What causes HNRNPU-related disorder?

The *HNRNPU* gene is located on chromosome 1. We have two copies of chromosome 1 and therefore two copies of the *HNRNPU* gene. HNRNPU-related disorder is caused by one copy of the *HNRNPU* gene not functioning properly. This may be due to a change (a variant/mutation) within the gene which disrupts its function, or to the loss (deletion) of the gene or part of it. The other copy of the *HNRNPU* gene is unaffected and so can carry out its usual function.This type of genetic change is called autosomal dominant, since the change occurred on an autosome (chromosomes 1-22) and symptoms are apparent with only one altered copy (dominant).

The *HNRNPU* gene has multiple roles in the genetic control of our development and functioning. The HNRNPU protein binds to DNA, RNA (a different type of genetic molecule encoded by our DNA) and chromosomes. Not all functions are fully understood but knowledge in these areas will progress as research continues. This gene is known to be active in the brain, heart, kidney and liver.

Why did this happen?

When children are conceived their parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random, rare changes occur in the genetic code of children that are not seen in the DNA of their parents. HNRNPU-related disorder occurs when one of these random changes affects the *HNRNPU* gene. These types of change happen naturally in all species - humans, plants and animals - and are not due to lifestyle or anything you did prior to, during or after pregnancy.

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 most families, this genetic change has happened for the first time in the child with HNRNPU-related disorder. This is called a '*de novo* mutation'. When the parents are unaffected, the chances of having another child with the same condition are very low. Very rarely, a parent may be identified as having germline mosaicism, which means the gene mutation can be present in the egg or sperm but is not detected in a standard blood test. Each family situation is different and a clinical geneticist or genetic counsellor can offer family specific advice.

Families say ...

" Progress with development is slow for us but our son is making progress so that's what matters. We did wonder how he would develop physically as he didn't walk until two but he can now run as fast as me! Language is still developing, music and singing has helped a lot with this and an awful lot of repetition. He is starting to understand toileting but at five years old he is still learning. The advice I would give is to ensure you have portage involved from a young age as this helped me learn to play and teach my son at the same time, take advantage of any training offered such as language development. Become your own expert in what is available to you and your child through your national health service and through local/community services and if you feel your child needs something then never feel afraid to ask for it. "- Age 5 years

Inform Network Support

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Websites:
HNRNPU foundation: http://hnrnpu.org/
Facebook groups:
www.facebook.com/groups/350878592068230/
www.facebook.com/hnrnpupage/

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!

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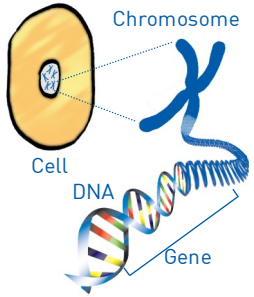
Unique
Understanding Chromosome & Gene Disorders

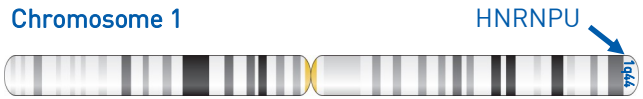
HNRNPU-related disorder

rarechromo.org

What is HNRNPU-related disorder?

HNRNPU-related disorder is caused by changes (also known as variants or mutations) in, or a deletion of, the *HNRNPU* gene. This gene is located at the end of the long 'q' arm of chromosome 1 in a region called 1q44. Its name is an abbreviation of the protein it codes for - heterogenous nuclear ribonucleoprotein U.





Children with HNRNPU-related disorder have neurodevelopmental difficulties. They have developmental delay with learning difficulties or intellectual disability. Their speech and language is affected and they also commonly experience seizures (abnormal electrical activity in the brain) and epilepsy (recurrent seizures).

HNRNPU-related disorder affects boys and girls, and there are both mildly and more significantly affected individuals of both sexes.

Most children have

- Developmental delay
- Moderate to severe learning difficulties or intellectual disability (ID)
- Seizures and epilepsy
- Language and speech difficulties, delay or absence
- Hypotonia (low muscle tone/floppiness)

Some children have

- Small head circumference (microcephaly)
- Unusual findings during brain MRI
- Heart problem
- Kidney abnormality
- Short fingers and toes (brachydactyly) with or without curved 5th finger (clinodactyly)
- Regression (under 5 years)

How common is HNRNPU-related disorder?

HNRNPU-related disorder is extremely rare, about 50 people have been identified worldwide (2019), although many people currently remain undiagnosed.

Medical concerns

The medical concerns experienced by children with HNRNPU -related disorder are extremely variable and impossible to predict. Below are some of the more common problems that a child may experience:

Seizures The majority, but not all, children with HNRNPU-related disorder reported so far (2019) have seizures, of varying types and severity. Seizures usually start prior to five years of age. Many children have also had unusual brain imaging results following an MRI.

Ears and hearing Some children have recurrent otitis media or glue ear (a build-up of fluid in the ear), which can cause temporary hearing loss. Some children have required grommet (small tube) insertions to relieve pressure inside the ear. No long term hearing issues appear to be associated with HNRNPU-related disorder

Eyes and eyesight Children with HNRNPU-related disorder may be more likely to have a squint (strabismus), where the eyes do not look in the same direction. Treatment can include patching, exercises, glasses, and surgery to bring the eyes into line. No long term vision issues appear to be associated with HNRNPU-related disorder.

Skeletal A few children with HNRNPU-related disorder have short fingers (brachydactyly) and some have curvature of the 5th finger (clinodactyly).

Teeth Some children have been reported as having tooth anomalies such as large incisors, irregular or extra teeth.

Heart Although heart anomalies have been reported in a few children, recent reports have not described a link.

Kidneys Although kidney anomalies have been reported in a few children, recent reports have not described a link.

Feeding About half of the children described in the medical literature have been described as having some form of feeding difficulty.

Management recommendations

- Seizure activity may need monitoring
- An assessment of special educational needs should be carried out so that extra help can be put in place at school
- Early input from speech and language, physio– and occupational therapists is important
- Input from a neurology/neurodevelopment team may be required

Development

Physical development

Children with HNRNPU-related disorder learn to walk alone, but this may be delayed slightly. Hypotonia and/or joint hyper-flexibility may play a role in delays.

Learning

Children with HNRNPU-related disorder typically have learning difficulties and are often given a diagnosis of intellectual disability (ID). While most children may attend a mainstream primary school with extra help, the extra demands of mainstream secondary school may prove too challenging. Some children will transfer to special schooling and others may remain in a mainstream school with an Educational Health Care Plans (EHCP). Those with chromosome deletions may have more significant problems, which are probably related to additional deleted genes.

Behaviour

Children with rare chromosome and gene disorders often have behavioural, social and/or communication difficulties and vulnerability in these areas means that children should be monitored and families offered early support. Some children with HNRNPU-related disorder have been identified as having autism or autistic like behaviours such as hand flapping or repetitive behaviour. Some are described as very sociable while others may show signs of aggression.

Speech

For the majority of children with HNRNPU-related disorder identified so far, speech is delayed and limited; some children are non-verbal. Hearing problems due to glue ear at an important stage of language development may worsen speech delay. Language abilities may also be linked to the level of learning disability or ID for each child. Some children have also shown regression in their ability to speak, that may be linked to seizure activity.

Growth

Babies with HNRNPU-related disorder are usually at the lower end of the birth weight scale. Normal to short stature has been reported.

Facial appearance

Various minor facial appearances have been reported in children with HNRNPU-related disorder such as a short nose with anteverted nares (nostrils that tip upwards) and bulbous tip or a thin upper lip. Children have also been reported with wideset eyes (hypertelorism) and deep set eyes, but every child's appearance is different and will change with age.