How common is CLTC-related ID?

CLTC-related ID is rare. Currently (2021) less than 30 children with this diagnosis have been reported in the medical literature. It is expected that more children will be diagnosed with this condition as awareness increases and genetic testing becomes more routine. It is important to know that most severely affected children are likely to be identified first so initial findings may not represent the possible spectrum of severity.

Why did this happen?

When children are conceived, the genetic material is copied in the egg and sperm that make a new child. The biological copying method is not perfect, and random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. This happens naturally and is not due to any lifestyle, dietary or environmental factors. No one is to blame and nobody is at fault. Such changes happen to everyone but it's only when a change affects an important gene that health and/or development are affected.

In most children diagnosed with CLTC-related ID so far, the change in the *CLTC* gene occurred by chance in that child (this is known as *de novo*) and was not found in their parents.

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. If the change in the *CLTC* gene has been shown to be *de novo*, that means neither parent was found to carry it, the chance of having another child with CLTC-related ID is low (less than 1%). If a parent is found to carry the genetic variant, the chances of having another child with CLTC-related ID is 50% for each pregnancy. A clinical geneticist can give you specific advice for your family.

Can it be cured?

CLTC-related ID cannot be cured at the present time however, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.

Families say .....

" Learning of our daughter's CLTC diagnosis was certainly scary, yet we were so grateful to finally know the root of all of her differences. It helped us tremendously understand her many deficits better and allowed us to become better advocates for her in both the medical and educational environments. " ~ Age 13 years.

" Whilst he finds some aspects of day to day life, especially school difficult, he never gives up & is always smiling. " ~ Age 15 years.

" When we first received the CLTC-Related Disorder diagnosis, it was overwhelming...but also a relief to finally have an answer. Finding out your child has a rare disease can feel isolating at times, but know that there are other kiddos and other families out there - you are not alone! None of the medical professionals that work with our son had ever even heard of his disorder, let alone treated a child with it. Finding a support community was key to being able to share information both amongst ourselves and with our medical team. " ~ Age 17 years.

Inform Network Support

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CLTC Facebook groups:

https://www.facebook.com/groups/214314335821558/

Join *Unique* for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org/donate Please help us to help you!

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. *Unique* does its best to keep abreast of changing information and to review its published guides as needed. This booklet was compiled by Dr Elaine Clark, Consultant in Neurodevelopment at Great Ormond Street Hospital and Unique (AP) and reviewed by Dr David Koolen, Clinical Geneticist, Radboud University Medical Centre, The Netherlands.
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Understanding Chromosome & Gene Disorders

CLTC-related ID

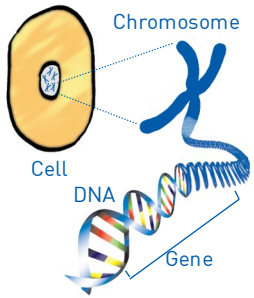
rarechromo.org

What is CLTC-related intellectual disability (ID)?

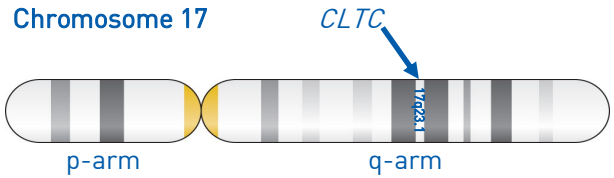
CLTC-related ID is a rare genetic condition that causes developmental delay and can affect a child's learning abilities and behaviour. As is common with genetic conditions, each person is affected differently. CLTC-related ID is also associated with subtle facial features, brain differences and seizures.

What causes CLTC-related ID?

CLTC-related ID is caused by specific changes (known as pathogenic variants) to, or a deletion of, a gene called *CLTC* (*CLTC* is an abbreviation of the gene's full name, Clathrin Heavy Chain).



The *CLTC* gene is located on the long 'q' arm of chromosome 17 in a region called 17q23.1 (see below).



We have two copies of chromosome 17 in our cells, so we also have two copies of the *CLTC* gene.

CLTC-related ID occurs when only one copy of the *CLTC* gene is affected, this is known as autosomal dominant since the change occurred on an autosome (any of the chromosomes numbered 1-22) and features are apparent when only one copy of the gene is altered (this is known as dominant).

The *CLTC* gene sequence is used to make the CHC1 protein. *CLTC* is highly expressed in the developing brain and is thought to play a role in the transmission of activity from one nerve cell to the next (via its impact on the release and recycling of chemicals in the space between nerve cells - the synapse). This may cause neurological difficulties such as those associated with learning and behaviour.

CLTC-related ID features

Most children with CLTC-related ID have:

- Developmental delay (motor and/or speech)
- Intellectual disability (ID) (mild to moderate/severe)
- Subtle facial differences (long face; high, narrow forehead; wide nasal bridge; wide-set eyes; large ears; a wide mouth and large front teeth)
- Behaviour differences such as ADHD and autism
- Brain anomaly identified by MRI
- Weak muscle tone (hypotonia)

Other possible features include:

- Seizures and epilepsy
- Poor motor coordination (ataxia) or muscle stiffness
- Small head size (microcephaly)
- Gastrointestinal problems
- Vision difficulties
- Hearing loss

Medical concerns

Hypotonia

Most children with CLTC-related ID reported so far have been found to have weak muscle tone (hypotonia).

Brain anomaly

Most children with CLTC-related ID who have had a brain MRI have been identified as having a structural brain difference but diagnoses vary.

Seizures

Just over a third of individuals with CLTC-related ID reported so far (2021) are known to experience seizures. The majority experience seizures before the age of 5 years but they can start anywhere between shortly after birth and adulthood. Seizures are fully controlled with antiepileptic medication.

Vision

Mild visual difficulties have been reported including squint (strabismus), involuntary eye-movement (nystagmus) or refractive errors (long or short sight) in a third of children with CLTC-related ID reported so far.

Hearing

Hearing loss does not appear to be common in children with CLTC-related disorder but some extent of hearing loss has been reported in four children with CLTC-related ID to date (2021).

Gastrointestinal and feeding

Feeding can be problematic for some children with CLTC-related ID. Gastroesophageal reflux (GER), constipation, blockage of the small bowel (ileal atresia) and difficulty swallowing (achalasia) have been reported.

Head circumference

Some children with CLTC-related ID have a smaller than usual head circumference.

Development

Intellectual Development and Learning

Most children with CLTC-related ID described to date (2021) have some level of learning difficulty or intellectual disability ranging from mild to severe. More severe intellectual disability is associated with brain anomalies and epilepsy.

Physical Development

Developmental delay of motor function, for example walking, has been reported in most children diagnosed with CLTC-related ID so far (2021).

Speech and language

Some form of speech and language developmental delay or difficulty has been reported in most children diagnosed with CLTC-related ID to date (2021).

Behaviour

The majority of children with CLTC-related ID have been diagnosed with differences in behaviour including ASD (autism spectrum disorder) and ADHD (attention deficit hyperactivity disorder) in a few children.

Management recommendations

Children with CLTC-related ID should be under the care of a multidisciplinary child development team which may include a community paediatrician, speech and language therapist, physiotherapist, occupational therapist and early years support. A referral should be made to an eye doctor (ophthalmologist). A specialist in epilepsy or movement may be required for some children.