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UNDERSTANDING GENES & CHROMOSOMES

CHAMP1-related neurodevelopmental disorders

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people with a CHAMP1-related neurodevelopmental disorder. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition.

What is a CHAMP1-related neurodevelopmental disorder?

A CHAMP1-related neurodevelopmental disorder (NDD) is an ultra-rare genetic condition caused by changes to a gene called CHAMP1. Historically, the condition has been referred to by other names, including Autosomal Dominant Intellectual Disability type 40 (MRD40) and Neurodevelopmental Disorder with Hypotonia, Impaired Language, and Dysmorphic Features (NEDHILD), so you may see these terms in older medical reports.

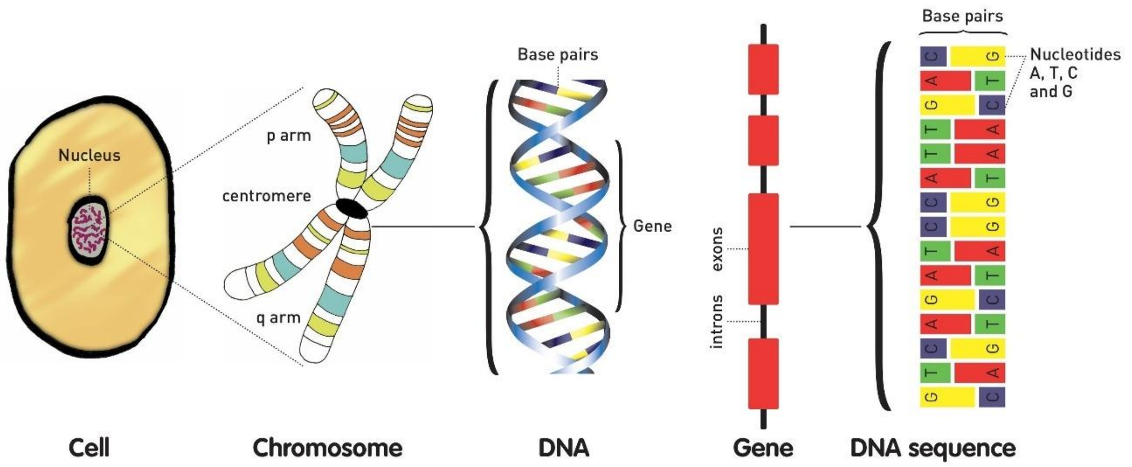
CHAMP1-related NDDs are conditions primarily characterized by developmental delay, varying degrees of intellectual disability, and significant speech and language impairment. Other core features that are very common include low muscle tone (hypotonia), motor and walking (gait) anomalies, feeding difficulties, atypical behaviours and distinctive facial features.

As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with a CHAMP1-related disorder will have all the possible features and each person with a certain feature won't necessarily be affected by it to the same level as other people with that feature.

Genes and chromosomes

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes therefore contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.

DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G, and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long.



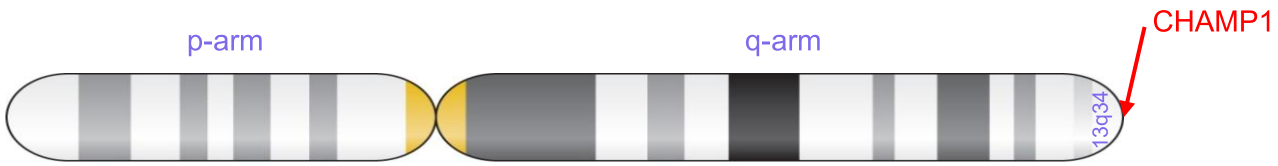
What causes CHAMP1-related NDD?

CHAMP1-related NDDs are caused by specific changes (known as pathogenic variants) to the DNA sequence of the CHAMP1 gene (CHAMP1 is an abbreviation of the gene's full name, CHromosome Alignment-Maintaining Phosphoprotein 1) or the loss of one copy of this gene due to a chromosome deletion.

Unique publishes a separate guide to deletions and microdeletions

The CHAMP1 gene is located at the end of the long 'q' arm of chromosome 13 in a region called 13q34 as shown in the image below.

Chromosome 13



We have two copies of chromosome 13 in our cells, so we also have two copies of the CHAMP1 gene. CHAMP1-related NDD occurs when only one copy of the CHAMP1 gene is affected; the second copy is fully functional. This is known as autosomal dominant since all numbered chromosomes are called autosomes and genetic conditions that occur when only one copy of an autosomal gene is affected are known as dominant.

Unique publishes a separate guide to single gene disorders – autosomal dominant inheritance

The role of the CHAMP1 protein

The CHAMP1 gene sequence is used to make the CHAMP1 protein. This protein has several fundamental jobs that are critical for our bodies to develop and function as expected. The widespread symptoms and features of CHAMP1-related NDD - including those on the brain, muscles, gut, and other systems - are a direct result of the changes to the CHAMP1 protein and their effects on its different roles in our cells.

- **Cell Division (Mitosis):** CHAMP1 protein's primary role, reflected in its name, is to act as a 'traffic control' for chromosomes during cell division. It ensures that chromosomes are correctly aligned and then separated into two new cells each time a cell divides. This process is vital for growth and development, especially in the brain, which undergoes massive and rapid cell division as it forms. When the CHAMP1 protein does not function as expected, this process can be disrupted, which may affect how different parts of the body develop.

- **Neuronal Development:** Studies have shown that CHAMP1 is essential for proper brain development. A deficiency of the protein can delay the development of neurons (brain cells) and impair their ability to migrate to the correct positions in the developing brain (Nagai 2022, Van Caugherty 2024). This directly contributes to the intellectual disability and other neurological features that people with a CHAMP1-related NDD have.

- **DNA Repair:** The CHAMP1 protein is also part of a system that helps repair damage to our DNA, specifically a type of damage called a double-strand break. This function helps maintain the stability and integrity of our genetic code.

Different types of genetic changes

The specific type of genetic change in the CHAMP1 gene is an important factor that could influence an individual's symptoms and features. Research suggests that different types of variants can affect the CHAMP1 protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with a CHAMP1-related NDD.

- **Gene Deletions:** In some individuals, one entire copy of the CHAMP1 gene is missing (deleted). This means the body has only one functioning copy of the gene to produce the CHAMP1 protein. This is called haploinsufficiency - having half the expected amount of protein is not enough for typical development. Generally, it is thought that individuals with a deletion of CHAMP1 have milder symptoms and features compared to those with gene sequence variants.

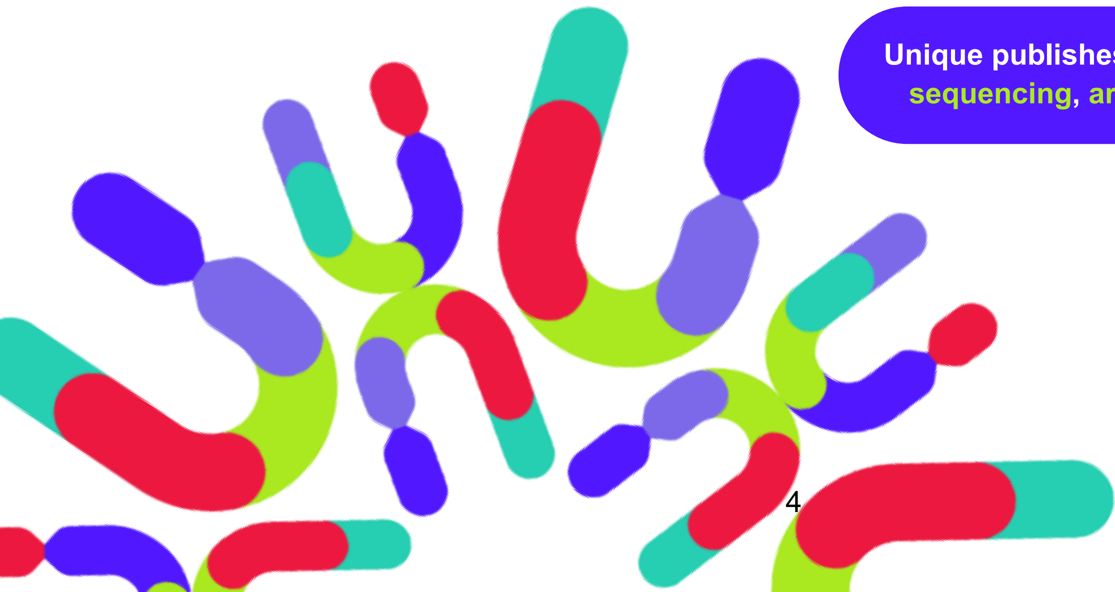
- **Gene Sequence Variants, Loss of Function (LOF):** People with a CHAMP1-related NDD are more commonly found to have a gene sequence variant, as opposed to a deletion of the entire gene. Such variants include 'nonsense' or 'frameshift' variants that have created a premature 'stop' signal in the gene's instructions. This stop signal causes the cell's molecular machinery to stop making the CHAMP1 protein before it has reached its full size. These variants are thought to be loss of function variants (LOFs), since the smaller protein is not able to perform its usual function. However, the smaller protein that is produced is thought to interfere with the normal function of the full-sized protein produced from the unaffected CHAMP1 gene on the other chromosome 13. This is known as a dominant-negative effect, rather than haploinsufficiency, as is the case for gene deletions.

- **Gene Sequence Variants, Gain of Function (GOF):** It is possible to have a different type of variant, known as a missense variant, that produces an altered protein, as opposed to a smaller protein. These altered proteins can sometimes gain a new or enhanced function, and the variants are then called gain of function variants (GOFs). CHAMP1 GOF variants are not often reported in the medical literature (Ben-Haim 2020, Amenta 2023, Yoshizaki 2024), but this type of variant can cause some different symptoms and features. So far (2025) the few people who have been found to have a missense variant, typically present at either the very mild or severe end of the spectrum dependant on the exact location of the change within the gene (CHAMP1 Research Foundation personal communication - based on 17 children/adults with a CHAMP1 missense variant).

Genetic Tests

A CHAMP1-related NDD can be diagnosed through genetic testing. Variants within the gene sequence are identified by a type of genetic test called sequencing, such as whole exome sequencing (WES) or whole genome sequencing (WGS). The loss of the gene (a deletion) can also be identified by sequencing but is more commonly found using a different type of genetic test called a chromosome microarray (CMA), also known as an arrayCGH or SNParray.

Unique publishes separate guides to DNA sequencing, arrayCGH and SNParrays



Genetic Test Results

The results of genetic testing are likely to be provided by a geneticist, a genetic counsellor or the clinician who ordered the test. Depending on the test that was carried out, someone with a CHAMP1-related disorder might have results that look like one of the following examples:

An example result of a DNA sequencing test (e.g. WES or WGS), that identifies a gene variant, is shown here for the CHAMP1 gene:

c.1192C>T p.Arg398* (A398Ter) CHAMP1 (NM_032436.3)

p.Arg398* (A398Ter)	Signifies the change to the protein: the amino acid Arginine (Arg) has been converted to a premature stop signal (signified by *) at position 398 in the sequence of amino acids that make up the protein. This is a type of nonsense variant
C>T	signifies the gene sequence change; the C nucleotide has been replaced by a T nucleotide
c.1672	signifies the base pair position of the change within the gene sequence (the position where the C nucleotide has been replaced by the T nucleotide)
CHAMP1	signifies the gene that is affected
NM_032436.3	This is the specific ‘reference sequence’ or blueprint of the gene that scientists use to identify the location of the variant

The result of a chromosome microarray (CMA) test (e.g. arrayCGH or a SNParray), that can identify deletions and duplications, is shown here for a microdeletion affecting the CHAMP1 gene:

arr[hg19] 13q34(114,857,341-114,902,670)x1 dn

arr	The analysis was by array (arr) comparative genomic hybridisation (cgh)
hg19	Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new ‘builds’ of the genome are made, and the base pair numbers may be adjusted. This means base pair positions change depending on the assembly used
13q34	The chromosome involved is chromosome 13 and the position of the deletion is in band q34
114,857,341-114,902,670	the base pairs between 114,857,341 and 114,902,670 have been shown to be deleted. Take the first long number from the second and you get 45,329 (0.045Mb or 45kb). This is the number of base pairs that are deleted
x1	means there is one copy of these base pairs, not two – one on each chromosome 13 – as you would normally expect, so this a deletion
dn	means *de novo*. The biological parents’ chromosomes have been checked and no deletion or other chromosome change has been found at position 13q34. The deletion is very unlikely to be inherited and has almost certainly occurred for the first time in this family with this child
	mat here would mean that the deletion has been inherited from the mother
	pat here would mean that it has been inherited from the father

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What features and symptoms do people with a CHAMP1-related NDD have?

As is common with many genetic conditions, children and adults with a CHAMP1-related NDD can have a range of features and symptoms. As more people are diagnosed, and information is shared, the range of features, and the likelihood of a child or adult having these features, will become clearer.

Common features

Most children with a CHAMP1-related NDD have:

- Some degree of developmental delay, often moderate to severe
- Some degree of intellectual disability (ID) or learning difficulties (LD), often moderate to severe
- Speech and language delay, expressive language is often more affected than receptive language. Many individuals are non-verbal or minimally verbal
- Gross motor delay, delays in sitting, crawling, and walking. The average age for independent walking is over 2 years old
- Low muscle tone (hypotonia)
- Joint hypermobility
- Feeding difficulties, especially in infancy, often related to hypotonia
- Behavioural differences, including a friendly/happy demeanour, autism spectrum disorder (ASD) or autistic traits, attention deficit hyperactivity disorder (ADHD) and anxiety
- Characteristic facial features including a thin or triangular-shaped (tented) upper lip, a short space between the nose and upper lip (philtrum), a flat or wide nasal bridge, low-set ears, skin folds at the inner corner of the eyes (epicanthal folds), up-slanting eyes and an open mouth posture
- Eye/vision anomalies, including squint (strabismus), long-sightedness (hyperopia), short-sightedness (myopia), and uncontrolled eye movements (nystagmus)
- Gastroesophageal reflux disease (GERD)
- Constipation
- Sleep issues, including difficulty falling or staying asleep, and sleep apnoea
- Recurrent respiratory infections

Other possible features include:

- Seizures or epilepsy
- Structural brain anomalies, may include a thin corpus callosum or white matter changes
- Small head size (microcephaly)
- Dental issues, including small or misaligned teeth and delayed loss of baby teeth
- Hernias, typically umbilical and midline hernias
- Cyclical vomiting syndrome (CVS)

Pregnancy and birth

While most pregnancies are unremarkable, concerns may become evident in the newborn period. Low muscle tone (hypotonia) and feeding difficulties are often among the first signs noted by parents and doctors. Some babies may require a stay in the neonatal intensive care unit (NICU) for additional support. Birth weight and length are typically within the average range, but may be on the lower end of the scale. There have been some reports by parents of an increased amount of nuchal fluid during the pregnancy (CHAMP1 Research Foundation personal communication).

Appearance

Certain facial features are observed more often in children with a CHAMP1-related disorder than in other children. These features are of no medical consequence but may mean that unexpected similarities are seen between children with the same diagnosis. These features are variable and can be subtle, and not every child will have them. They include an open mouth posture, a thin or triangular-shaped (tented) upper lip, an everted lower lip, a short space between the nose and upper lip (philtrum), a flat or wide nasal bridge, low-set ears, skin folds at the inner corner of the eyes (epicanthal folds), and up-slanting eyes.

Development

Gross and fine motor skills

Developmental delay is a universal feature of CHAMP1-related disorders. Developmental 'milestones' are often significantly delayed. This is largely due to hypotonia (low muscle tone), which is present in the vast majority of individuals, and joint hypermobility (unusually flexible joints). Most children learn to walk independently, but this milestone is typically reached after the age of 2 years, with an average age of around 26 months (Levy 2022). Some individuals may have an unusual or uncoordinated walk (ataxic gait) due to challenges with balance and muscle control. Fine motor skills, such as using hands purposefully for tasks like playing with toys, using cutlery, or dressing, are also delayed (Levy 2022). Many children benefit from early and consistent intervention with physiotherapy (PT) to build strength and coordination, and occupational therapy (OT) to develop fine motor and daily living skills.

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Just after her fifth birthday, our daughter learned to ride a balance bike. For a long time, it didn't seem like she ever would. Even after lots of practice, there was very little progress—but then, all of a sudden, she got the hang of it! She has surprised us like that many times, and we've learned to never say never".

"When our daughter was diagnosed, I never would have imagined her talking as well as she does, running, having friends, ice skating, dancing, singing her favorite songs, making her breakfast, packing her lunch, sleeping through the night, handling her big emotions with breath work,

emotionally appropriate response or questions, a sense of spirituality, love of community, thriving at school … and so much more. Everyone's diagnosis is different. Our daughter has the most common variant when it comes to CHAMP1, so I share this to say, I didn't have a ton of hope, but now I do. Fight for the supports your kid needs - little improvements compound and it's incredible to see"!

Intellectual development and learning

All individuals with a CHAMP1-related disorder have some degree of intellectual disability (ID), ranging from mild to severe. This means they will experience challenges with learning, reasoning, and problem-solving. Most children will require significant additional support with their learning throughout their education. Early intervention services and the creation of a formal, individualized education plan (IEP) or equivalent are essential to help each child reach their full potential.

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At five years old our daughter can work with amounts up to five and complete jigsaw puzzles with up to 16 pieces. It took a lot of patient, sometimes tedious practice, but now she actually enjoys games that involve counting and sometimes even plays puzzle games on her own. The hard work always pays off"!

"Try not to focus on what your child can't do, focus on what they can. Because one day you might turn around and they've done it at their own pace and you've worried about something you didn't need to worry about".

Speech and language

Severe speech and language impairment is also a universal feature of a CHAMP1-related NDD. Many individuals are non-verbal or minimally verbal, using only a few single words or signs. For those who do develop speech, the first words are typically achieved late, around 3.5 years on average (Amenta 2023, Houvener 2025). A common observation is that a child's understanding of language (receptive language) is significantly better than their ability to speak (expressive language). This gap can be a major source of frustration.

Early assessment by a speech and language therapist is crucial. For individuals with limited or no speech, Augmentative and Alternative Communication (AAC) methods are vital. These can range from low-tech options like picture boards (PECS) and sign language to high-tech speech-generating devices, enabling individuals to communicate their thoughts, needs, and feelings effectively.

Unique publishes a separate guide to Communication

We always knew she understood a great deal, but it was difficult to fully connect with her until we experienced the miracle of her being able to tell us what she thinks, dreams of, wishes for, and feels. Sign language was an enormous help in bridging the gap before her speech had developed far enough".

Feeding

Feeding issues are common, affecting over half of infants with a CHAMP1-related NDD. These difficulties are often present from birth and are linked to hypotonia, which can make sucking and swallowing inefficient. Gastro-oesophageal reflux (GERD), where stomach contents come back up the food passage, is also common, affecting just under half of those with a CHAMP1-related NDD (Houvener 2025, Simons Searchlight CHAMP1 Gene Guide). Some children may require specialized feeding support, such as high-calorie formulas or, in severe cases, a feeding tube (NGT or G-tube) to ensure adequate nutrition. Constipation is another frequent gastrointestinal concern.

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Growth and stature

While most babies with a CHAMP1-related disorder have birth measurements in the standard range, growth can be affected over time. Small stature (height below the 3rd percentile) is a known feature (Tanaka 2016, Houvener 2025). Head size is also frequently affected. A head size smaller than expected (microcephaly) is common, seen in about half of individuals (Tanake 2016). Less commonly, an unusually large head size (macrocephaly) is reported (Raad 2023).

Behaviour

The behavioural profile of CHAMP1-related NDDs is complex and multifaceted. One of the most frequently noted characteristics is a happy, friendly, charming, and endearing demeanour. Parents and clinicians often describe children as very sociable and joyful.

However, this sociable nature often coexists with significant neurobehavioral challenges. It is essential for parents, educators, and therapists to understand that these are not contradictory traits but rather different facets of the same underlying neurological condition. Challenging behaviours are not a reflection of a child's character but often stem from underlying difficulties with attention, anxiety, or sensory processing. High rates of the following have been formally diagnosed in studies:

- **Attention-Deficit/Hyperactivity Disorder (ADHD):** Around 60% of individuals meet the criteria for ADHD (Levy 2022, Houvener 2025), showing significant challenges with inattention, hyperactivity, and impulsivity.
- **Autism Spectrum Disorder (ASD):** Around a third of individuals (33%) meet the diagnostic criteria for ASD (Levy 2022, Houvener 2025). Many more show autistic traits, such as repetitive behaviours (e.g., hand movements) and sensory sensitivities.
- **Anxiety:** Anxiety is very common, reported in over 70% of individuals (Levy 2022, Houvener 2025).
- **Sensory Processing Differences:** Many individuals have unusual responses to sensory input. They may be sensory-seeking (craving intense input) or have hyper- or hypo-reactivity to sounds, touch, or other stimuli. A decreased sensation of pain has also been reported (Levy 2022, Houvener 2025).

Understanding this complex profile is key to providing effective support. Management strategies should focus on addressing the root causes of challenging behaviours - such as providing sensory supports, using strategies to manage anxiety, and creating structured environments to help with attention - while nurturing the child's inherently friendly and sociable personality.

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What's still difficult for our five-year-old daughter at this age is connecting with peers. She went through a phase of hitting and pinching other children a lot. This has improved with language development and guidance, but social interaction still doesn't come intuitively to her. She is very interested in other people, yet her many autism-related traits make smooth interactions more challenging. She also has sensory issues, mostly with noise. However, when we prepare her for what she is going to hear and give her noise-cancelling headphones, she is able to tolerate most situations".

"Our five-year-old daughter is immensely caring, often cheerful and motivated, and has a wonderful sense of humor. At the same time, she constantly needs something, becomes aggressive when stressed, and is fidgety much of the time. She is also very good at sticking to plans and keeps reminding us of what we agreed on. This can sometimes be exhausting, but it actually helps immensely in everyday life".

Puberty

There is limited information available about puberty in children with a CHAMP1-related NDD. Parents of children with a CHAMP1-related NDD have reported that most boys and girls appear to go through puberty late (CHAMP1 Research Foundation personal communication).

Some families of children with chromosome disorders and behavioural or learning difficulties can be particularly concerned at their daughter's ability to cope with menstruation, and for some discussing menstrual regulation options with a paediatrician may be beneficial.

Unique publishes a separate guide to Puberty

Sleep

Sleep problems are a common concern for families. These can include difficulty falling asleep, frequent night wakings, and abnormal breathing patterns during sleep, such as sleep apnoea (where breathing temporarily stops). If sleep apnoea is suspected due to snoring or observed pauses in breathing, an evaluation by a specialist and a sleep study may be recommended.

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Adulthood

As CHAMP1-related NDDs have only been identified relatively recently, information on adulthood is still emerging. Experiences are likely to vary considerably depending on the severity of an individual's intellectual disability and any ongoing medical concerns. Based on the universal presence of ID, it is expected that most adults will require lifelong support with daily living. A case report of a 21-year-old individual noted ongoing ID and neurodevelopmental challenges but good general health. Adults will have varying levels of independence, with most likely continuing to live with their parents or in supported settings such as a group or residential care home.

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Medical concerns

The following medical concerns have been found in children with a CHAMP1-related NDD. They are not found in all children so not all children with a CHAMP1-related NDD will be affected.

Brain

A small head size (microcephaly) is common in children with a CHAMP1-related NDD. Structural brain anomalies have been detected by an MRI (magnetic resonance imaging) scan in over a third of individuals (37%) tested (Simons Searchlight CHAMP1 Gene Guide 2024). The changes seen vary but most commonly include underdevelopment (hypoplasia) of the white matter connecting the two halves of the brain (corpus callosum), a reduction in the size of the cerebellum (an area at the back of the brain important for coordination), and other changes to the brain's white matter, such as delayed myelination.

Seizures

Current studies suggest about 1 in 5 (21%) of children with a CHAMP1-related NDD experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain) (Houvener 2025, Simons Searchlight CHAMP1 Gene Guide 2024). Depending on the part(s) of the brain affected, symptoms vary, but include temporary confusion, uncontrollable jerking movements and loss of consciousness or awareness. Age of onset can vary considerably, while seizures may be isolated to a single incident or occur more regularly. More than one type of seizure may be present in the same individual. Electroencephalograph (EEG) and video telemetry (video EEG) are medical tests that can be used to measure and record the electrical activity of the brain and are tools that, when used alongside other tests, can help diagnose the type of seizure experienced.

Seizures can cause a lot of worry for families and can be frightening to observe, but in the majority of cases they self-resolve or resolve with medical treatment. If your child has a seizure for the first time, it is important to remove nearby hazards so they can't hurt themselves, and contact a medical professional.

Seizure types reported in children with CHAMP1-related NDD include:

Febrile seizures: Episodes only occur when the child has a high temperature.

Absence seizures: A change in behaviour as if the child 'switches off', sometimes with staring, eyelid flickering or lip smacking. Absences are very brief, often lasting less than half a minute.

Atypical absence seizures: Child may appear confused and unresponsive for minutes (very different from a typical absence seizure).

Generalised tonic-clonic seizures: At the onset of a seizure, the abnormal electrical activity involves both sides of the brain. The seizure involves a phase of stiffening followed by jerking of the body

Eyes and sight

Eye and vision anomalies are common in children with CHAMP1-related NDD. A thorough evaluation by a paediatric ophthalmologist is recommended at diagnosis. Known concerns include:

Refractive errors: Long-sightedness (hyperopia) and short-sightedness (myopia) that can be corrected with glasses.

Strabismus: A squint, where one or both eyes turn inward, outward, up, or down. This may be treated with patching, glasses, or surgery.

Nystagmus: Uncontrolled, repetitive eye movements.

Amblyopia: A ‘lazy eye,’ which can result from untreated strabismus.

Gastrointestinal System

Constipation is common among children with CHAMP1-related NDD and can be related to low muscle tone, little exercise, a low-bulk diet and small fluid intake, among other reasons that are not fully understood. It is important that possible causes are discussed with a health visitor or doctor, who may recommend adapting diet or giving stool softeners or laxatives. GERD (gastroesophageal reflux, where feeds return readily up the food passage) is also common and may require treatment, including careful positioning for feeds, medication or nutritional supplements, or, in severe cases, a feeding tube (NGT or G-tube) to ensure adequate nutrition.

Some individuals experience Cyclical Vomiting Syndrome (CVS). CVS is a distinct condition characterized by severe, recurring episodes of nausea and vomiting that can last for hours or days, followed by periods of relative wellness. Management of CVS often requires a gastroenterologist and may involve medications to prevent or shorten episodes.

Joints

Joint anomalies are a known feature of CHAMP1-related NDDs. These include extremely loose (hypermobile) joints (elbows, wrists, knees and hips), which mean babies and children can move their limbs into positions others find impossible. While this may cause no problems, hypermobility is sometimes associated with pain and stiffness in the joints and muscles, joints that dislocate (come out of position) easily, and injuries including sprains. Children with very loose joints may need physiotherapy, massage or additional braces (supports, splints) before they are able to walk.

Hearing

A few children with a CHAMP1-related NDD have a hearing impairment, but hearing is unaffected in most children and hearing tests at birth often give a clear response. A hearing loss may be conductive, where sound is unable to travel effectively to the inner ear; sensorineural, where there are problems with the inner ear, sometimes with the cochlea or auditory nerve (the nerve that sends signals to the brain about sound); or a combination of both conductive and sensorineural hearing loss.

Many types of hearing loss can be managed by using hearing aids. As children are at risk of speech delay, parental concerns should be acted on early and home- or school-based therapy provided.

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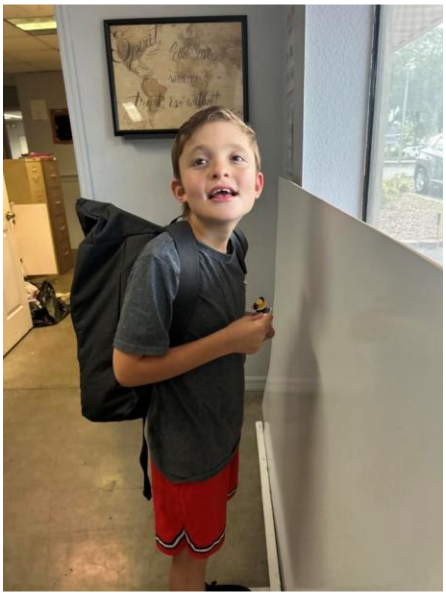
Breathing

Babies and children with rare chromosome and gene disorders tend to have a higher rate of respiratory concerns, which may become less frequent with age and maturity, although they can persist throughout childhood. Children may also be prone to allergies and asthma, sometimes triggered by respiratory infections. Other issues may include sleep apnoea (when there is an abnormal breathing pattern during sleep).

Teeth

Dental concerns are very common in children with genetic conditions. A number of issues have been described by parents of children with a CHAMP1-related NDD including unusual dental development; tooth grinding (bruxism), which can prematurely wear down the enamel, teeth emerging late and milk teeth being late to fall out. A high standard of dental care is important to minimise damage by decay and erosion (by grinding). Children and adults may also benefit from specialist hospital dental services and may require treatment under general anaesthetic.



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Hernias

Some babies with a CHAMP1-related NDD are born with a hernia, where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue. These include instances of hernias at or near the belly button (umbilical), concerning the abdomen (abdominal), involving the muscle that separates the chest cavity from the abdominal cavity (diaphragmatic) and the upper stomach (hiatal). In some cases the hernias healed naturally without the need for treatment, but in the majority of cases surgical repair was required.

Other medical concerns

Spine: A sideways curvature of the spine (scoliosis) or a rounding of the upper back (kyphosis) can occur (Raad 2023, Houvener 2025).

Kidneys and Urinary Tract: While less common, anomalies of the kidneys or urinary tract have been reported in some individuals (Houvener 2025, CHAMP1 Research Foundation personal communication).

Heart: Congenital (present at birth) heart defects have been reported rarely (Tanaka 2016, Houvener 2025). A baseline evaluation by a cardiologist may be considered.

Cancer: There have been very rare reports of leukaemia in individuals with CHAMP1 variants (Garrity 2021). At present, it is unclear if this represents a true association. Routine cancer screening is not currently recommended, but it is an area of ongoing research.

How common is a CHAMP1-related NDD?

A CHAMP1-related NDD is extremely rare. As of 2025, less than 250 individuals with a CHAMP1-related NDD have been identified worldwide through patient registries and medical literature. However, because the condition was only first described in 2015 (Deciphering Developmental Disorders Study 2015, Hempel 2015) and is not yet on all standard genetic testing panels, it is likely underdiagnosed. It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.


2 years

Why did this happen?

When children are conceived, their parents' genetic material (DNA) is copied in the egg and sperm that makes a new child. The biological copying method is not perfect, and random changes occur in the genetic code of all children that are not seen in the DNA of their parents. This happens naturally and is not due to the parents' diet, environment or lifestyle. Most of these DNA changes have no obvious effect. But in rare instances these random DNA changes can lead to health issues or affect development. When such a random change disrupts the function of the CHAMP1 gene then a child will have a CHAMP1-related NDD. In almost all people identified so far (2025) with a CHAMP1-related NDD, the genetic change was a random (or '*de novo*') change, meaning the change occurred for the first time in that family in the affected individual. Very rarely, one parent may have a chromosomal rearrangement that led to the CHAMP1-related NDD in their child, or one parent may have the same change (or variant) in some of their egg or sperm cells and pass it on to their child (this is known as germline mosaicism). However, it is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when a new DNA change occurs in their child.

Accepting the diagnosis of the disease is a long, sometimes discouraging, sometimes tiring, journey, but it also allows us to discover unsuspected strengths and boundless courage. Our daughter taught us to live day by day. To put things into perspective. To savor the small victories and the big progress more. We experience everything more intensely. With the CHAMP1 parent group, you'll feel like you're joining a new family, a cocoon where everyone is always there to listen, help, and support you".

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. In almost everyone reported with CHAMP1-related NDD so far (2025) the genetic alteration has been found to be *de novo* (dn), which means neither parent was found to have the same CHAMP1 gene change as their child, and neither parent was found to have a chromosomal rearrangement that might have resulted in a CHAMP1 deletion in their child. Therefore, the chance of having another child with a CHAMP1-related NDD is usually less than 1%.

One reason why there is some residual chance of recurrence is due to the rare phenomenon called germline mosaicism that was mentioned above. This is when a parent carries a genetic change, but it is limited to some of their egg or sperm cells. The genetic change would not, therefore, be detected in the parents' blood tests.

Unique publishes a short general guide to Mosaicism

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with a CHAMP1-related NDD.

Unique publishes separate guides to Planning your next child, Prenatal genetic testing and diagnosis, A clinical genetics appointment and Supporting siblings of children with a rare genetic condition

Can a CHAMP1-related NDD be cured?

There is no cure for a CHAMP1-related NDD since the effects of the genetic change took place during a baby's formation and development. However, knowing the diagnosis means that appropriate monitoring and interventions can be put in place.

Management

No clinical practice guidelines for CHAMP1-related NDDs have been published (2025). The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with a CHAMP1-related NDD, to improve quality of life and reduce complications.

Children and adults with a CHAMP1-related NDD should be under the care of a multidisciplinary team. The team should include a geneticist and paediatrician (for children) who can oversee care so that development and behaviour can be monitored, and the best help given in the form of therapies. Individuals may also have evaluations with various specialist doctors.

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of CHAMP1-related NDDs that are present in the child or adult who has been diagnosed with this genetic condition should be carried out. This can determine which of the features of CHAMP1-related NDDs are present and how severe they are.

Supportive care

How a person with a CHAMP1-related NDD is cared for is likely to require co-ordinated care by a multidisciplinary team of specialists, which may include:

Paediatrician – a doctor who specialises in the physical, mental and social health of children from birth to young adulthood.

Neurologist – a doctor who specialises in conditions of the brain, spinal cord and nervous system.

Cardiologist – a doctor who specialises in heart conditions.

Endocrinologist – a doctor who specialises in hormones and their effect on the body.

Urologist – a doctor who specialises in diagnosing and treating conditions affecting the urinary system.

Nephrologist – a doctor who specialises in conditions affecting the kidneys.

Surgeon – doctor who is specially trained to perform medical operations.

Ophthalmologist – a doctor who specialises in conditions affecting the eyes.

Audiologist – a health care professional who diagnoses, treats and helps manage a condition that involves hearing or balance.

Occupational therapist (OT) – a health care professional who uses activities to aid self-management of a condition and can provide equipment.

Physiotherapist (PT) – a health care professional who uses exercise, movement, manual therapy, education and advice to help with the body's strength and mobility.

Speech and language therapist (SALT) – a health care professional who helps with speech, language communication and sometimes feeding/swallowing difficulties.

Psychiatrist – a doctor who specialises in mental health.

Specialist nurses and/or other healthcare professionals may need to systematically and comprehensively plan a child or adult's treatment.

Treatments and therapies

Treatment will depend on the specific features and symptoms experienced by the person with a CHAMP1-related NDD but may include:

Physiotherapy for low muscle tone (hypotonia) and gross motor delays, which usually includes exercises to build core strength, improve balance, and enhance coordination for/to help children achieve motor milestones like sitting, crawling, and walking, and to improve overall mobility.

Occupational therapy for fine motor skill delays and sensory sensitivities, which can include activities to improve hand strength and coordination for daily tasks (e.g. feeding and dressing) and sensory integration therapy for/to help individuals better process and respond to sensory information from their environment.

Speech therapy for severe speech and language impairment, which can include regular sessions focusing on Augmentative and Alternative Communication (AAC) methods (e.g. sign language, picture exchange systems and high-tech communication devices) for/to provide a functional means of communication for individuals who are non-verbal or have very limited speech.

Behavioural therapy for features of autism, ADHD, and anxiety, which can include structured therapies like Applied Behaviour Analysis (ABA) for/to help manage challenging behaviours, improve social skills, and develop coping strategies.

Medications may be prescribed such as anti-seizure medications (ASMs) to help control or prevent seizures.

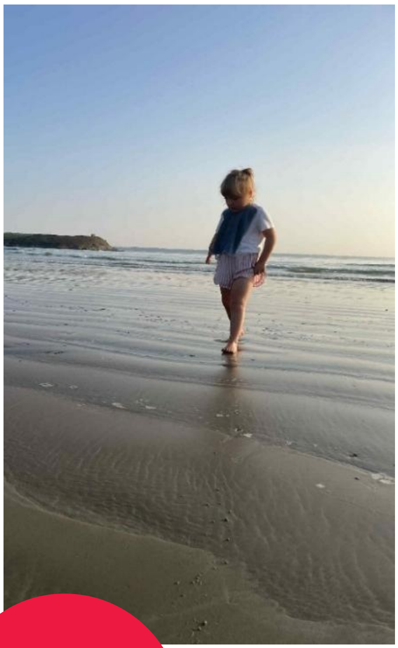
Diet, such as a high-fibre diet or stool softeners and/or laxatives may be recommended to help relieve constipation.

Surgery, such as the placement of a gastrostomy tube (G-tube) for severe, long-term feeding difficulties, or procedures to correct a squint (strabismus) to ensure adequate nutrition and improve vision.

Research into new treatments for CHAMP1-related NDDs

The genetic change causing a CHAMP1-related NDD affects the development of the brain and other parts of the body before birth. Therefore, a complete cure is unlikely, even in the future, since the brain has already formed by the time a diagnosis is made. However, research into improved treatments and management for various features of the disorder, like ASD and epilepsy, is ongoing.

In addition, the CHAMP1 gene and its role in the cell are the subject of active research. Patient organizations like the CHAMP1 Research Foundation are working to accelerate this research by funding studies, creating animal and cell models with changes to the CHAMP1 gene, and building patient data registries.



One area of research is drug repurposing, which aims to identify existing and approved medications that could help manage the symptoms of CHAMP1-related NDDs.

A key area of future research is the development of genetic therapies. Because different genetic variants cause the disorder through different mechanisms (haploinsufficiency or loss of function dominant-negative and possibly gain of function), different therapeutic approaches may be needed. Research is exploring strategies like RNA-based therapies [e.g. antisense oligonucleotides (ASOs)] that could potentially either boost the function of the healthy gene copy or silence the gene copy with the variant. These approaches are still in the very early stages of research and are not yet available as treatments.

Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

Families say ...

We received our daughter's diagnosis in December 2023 after a year and a half of waiting, she was 3 years old. When we received the results, we were relieved to be able to put a name to her symptoms. However, it also threw us into an unfamiliar world of being parents of a child with a very rare genetic disease".

"Hearing our daughter has a genetic condition that's ultra-rare was tough information to receive, but we were relieved to finally have answers to so many medical concerns that seemed so unrelated. What I didn't anticipate was such incredible support getting to know our CHAMP1 community. We have amazing families advocating for everything our kids need. We are all chasing quality of life for our kids and for our families - the family support and CHAMP1 foundation have been such a blessing. I often say, for the tough news and road we've traveled with this condition, we've won the lottery when it comes to support. Thankful for people like Jeff and Katis willing to give so much to our foundation, fighting for better quality of life and someday a cure for our kiddos".

"Our son's diagnosis has helped us to help other families that are newly diagnosed. We have lived experiences which help much more than any information from professionals. We understand the loneliness of diagnosis and hope that new families reach out to our community to help them through the start of theirs".

"Whilst receiving a CHAMP diagnosis can feel scary, it's been an experience filled with progress and triumphs. Many of the things we thought wouldn't happen for us have slowly emerged and we get to enjoy this journey with a new sense of perspective".

"My daughter having CHAMP1 changed my life. And not necessarily in the ways you may think. Yes, life is at times, hard. When we received the diagnosis I cried for days, grieving the life I thought our daughter would have, not knowing what her future held and unsure how to best support her. But once I'd processed what had happened, I found the most amazing community in our fellow CHAMP1 families. The support, love and care they continually show is the best. They know exactly how I'm feeling and will always help and offer comforting words of support in tough times, helping us know what to ask for from medical professionals. They share our successes too and champion our daughter".

"So to say having a child with CHAMP1 was life changing is true. We've travelled across the world to meet the most amazing people. We have the most supportive community and the best scientific team who are working tirelessly for us. I am a completely different person because of CHAMP1, in the best way. I am stronger, more confident and more resilient than I was before having my daughter".

"Yes, life can be tough but my goodness I wouldn't change our daughter for the world".

Sources

The information in this booklet is drawn from the published medical literature, CHAMP1 patient organisations and information from Unique members. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (**pubmed.ncbi.nlm.nih.gov/**).

References

*Garrity *et al*. (2021) Neurodevelopmental phenotypes in individuals with pathogenic variants in CHAMP1. Cold Spring Harb Mol Case Stud, 7(4): a006093.
pubmed.ncbi.nlm.nih.gov/34021018/

*Deciphering Developmental Disorders Study (2015). Large-scale discovery of novel genetic causes of developmental disorders. Nature 519: 223-228.
pubmed.ncbi.nlm.nih.gov/25533962/

*Hempel *et al.* (2015) De Novo Mutations in CHAMP1 Cause Intellectual Disability with Severe Speech Impairment. Am J Hum Genet, 97(6): 923-30.
pubmed.ncbi.nlm.nih.gov/26340335/

*Levy *et al.* (2022) CHAMP1 disorder is associated with a complex neurobehavioral phenotype including autism, ADHD, repetitive behaviors and sensory symptoms. Hum Mol Genet, 31(15): 2582-2594.
pubmed.ncbi.nlm.nih.gov/35271727/

*Levy *et al.* (2023) Prospective phenotyping of CHAMP1 disorder indicates that coding mutations may not act through haploinsufficiency. Hum Genet, 142(9): 1385-1394.
pubmed.ncbi.nlm.nih.gov/37454340/

*Nagai *et al.* (2022) Deficiency of CHAMP1, a gene related to intellectual disability, causes impaired neuronal development and a mild behavioural phenotype. Brain Commun, 4(5): fcac220.
pubmed.ncbi.nlm.nih.gov/36106092/

*Tanaka *et al.* (2016) De novo pathogenic variants in CHAMP1 are associated with global developmental delay, intellectual disability, and dysmorphic facial features. Cold Spring Harb Mol Case Stud, 2(3): a000918.
pubmed.ncbi.nlm.nih.gov/27148580/

*Raad *et al.* (2023) CHAMP1-Related Disorder: Sharing 20 Years of thorough Clinical Follow-Up and Review of the Literature. Genes (Basel), 14(8): 1546.
pubmed.ncbi.nlm.nih.gov/37628598/

*Ben-Haim *et al.* (2020) CHAMP1 mutations cause refractory infantile myoclonic epilepsy. J Pediatr Neurol. 18:027–32.
research.champ1foundation.org/papers-details?recordId=recBRWBaeYlp879Yn

*Van Caugherty *et al.* (2024) The Genomics of CHAMP1: Insights into their Cell-Type Specificity and Developmental Trajectories.
research.champ1foundation.org/papers-details?recordId=recEgelaTNE8WI5up

*Houvener *et al.* (2025) A disease conceptual model for CHAMP1-related disorder.
research.champ1foundation.org/papers-details?recordId=recBvwhfNrm6pvvvU

*Yoshizaki *et al.* (2024) CHAMP1 premature termination codon mutations found in individuals with intellectual disability cause a homologous recombination defect through haploinsufficiency. Sci Rep. Dec 30;14(1):31904.
pubmed.ncbi.nlm.nih.gov/39738383/

*Simons Searchlight CHAMP1 Gene Guide
simonssearchlight.org/gene-guide/champ1/

Inform Network Support

Rare Chromosome Disorder Support Group
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Tel: +44(0)1883 723356
help@rarechromo.org I rarechromo.org

Join Unique for family links, information and support:

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Please help us to help you!

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- CHAMP1 UK (Charity)
- CHAMP1 UK Facebook Page
- CHAMP1 UK WhatsApp
- CHAMP1 Family Support Private Facebook Group
- CHAMP1 Research Foundation (Non-Profit)
- CHAMP1 Research Foundation Facebook Page
- CHAMP1 Research Portal

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change.

This guide was written by CHAMP1 UK, The CHAMP1 Research Foundation and Unique (AP) and reviewed by the CHAMP1 Research Foundation's Scientific Advisory Board members Dr. Wendy Chung, M.D., Ph.D. and Dr. Stefano Berto, Ph.D.

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