UNIQUE

UNDERSTANDING GENES & CHROMOSOMES

DYNC1H1-related disorders (DYNC1H1)

rarechromo.org

This guide is designed to help families and healthcare professionals looking after people DYNC1H1-related disorders (DYNC1H1). 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 are DYNC1H1-related disorders?

DYNC1H1-related disorders share several overlapping symptoms and features. This can sometimes make it hard to distinguish between the different types. Depending on which features and gene changes are present, a child may be diagnosed with one of the three following disorders: Charcot-Marie-Tooth Disease Type 2O (CMT2O), Complex Cortical Dysplasia with other Brain Malformations 13 (CDCBM13) or Spinal Muscular Atrophy, Lower Extremity-Predominant 1 (SMALED1).

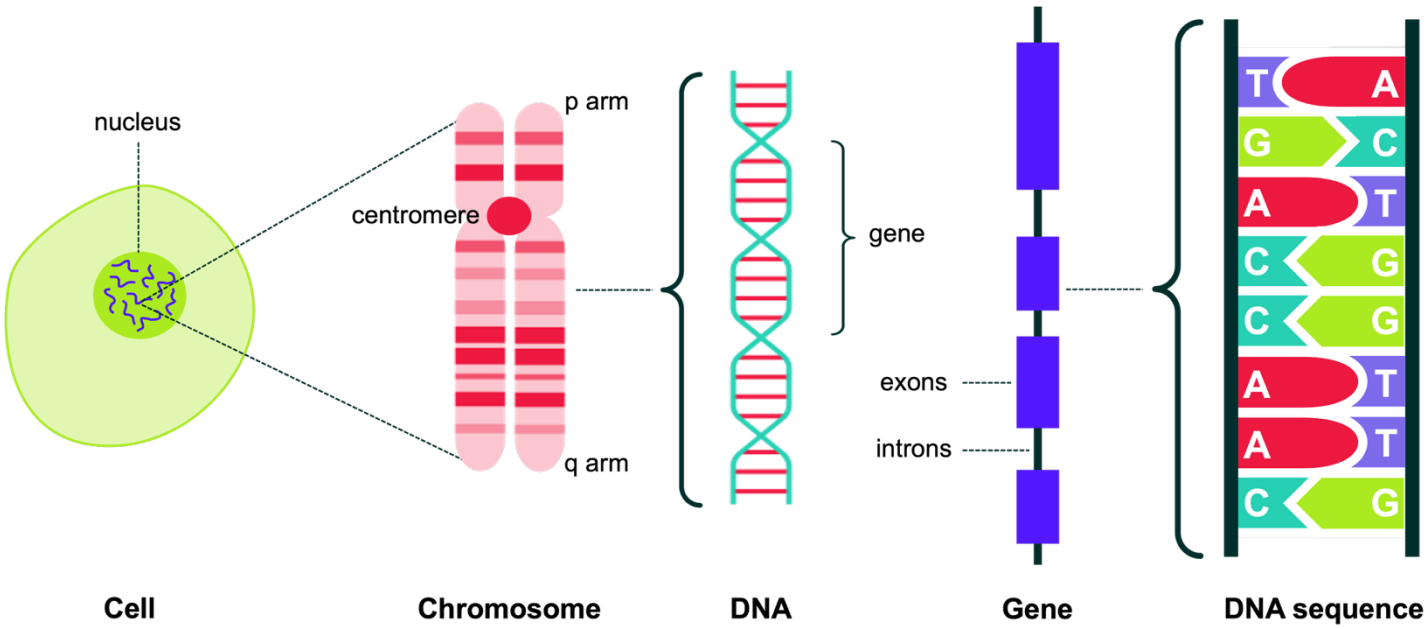
These are all rare genetic conditions in which a range of features may be present, including developmental delay, progressive muscle weakness, unusual skeletal formation, varying degrees of learning (intellectual) disability and behavioural differences, including attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). As is common with genetic conditions, each person can be affected differently - even among affected members within the same family. Not everyone with a DYNC1H1-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.

DYNC1H1-related disorders are caused by certain changes (variants) in the DYNC1H1 gene.

What causes DYNC1H1-related disorders?

Genes are instructions that 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 we would expect, which can lead to changes in how their body works.

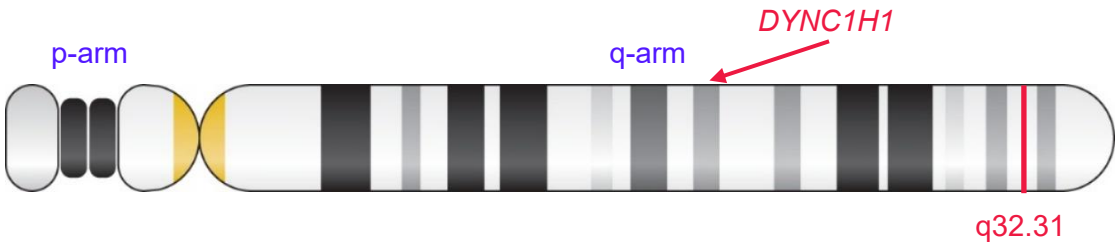
DNA is made up of building blocks called 'bases' or 'nucleotides'. There are four DNA bases which can be abbreviated to the letters A, C, G, and T. These DNA bases are paired up in the DNA structure into 'base-pairs'. The full sequence of our DNA is over three billion base-pairs long. There are changes in the DNA sequence (variants) present in everyone's genes. It is variants in our genes that make each one of us unique individuals.



DYNC1H1-related disorders are caused by specific changes (known as pathogenic variants) to the DNA sequence of a gene called DYNC1H1 (DYNC1H1 is an abbreviation of the gene's full name, Dynein Cytoplasmic 1 Heavy Chain 1).

The DYNC1H1 gene is located in the long 'q' arm of chromosome 14 in a region called 14q32.31 as shown in the image below.

Chromosome 14



We have two copies of chromosome 14 in our cells, so we also have two copies of the *DYNC1H1* gene. DYNC1H1-related disorders occur when only one copy of the DYNC1H1 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 DYNC1H1 gene sequence is used to make the Cytoplasmic Dynein 1 Heavy Chain 1 protein. This protein has an important role in transporting proteins around nerve cells and ensuring correct orientation of cell machinery during cell division.

Genetic Tests

DYNC1H1-related disorders are caused by gene sequence variants and can be identified by a type of genetic test called sequencing (e.g. whole exome sequencing (WES) or whole genome sequencing (WGS)).

Unique publishes separate guides to DNA sequencing

Genetic Test Results

The results of genetic (genomic) testing are likely to be given to you by your geneticist, a genetic counsellor or the clinician who ordered the test. Depending on the test that was carried out, someone with DYNC1H1-related disorders might have results that look like the following example result of a DNA sequencing test (e.g. whole exome sequencing (WES) or whole genome sequencing (WGS)), that can identify gene variants, is shown on the next page for the DYNC1H gene:

p.His306Arg (H306R) (CAC>CGC): c.917A>G in exon 5 of the *DYNC1H1* gene (NM_001376.5)

p.His306Arg (H306R)	signifies the change to the protein: the amino acid Histidine (H) has been replaced by the amino acid Arginine (R) at position 306 in the sequence of amino acids that make up the protein
CAC>CGC	signifies the gene sequence change; the A nucleotide has been replaced by a G nucleotide
c.917	signifies the base pair position of the change within the gene sequence (the position where the A nucleotide has been replaced by the G nucleotide)
exon 5	signifies which part of the gene has been altered, in this case exon 5
DYNC1H1	signifies the gene that is affected
NM_001376.5	denotes the reference sequence used

Unique publishes a separate guide to Interpreting Genetic Test Results

What features and symptoms do people with DYNC1H1-related disorders have?

As is common with many genetic conditions, children and adults with DYNC1H1-related disorders 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 DYNC1H1-related disorders have:

- Low muscle tone (hypotonia)
- Some degree of motor developmental delay, ranging from mild to profound
- Some degree of learning intellectual disability (ID) or learning difficulties (LD), ranging from mild to profound
- Behavioural differences, such as attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD)
- Speech and language delay
- Feeding difficulties
- Gastro-oesophageal reflux (GERD/GORD)
- Skeletal anomalies
- Anomalies of the hands and feet
- Sleep disturbance

Other possible features include:

- Small head size (microcephaly)
- Brain anomalies (polymicrogyria)
- Seizures
- Progressive muscle weakness
- Unusual gait
- Feelings of pain, numbness or tingling (sensory neuropathy)

Pregnancy and birth

While many pregnancies are unremarkable and proceed without complication, occasional concerns during pregnancy have been reported, sometimes following mid-pregnancy anomaly scans. Where a cause for concern was noted, most often parents reported fixed joints and reduced fetal movement in utero (fetal dyskinesia).

The majority of pregnancies go to term but a few babies are born prematurely. Some babies show some signs of difficulty at birth, related to difficulties with feeding and anomalies affecting the feet. Birth weights are usually average. A small number of babies grow very slowly in the womb and are tiny at birth.

Appearance

Certain facial features are found more often in children with DYNC1H1-related disorders (especially CDCBM13) than in other children. These features may mean that you see unexpected similarities between your child and others with DYNC1H1-related disorders. The most common characteristic features include down-slanting eyes and reduced muscle tone in the face (hypotonic face).

Development

Gross and fine motor skills

Developmental delay has been reported in most children with DYNC1H1-related disorders so far [2025]. The degree of delay ranges from mild to profound. Developmental "milestones", including rolling, sitting, walking, playing with toys, using cutlery, using zips and buttons, and toilet training, are often delayed, although there is a wide range of eventual ability, with some children acquiring mobility and other skills around the same age as "typical" children and others showing more obvious delay. Low muscle tone (hypotonia) is common and may affect mobility. Most children may have an unusual gait when walking because of stiffness, or balance issues (known as ataxia). For some, independent walking may not be achieved. Many benefit from early intervention with treatments or therapies such as orthotics e.g. insoles, braces, splints and callipers; occupational therapy (OT); and physiotherapy (PT).

> ***He has altered muscle tone. Age 7, he took his first independent steps after years of very intensive physiotherapy."***

Unique publishes separate guides to Therapies and Toilet training and continence

Intellectual development and learning

Some children with DYNC1H1-related disorders have intellectual disability (ID) or learning difficulties, most commonly seen in CDCBM13. ID ranges from mild to profound but is usually in the mild to moderate range and most children have needed additional support with their learning. Early intervention can prove particularly beneficial and formal testing to assess specific, individual needs is recommended.

> ***He attends a specialist school, where he is thriving."***

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Speech and language

Children with DYNC1H1-related disorders may experience some degree of speech and language delay and a few may find it difficult to co-ordinate movement of their lips, jaw and tongue to make the right sounds (apraxia of speech). The eventual range of achievement is broad, but some may remain non-verbal. Those who do develop speech may achieve single words, short phrases or basic sentences and some go on to develop conversational skills and a broad vocabulary. Many parents believe that their child can understand a lot more than they can express.

An assessment by a speech therapist should be able to identify your child's specific difficulties, allowing regular therapy sessions tailored to your child's specific areas of need. Where individuals have no speech or very few words, Augmentative and Alternative Communication (AAC) methods, including pointing, pictograms, gestures, facial expression and simplified sign language and high-tech communication systems (aided communication) have enabled many to communicate their thoughts and needs well.

> ***He uses an electronic device and has the manual dexterity to be able to select photo symbols at quite a small size, with a grid overlay. Using this he's been able to happily tell us the dinner we cooked was 'disgusting'! As mum, I've never been so pleased to hear that about my food!"***

Unique publishes a separate guide to Communication

Feeding

Feeding issues in the new-born period are common. Low muscle tone may contribute to difficulties with swallowing and some babies will suck weakly and may need high energy milks to encourage weight gain. Many babies also suffer from gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), which may require treatment, including careful positioning for feeds, medication, nutritional supplements or, in some cases, insertion of a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy tube (PEG/G-tube). Other issues that have been reported include aspiration (where fluid, food or saliva enters the airway or lungs). Some children have benefited from attending a feeding clinic where an assessment can be made, and advice to help treat any eating and drinking difficulties provided.

Unique publishes a separate guide to Feeding

Growth and stature

Most children with DYNC1H1-related disorders described in the medical literature so far (2025), generally exhibit growth patterns within the expected range, although some may experience growth delays. Many of these children also have smaller than expected head size (microcephaly). Beyond infancy, height and weight is variable.

Behaviour

Children with DYNC1H1-related disorders typically tend to have behaviour in keeping with their overall degree of developmental delay, and most have a happy disposition and sociable nature. Many children have an autism spectrum disorder (ASD) diagnosis or traits. Other behaviours including attention deficit hyperactivity disorder (ADHD), anxiety and less commonly aggressive behaviours have also been reported. Some children also have sleep problems.

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. Efforts to take into account and introduce strategies to tackle communication and other difficulties can also be beneficial.

"Our son is very happy; he smiles a lot, he loves the wind in his face, eating yoghurts, checking every car has four wheels and investigating every sign (fire exits are best!). He is very expressive and you are never in doubt of his mood or requests."

Unique publishes separate guides to Challenging Behaviour and Sleep

Puberty

There is limited information available about puberty in children with DYNC1H1-related disorders. We do know that a few appeared to go through puberty as expected. 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

Adulthood

Experiences of adulthood are likely to vary considerably and will depend on many factors. These include the level of any LD/ID, possible on-going medical concerns and improvements in early intervention and therapies/treatments.

Adults with DYNC1H1-related disorders have varying levels of independence. A few have gone on to have families of their own and manage to run their own households and work. Most continue to live with their parents or in supported settings such as a group/residential care home, with caregivers who can provide support. Some may live independently but require some support from family or friends with certain tasks. Levels of employment and the nature of employment varies but a few do undertake some form of paid or unpaid employment.

Unique publishes a separate guide to Transition

Medical concerns

The following medical concerns have been found in children with DYNC1H1-related disorders. They are not found in all children so not all children with DYNC1H1-related disorders will be affected.

Heart

A heart condition(s) has been found in a few people reported so far with DYNC1H1-related disorders, which can be present at birth (congenital) or develop later in life. Due to the frequency of heart conditions in the general population, it is thought their presence alongside DYNC1H1 could be incidental. In children for whom heart problems are suspected, these can be diagnosed using tests like an electrocardiogram (ECG) (recording the electrical activity of the heart), echocardiogram (ultrasound scan of the heart), or chest X-ray.
The type of heart condition(s) is variable but include anomalies affecting the size and structure of the heart muscle and valves. Most often these include:

- Mild leaking of the aortic valve (aortic valve insufficiency)
- Narrowing of the vessel carrying blood from the heart to the lungs (pulmonary stenosis)
- A valve with two flaps instead of three (bicuspid aortic valve)
- The pulmonary veins draining into the wrong part of the heart (anomalous pulmonary venous drainage)
- A small hole in the wall between the heart's two atria (atrial septum defect), resulting in the thickening of the walls of the heart's ventricles (ventricular hypertrophy)

Many of these conditions are relatively minor and resolve naturally in time. Medical treatment may be necessary for others, and some may require surgery.

Brain

Some children have a structural brain anomaly, which can be detected by MRI (magnetic resonance imaging) or a CT (computerised tomography) scan of their brain. The changes seen vary but include:

- Partial/complete absence (agenesis) of the white matter connecting the two halves of the brain (corpus callosum)
- Enlarged fluid-filled cavities in the brain (dilated ventricles)
- Ventricles of the brain that are larger than normal (ventriculomegaly)
- The presence of tissue containing nerves in atypical locations of the brain (grey matter heterotopia)
- A reduction in the size of the part of the brain that helps control balance, movement and basic body functions, called the cerebellum and brainstem (pontocerebellar hypoplasia)
- (More rarely) atypical tissue connections of the brain (atypical white matter)

Seizures

Occasionally children with DYNC1H1-related disorders experience some form of seizure (a sudden and unexpected change in the electrical activity in the brain). In the majority of cases seizures are infantile onset. 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 some cases they self-resolve or resolve with medical treatment. Vigabatrin is reported as the best medication for seizure control,

especially for infantile spasms. 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 individuals with DYNC1H1-related disorders include:

Infantile spasm Type of seizure usually occurring in clusters in babies between 3-10 months. Seen most often when a baby wakes and may be obvious or subtle.

Generalised tonic clonic 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.

Myoclonic generalised seizure Involving jerky or shock-like contraction of different muscles anywhere in the body but usually the arms or legs. Each myoclonic seizure lasts for a fraction of a second or a second at most.

> ***In utero we learnt he has brain structural anomalies and an enlarged head. At age 6 he started having seizures."***

Constipation

Constipation is sometimes observed among children with DYNC1H1-related disorders 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. Some children have benefitted from enemas when symptoms were particularly severe.

Eyes and sight

Problems with eyes and vision are fairly common in children with DYNC1H1-related disorders. A wide range of conditions have been reported, and an individual may have more than one vision or eye-related concern. Known concerns include cataracts (when the usually clear lens of the eye develops cloudy patches) and severe dry eyes.

Ears and Hearing

A few children 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, with sensorineural hearing loss being the most common type observed in children with DYNC1H1-related disorders. 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.

Unique publishes a separate guide to Hearing

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 with DYNC1H1-related disorders (particularly SMALED1) have been observed to have breathing difficulties, including irregular breathing patterns during sleep where breathing stops and starts

(sleep apnoea). Since SMALED1 causes muscle weakness and a decrease in muscle size (atrophy), breathing can be affected when respiratory muscles are affected.

Hands and feet

Children with DYNC1H1-related disorders often have anomalies of the feet, and sometimes anomalies of the hands due to muscle weakness.
Most common among these anomalies of the feet are:

- 'Claw foot' (pes cavus)
- The foot being held in a downwards position (pes equinus)
- The foot pointing downwards and inwards (pes equinovarus)
- So-called 'banana foot', where the toes point inwards (pes adductus)
- Rocker bottom feet (the sole is curved without an instep, like a chair rocker) (talus verticalis)
- Shortened forefoot
- Slender/hammer toes
- The foot pointing upwards (pes calcaneus)
- Hyperextension anomalies
- Bilateral foot drop, where the toes drag when walking

Some children are only mildly affected, and any condition will not require treatment. Others may benefit from massage, orthotics and physiotherapy. Treatment is tailored to the individual child, and in some cases surgical correction will best enhance eventual mobility.

Spine

A few babies are born with or develop a spinal curvature, either a sideways curve of the spine (scoliosis), a rounding of the upper back (kyphosis) or kyphoscoliosis (a combination of kyphosis and scoliosis). The curvature can be treated with physiotherapy and exercises, or a support brace or surgery may be needed.

> ***Our son developed severe scoliosis when he went through a puberty growth spurt at age 13, and recently had spinal fusion surgery at age 14 to correct this. This was a particularly challenging time, as we weren't aware of anyone else with a DYNC1H1-related disorder who has had this surgery. His surgical team hadn't come across DYNC1H1 before but were very thorough in carrying out pre-op assessments to ensure he was fit for surgery. Our son approached this major surgery in his usual determined way and is recovering really well from it."***

Joints

Joint anomalies are a known feature of DYNC1H1-related disorders. These include extremely loose (hyper-mobile) joints (elbows, wrists, knees, hips), which mean babies and children can move their limbs into positions others find impossible. While this may cause no problems, hyper-mobility 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. Some children have a degree of hip dysplasia, in which the hip joints are easily dislocated. This usually happens because the muscles around the joints become weak over time, which makes it harder for the joints to stay stable. This may be apparent at birth or develop later. In either case it is treated with splinting and, if necessary, immobilisation in plaster and possibly surgery.

Hernias

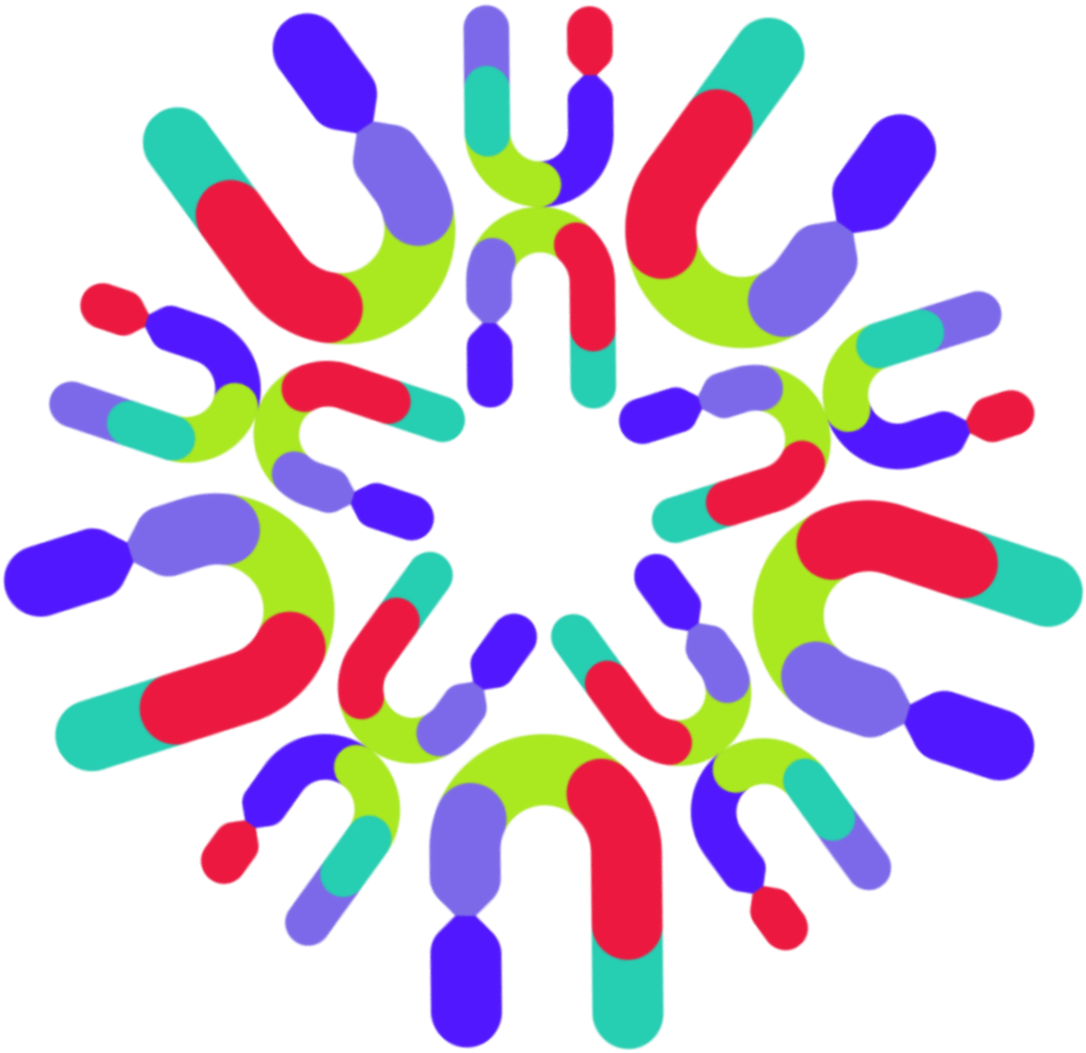
Some babies have been reported as being born with a hernia, where an organ or fatty tissue pushes through a weak spot in a surrounding muscle or tissue. The cases reported have been diaphragmatic (the muscle that separates the chest cavity from the abdominal cavity). In the majority of cases surgical repair was required.

Palate

Anomalies of the palate (roof of the mouth) ranging from those that may be invisible to the casual onlooker such as a high/arched palate to more obvious conditions such as a cleft palate, have been reported in some individuals. Anomalies of the palate, particularly clefting, can cause difficulties in feeding, hearing, teething and speech production. As well as helping aesthetically, surgical repair eases these problems and may even eliminate them altogether.

Kidney and urinary tract

Some babies are born with minor anomalies of the kidneys and urinary tract. Urinary tract infections (UTIs) are relatively common and may need to be treated with antibiotics. Repeated urinary infections may require preventive treatment with antibiotics. Reported anomalies include enlarged kidney(s) (hydronephrosis) due to a build-up of urine inside, which may sometimes be diagnosed during mid-pregnancy anomaly scans. In mild cases this requires monitoring but no treatment. More serious cases can cause UTIs, which can be treated with antibiotics or, very occasionally, a catheter may need to be inserted to remove the build-up of urine and prevent damage to the kidney.



How common is DYNC1H1-related disorder?

DYNC1H1-related disorders are extremely rare. Currently [2025] about 300 individuals with about 150 gene variants reported in the medical literature, but more are known to have been diagnosed. It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.

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 DYNC1H1 gene then a child will have a DYNC1H1-related disorder, which may be one of: CMT2O, SMALED1, or CDCBM13. In most people identified so far [2025] with a DYNC1H1-related disorder, 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 a DYNC1H1-related disorder 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.

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 a DYNC1H1-related disorder so far (2025) the genetic alteration has been found to be *de novo* (dn), which means neither parent was found to have the same DYNC1H1 gene change as their child, and neither parent was found to have a chromosomal rearrangement that might have resulted in a DYNC1H1 deletion in their child. Therefore, the chance of having another child with a DYNC1H1-related disorder 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

In families where the DYNC1H1 variant has been inherited from a parent, the possibility of having another child - either a girl or a boy - with a DYNC1H1-related disorder rises to 50% (1 in 2) in each pregnancy. However, the effect on the child's development, health and behaviour cannot be reliably predicted. Your genetics centre should be able to offer counselling before you have another pregnancy.

If your child with a DYNC1H1 variant goes on to have children of their own, the chances of passing on the variant to their child are 50% in each pregnancy. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

Parental genetic testing has been reported in the medical literature for over 150 individuals with DYNC1H1-related disorders and parental mosaicism for a DYNC1H1 variant has been reported only a few times.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with a DYNC1H1-related disorder.

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 DYNC1H1-related disorders be cured?

There is currently no cure for DYNC1H1-related disorders since most of 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 DYNC1H1-related disorders have been published [2025]. The following suggestions have been provided by clinicians, who have personal experience of managing/treating individuals with DYNC1H1-related disorders, to improve quality of life and reduce complications.

Children and adults with DYNC1H1-related disorders 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 physiotherapy, occupational therapy, speech therapy and, if needed, behavioural therapy. Individuals may have evaluations with neurology to assess how the brain and nerves are working. This may include tests such an EMG, EEG, or MRI to look for signs of nerve problems (axonal neuropathy), seizures, or issues with the brain.

Immediately following diagnosis

When not carried out as part of the diagnostic process, an evaluation of the features of the DYNC1H1-related disorder that are present in the child or adult who has been diagnosed with this genetic condition is recommended. This can determine which of the features of the DYNC1H1-related disorder are present and how severe they are.

Supportive care

Children with DYNC1H1-related disorders are likely to be under the care of a multidisciplinary team. The team should include a community or hospital paediatrician who can oversee care; monitor growth, development and behaviour; and link in with affiliated services.

How a person with a DYNC1H1-related disorder is supported is likely to require co-ordinated care by a 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.

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 – a 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.

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

Treatments and therapies

Early intervention can be beneficial and formal testing to assess specific, individual needs is recommended. An education, health and care plan (EHCP) in the UK, individualized education plan (IEP) in the US, or equivalent document in other countries, may be issued after a child has undergone an assessment, to help ensure that the educational, health and social provisions deemed necessary to support the child's needs are delivered.

Treatment will depend on the specific features and symptoms experienced by the person with the DYNC1H1-related disorder but may include:

Physiotherapy for motor dysfunction, which usually includes stretching and strengthening exercises to improve gross motor skills and mobility.

Occupational therapy for developmental delay, which can include developing fine motor skills, using specialist equipment, or aiding with everyday tasks to improve self-management.

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

Behavioural therapy for ADHD, anxiety, and/or aggressive behaviour, which can include cognitive behavioural therapy to manage/improve behavioural and/or social development.

Medications may be prescribed such as anticonvulsants to reduce/prevent seizures, or NSAIDs to help manage pain.

Diet, such as a high-fibre diet or stool softeners and/or laxatives may be recommended to help relieve constipation. Some benefit from enemas when symptoms are particularly severe.

Surgery such as orthopaedic and/or soft tissue surgery to correct spinal curvature (scoliosis or kyphosis) or foot/ankle issues, such as "claw foot" (pes cavus) or "banana foot" (pes adductus).

> ***He has involvement from genetics, neurology, paediatrics, OT, physio, SALT, ENT, ophthalmology, orthotics and dieticians."***

Surveillance

It is recommended that the following evaluations are carried out/considered to monitor an individual's existing symptoms, how they respond to care and treatment and whether any new symptoms emerge over time:

- Regular dental check-ups
- Consider a palate review (particularly if there are feeding difficulties or speech concerns)
- Consider an annual cardiac review
- Consider a neurologic review (including MRI and EEG, if indicated by seizures)
- Consider a skeletal review
- Consider an abdominal ultrasound and review
- Assessment of the need for social support, such as respite care and home nursing care, or genetic counselling and family planning advice

Research into new treatments for DYNC1H1-related disorders

The genetic change causing DYNC1H1-related disorders affects 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 DYNC1H1-related disorders, like autism, epilepsy and ADHD, is ongoing. In addition, although DYNC1H1-related disorders are rare conditions, the DYNC1H1 gene is the subject of a lot of research. Whilst no DYNC1H1 specific treatments are currently being trialled, extensive effort is being invested into understanding the function and involvement of DYNC1H1 in its associated disorders. However, there are several pharmacological drugs currently in trial that may benefit DYNC1H1-related disorders (notably SMALED1 and CMT2O) by targeting proteins involved in muscle growth and movements, aiming to improve their strength.

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

Families say ...

"Our son is 14; he was diagnosed with a DYNC1H1-related disorder when he was 8. It was a huge relief to finally get a diagnosis after years of not knowing what had caused his multiple physical and learning disabilities. We were told at the time there were only a handful of people worldwide with a DYNC1H1 variant, and were given very little information about it, and nothing aimed specifically at families. The DYNC1H1 community has grown a lot since then, and it's been great to get in touch with other families and have a network of support around us.

Despite all of his challenges, our son is a very happy, chatty and friendly boy who loves playing games with his friends and laughing and joking with them. He's so determined in everything he does and makes us proud every single day."

"Our son has a unique de novo genetic variant in DYNC1H1. He's a non-identical twin and his twin doesn't have the variant. His development has been an interesting journey, and we believe the best and worst aspects are the fact he is unique. It's tedious telling people about his diagnosis constantly, professionals relying on us for information and there being no certainty about anything... but that's also the best part. His physio said he'd never walk, but we didn't give up and seven years on he's enjoying slopes where he can speed up on the downhill! Being unique means a blank piece of paper. People have to know him for who he is and not by his diagnosis, or what they've read."

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. In 2025, Unique had 16 members with DYNC1H1-related disorders. 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

Amabile, S. et al. (2020). DYNC1H1-related disorders: A description of four new unrelated patients and a comprehensive review of previously reported variants. *American journal of medical genetics. Part A*, 182(9), 2049–2057. **Link to article**

*Birk Möller, M. et al. (2024). DYNC1H1-related disorders. *GeneReviews*® [online]. **Link to article**

*Birk Möller, M. et al. (2024). The expanding clinical and genetic spectrum of DYNC1H1-related disorders. *Brain*, 148(2), pp.597–612. **Link to article**

*Derksen, A. et al. (2021). A novel de novo variant in DYNC1H1 causes spinal muscular atrophy lower extremity predominant in identical twins: A case report. *Child Neurology Open*. **Link to article**

*Liu, W. et al. (2023). DYNC1H1-related epilepsy: Genotype-phenotype correlation. *Developmental medicine and child neurology*, 65(4), 534–543. **Link to article**

*OMIM.org (2011) [updated 2017]. *Charcot-Marie-Tooth Disease, Axonal, Type 2O, CMT2O*. [online] OMIM. **Link to article**

*OMIM.org (2012) [updated 2023]. *Cortical Dysplasia, Complex, with Other Brain Malformations 13; CDCBM13*. [online] OMIM. **Link to article**

*OMIM.org (1986) [updated 2019]. *Spinal Muscular Atrophy, Lower Extremity-Predominant, 1; SMALED1*. [online] OMIM. **Link to article**

Smauk.org.uk. (2022). *Drugs Currently Being Tested in Clinical Trials – SMAUK*. [online] **Link to article**

*Zillhardt, J.L. et al. (2015). Mosaic parental germline mutations causing recurrent forms of malformations of cortical development. *European Journal of Human Genetics*, [online] 24(4), pp.611–614. **Link to article**

Note: an asterisk indicates articles which are “open access” and available to everyone at **pubmed.ncbi.nlm.nih.gov**

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Inform Network Support

Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted, Surrey, RH8, 9EE, UK
Tel: +44(0)1883 723356
help@rarechromo.org I rarechromo.org

Join Unique for family links, information and support:

Become a member

Please help us to help you!

Unique is a charity without government funding, existing entirely on donations and grants.
If you can, please make a donation:

Donate via our website

Facebook groups and other links:

- DYNC1H1 Association
- DYNC1H1 Family Support Private Facebook Group
- Simons Searchlight DYNC1H1 Gene Guide
- Rare Epilepsy Network

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.

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