

What causes BWCF syndrome?

Changes (mutations) in the *ACTB* and *ACTG1* genes cause BWCF syndrome. These genes code for proteins that have a crucial role in many functions of the cells of the body. Changes in *ACTB* and *ACTG1* that result in the production of altered proteins interfere with these functions. For example, these genes are required to make proteins which are needed for the normal development of brain cells (neurons). So far the majority of children and adults with BWCF have been found to have mutations in *ACTB*. However, there are no obvious differences between people with mutations in either gene. Changes to *ACTB* that results in the loss of the *ACTB* protein (as opposed to an altered *ACTB* protein being made) causes a different outcome.

Why did this happen?

When children are conceived your genetic material is copied in the egg and sperm that make 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. These types of changes happen naturally in all species, including humans, and are not due to your lifestyle or anything you did. BWCF syndrome occurs when one of these random changes affects the *ACTB* or *ACTG1* genes. In most families, these changes occur out of the blue (*de novo*). In a minority of families, one parent may have the same genetic change as their child, but this is very rare.

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. For BWCF syndrome, where parents do not carry the genetic change, the chance of having another child is almost always very low. If the genetic analysis of the parents of a child with BWCF shows they carry the same variant, the chance of it happening again is much higher. Each family situation is different and a clinical geneticist can give you specific advice for your family.

Can it be cured?

BWCF syndrome cannot be cured at the present time. However, treatment is available for many of the medical problems, like epilepsy, which can be associated with the condition.

Families say ...

“ Having a diagnosis was daunting at first, however we realised that as there is such a wide spectrum of difficulties and such a small number of individuals diagnosed, it gives our son the chance to reach his full potential, whatever that might be. ”

“ We were told the future was uncertain in regards to intellectual disability but that stimulation was key to our son reaching his full potential. We have therefore provided him with as many opportunities to develop as possible, engaging fully with therapies as well as normal baby groups. He is continuing to surprise the professionals everyday with his progress. ”



Inform Network Support



Rare Chromosome Disorder Support Group,

The Stables, Station Road West,
Oxted, Surrey RH8 9EE, UK
Tel: +44(0)1883 723356

Understanding Chromosome & Gene Disorders info@rarechromo.org | www.rarechromo.org

Facebook Groups

<https://www.facebook.com/groups/963637817091894>

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Understanding Chromosome & Gene Disorders

Baraitser-Winter (BWCF) syndrome



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What is BWCFF syndrome?

Baraitser-Winter Cerebrofrontofacial syndrome (BWCFF) is a genetic condition, caused by changes in the *ACTB* and *ACTG1* genes that cause production of proteins with altered function. It is associated with distinct face and eye anomalies, intellectual disability and abnormal development of the grey matter of the brain.

The *ACTB* gene is found on chromosome 7, in the band numbered 7p22.1, between base pairs 5,527,147 and 5,530,600.

The *ACTG1* gene is found on chromosome 17 in the band numbered q25.3 between base pairs 81,509,970 and 81,512,865.

Base pairs are the chemicals in DNA that form the ends of the 'rungs' of its ladder-like structure. There are millions of base pairs in every chromosome.



Other names

The term Baraitser-Winter Cerebrofrontofacial syndrome includes several conditions which were previously known by different names, before the gene changes underlying the disorders were discovered. The syndrome was first named Baraitser-Winter syndrome (BWS) after the doctors who described it in 1988. Another two conditions, Cerebrofrontofacial syndrome (types 1 and 3) and Fryns-Aftimos syndrome are now known to also be caused by changes in the same genes, *ACTB* and *ATCG1*, as BWCFF, and they are considered part of the same syndrome.

Most people with BWCFF have:

- Intellectual disability or slow learning
- Developmental delay and learning difficulties (degree differs between individuals)
- Characteristic facial features, such as hypertelorism (widely spaced eyes)
- Ptosis (drooping of the eye lids)
- Pachygyria (thickened grey matter of the brain with reduced folds).

Medical concerns

■ Vision (ptosis and coloboma)

Drooping eyelids (ptosis) are very common. Significant ptosis may require surgery to lift the eye lid.

Coloboma is a gap in the eye structure, for example the iris, or the retina (the back of the eye). Depending on the location of the coloboma in the eye, vision may be affected. A few children have small eyes (microphthalmia), a squint or are short-sighted.

■ Hearing

Variable sensorineural hearing loss (permanent nerve deafness) can develop, and can be progressive. Hearing aids may be required.

■ Epilepsy

If there are any anomalies of the brain structure, particularly pachygyria, it is likely a child with BWCFF will develop epilepsy. This is a seizure disorder, which usually needs to be treated with medication. Seizures commonly start before the age of five years. No cases of epilepsy have been seen when the brain scan looked normal.

■ Heart anomalies

Several different heart conditions are known to be associated with BWCFF. These are present from birth. They may require surgery and/or medication.

■ Cleft lip and palate

Some babies are born with a gap in the lip and/or roof of the mouth that requires surgical repair.

■ Hernia

Some babies are born with a hernia, or this appears later. Usually it is an umbilical hernia, which is seen as a swelling around the navel (tummy button). They mostly close on their own after a few years, but sometimes an operation is required.

■ Kidneys

Structural anomalies of the kidneys and urinary system have been found in a small number of children with BWCFF. This includes hydronephrosis – swelling of the kidneys – which has many causes; the treatment depends on the cause.

Is there a typical facial appearance?

Children and adults with BWCFF usually have a distinct appearance. Common features include a ridge down the middle of the forehead (metopic ridge) and a narrow forehead (trigonocephaly); arched eyebrows; ptosis; a short nose; a flat tip of the nose; a long philtrum (the area between the nose and upper lip) and a wide mouth.

Development

■ Learning

Developmental delay and intellectual disability is very variable, ranging from mild to severe. The degree of severity often corresponds to the amount of structural/grey matter change in the brain. Children and adults with a normal brain structure appear to have only mild to moderate problems.

■ Behaviour

Specific behavioural challenges have so far not been distinguished in children with BWCFF syndrome.

■ Speech

Speech development is commonly delayed, and in some children does not develop, or remains limited.

■ Growth

Some children may have a mild to moderate short stature and mild microcephaly (small head).

■ Physical development

Kyphosis (rounding of the back or spine) and scoliosis (curvature of the spine) can develop in some children.

Some adults develop a 'rounded back' posture with forward facing shoulders and slightly bent elbows and knees. This is thought to be a muscular problem.

Some adults may develop increasing problems with walking, possibly due to very gradually progressive muscle weakness.

Hearing problems can be progressive.

Management recommendations

At the time of diagnosis, screening for colobomas, hearing problems, and heart and kidney anomalies should be undertaken, if not done previously. A brain scan is important if seizures are present, and/or moderate to severe developmental delay/learning difficulties; with only mild delay, the need for a brain scan can be discussed.