Why did this happen?

A blood test to check both parents' chromosomes is needed to find out why the 16p13.11 microduplication occurred. The vast majority of children are believed to inherit the 16p13.11 microduplication from a parent. However, in some cases the microduplication occurs when both parents have ordinary chromosomes. The term that geneticists use for this is *de novo* (dn) which means 'new'. *De novo* 16p13.11 microduplications are caused by a change that occurred when the parents' sperm or egg cells formed, or possibly during formation and copying of the early cells after the egg and sperm joined.

Whether the microduplication is inherited or *de novo*, as a parent there is nothing you did to cause the 16p13.11 microduplication and nothing you could have done would have prevented it from occurring in your baby. No environmental, dietary or lifestyle factors are known to cause these chromosome changes. There is nothing that either parent did before or during pregnancy that caused the microduplication – so no-one is to blame and there is no reason for anyone to feel guilty.

Can it happen again?

The possibility of having another pregnancy with a 16p13.11 microduplication depends on the parents' chromosomes. If both parents have "normal" chromosomes on a blood test, the possibility of having another child with a 16p13.11 microduplication is low. It is possible that the duplication occurred during the formation of the egg or sperm cells in a parent, meaning there could be more than one egg or sperm carrying the duplication (called germline mosaicism). When this occurs there is a tiny chance that parents with apparently unaffected chromosomes could have another affected pregnancy.

In families where the microduplication has been inherited from a parent the possibility of having another child with the microduplication rises to about 50 percent (1 in 2) in each pregnancy. However, the effect of the microduplication 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 one person in a family is mildly affected, will others in the same family also be?

Not necessarily. There is a lot of variation between different members of the same family who have the same microduplication. We know that if one person is mildly affected or unaffected, others may be more severely and obviously affected.

What is the outlook?

We can't be sure yet but there appears to be no reason why people who are healthy should not enjoy a normal lifespan. An ever-increasing number of adults with 16p13.11 microduplications have been reported and many have no developmental delay or health issues and only discovered they carried the microduplication after their child was diagnosed. A number of adult members of *Unique* live an independent life having successfully completed their schooling and gone on to work in a variety of occupations, including nursing and management. Some adults with a 16p13.11 microduplication have developed adult-onset conditions, including a cardiovascular disorder called thoracic aortic aneurysm dissection (TAAD). It has been suggested that routine screening from childhood onwards is carried out to identify and monitor cases of aortic dilation.

Inform Network Support

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Join *Unique* for family links, information and support

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This 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 information guide was compiled by Unique (CA) using information from the comprehensive Unique information guide to 16p13.11 microduplications (2024) and reviewed by Dr Hannah Titheradge, Consultant in Clinical Genetics at Birmingham Women's and Children's NHS Foundation Trust, UK.

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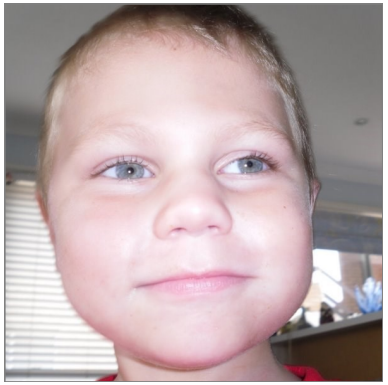
Understanding Chromosome & Gene Disorders

16p13.11 microduplications



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What is a 16p13.11 microduplication?

A 16p13.11 microduplication is a very rare genetic variation in which there is an extra copy (duplication) of a tiny piece of chromosome 16. The duplication is found near the middle of the short arm of the chromosome at a place called p13.11. Because the extra bit is very tiny indeed, you will sometimes see it called a microduplication.

Are all people with a 16p13.11 microduplication affected in the same way?

Most of what we know about 16p13.11 microduplications comes from studying people who have a reason for having a genetic test. The reason might be developmental delay, unusual behaviour or a health concern, or perhaps the 16p13.11 microduplication has been found in someone else in their family. This gives us a biased sample; however, what is clear is that the effect on a carrier of a 16p13.11 microduplication can range from "silent", meaning there are no obvious unusual features, to having additional learning needs and/or medical concerns.

You may read or hear the terms "incomplete penetrance" and "variable expressivity" in relation to 16p13.11 microduplications. This is because the features of people with a 16p13.11 microduplication vary widely, even among members of the same family. Some people can have developmental delay, learning difficulties and behavioural concerns, but many people with the microduplication have no apparent physical, learning or behavioural concerns.

Why people show such variability in the range and severity of features, even when they have the same – or very similar - genetic change, are complex and not yet fully understood. It is likely to be a combination of other genetic variants across the genome as well as different environmental factors.

Development

Gross and fine motor skills

While gross motor skills, including rolling over, sitting and walking, can be unaffected, one of the first signs may be a delay in reaching these milestones. Mobility may be affected by high muscle tone (hypertonia) or more commonly low muscle tone (hypotonia), which generally improves with maturity. Regular physiotherapy helps, and the use of orthotics such as support boots may also help increase mobility.

A delay in the development of hand use and hand-eye coordination (fine motor skills) may be observed. Some children have occupational therapy to try to help overcome these difficulties.

Features of 16p13.11 microduplications

The features associated with 16p13.11 microduplications are believed to be caused by the presence of three copies of the genes in this region instead of the normal two copies. Features vary, even between members of the same family, and they do not affect everyone. In any individual, when present, a feature can be more or less obvious.

- Some degree of developmental delay
- Some degree of learning (intellectual) disability/learning difficulties
- Speech and language delay
- "Challenging" behaviours & social, emotional & anxiety disorders

Less common features include:

- Feeding difficulties
- Heart conditions (including Aortic dilation and thoracic aortic aneurysm dissection (TAAD))
- Seizures
- Skeletal anomalies
- Vision/structural eye anomalies
- Skeletal anomalies
- Hearing concerns
- Anomalies of the brain, kidneys, urinary or genital systems
- Anomalies of the hands and feet

Learning

Children may need support with learning. While some children don't have any learning (intellectual) disability and/or learning difficulties, most have mild to moderate learning disability, but for a few a severe or profound learning disability has been reported. The amount of support needed by each child will therefore vary, although most benefit from supportive services for special needs.

Behaviour

In general, children are happy and affectionate. However, they are as vulnerable to frustration as other children with a communication difficulty and a small minority succumb to temper tantrums and aggression.

Alongside this, one of the most common features of 16p13.11 microduplications are behavioural and emotional disorders. The most common of these, certainly among members of *Unique*, are an autism spectrum disorder (ASD) and/or attention deficit hyperactivity disorder (ADHD).

It has also been proposed that duplications of 16p13.11 increase the chance of developing mental health concerns such as schizophrenia. These occur as the result of multiple physical, genetic, psychological and environmental risk factors, rather than just one single genetic difference such as 16p13.11 microduplication. Carriers may therefore never develop any of these mental health conditions. Schizophrenia can be treated using a combination of medical treatments, such as antipsychotic medicines, and psychological interventions, such as cognitive behavioural therapy.

Speech and language

Some, although not all, children have a delay in acquiring speech and language skills and a few are described as non-verbal. There are also a few cases where children have experienced regression in their level of speech. Where a speech delay is suspected, parental concerns should be acted on early to ensure home- or school-based therapy is provided. Speech therapy can prove extremely effective.

Feeding

Feeding difficulties do not appear to be a consistent feature but there are a number of cases of babies and children who were very fussy eaters. Several babies experienced acid reflux. Where feeding difficulties were linked to a 'failure to thrive', a few children have needed a nasogastric tube for several weeks or months. Other children benefit from seeing a dietician. There are several cases of chronic constipation that required treatment, including the use of laxatives. Several children are described as having food intolerances and allergies.

Medical concerns

Heart conditions

For a few babies the heart is affected, with conditions including ventricular septal defect (VSD), atrial septal defect (ASD), pulmonary stenosis, and hypoplastic left heart syndrome. A 16p13.11 microduplication has also been suggested to be a susceptibility factor that increases the chance of developing aortic dilation, which is the widening of the main blood vessel from the heart. This can be managed with medication and, where indicated, surgery, to present dissection (rupture of the main blood vessel), also called TAAD. The majority of individuals with 16p13.11 duplication do not develop TAAD.

Other conditions

Occasionally, other medical conditions such as seizures; skeletal anomalies; hearing concerns; vision/structural eye anomalies; anomalies of the brain, kidneys, urinary or genital systems; and anomalies of the hands and feet, have been reported.