This leaflet 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. The information is believed to be the best available at the time of publication. It was compiled by Unique and reviewed by Dr David Koolen, The Radboud University Nijmegen Medical Centre, Netherlands and Dr Bernard Grisart, Institut de Pathologie et de Génétique, Belgium.

2013 Version 1 [SW]
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17q21.31 microduplications
A 17q21.31 microduplication is a rare genetic condition caused by an extra part of one of the body’s 46 chromosomes – chromosome 17. For healthy development, chromosomes should contain just the right amount of genetic material (DNA) – not too much and not too little. Even a tiny piece of extra material can influence development.

Background on Chromosomes
Chromosomes are structures found in the nucleus of the body’s cells. Every chromosome contains thousands of genes which may be thought of as individual instruction booklets (or recipes) that contain all the genetic information telling the body how to develop, grow and function. Chromosomes (and genes) usually come in pairs with one half of each chromosome pair being inherited from each parent. Humans have 23 pairs of chromosomes giving a total of 46 individual chromosomes. Of these 46 chromosomes, two are the sex chromosomes that determine gender. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22 approximately from the largest to the smallest. Each chromosome has a short (p) arm (shown at the top in the diagram on page 3) and a long (q) arm (the bottom part of the chromosome).

Chromosome Duplications
A sperm cell from the father and an egg cell from the mother each carry just one copy of each chromosome. When they join together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make all of the many cells that form during human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently from usual. People with a 17q21.31 microduplication have two intact chromosome 17s, but also an extra piece from the long arm of chromosome 17. It is believed that at least part of the clinical difficulties are caused by having three copies (instead of the usual two) of a gene or number of genes from the extra piece of chromosome 17. We are still learning about the specific jobs or functions of the genes in this region. However, it is likely that other genes, environment factors and your child’s unique personality also help to determine future development, needs and achievements.
Families say..................

“Contagious laugh. Lovely cuddles.”
“He can be very nurturing to his younger brother.”
“She is a very happy child who loves singing and dancing. She has a great sense of humour. She is just a delightful child/young adult.”

References


Looking at 17q21.31

Chromosomes can be seen using a microscope. After staining, each chromosome has a distinctive pattern of light and dark bands. These bands are depicted in the diagram of chromosome 17 on the right. Band 17q21.31 contains around 4 million base pairs. Base pairs are the chemicals in DNA that form the ends of the ‘rungs’ of its ladder-like structure. The recurrent 17q21.31 microduplication encompasses a part of band 17q21.31: approximately 500-600 thousand base pairs. This sounds a lot but it is actually quite small and is only 0.01 per cent of the DNA in each cell and only 0.6 per cent of the DNA on chromosome 17.

People who have extra chromosome material are said to have duplication but when the amount is so small that it can’t be seen even under a high-powered microscope, it is called a microduplication. The 17q21.31 microduplication can often only be found using molecular or DNA technology, in particular a technique using microarrays (array-CGH), that shows gains and losses of tiny amounts of DNA throughout the genome and can demonstrate whether particular gene(s) are present or not.

Genetic Report

Your geneticist or genetic counsellor will be able to tell you about the changes found in your child’s chromosomes. With a 17q21.31 microduplication, the results are likely to read something like the following example:

arr[hg19] 17q21.31 (43,717,703-44,345,038)x3

arr The analysis was by array [arr] comparative genomic hybridisation (cgH) 

hg19 Human Genome build 19. This is the reference DNA sequence that the base pair numbers refer to. As more information about the human genome is found, new “builds” of the genome are made and the base pair numbers may be adjusted. At present hg19 is the latest version

17q21.31 The chromosome involved is 17 and part duplicated is in band q21.31

43,717,703-44,345,038 The base pairs between 43,717,703 and 44,345,038 have been duplicated. Take the first long number from the second and you get 627,335 or 627 kb. This is the number of base pairs that are in the duplication.

x3 means there are three copies of these base pairs, not two as you would normally expect
17q21.31 microduplications
The first published description of a person with a 17q21.31 microduplication was in 2007. There have since been around 8 cases reported in the medical literature worldwide. The duplication occurs equally often in boys and girls (Kirchoff 2007; Grisart 2009; Kitsiou-Tzeli 2012).

17q21.31 microdeletions
Many more people have been described with a different disorder known as 17q21.31 microdeletion syndrome or Koolen-De Vries syndrome where the same piece of band 17q21.31 is not extra but is missing. Unique publishes a separate information guide to Koolen-De Vries syndrome.

How much do we know?
17q21.31 microduplications have only been recently discovered and therefore the number of people identified is very low. This means it’s rather difficult to draw a clear picture of the features of the microduplication. Comparing different children and adults with 17q21.31 duplications shows that some effects seem to be broadly similar. This information guide tells you what is known about those effects. Comparing your child’s array results with others, both in the medical literature and within Unique, can help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with an apparently similar array result. It is very important to see your child as an individual and not to make direct comparisons with others with the same chromosome test results. After all, each of us is unique.

Most common features
Every person with a 17q21.31 microduplication is unique and so each person will have different medical and developmental concerns. Additionally, no one person will have all of the features listed in this information guide. However, a number of common features have emerged:
- Speech and language delay
- Behavioural difficulties such as autism spectrum disorder
- Some children need support with learning
- Hypotonia (low muscle tone or floppiness) in some
- Otherwise generally healthy

Are there people with a 17q21.31 microduplication who are healthy, have no major birth defects and have developed normally?
There are several people with the microduplication who had no major birth defects and only discovered they had the microduplication when it was detected in their child (Kitsiou-Tzeli 2012; Decipher; Unique).

It is important to remember that while identifying the gene(s) responsible for certain features of the 17q21.31 microduplication syndrome is valuable and may help guide future studies, it does not lead directly to immediate improved treatment. Additionally, even if the supposedly responsible gene is extra, it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.

How did this happen?
In a few cases the 17q21.31 microduplication was inherited from a parent (Kitsiou-Tzeli 2012; Decipher; Unique). In some people the 17q21.31 duplication has occurred out of the blue for no obvious reason. The genetic term for this is de novo (dn) and a blood test shows that both parents have normal chromosomes. De novo 17q21.31 microduplications are caused by a mistake that is thought to occur when the parents’ sperm or egg cells are formed or in the very earliest days after fertilisation.

What is certain is 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 17q21.31 microduplications. There is nothing that either parent did before or during pregnancy that caused the microduplication.

Could this happen again?
Where one parent has the same microduplication as the child, the possibility of having another child with the microduplication can be as high as 50 per cent in each pregnancy. For parents whose blood test showed normal chromosomes, it is unlikely that another child will be born with a 17q21.31 microduplication or any other chromosome disorder. Very rarely, both parents have normal chromosomes by a blood test, but a few of their egg or sperm cells carry the 17q21.31 microduplication. Geneticists call this germline mosaicism and it means that parents whose chromosomes appear normal when their blood is tested can have more than one child with the microduplication. This has never been reported in the medical literature or seen at Unique.

If they wish, parents should have the opportunity to meet a genetic counsellor to discuss the specific recurrence risks and options for prenatal diagnosis and preimplantation genetic diagnosis (PGD). Prenatal diagnosis is technically possible by chorionic villus sampling (CVS) at 11-13 weeks or amniocentesis at 15-18 weeks, if that is what you choose. However, it is not yet possible to predict how mildly or severely any child with this microduplication will be affected. PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother’s uterus. Testing is generally very accurate, although not all of these tests are available in all parts of the world.

Will my child have similarly affected children?
It is too early to know whether this duplication affects fertility. One person has been reported to have hypogonadism (diminished functionality of the testicles) which may have an impact on fertility. However, there are at least three reports of people with a 17q21.31 microduplication having children so it is likely that fertility is normal. In each pregnancy, someone with the microduplication is likely to have a 50 per cent risk of passing it on and a 50 per cent chance of having a child without it. We haven’t known about this microduplication for long enough to be certain of the range of possible effects or how obvious they will be (Grisart 2009; Kitsiou-Tzeli 2012; Decipher; Unique).
surgically if necessary) and two adults had hypertension (high blood pressure) (Kitsiou-Tzeli 2012; Unique).

**Other**

Other health concerns which may or may not be linked with the microduplication (because they have only been reported in one person) include asthma; small cysts on liver and spleen; slight pigeon chest; kidney inflammation (nephritis) (Kirchoff 2007; Unique).

**17q21.31 triplication**

Most people with a 17q21.31 duplication have just one extra copy of this region making a total of three copies (instead of the usual two). However, a 16-year-old in the medical literature has been reported with two extra copies (resulting in a total of four copies) of 17q21.31. He has moderate learning disability, a heart defect and urogenital anomalies (Gregor 2012).

**Research involving 17q21.31**

The microduplication involving 17q21.31 is usually encompasses five known genes: MAPT, CRHR1, IMP5, STH and KANSL1.

It has been shown that loss of KANSL1 is sufficient to cause Koolen-De Vries syndrome (17q21.31 microdeletion syndrome). It is not yet known what the consequence of having an extra copy of this gene is but it is likely to play a role in the features of 17q21.31 microduplication syndrome.

The duplication of the genes MAPT and CRHR1 has been suggested to be responsible for the learning disability and/or the delay in motor skills. Both genes are expressed (active) in the brain (Grisart 2009). CRHR1 has also been shown to be involved in stress response and anxiety related behaviour so a duplication of this gene may be responsible for the behavioural features and poor social interactions which affect some people with this duplication (Grisart 2009).

If one person in a family with the 17q21.31 microduplication is mildly affected, will others in the same family also be mildly affected?

Not necessarily. There seems to be 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 (Kitsiou-Tzeli 2012; Decipher; Unique).

**What is the outlook?**

We can’t be certain yet but there appears to be no reason why people who are healthy should not enjoy a normal lifespan and there are a number of adults both at Unique and in the published medical literature (Kitsiou-Tzeli 2012; Decipher; Unique).

**Pregnancy**

Many pregnancies were uncomplicated, and babies were born at or near their expected due date.

Many mothers (7/10) carrying babies with a 17q21.31 microduplication experienced no pregnancy problems, had a normal delivery and only discovered their baby was affected after the birth. However, pregnancy complications in mothers carrying a baby with a 17q21.31 microduplication have been reported. One mother had an amniocentesis and genetic testing after the triple screening test revealed a high risk of a baby with a chromosome disorder. Due to the small size of the microduplication it was not detected. This baby was also shown to have a single umbilical artery (the umbilical cord usually has three blood vessels – two arteries and a vein) and was induced a few days before the due date because of slowed growth. One baby was born premature at 29 weeks. Other features such as a low-lying placenta and a detached placenta are unlikely to be connected to the chromosome duplication (Kirchoff 2007; Grisart 2009; Unique).

**Newborn**

Babies are generally born around the expected due date. Typically, their birth weight, length and head circumference are in the usual range. Where birth weights are known, they are all within the normal range, with an average of 3.32 kg (7lb 5oz). One baby (out of 12) was born early (before 36 weeks) (Kirchoff 2007; Grisart 2009; Unique).

**Range of birth weights (at or near term):**

2.5 kg (5lb 8oz) to 5.1 kg (11lb 4oz)

There are generally no major medical problems although four babies were born with an inguinal hernia (a bulge of tissue from the intestines located in the lower abdomen, see page 11) which usually requires a routine surgical procedure (Grisart 2009; Decipher).
Feeding and growth does not seem to be affected in children with a 17q21.31 microduplication. The majority of children with a 17q21.31 microduplication have normal growth. However, two babies were described as ‘failure to thrive’ (slower growth than expected) and two are described as small [Kirchoff 2007; Unique]. Four people had a small head [microcephaly] (Kirchoff 2007; Grisart 2009; Decipher; Unique).

Feeding problems have not been described in the medical literature but have been seen in several Unique members. The hypotonia (low muscle tone) that is common in babies with a 17q21.31 microduplication may lead to difficulties with sucking and swallowing, and/or latching onto the breast. The floppiness can also affect their food pipe and contribute to gastro-oesophageal (GO) reflux (in which feeds return readily up the food passage).

Three people have been reported with obesity (Grisart 2009; Kitsiou-Tzeli 2012; Decipher).

- He doesn’t have any feeding issues now but he did have serious feeding problems from birth. He cried and vomited a lot. He had failure to thrive until about 2 years – 5 years
- He breast fed well for 5 months although did suffer with GO reflux which was treated with medication. He was slow to move from liquidized food to lumpy foods – 5 years

Motor skills (sitting, moving, walking)
Children with a 17q21.31 microduplication are often delayed in learning to sit and walk. One of the causes of the delay in mobility in children with a 17q21.31 microduplication is low muscle tone, reported in a number of individuals. This makes a child or baby feel floppy to handle and generally improves and may disappear with physiotherapy and exercises. However, this means it may take a little longer for them to roll over, sit, crawl and walk. From the limited information that is available, sitting unaided has been mastered between 10 months and 2 years (at an average of 15 months); crawling has been mastered between 11 months and 3 years (at an average of 21 months) and walking has been mastered between 1 year and 5 years (an average of 2 years). Several children have been described as being clumsy or having an unusual gait. Two children have a tendency to walk on tiptoes [Kirchoff 2007; Grisart 2009; Kitsiou-Tzeli 2012; Unique].

What do children enjoy?
- His favourite toys are trains and cars. He also likes puzzles and blocks and books. He likes watching pictures on TV, music and he enjoys painting or making things with Plasticine. He loves dogs. He enjoys playing in the park a lot. He likes to swing in the swings. He also likes playing shops and cooking. – 5 years
- Toy cars; touch screen computer; playing football with brothers; riding bike; listening to music; dancing; playing shops; making dens; going to the park. – 5 years
- Playing with her dolls and watching TV. LOVES the cinema and musicals. LOVES make-up and earrings. Loves her dog and budgie. Her strengths are singing, drama, music, dancing. She loves performing. – 13 years

Health matters
- Inguinal hernia
  Four babies were born with an inguinal hernia [a bulge of tissue from the intestines located in the lower abdomen (groin)] [Grisart 2009; Decipher; Unique].
- Loose or overly flexible (‘bendy’) joints are common in all young children but seem to be more common in children with a 17q21.31 duplication. Virtually any joints can be affected [Kirchoff 2007; Unique].
- Constipation
  Constipation has been described in some children with this microduplication. Dietary changes and/or medication can help to manage the problem [Kirchoff 2007; Unique].
- Eyesight
  Three people had astigmatism (an abnormal curve of the cornea – the clear cover over the iris and pupil) and one person had a squint (where the eye turns inwards, outwards, up or down) [Kirchoff-Tzeli 2012; Unique].
- Hearing
  Generally speaking children have had normal hearing, although four young children had the fluctuating temporary hearing loss caused by a build-up of fluid behind the eardrum (glue ear), but they outgrew this naturally. If it is severe or persistent, tubes (grommets) may be inserted into the eardrum to aerate the space (the middle ear) behind it and improve hearing (Unique).
- Teeth
  Generally speaking, children with chromosome disorders appear to have somewhat more dental problems than others. A few children have a tooth or teeth that are larger than expected (Decipher; Unique).
- Genital anomalies
  Minor anomalies of the genitals and reproductive system appear to be somewhat more common among babies and children with a chromosome change than among others. One boy had an orchidectomy (one testicle removed); one boy had a small penis and one boy had large testicles [Grisart 2009; Decipher; Unique].
- Heart
  Cardiac problems have been rarely reported. One child had a small hole in the muscle wall of the heart [holes often close spontaneously by themselves but can be corrected...
“He is a lovely natured child but he can get upset and because of his communication difficulties he can struggle to let you know what he wants to tell you. He speaks easily especially during the night or in a new environment. He has friends at school and plays with his brothers. He can appear over friendly and is very trusting of others” – 5 years

“He has to be reminded to complete tasks as she loses concentration and gets distracted by other things. She has to close doors; she will not allow anyone into her bedroom or touch her things. If she forgets something she hits her forehead – it’s something we are slowly getting her to stop doing. Although she is friendly and smiley she has difficulty maintaining conversations. She is more social at school but will choose to be on her own also. She has been diagnosed with OCD, anxiety and germ phobia” – 13 years

Sleep
Sleep problems affect some children with a 17q21.31 microduplication; most commonly multiple night-wakings. Some children take medication to help with sleep problems. Unique publishes a separate guide to Sleep Problems in Children with Chromosome Disorders (Kirchoff 2007; Unique).

“Had serious sleep problems and just couldn’t stay asleep for very long until he was nearly 4. He stayed awake during the night and wanted to do the same things he did during the day. He sleeps much better now but he continues to wake up several times at night” – 5 years

“He goes to sleep fine but has problems staying asleep. He has melatonin once a day, which helps a little as although he still wakes it is for shorter periods” – 5 years

Appearance

Facial appearance
Children with 17q21.31 microduplication may have a subtle characteristic facial appearance.

Babies and children with this microduplication may have subtly different facial features that would not, however, make them stand out from a crowd of other children. Geneticists trained to note unusual features may find features such as large, unusual ears (with fewer folds than is usual), a short nose, and a small chin and mouth (Unique).

Body
Some people with a 17q21.31 duplication have a tendency to have more body hair than expected (hirsutism) (Kirchoff 2007; Kitsiou-Tzeli 2012; Decipher; Unique).

Hands and feet
Hand and feet anomalies affect some of those with 17q21.31 microduplication. Three people have incurring little fingers (5th finger clinodactyly, a feature that is very common in people with a chromosome disorder and quite common in the general population); two people have tapering fingers and one person has short, broad thumbs and another is described as having small thumbs. Three people have partial or full syndactyly (fingers fused together) and two people are described as being flat footed. Overall, the pattern is of variable minor hand and feet anomalies (Kirchoff 2007; Grisart 2009; Decipher; Unique).

“He is very flexible and he loses his balance sometimes. He is also flat footed. He walks in an unusual manner because his left foot turns towards his right foot. He is improving with stairs. He can’t jump or squat. He likes crawling (and pretending to be a dog!). He also likes running and is learning to swing which he enjoys” – 5 years

“He can walk and run but he is more prone to falling over; seems to trip over his own feet. He is cautious going up and down stairs, he holds onto railings/banisters. He does appear wobbly but enjoys football with his brothers and is starting to be more confident in the swimming pool. He can ride a bike with stabilisers” – 5 years

“He has clumsy movements” – 11 years

Fine motor skills and self care
Fine motor skills may be affected in children with a 17q21.31 microduplication. Hypotonia can also affect fine motor skills in children with a 17q21.31 microduplication, and they may take longer to reach for and grab toys and hold a bottle or cup. This can lead to delays in children being able to self-feed, dress themselves (zips and buttons can be especially problematic) and hold a pen to write or draw. Special chunky cutlery, cups with handles and cutting up food have helped some children. For those children who have problems holding and controlling a writing implement, mastering a keyboard or touch screen computer can often be easier. Toilet training may also be affected (Grisart 2009; Unique).

“His fingers are very flexible. He had physiotherapy from the age of 18 months and 2 years. He holds his hands in an unusual position (with the palms outwards). Despite this he has good psychomotor activity but needs help, for example when eating with a fork. He is in nappies day and night. He can wash himself and brush his teeth but needs help” – 5 years

“He has poor fine motor skills but can feed himself well and uses both left and right hand to eat with a spoon. Holds a pencil but writing and drawing are very delayed. A writing slope and touch screen computer can often be easier. Toilet training may also be affected (Grisart 2009; Unique).

“His fingers are very flexible. He had physiotherapy from the age of 18 months and 2 years. He holds his hands in an unusual position (with the palms outwards). Despite this he has good psychomotor activity but needs help, for example when eating with a fork. He is in nappies day and night. He can wash himself and brush his teeth but needs help” – 5 years

“Has independent with prompts and encouragement” – 11 years

“She was delayed reaching all of her milestones. She had difficulty crossing her midline so using cutlery was difficult for her. She also found it difficult or uncomfortable to sit up and needed a slouch cushion at school. She is toilet trained. She needs help brushing her teeth, showering, hair washing, dressing and generally organizing herself” – 13 years

Learning
A 17q21.31 microduplication has a variable impact on learning ability
Out of 13 people with a known level of learning, five were described as having no learning disability; five were described as having a mild level of disability; two had a moderate to severe learning disability and one had a severe learning disability. Six further children were described as having an unspecified learning disability. A child with a learning disability is likely to need some learning support and many children benefit from attending a special educational school (Kirchoff 2007; Grisart 2009; Kitsiou-Tzeli 2012; Decipher; Unique).
He has a really good memory. His degree of difficulty is not known yet. He sometimes has difficulty with concentration (if there is something/someone more interesting) – 5 years

He has a moderate – severe learning disability. He has a good memory and is a visual learner. He loves being read to and is very proud of the reading books from school. He can write the first letter of his name and draws well on a touch screen computer; with a finger he can draw a face. He is in mainstream school with fulltime 1:1 support – 5 years

He has a mild learning disability and his strength is maths. He struggles with other subjects particularly literacy. He is in a mainstream school in a ‘base’ for children with additional needs. Calm and consistent instructions help him to learn – 11 years

She has a moderate-severe learning disability. She has difficulty understanding concepts so learning maths or science is difficult for her. Learning songs is one of her strengths as she loves music. Although she is behind, she has done well in reading, probably because she enjoys books. She loves drawing all sorts of subjects and writes short stories. She attends a special needs school and receives learning support all day – 13 years

Speech and communication
Speech and language delay is common in children with a 17q21.31 microduplication. Speech and language development was often delayed (13/19), but it is not known whether the delay was in line with the child’s cognitive abilities. Speech is variable in those with a 17q21.31 microduplication, with some people whose speech is not affected at all, but some who have limited speech. Picture exchange communication system (PECs) methods are helpful, including those on devices such as the iPad. Sign language may be useful. Speech therapy is regularly used to develop more language (Kirchoff 2007; Grisart 2009; Kitsiou-Tzeli 2012; Decipher; Unique).

He uses single words but is starting to link two words together. He had his first word at one but he took a long time to say any other words. He uses pictures, pictograms, computer programs and does exercises with his mouth, tongue and lips to help his speech and communication – 5 years

He talks normally now but didn’t talk much at 2½ years – 11 years

His words are limited but probably around 15 months he could say mama/dada, but by 2 years he had obvious delay. He missed the baby babbling stage. He was referred to a speech therapist at 21 months. He started using Makaton signing at 2½ years. He now combines word attempts with Makaton signing. He can link 3-4 signs together and his speech is progressing – 13 years

She has found speech and language therapy very useful. She has also enjoyed signing, visual aids, one to one speech therapy and small group therapy. She uses small sentences. Her understanding is not always as good as it might appear. She will often say something but she does not always understand what she has said herself – 13 years

Behaviour
Some children with 17q21.31 microduplications have behavioural difficulties. Children with this microduplication are often described as happy and loving with a good sense of humour. However, some children have behavioural difficulties. One child in the medical literature has Asperger’s syndrome and a further four children have been described with autistic spectrum disorder (ASD) or ASD traits. In line with the features of ASD people with a 17q21.31 microduplication often have problems with social interactions and can find making close friendships difficult. Two people have anxiety. Four people had attention deficit hyperactivity disorder (ADHD), hyperactivity or attention problems. Three children have problems with aggression. Two children have obsessional behaviour; one of whom also has a germ phobia. One father described in the medical literature had bipolar disorder but no other behavioural problems. Bipolar disorder, previously called manic depression, is a condition that affects a person’s moods, which can swing from one extreme to another. Someone who has bipolar disorder will have periods or episodes of depression and mania (Kirchoff 2007; Grisart 2009; Kitsiou-Tzeli 2012; Decipher; Unique).

He is really friendly, sociable, smiling and loving. He is really good and has a good sense of humour. He ‘speaks’ with everybody (he doesn’t know that he mustn’t go with everybody). He always tries hard to do the things that he can’t do. For example, he couldn’t pick up things that were on the floor (due to his rigid body movements) so he threw toys on the floor to practise it and he got it – 5 years

He bores of things quickly. He has a very challenging nature and needs consistent supervision and structure – 11 years