger speakers. The amount of storage needed, built-in features, accessories, and of course cost are all things to take into consideration when picking out an iPad.

Once you have an iPad for your child, in order for them to get the full benefit you will both need expert guidance on which apps to use to reach goals. Apps can be used for communication, social interaction, education, and even distraction during medical procedures. When choosing apps for your child to use, bear in mind that the ones that cost money are not necessarily the most useful. While many apps cater to children with special needs, mainstream apps can be helpful as well. The iPad itself has a lot of useful tools built in, such as video chat and the internet connection. If a child is using an iPad for communication, no one other than the child should use it. Also bear in mind that the iPad is not the only useful technology out there.

Learn more about the latest and most liked apps at:

- Mac/Apple http://www.apple.com/education/special-education/ios/
- PC/Android https://play.google.com/store/search?q=special%20education&c=apps

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We must also thank the entire Simons Searchlight study team — including the investigators, study coordinators, project managers, and administrators, as well as our website developer, Tempus Dynamics — who have dedicated many hours to meeting with families and making sure the project runs smoothly. Their work, along with that of other collaborators, has led to numerous publications about 16p11.2 CNVs (listed below).

Most importantly, we owe a huge debt of gratitude to the many families who have participated in the Simons Searchlight study. Since 2010, over 200 people with a 16p11.2 deletion have participated in this research project, with many families still contributing updates to this day. This guidebook has been made possible thanks to the time, energy and information they have committed to sharing with us.

A special thank you is extended to our 2015 summer intern, Elly Brokamp, for developing the initial draft of this comprehensive guide. Thank you for your contribution, Elly. Your work has had a tremendous impact.

Resources

Web resources
The Simons Searchlight website www.simonssearchlight.org
The Simons Searchlight (and Simons VIP Connect) webinars archive www.youtube.com/c/simonssearchlight
Simons Searchlight 16p11.2 deletion article summaries www.simonssearchlight.org/research/what-we-study/16p11-2-deletion/
Unique – Understanding Chromosome Disorders www.rarechromo.org
GeneReviews – 16p11.2 Microdeletion www.ncbi.nlm.nih.gov/books/NBK11167/
Genetics Home Reference – 16p11.2 deletion syndrome www.ghr.nlm.nih.gov/condition/16p112-deletion-syndrome

References

Articles Using Simons Searchlight Data

Year Published	Title	Authors
2012	Simons Variation in Individuals Project (Simons VIP): A genetics-first approach to studying autism spectrum and related neurodevelopmental disorders www.ncbi.nlm.nih.gov/pubmed/22445335	The Simons VIP Consortium
2012	A 600 kb deletion syndrome at 16p11.2 leads to energy imbalance and neuropsychiatric disorders www.ncbi.nlm.nih.gov/pubmed/23054248	Zufferey *et al.*
2014	Aberrant white matter microstructure in children with 16p11.2 deletions www.ncbi.nlm.nih.gov/pubmed/24790192	Owen *et al.*
2014	Opposing brain differences in 16p11.2 deletion and duplication carriers www.ncbi.nlm.nih.gov/pmc/articles/PMC4138332/	Qureshi *et al.*
2014	Eating in the absence of hunger but not loss of control behaviors are associated with 16p11.2 deletions www.ncbi.nlm.nih.gov/pubmed/25234362	Gill *et al.*
2015	The role of parental cognitive, behavioral, and motor profiles in clinical variability in individuals with chromosome 16p11.2 deletions www.ncbi.nlm.nih.gov/pubmed/25493922	Moreno-De-Luca *et al.*
2015	The cognitive and behavioral phenotype of the 16p11.2 deletion in a clinically ascertained population www.ncbi.nlm.nih.gov/pubmed/25064419	Hanson *et al.*

2015	Genotype-first analysis of the 16p11.2 deletion defines a new type of “autism” www.ncbi.nlm.nih.gov/pubmed/25843334	Duyzend and Eichler.
2015	A potential contributory role for ciliary dysfunction in the 16p11.2 600 kb BP4-BP5 pathology www.ncbi.nlm.nih.gov/pubmed/25937446	Migliavacca *et al.*
2015	Modulation of mu attenuation to social stimuli in children and adults with 16p11.2 deletions and duplications www.ncbi.nlm.nih.gov/pubmed/26213586	Hudac *et al.*
2015	Abnormal auditory and language pathways in children with 16p11.2 deletion www.ncbi.nlm.nih.gov/pubmed/26413471	Berman *et al.*
2016	Mirror extreme BMI phenotypes associated with gene dosage at the chromosome 16p11.2 locus www.ncbi.nlm.nih.gov/pubmed/21881559	D’Angelo *et al.*
2016	Deletion and duplication of 16p11.2 are associated with opposing effects on visual evoked potential amplitude www.ncbi.nlm.nih.gov/pubmed/27354901	LeBlanc and Nelson.
2016	Maternal modifiers and parent-of-origin bias of the autism-associated 16p11.2 CNV www.ncbi.nlm.nih.gov/pubmed/26749307	Duyzend *et al.*
2016	A highly penetrant form of childhood apraxia of speech due to deletion of 16p11.2 www.ncbi.nlm.nih.gov/pubmed/26173965	Fedorenko *et al.*
2016	Auditory evoked M100 response latency is delayed in children with 16p11.2 deletion but not 16p11.2 duplication www.ncbi.nlm.nih.gov/pubmed/25678630	Jenkins *et al.*

2016	Relationship between M100 auditory evoked response and auditory radiation microstructure in 16p11.2 deletion and duplication carriers www.ncbi.nlm.nih.gov/pubmed/26869473	Berman *et al.*
2016	Reciprocal white matter alterations due to 16p11.2 chromosomal deletions versus duplications www.ncbi.nlm.nih.gov/pubmed/27219475	Chang *et al.*
2016	Emergence of a Homo sapiens-specific gene family and chromosome 16p11.2 CNV susceptibility www.ncbi.nlm.nih.gov/pubmed/27487209	Nuttle *et al.*
2016	Characterizing cognitive control abilities in children with 16p11.2 deletion using adaptive 'video game' technology: A pilot study www.ncbi.nlm.nih.gov/pubmed/27648915	Anguera *et al.*
2016	16p11.2 deletion and duplication: Characterizing neurologic phenotypes in a large clinically ascertained cohort www.ncbi.nlm.nih.gov/pubmed/27410714	Steinman *et al.*
2018	Brain MR imaging findings and associated outcomes in carriers of the reciprocal copy number variation at 16p11.2 www.ncbi.nlm.nih.gov/pubmed/28786752	Owen *et al.*
2018	Abnormal speech motor control in individuals with 16p11.2 deletions www.ncbi.nlm.nih.gov/pubmed/29352208	Demopoulos *et al.*
2018	Deep phenotyping of speech and language skills in individuals with 16p11.2 deletion www.ncbi.nlm.nih.gov/pubmed/29445122	Mei *et al.*
2018	Autism-associated 16p11.2 microdeletion impairs prefrontal functional connectivity in mouse and human www.ncbi.nlm.nih.gov/pubmed/29722793	Bertero *et al.*

2018	Quantifying the effects of 16p11.2 copy number variants on brain structure: A multisite genetic-first study www.ncbi.nlm.nih.gov/pubmed/29778275	Martin-Brevet *et al.*
2019	Psychiatric disorders in children with 16p11.2 deletion and duplication www.ncbi.nlm.nih.gov/pubmed/30664628	Niarchou *et al.*
2019	Atypical neural variability in carriers of 16p11.2 copy number variants www.ncbi.nlm.nih.gov/pubmed/31260176	Al-Jawahiri *et al.*
2019	Sensorimotor cortical oscillations during movement preparation in 16p11.2 deletion carriers www.ncbi.nlm.nih.gov/pubmed/31270155	Hinkley *et al.*
2019	Psychotic symptoms in 16p11.2 copy number variant carriers www.biorxiv.org/content/10.1101/621250v2.full	Jutla *et al.*
2019	Quantitative gait assessment in children with 16p11.2 syndrome www.jneurodevdisorders.biomedcentral.com/articles/10.1186/s11689-019-9286-9	Goldman *et al.*

Other Articles about 16p11.2 Deletion Syndrome

Year Published	Title	Authors
2008	Association between microdeletion and microduplication at 16p11.2 and autism www.ncbi.nlm.nih.gov/pubmed/18184952	Weiss *et al.*
2009	Extending the phenotype of recurrent rearrangements of 16p11.2: Deletions in mentally retarded patients without autism and in normal individuals www.ncbi.nlm.nih.gov/pubmed/19306953	Bijlsma *et al.*

2010	Evidence for a recurrent microdeletion at chromosome 16p11.2 associated with congenital anomalies of the kidney and urinary tract and Hirschsprung disease www.ncbi.nlm.nih.gov/pubmed/20799338	Sampson *et al.*
2010	Expanding the clinical spectrum of the 16p11.2 chromosomal rearrangements: Three patients with syringomyelia www.ncbi.nlm.nih.gov/pubmed/20959866	Schaaf *et al.*
2010	A new highly penetrant form of obesity due to deletions on chromosome 16p11.2 www.ncbi.nlm.nih.gov/pmc/articles/PMC2880448	Waters *et al.*
2010	Cognitive and behavioral characterization of 16p11.2 deletion syndrome www.ncbi.nlm.nih.gov/pubmed/20613623	Hanson *et al.*
2010	Recurrent reciprocal 16p11.2 rearrangements associated with global developmental delay, behavioral problems, dysmorphism, epilepsy, and abnormal head size www.ncbi.nlm.nih.gov/pubmed/19914906	Shinawi *et al.*
2010	Phenotypic spectrum associated with de novo and inherited deletions and duplications at 16p11.2 in individuals ascertained for diagnosis of autism spectrum disorder www.ncbi.nlm.nih.gov/pubmed/19755429	Fernandez *et al.*
2010	Speech delays and behavioral problems are the predominant features in individuals with developmental delays and 16p11.2 microdeletions and microduplications www.ncbi.nlm.nih.gov/pubmed/21731881	Rosenfeld *et al.*
2011	Intra-family phenotypic heterogeneity of 16p11.2 deletion carriers in a three-generation Chinese family www.ncbi.nlm.nih.gov/pubmed/21302351	Shen *et al.*
2011	Mirror extreme BMI phenotypes associated with gene dosage at the chromosome 16p11.2 locus www.ncbi.nlm.nih.gov/pubmed/21881559	Jacquemont *et al.*

2016	The number of genomic copies at the 16p11.2 locus modulates language, verbal memory, and inhibition www.sciencedirect.com/science/article/pii/S0006322315009178?via%3Dihub	Hippolyte *et al.*
2017	Rare and common variants at 16p11.2 are associated with schizophrenia www.sciencedirect.com/science/article/abs/pii/S0920996416305242?via%3Dihub	Chang *et al.*