Understanding Chromosome & Gene Disorders

15q11q13 Duplications (interstitial)

rarechromo.org

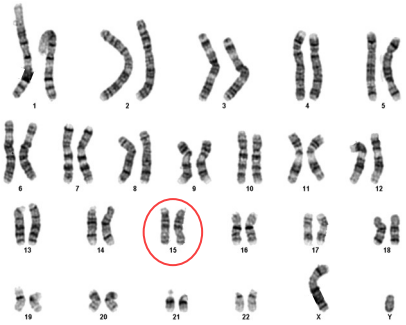
15q11q13 duplications

A 15q11q13 duplication is a rare genetic condition caused by a duplicated piece of genetic material from one of the body's 46 chromosomes – chromosome 15.

For typical and healthy development, chromosomes should contain the expected amount of genetic material. Like many other chromosome disorders, having an extra piece of chromosome 15 may affect a child's development and intellectual abilities. The outcome of having a 15q11q13 duplication is very variable and depends on a number of factors including what and how much genetic material is duplicated and whether the duplicated DNA is from the chromosome 15 inherited from the mother or the one inherited from the father.

Background on chromosomes

Our bodies are made up of different types of cells, almost all of which contain the same chromosomes. Each chromosome consists of DNA that codes for hundreds to thousands of genes. Genes can be thought of as individual instruction booklets that contain all the genetic information that tells the body how to develop, grow and function. Chromosomes (and hence genes) usually come in pairs with one member of each chromosome pair being inherited from each parent. Most cells of the human body have a total of 46 (23 pairs of) chromosomes. The egg and the sperm cells, however, have 23 unpaired chromosomes, so that when these cells join together at conception, the chromosomes pair up to make a total of 46. Of these 46 chromosomes, 44 are grouped in 22 pairs, numbered 1 to 22. The remaining two are the sex chromosomes that determine biological sex. Males usually have one X chromosome and one Y chromosome, and females usually have two X chromosomes.



Chromosomes pairs 1-22, X and Y (male)
Chromosome pair 15 is circled in red

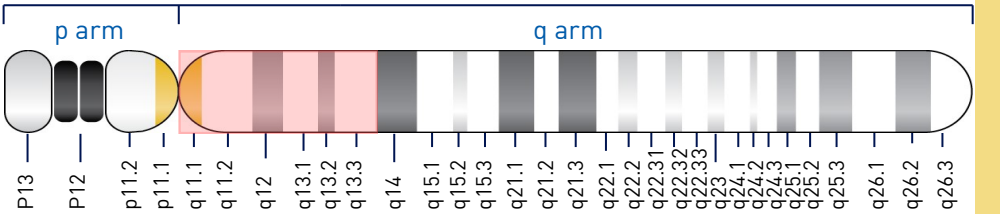
Sources

The information in this booklet is drawn from published medical literature, information from *Unique* members, Dup15 Alliance members and the DECIPHER database. The first-named author and publication date from articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (http://www.ncbi.nlm. nih.gov/pubmed). If you wish, you can obtain most articles from *Unique*. Information gathered from DECIPHER (DatabasE of genomiC varIation and Phenotype in Humans using Ensembl Resources) is open access and can be found at https://decipher.sanger.ac.uk. 18 families competed a *Unique* survey in 2016.

Looking at 15q11q13

Chromosomes can't be seen with the naked eye but if cells are prepared in a specific way, the chromosomes can be stained and viewed under a microscope to show a distinctive pattern of light and dark bands. You can see the banding pattern for each chromosome in the image on page 2, and a more detailed diagrammatical view for chromosome 15 in the image below.

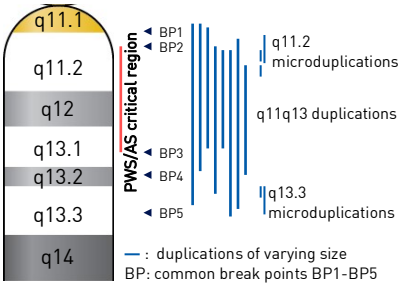
Chromosome 15



Each chromosome has a short (p) arm and a long (q) arm. Bands are numbered outwards starting from where the short and long arms meet, at a point called the centromere (coloured yellow in the image above). Region q11 to q13 is close to the centromere on the long arm (q) of chromosome 15 (shaded red in the image above), it can be split further into bands q11.1, q11.2, q12, q13.1, q13.2 and q13.3 as shown by the numbering above and in the image below.

Duplications in region 15q11q13

Since there are regions in this part of chromosome 15 where breakage and duplication are more likely to occur, some people will have very similar duplications but others will have a slightly larger or smaller duplication that will contain different genes. The type of duplication discussed in this information guide is commonly referred to as 15q11.2q13.1, however, since families will receive slightly different genetic test results, for simplicity, duplications will be referred to as 15q11q13 in this guide unless otherwise specified. Unique has a separate guide for 15q13.3 microduplications (relatively small duplications) and a 15q11.2 microduplication guide is planned (2019). If your child's duplication extends to one or both of these regions you may wish to also read these guides.



The duplication described in this guide is known as an interstitial duplication, which means that the duplicated piece of DNA is added to an existing chromosome (presumed to be chromosome 15 next to the original piece of DNA). It is also possible to have two extra copies of this region of chromosome 15 that form an additional small chromosome. This is known as isodicentric 15 or idic(15), Unique has a separate information guide for this chromosomal rearrangement.

Many years ago, a duplication at 15q11q13 would have been identified by the basic band staining procedure shown on page 2. A laboratory technique called FISH (fluorescence *in situ* hybridisation) was later developed which enables sections of chromosomes to be analysed in more detail. This technique uses fluorescently labelled pieces of DNA that match the DNA in specific places on a chromosome so is only offered as a test if there is a suspected change in a specific region of a chromosome. The most recent test now available that allows DNA to be analysed in greater detail is called microarray comparative genomic hybridisation (array CGH). An array CGH test can detect very small duplications even when a specific diagnosis is not suspected but it cannot identify if the new piece of DNA is located next to the original piece of DNA on the same chromosome, or if it is located in a different place, or on a different chromosome, or has formed an additional small chromosome.

Chromosome test results

Your geneticist or genetic counsellor will have given you more information about the piece of DNA that has been duplicated in your child. Nowadays, this will most likely include an arrayCGH test result such as that detailed below.

Array CGH example:

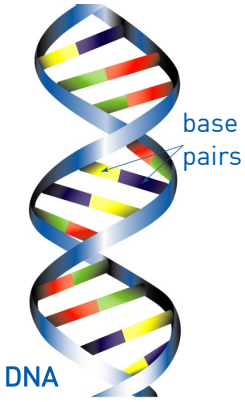
arr[hg19] 15q11.2q13.1 (23651578-28664977)x3 dn

arr The analysis used microarray technology

hg19 This is the reference DNA sequence that the base pair numbers refer to, in this case Human Genome build 19 (for more information, see page 5)

15q11.2q13.1 The analysis revealed a DNA anomaly on chromosome 15, region q11.2 to q13.1

(23651578-28664977) The DNA anomaly is identified by its base pair numbers (the points where the chromosomal change has occurred). In this example, the DNA anomaly lies between base pairs 23651578 bp and 28664977 bp. This region covers 5,013,399 base pairs, or more simply ≈5 Mb (1 Mb = 1,000,000 base pairs)



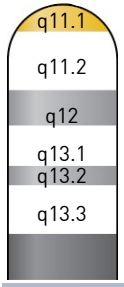
x3 There are three copies of the piece of DNA specified. Since there should be 2 copies of chromosome 15, this shows that the DNA anomaly is a duplication

dn The duplication occurred *de novo* (as a 'new event'). The parents' chromosomes have been checked and no duplication has been found in this region of chromosome 15

If a duplication is identified as *de novo*, it is very unlikely to have been inherited. If a test result is followed by mat, the duplication has been inherited from the child's mother (maternal); if it is followed by pat, the duplication has been inherited from the child's father (paternal).

If a duplication is found to be inherited, other family members can have a DNA test such as a microarray, FISH or qPCR (quantitative Polymerase Chain Reaction; a quick test that can be designed specifically for the duplicated piece of DNA to identify any increase in copy number). A FISH test (see page 3) can also show whether the extra piece of genetic material has been placed on chromosome 15 next to the original piece or if it has been placed elsewhere. FISH may also be able to detect mosaicism. Mosaicism is when not all cells in the body contain the extra piece of genetic material. In such a case, the outcome of having this duplication may depend on which cells in the body contain the extra DNA.

Some families are also offered a test to establish if the duplicated piece of genetic material is from the chromosome 15 inherited from the mother or the one inherited from the father. This is because there are genes in this region of chromosome 15 that are subject to genomic imprinting which means the expression of these genes depends on the 'parent of origin'. Imprinted genes are 'switched off' and this is a normal process required for normal neurodevelopment. In this region of chromosome 15, there are genes known to be 'switched off' on the mother's chromosome 15 and that of the father (see below). It is thought that the effects of a 15q11q13 duplication may vary depending on the parental origin of the duplicated DNA. This is known to be the case when this piece of chromosome 15 is deleted, which causes Prader-Willi/ Angelman syndrome (PWS/AS) depending on which parent the chromosome with the deletion was inherited from.



Important genes identified within the PWS/AS region include:
NDN, SNRPN, MKRN3, MAGEL2 (only copies inherited from the father are usually active in certain cells)
ATP10A and UBE3A (only copies inherited from the mother are usually active in certain cells)
GABRB3, GABRA5 and GABRG3 (GABA receptor genes are important for brain development and function)
OCA2, HERC2, CYFIP1, NIPA1, NECDIN, MKRN3, MAGEL2, snoRNAs.

Genome Assemblies

The human genome project, an international effort to sequence the entire human genome and map all of its genes, was announced complete in 2003. However, there were many gaps in the sequence and mapping data, and scientists have since been working continuously to identify the missing information. When new sequence information is identified, the base pair numbers of each chromosome change slightly and hence the duplication coordinates can shift.

Each new version of the genome is often referred to as an 'assembly'. Every few years a new assembly is released. The genetic information in this guide is based on the Genome Reference Consortium (GRC) human (h) genome assembly number 37 (GRCh37), which was released in 2009. You will often see the DNA sequence data for this assembly referred to as hg19 (human genome 19) on a genetic report.

The databases commonly used by clinical geneticists and Unique will soon move to a more recent assembly named GRCh38/hg38, which was released in 2014. Genetic reports will at some point also be altered, so genes and genetic changes may have new base pair numbers.

You may wish to compare your child's results with others who have the same or a similar duplication to help understand your child's development. While this may help identify common consequences, it is important to remember that the same duplication can have very different effects on different people. Siblings with the same parents and the same duplication can have different outcomes. A child's other genes, environment and unique personality help to determine their future development, needs and achievements. It is very important to see your child as an individual and not to rely on direct comparisons with others who appear to have the same or a similar duplicated piece of DNA.

How common are 15q11q13 duplications?

It is difficult to estimate the prevalence of 15q11q13 duplications since many children will not have been diagnosed, and many of those who are diagnosed are not reported in the literature and may not join support groups. There are currently less than 100 case reports in the medical literature and database reports. A recent study combining results from over 50 thousand children/adults with developmental delay and/or behavioural difficulties identified just over 50 children with an interstitial 15q11q13 duplication (Isles 2016).

It is very important to note that 15q11q13 duplications have also been identified in the general population, i.e. people without any obvious symptoms. Such people are often referred to as healthy carriers, and include parents from whom a duplication has been inherited. A recent publication (Isles 2016) noted that roughly 60% of reports in the medical literature describe a 15q11.2q13.3 interstitial duplication as being *de novo*, which means the duplication occurred as a new event in that person. The same publication estimates that, in the general population, duplications of a maternal origin are twice as likely to occur than duplications of the paternal chromosome in this region of chromosome 15. Interstitial 15q11q13 duplications are more commonly identified as being of maternal origin in people with developmental delay and neurodevelopmental difficulties and are less frequently reported than Idic15 (Isles 2016, Funicane 2016). The reason that duplications of the paternally inherited chromosome are less frequently identified may be partly due to the fact that children with such a duplication are thought to be less affected, or not affected by their extra piece of DNA, and would therefore be less likely to be offered a genetic test, but it is also apparent that paternally inherited duplications are less frequent in the general population than those inherited from the mother.

Unique currently has 73 members (63 families) with an interstitial duplication that includes region q11q13 of chromosome 15 who live worldwide. Seven of these families also have anomalies on other chromosomes or additional changes on chromosome 15. Unique has many other members with Idic(15) as described on page 4 or microduplications in 15q11.2 or 15q13.3 which are, or will be, explained in separate Unique guides. Only those with an interstitial 15q11q13

duplication (and no other chromosomal anomaly) will be considered in this guide since, for others, the reason for some of their clinical features may be due to additional chromosomal anomalies. This guide may however be of use to such families to partly explain their child's difficulties. Unique currently has 62 members (56 families) with such a 15q11q13 interstitial duplication; 18 families completed a survey in 2016.

Why did this happen?

When sperm and egg cells join they form a single cell and this cell must continuously make copies of itself (and all its genetic material) in order to produce the billions of cells that are necessary for human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated replication process, parts of a chromosome are lost, duplicated and/or become rearranged. The reason the duplication occurred in this specific region of chromosome 15 is thought to be due to the repetitive nature of the DNA sequence in this region. It is important to know that as a parent there is nothing you could have done to prevent this from happening. No environmental, dietary or lifestyle factors are known to cause 15q11q13 duplications. There is nothing that either parent did before, during or after pregnancy that caused the duplication.

Can it happen again?

If a parent is found to have the same duplication as their child, the possibility of having another child with this duplication is 50% in each pregnancy. If neither parent is found to have this chromosomal change, it is unlikely that they will have another child with a 15q11q13 duplication. Very rarely, parents are identified as having unaffected chromosomes by a blood test, but a few of their egg or sperm cells carry a chromosomal change. Geneticists call this germline mosaicism and it means that such parents can have more than one child with the same chromosome disorder. If they wish, parents can discuss with a genetic counsellor the specific recurrence risks and options for prenatal and preimplantation genetic diagnosis (PGD).

If your child with a 15q11q13 duplication goes on to have children of their own, the chances of passing on the duplication to their child is 50%. We have not known about the condition for long enough to be certain if this duplication affects fertility but it is unlikely given the frequency of duplications that are inherited. Your child's ability to look after their own child is very likely to be closely related to their own learning ability and behaviour.

Possible features

Features vary considerably for those affected by their 15q11q13 interstitial duplication, some effects appear to be more common than others. The following is a list of possible features:

- Learning difficulties or intellectual disability
- Speech and language difficulties or absent speech
- Autism spectrum disorder or other behavioural difficulties
- Seizures including infantile spasms
- Developmental delay
- Sensory processing disorder
- Anxiety and/or emotional lability (rapid change in type/strength of emotion)
- Hypotonia (low muscle tone)
- Smaller or larger head size
- Slightly unusual facial features

It is important to note that no one person will have all of the features listed in this information guide and each person will have different developmental and medical concerns. A number of people with a 15q11q13 duplication have none of the features while a few may have a number of them. The outcome will also depend on the size and content of the duplication, the chromosome of origin, as well as the unique genetic makeup of each person. Other less common features have also been reported in association with 15q11q13 duplications and are discussed later in this information guide.

Pregnancy and birth

Almost all Unique members carrying babies with a 15q11q13 duplication have reported an uncomplicated pregnancy and babies were born at or near their due date. A couple of mothers mentioned their child was not very mobile during pregnancy but other than that, no recurrent problem has been identified.

Newborn

A number of families informed us that their babies experienced some difficulties during the newborn period. While most babies with a 15q11q13 duplication were born with a birth weight within the normal range, a few were born with a low birth weight and some had feeding difficulties and struggled to gain weight as discussed on pages 9 and 10.

Some babies with a 15q11q13 duplication are described as 'floppy' in the newborn period. Professionals call this hypotonia and it can lead to difficulties with sucking and swallowing, and/or latching onto the breast. Hypotonia can also result in delays reaching developmental milestones such as rolling, sitting, crawling and walking.

First signs

Since the outcome of having a 15q11q13 duplication is so variable, babies and children are diagnosed at various stages of development. Babies with a 15q11q13 duplication are not commonly reported as having physical problems such as hernias, or strong facial features that have been associated with other genetic changes. The majority of Unique members reported that their child was offered a genetic test due to concerns such as developmental delay, delayed speech, hypotonia or delayed motor skills. Others have been identified due to behavioural characteristics such as ADHD (attention deficit hyperactivity disorder) or Autism/ASD (autistic spectrum disorder). Some were offered a genetic test due to seizures.

Appearance

Children with a 15q11q13 duplication may have subtle facial features that are not obvious to a parent but can be identified by a paediatrician or clinical geneticist. Such features include skin folds across the inner corner of the eye (epicanthic folds); a flat nasal bridge and/or button nose; high forehead; strabismus (when eyes do not look in the same direction, this is also known as a squint or more commonly cross eyes). A number of families mentioned their child has patches of darker skin that some describe as 'cafe au lait' spots. They do not appear to be specific to any part of the body but are also reported in the medical literature. Facial features can be very subtle and children may not look very different to other children and may closely resemble their siblings and/or parents.

Feeding and growth

About half of the families who have provided information about feeding have mentioned that their child with a 15q11q13 duplication had feeding problems as a baby. This can be due to a number of reasons. Babies with hypotonia (low muscle tone) may find breast feeding or bottle feeding very tiring. They may take a long time to feed or need to be fed more often. If a baby's nutritional needs cannot be met, they may require supplementation with a high energy formula or via a nasogastric tube (a tube leading to the stomach that is inserted via the nose to allow all feeds and medicines to be taken directly).

Some babies have reflux, where feeds readily return up the food pipe from the stomach. If necessary, this can be controlled with medication and feed thickeners as well as careful positioning. Some babies may be reluctant to feed since their sucking reflex is not developed or they find it difficult to co-ordinate sucking, swallowing and breathing.

Feeding may also be affected by constipation, which is common in children with interstitial 15q11q13 duplications and is discussed further on page 17. One family mentioned their baby was diagnosed with pyloric stenosis at 6 weeks and required corrective surgery. This is a narrowing of the opening from the stomach to the first part of the small intestine and causes projectile vomiting following a feed.

“ She struggled to gain weight. Was hard to wake her up to feed her. ”

“ She was colicky and had trouble latching to the breast. ”

“ Slow to suck and tube fed for first 24 hours. ”

“ She was low birth weight and kept in the extra help nursery at the hospital for a week. ”

“ He struggled to breast feed in the first few weeks, he lost a lot of weight. Finally mastered it after about 2 months. ”

“ A tongue tie made sucking a bit difficult, but he fed well. ”

Sleep

Almost half of the families who gave us information about their child's sleeping habits remarked that their child has (or has had) some form of regular sleep disruption. Families informed us that their children find it difficult to 'switch off' and fall asleep at night, some children do not sleep for long periods of time and wake repeatedly in the night, some wake far too early in the morning. The reasons for sleeping difficulties are not yet well understood and may be different for each child. They do not however appear to be severe and only one family mentioned the intermittent and temporary use of melatonin (a hormone naturally produced by the body in response to day/night cycles that can help synchronise a child's body clock). One family mentioned sleep difficulties developed at the onset of puberty.

Children

Once your child has shown their individual pattern of development it will become easier to predict their abilities and possible longer term difficulties. Unique members have reported a wide range of difficulties in their children. Developmental delay has been described by over half of the families who shared this information about their child, ranging from mild to severe/global.

Gross motor skills and mobility

Roughly half of the families for whom we have information regarding motor skills mentioned that their child's gross motor skills are affected. This is likely to be related to hypotonia and most families have mentioned their child has been diagnosed with hypotonia.

“ Motor skills have come late but follow pattern of developmental delay. ”

❝ He has a broad based gait, and needs to put 100% more effort, than anyone else, to take each step. ❞

❝ Difficulty sitting unassisted until 10 months. Started early intervention physical therapy. She was diagnosed with low-tone, but not too severe. Gross motor skills are picking up with the help of therapy. She's still behind overall. ❞

❝ No rolling over or sitting at 10 months, at 14 months was crawling, walking started at 20 months with ongoing balance issues. ❞

Fine motor skills

Half of the families who provided information regarding fine motor skills mentioned their child with a 15q11q13 duplication had difficulties with fine motor skills ranging from mild to severe. Most parents mentioned poor hand use and coordination and delays in meeting milestones.

❝ Because she is hypermobile she has a problem with fine motor skills. She started to draw lines and circles when she was 4. She is 6 and she can copy her name and draw some pictures. ❞

❝ She achieves her milestones but is developmentally delayed by 1-2 years. ❞

❝ Poor fine motor skills - that of about a 3-year-old, while true age is 14. ❞

❝ She struggles to write but we've finally found a pencil grip that works. ❞

❝ OT at school was amazed how helpful drum lessons were for him. ❞

Self-Care

Families have informed us that self-care is commonly delayed but eventually achieved. Toilet training is commonly delayed, perhaps more so at night. A few parents also mentioned that their children needed help to get dressed during and after teenage years due to putting clothes on back to front, or in the wrong order, or not choosing appropriate clothing for the outdoor climate.

❝ Problem with cleaning teeth, very clumsy. Toilet trained when she was 3. No nappies for night about 5years old. ❞

❝ Late to toilet train, around age 5, and that was with intense therapy. Able to wash and get dressed with prompts. ❞

❝ She's eight and I still help her with all of these. ❞

❝ Took much longer than normal. He has to be reminded to dress for the weather, summer and winter (Age 26). ❞

Ability to learn

Most children affected by their 15q11q13 interstitial duplication described in the literature and members of Unique experience learning difficulties and for some this may be compounded by hearing and/or vision problems. While some children are identified as having a mild learning difficulty, the learning abilities of others are more severely affected and they are diagnosed as having intellectual disability. Some children attend a mainstream school and some have a dedicated support worker, others attend a school specifically for children with special educational needs. If your child is diagnosed early enough they may benefit from early intervention programmes. Children may also benefit from speech and occupational therapy sessions. While learning difficulties have been reported by most families, less than half have reported a diagnosis of intellectual disability.

“ He is at a special school for pupils with communication difficulties and moderate learning disabilities. He has always been at a special school. He attempted 6 GCSEs, got B in art and music, C in maths. He is quite good at maths but the language of maths tripped him up. ” - Age 18

“ She does try to avoid learning new things unless she is very motivated. She needs a lot of repetition. ” - Age 11

“ It's difficult for her because she doesn't believe in herself. But once she sees she can manage to do it she loves it. She is learning to write this year at the school. ” - Age 6

“ Does not want to try anything new & takes much longer than others to learn. ” - Age 12

“ Started to read at 8. Started to write at 8 years 6 months. ”

“ Started to read and write at 6 years. ”

Speech, communication and sociability

The ability to learn and to be sociable are strongly associated with the ability to understand and use language. The majority, but by no means all Unique members informed us that their child with a 15q11q13 duplication had or has delayed speech. Parents mention that their children's comprehension of language is better than their ability to communicate using language but difficulties understanding humour, abstract concepts, non-literal or figurative language (where the meaning of the conversation does not correspond exactly to the meaning of each word) were mentioned. Children can also show difficulties with appropriate language use in social situations (pragmatic speech). While children do develop language skills at varying levels, a number of families mentioned their child did not start to speak until age 4 or 5. Non-verbal children (over the age of 5) with an interstitial 15q11q13 duplication have been reported but most children develop language skills of varying levels.

One parent reported their child was diagnosed with an auditory processing disorder (when the brain processes sounds in a different way to that expected). Another family mentioned their child has echolalia (automatically repeating what other people say).

An assessment by a speech and language therapist should be able to identify specific difficulties and regular therapy sessions should be tailored to a child's specific areas of need. While behaviour and sociability are affected by language abilities, other neurodevelopmental behavioural difficulties may also be involved (as described below).

" By 12 years speech has greatly improved. She speaks well but has difficulties with appropriate use of language, comprehension, semantic and pragmatic skills. " - Age 12

" He is socially awkward, he interrupts. " - Age 14

" She takes everything seriously. " - Age 6

" He is friendly and social although has limited speech. He is able to communicate what he wants, needs, sees, likes, etc. Not much more than that. " - Age 14

" Getting better. Comes out with random comments & doesn't follow conversation. Doesn't listen - too busy wanting to talk. Talks so fast too so don't understand her! Getting there. " - Age 22

" Socially awkward. Over friending to totally blocking a person out. It all varies depending on the company or the social setting. " - Age 6

" Her social skills are basic. Although I would call her very social she gets on with children aged around 5 years of age, and doesn't fully grasp the rules of social behaviour. " - Age 11

Behaviour

Not all children or adults with a 15q11q13 duplication have behavioural difficulties, but as a group, they appear to show a higher incidence of behavioural, social and communication difficulties. It is not yet known exactly what causes this but a known vulnerability in this area means that children should be monitored and families offered early support. Diagnoses that have been associated with people with a 15q11q13 duplication are as follows:

- Autism or ASD: Autism spectrum disorder
- ADHD: Attention deficit hyperactivity disorder
- OCD: Obsessive compulsive disorder
- SPD: Sensory processing disorder
- PDD-NOS: Pervasive developmental Disorder (now known as ASD)
- Anxiety

Other behaviours may include antisocial behaviour, bad temper outbursts, stubborn refusal to conform and autistic like behaviour. Self-harming and substance abuse have been reported in a few young adults (Isles 2016) as has schizophrenia, which is primarily associated with duplications of maternal

origin. Some behaviours may be anxiety based due to other difficulties in areas such as comprehension and communication. The type of behavioural difficulty may be linked to the chromosome of origin i.e. whether the duplicated piece of DNA comes from the chromosome inherited from the mother or the father (Isles 2016).

From birth to at least 3 years of age, most children are routinely screened for developmental milestones. If there are any concerns about a child's development (either from the doctor or a parent or carer) they should be referred for developmental evaluation, which may include a hearing test and autism specific screening.

There is not a 'medical test' that can diagnose autism, children undergo an autism-specific behavioural evaluation usually carried out by a specially trained physician and psychologist. The evaluation may be multidisciplinary and include a speech and language therapist as well as an occupational therapist, it is also tailored to the age of the child. Depending on the outcome, further evaluation by a specialist such as a developmental paediatrician, neurologist, psychiatrist or psychologist may be offered.

Duplications of 15q11q13 are associated with an estimated 1 to 3% of all autism cases, making this duplication one of the most frequent chromosomal changes associated with autism spectrum disorder (ASD; Germain 2014). More recent estimates however place this value at approximately 0.1% (Isles 2016).

Five children with an interstitial 15q11q13 duplication known to Unique have been given a diagnosis of autism or autistic spectrum disorder. Two families mentioned their child had undergone an autism specific evaluation due to autistic like behaviours but no autism or ASD diagnoses were given. Autism is a spectrum disorder meaning that the same diagnostic 'name' is given for a number of different but closely related disorders. If a child doesn't 'tick enough boxes' to fall into the spectrum they may be described as having autistic like behaviour. The reasons for such behaviour are not always understood but are thought to have a neurological basis.

Some children with interstitial 15q11q13 duplications are described as having a sensory processing disorders (SPD). This means they have difficulties processing sensory input which can lead to behavioural difficulties as well as affecting social interactions and learning abilities. While most professionals diagnose and treat SPD nowadays, not everyone is aware of this neurological disorder. If you think your child has an unusual reaction to sight, sound, touch, taste and smell, they may have an SPD that may be affecting their behaviour. Movement, balance and body position can also be affected.

❝ Very sensitive to touch especially around her face, ears and hair. She is also somewhat sensitive to noise and can be easily overwhelmed.❞ - Age11
❝ She definitely has a processing disorder although undiagnosed. Bites everything, touches everything and this is ongoing. Very sensitive to smell especially but also touch and noise.❞ - Age 12
❝ Has SPD. As a kid couldn't wear clothes = Velcro or certain material or too tight.❞ - Age 22
❝ Sensitive to touch, noise, lights taste. Nothing noticed for smell and clothing. ❞
❝ He has very sensitive hearing.❞ - Age 18

Children with behavioural difficulties may benefit from specialist therapy such as that provided by a speech and language therapist (SALT) and occupational therapists (OT) but families have also mentioned their use of BT (behavioural therapy), ABA (applied behaviour analysis) therapy, hippo therapy (horse riding), music therapy and RDI (relationship development intervention (helping children to develop different aspects of social connections)).

Pain Threshold

10 families informed us that their child appears to have a high pain threshold, which means they appear to be less sensitive to pain. Although the point at which a person perceives a stimulus as painful varies between people and over time, it's possible that some people with a 15q11q13 duplication may have an altered pain sensitivity. The reason for this is not well understand but is likely to be of a neurological basis.

Puberty

There is limited information available about puberty in children with a 15q11q13 duplication although, at the time of writing, Unique had just over 30 members with a child aged 12 or above with a 15q11q13 duplication and no other known genetic variation. One family mentioned delayed puberty in their son and another mentioned their daughter had an irregular menstrual cycle but no other family has mentioned anything unusual about their child going through puberty.

Adults

Since it is possible to identify this duplication by looking at chromosomes under a microscope, this diagnosis has been available for longer than that of smaller microduplications which require more modern technology for identification. There are hence relatively more adults who were diagnosed at a younger age compared with other genetic variations. However, there is limited detailed information available about adults with a 15q11q13 duplication. When this guide was written in 2017, Unique had just over 20 adult members (between the age of 18 and 60) with a 15q11q13 duplication and no other known genetic variation. A number of unaffected or mildly affected adults are also identified as having a 15q11q13 duplication as a consequence of their child's investigation, they were otherwise unaware of their duplication. Occasionally, more severely affected adults are identified in large scale screening studies of adults with intellectual disability or a developmental disorder.

❝ He loves board games, sudokus (he is brilliant at these), and he is very musical. He learns and remembers music quickly, and is a reliable and trustworthy member of two mainstream music ensembles. He achieved Grade 6 orchestral percussion with distinction in 4.5 years of learning. He has perfect pitch, and can identify the key of any piece of music he hears.❞ - Age 18

Medical concerns

Occasionally babies with a 15q11q13 duplication are born with a physical change such as a cleft lip and/or palate, but this is rare. The most commonly reported medical causes of concern are seizures and gastrointestinal problems. Other problems include recurrent respiratory infections in childhood but most families report that their child with an interstitial 15q11q13 duplication is consistently in generally good health. No unusual findings from routine blood tests have been noted (apart from one family who mentioned previously elevated thyroid levels).

❝ His general state of health is incredibly good, he had a cold last winter, and had a week off school, - his only absenteeism from school since having chicken pox 13 years ago. ❞ - Age 18

Seizures

About half of the families known to Unique, reported their child has or has had seizures (a sudden change in electrical activity of the brain that causes momentary brain dysfunction), the other half reported that their child had no signs of any seizure activity (with ages ranging from baby to adulthood).

Reported seizures types vary and include tonic clonic (loss of consciousness with rigidity of the body (tonic) and then jerking (clonic)), myoclonic (a sudden jerk-like movement), drop fits (atonic seizures; loss of muscle tone causing the head and/or body to go limp), infantile spasms ('lightning', 'nodding' and 'jack-knife' attacks), West syndrome (three infantile spasm types with a specific EEG (electroencephalogram) pattern and developmental regression (the international definition only requires two of these elements)) and night seizures (seizures triggered by sleep or fatigue)and epileptic (recurrent seizures). The age at which seizures start varies between baby and adulthood and often only a few seizures occur, or seizures stop after a certain amount of time.

❝ Not "true" seizures, but infantile spasms. We thought they were seizures at first but no seizure activity ever registered on EEG. We never treated them and they went away by the time he was 1. ❞ - Age 12

❝ Tonic clonic seizures started at age 20. Probably had Absences before that. ❞ - Age 26

❝ Initial myoclonic seizures were treated. Transformed into epileptic spasms. EMU (Epilepsy Monitoring Unit) showed potential to transport to infantile spasms. ❞

❝ She has been treated for seizures since age 7 and has had good control, medication was topped up when absence seizure was seen. We are currently trialling coming off meds after 3 years with no seizures. ❞ - Age 12

❝ Two drop fits as pre-schooler. ❞ - Age 12

❝ Diagnosed with West Syndrome / Infantile spasms at 8 months old, seizure free (to our knowledge) since 10 months old. ❞ - Age 3

❝ Concerned about possible night-time fits. Referred for EEG. ❞ - Age 6

❝ He had 2 major seizures 9y (in the beginning of his puberty). No seizures since. Takes no medicine. ❞

Gastrointestinal problems

Food consumption and passage can be affected in a number of ways and ~ 3/4 of families of children with an interstitial 15q11q13 duplication have reported gastrointestinal problems. When we eat, our body has to break down the food in order to absorb nutrients, then move any waste through our system to the point of excretion. Difficulties can occur at any point of this process, and even before.

Our body tells us we need to eat when our stomach is empty and our blood sugar levels are low—if a child's brain does not receive these signals they are more likely to have a poor appetite or not realise they are hungry. Children who have difficulties such as autism or OCD may refuse certain foods due to texture or colour resulting in a limited diet. Once swallowed and digested, the movement of food through our bodies (peristalsis) is a regulated process that can also be affected by diet, medication, the nervous system and hormones. Stool retention (functional faecal retention; often due to a fear of passing stools) can also occur which is often accompanied by soiling of underwear (encopresis or faecal soiling) when gas is released. Constipation is commonly reported in children with an interstitial 15q11q13 duplication and may be due to one or more of the above reasons. It is important to identify the possible cause of the constipation and if treatment is needed, the use of a low dose of stool softener when necessary is recommended.

Some children with an interstitial 15q11q13 duplication also have problems with retaining food in their stomach. Families have mentioned reflux (gastroesophageal reflux (GERD) when food returns up the food pipe) and vomiting. There are many different reasons why this can occur (e.g. trouble swallowing, delayed emptying of the stomach, sphincter is too tight, blockage) so it is important the correct diagnosis is made to enable the most appropriate choice of treatment.

Eyes and vision

Although eye and vision problems are not commonly reported in association with 15q11q13 duplications, 6 families have reported that their child has an eye or vision problem. Two families informed us their child is short sighted, one child is longsighted with a strabismus (misaligned eye), another child has uneven vision and an astigmatism (blurred vision that may be due to curvature of the cornea or lens) and one child was born with a cataract (clouding of the lens).

Ears and hearing

Several Unique members have mentioned that their child with an interstitial 15q11q13 duplication suffered numerous ear infections when young. Having frequent ear infections can be annoying and painful for a child and commonly necessitates use of antibiotics. Children can be fitted with ear tubes to equalise the air pressure either side of the eardrum and to improve hearing. Glue ear (when the middle ear becomes filled with fluid) and the consequent effect on hearing at a stage crucial for language development can be frustrating for a child. Permanent hearing problems are not commonly reported in association with this duplication.

Teeth

It is not uncommon for children with chromosomal changes to have problems with dentition. Although no consistent unusual dental anomalies have been observed in children with an interstitial 15q11q13 duplication, one family mentioned overcrowding of teeth, others mentioned early and late tooth eruption and one mentioned decay due to poor enamel. A few families reported that their child grinds their teeth.

Bones, joints and spine

There are reports in the medical literature of scoliosis (curvature of the spine) in association with an interstitial 15q11q13 duplication and two Unique members with this duplication are known to have scoliosis. One family mentioned hypermobility and joint pains, another mentioned hip dysplasia (deformation or misalignment of the hip).

Families say .....

❝ Join a support group. It gets better and they enrich your life in unexpected ways. There is always some grief but you learn to celebrate different milestones. ❞

❝ Just love your children and do your best to help them to improve, they are normal children and want to be loved like the others. Let them have more autonomy and freedom if you can, it will help them. ❞

❝ Get one doctor (e.g. paediatrician) to be main point of contact. Our paediatrician only knew about dup15 by googling. We did all of the research, made appointments etc. ourselves. At one stage we had 15 specialists. It would have been nice to have one contact to guide us and make suggestions. ❞

❝ At school, make sure you and the support network are on the same page. Some teachers don't 'get it'. ❞

❝ Get your child a good psychologist - your child needs to vent and to get guidance on friendships etc. ❞

Websites, Facebook groups

Please be aware that many of the websites and Facebook groups listed below are for idic15.

http://www.dup15q.org/Dup15q
Dup15q Alliance provides family support and promotes awareness, research and targeted treatments for chromosome 15q11.2-13.1 duplication syndrome.

UK
www.facebook.com/groups/1436105923301221/
www.facebook.com/groups/201770003266536/
www.facebook.com/groups/youkmowyouhaveakidwithidic15/?fref=ts
Parents of Idic 15 adults www.facebook.com/groups/255127651274011/
(secret group, please email marion@rarechromo.org to request to join)
Interstitial Idic 15 www.facebook.com/groups/287059141761737/

USA
Website: www.idic15.org
BigTent: www.bigtent.com/groups/dup15q
Facebook: www.facebook.com/groups/434813163252172/

France: www.facebook.com/pg/dup15qFrance
Germany www.facebook.com/groups/1724557007821374/
Italy www.idic15.it/
Spain www.idic15q.com/ facebook page www.facebook.com/pages/idic15-invdup15-Espa%C3%B1a/189248794453964
Australia www.facebook.com/Dup15qAustralia/
Australia and New Zealand www.facebook.com/groups/229118593766651/
Canada www.idic15canada.ca/ Facebook page www.facebook.com/Idic15Canada
South Africa www.facebook.com/groups/idic15sa/
Norge www.facebook.com/groups/851458564881875/

Inform Network Support

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

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 http://www.rarechromo.org/donate Please help us to help you!

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

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 written and compiled by Unique (AP) and reviewed by Prof Anthony Isles, Professor of Molecular and Behavioural Neuroscience, Cardiff University, UK, 2017.

Rare Chromosome Disorder Support Group
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