How common is BRPF1-related disorder?

BRPF1-related disorder is very rare. Currently (2021) less than 50 children with a pathogenic *BRPF1* gene variant have been reported in the medical literature. With increasing knowledge and availability of genetic testing, it is expected that more children and adults will be diagnosed with this condition over the next few years.

Why did this happen?

When children are conceived, the genetic material is copied in the egg and sperm that makes them. The biological copying method is not perfect, and random rare changes occur in the genetic code of children, which 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. We all carry different changes in our DNA, it's only when a change alters the functioning of an important gene that effects are seen.
In most children with BRPF1-related disorder diagnosed so far, the change in the *BRPF1* gene occurred by chance in the child (this is known as *de novo*) and was not found in their parents. However, a few parents have been found to carry a pathogenic *BRPF1* gene variant in a few, but not all, of their cells (this is known as mosaicism).

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 *BRPF1* gene has been shown to be *de novo*, it means that neither parent was found to carry it. When the gene change occurs *de novo*, the chance of having another child with BRPF1-related disorder is low (less than 1%). The risk is not zero, since occasionally a parent may carry the gene change in their egg or sperm (this is called gonadal mosaicism). If a parent is found to carry a *BRPF1* gene variant, there is a 50% chance of it being passed on in each pregnancy, unless the parent does not have the variant in all of their cells (this is called somatic mosaicism), in such cases, the chances are lower than 50%. A clinical geneticist or genetic counsellor can give you specific advice for your family.

Families say ...

" 'Unique' describes our son. Physically mobile, robust and resilient, his ASD, ADHD and PDA describe a complex young man with learning delay and huge hunger for activity and knowledge. Emotionally fragile, he is loving but volatile, with aggression arising from his anxieties. Being around him is an adrenaline rush in uncharted territory! " ~ 12 years.

" She sees an occupational therapist who works on a variety of areas due to her GDD but mostly self help skills. We have had a lot of trouble with toilet training and doing things for herself. She also struggles to stay on task and often gives up new experiences before even trying. She also has trouble retaining information, she seems to regress in areas she has learnt when moving on to a new skill. " ~ 5 years.

Inform Network Support

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

Websites, Facebook groups and other links:

https://www.facebook.com/groups/brpf1Support

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

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 Unique (AP) and Dr Rebecca Poole, Specialty Registrar in Clinical Genetics, South East of Scotland Clinical Genetics Service, Edinburgh, and reviewed by Dr Lara Menzies, Specialty Registrar in Clinical Genetics and Dr Francesca Faravelli, Consultant in Clinical Genetics, Great Ormond street Hospital, London, UK.

Version 1 (AP) 2021

Rare Chromosome Disorder Support Group
Registered in England and Wales
Charity Number 1110661
Company Number 5460413

Understanding Chromosome & Gene Disorders

BRPF1-related disorder

rarechromo.org

What is BRPF1-related disorder?

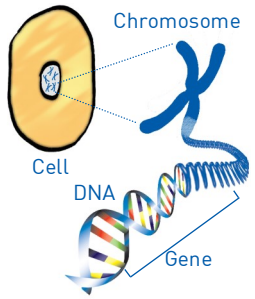
BRPF1-related disorder, also known as IDDDFP (intellectual developmental disorder with dysmorphic facies and ptosis) is a rare genetic condition that has been reported in less than 50 people to date (2021).

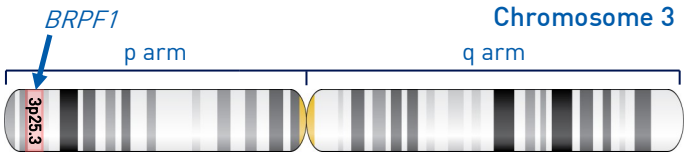
Children with BRPF1-related disorder have global developmental delay and their intellectual abilities are affected. Babies and young children may have feeding difficulties and decreased muscle tone (hypotonia). Many children identified with BRPF1-related disorder have difficulties with expressive speech and language and some children have behavioural difficulties. Children with BRPF1-related disorder may also have other features such as distinctive facial features or joint hypermobility (joints that stretch more than expected).

What causes BRPF1-related disorder?

BRPF1-related disorder is caused by specific changes (known as pathogenic variants) or deletions, of a gene called *BRPF1*.

The *BRPF1* gene is located on the short 'p' arm of chromosome 3 in a region called 25.3 as shown in the image below. We have two copies of chromosome 3 in our cells, so we have two copies of the *BRPF1* gene.





BRPF1-related disorder occurs when one copy of the gene is affected. This is known as autosomal dominant since the change occurs on an autosome (any of the chromosomes numbered 1-22) and the features are apparent when only one copy of the gene is altered (dominant).

The *BRPF1* gene codes for the BRPF1 protein which plays an important role in brain development and functioning.

BRPF1-related disorder features

Most children with BRPF1-related disorder have:

- Global developmental delay (GDD)
- Intellectual disability (ID)
- Expressive speech delay
- Gross and/or fine motor delays
- Eye anomalies

Some children with BRPF1-related disorder have:

- Joint hypermobility
- Spinal anomaly (fusion of neck vertebrae)
- Distinctive facial features
- Brain anomaly detected by MRI
- New-born feeding difficulties
- Seizures

Medical concerns

Eye anomalies

Most children with BRPF1-related disorder have an eye anomaly including droopy upper eyelids (ptosis) or underdeveloped eyelids (blepharophimosis), where the eyes may not appear fully open. In some cases, this may need surgery. Some children may have mild problems with their vision, for example, they may be long-sighted, near-sighted or have a squint (strabismus).

Joint hypermobility

Hypermobile joints have been identified in several children with BRP1-related disorder described so far and can cause difficulties with motor development, for example delayed walking. Children may also tire more easily. Physiotherapy can be helpful.

Brain and spinal anomalies

For those who have had a brain MRI, about half showed unusual findings, these were different for each child. Fusion of neck vertebrae (C2-C3 of the cervical spine) have also been reported in four children to date (2021). Review by a spinal doctor should be considered for individuals with a spinal anomaly, in particular if they have any related pain or mobility difficulties.

Seizures

Seizures have occurred in a few children with BRPF1-related disorder and possible seizure episodes should be investigated.

Development

Physical development

Children with BRPF1-related disorder may show delays in reaching motor milestones. Some children learn to crawl and walk slightly later than the average expected age.

A small number of children have been noted to have possible early puberty with early growth of pubic hair. Such features should be investigated by an endocrinologist (a doctor who specialises in glands and hormones).

Intellectual development and learning

Children with BRPF1-related disorder usually have learning difficulties or intellectual disability, which can be mild, moderate or severe. Most children need additional support at school, and some may benefit from the additional resources offered in special schooling.

Speech and language

Children with BRPF1-related disorder typically have delayed speech and language. The ability to speak may be more affected than the ability to understand language. Children may find additional ways to communicate. Input form a speech and language therapist may be helpful.

Behaviour

Challenging behaviours have been reported in some children with BRPF1-related disorder. Autism spectrum disorder (ASD) and/or ADHD have also been reported in a few children. Input from a psychologist may be helpful.

Can it be cured?

BRPF1-related disorder cannot be cured at the present time. However, knowing the diagnosis means that appropriate support, monitoring and management can be put in place for individuals and their families.

Management recommendations:

Children with BRPF1-related disorder are usually under the care of a multidisciplinary team including a neonatologist, community paediatrician, clinical geneticist, ophthalmologist, physiotherapist and speech and language therapist. A neurologist may also be involved if there is concern about possible seizures, or an orthopaedic review may be considered for spinal anomalies.