DYRK1A and 21q22.13 deletion syndrome

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What is DYRK1A syndrome?

DYRK1A is a gene that is involved in brain development. It was first characterised in 1996 but only recognised to be associated with a neurodevelopmental condition in 2008. The *DYRK1A* gene is on chromosome 21 in a region called q22.13. It is one of the genes that is missing in 21q22.13 deletion syndrome. Children with 21q22.13 deletion syndrome and those with changes in the *DYRK1A* gene have many similar features. It is now clear that the key features of 21q22.13 deletion syndrome are caused by loss of function of one copy of the *DYRK1A* gene.

Most children and adults with DYRK1A syndrome have a small alteration (often a single letter change in the gene's DNA sequence) affecting the *DYRK1A* gene. This is known as a gene sequence variant. Around 13% of people with DYRK1A syndrome have a chromosome 21 deletion that has removed part or all of the *DYRK1A* gene, and around 3% have a chromosomal rearrangement (called a translocation) that has caused a break in the gene (Fenster 2022). Some deletions also include other genes that may cause additional features that individuals who have lost only the *DYRK1A* gene do not have.

Most common features of DYRK1A syndrome

All children with DYRK1A syndrome have at least a moderate degree of developmental delay or learning disability. A research project (Fenster 2022) reviewed the information available for 97 individuals with DYRK1A syndrome and reported the following features as frequently observed:

- Small head (microcephaly) (94%)
- Delayed or absent speech (91%)
- Delayed walking (88%)
- Feeding difficulty (85%)
- Visual problems (61%)
  (mostly long or short sightedness, but also some other anomalies)
- Poor muscle tone (hypotonia) (54%) / stiff muscles (hypertonia) (35%)
- Gastro-oesophageal reflux (52%) / constipation (52%)
- Seizures, including febrile seizures (seizures associated with a fever) (81%)

Children with DYRK1A syndrome are often reported as having a lower birth weight and short stature, but there are also many individuals with birth weight / height measurements within the expected range.

Just under half of individuals with DYRK1A syndrome, have received a diagnosis of autism spectrum disorder (ASD) and 70% have at least one ASD feature such as ritualised behaviour (Earl 2017).

Heart problems have been reported in 20% of the 97 individuals described in the 2022 research project findings (Fenster 2022).

Although many children with DYRK1A syndrome may not have any obviously unusual facial features, there are some typical features associated with this syndrome such as deep-set eyes, swelling (oedema) of the upper eyelid, unusually shaped ears, thin upper lip and a small chin (Courraud, 2021).

Recurrent ear infections have been reported in many individuals (Morison 2022).

Children and adults with DYRK1A syndrome have various combinations of features that are also found in people with many other genetic conditions, so genetic investigations are important in making the correct diagnosis. It should also be noted that one or more features seen in an individual may not necessarily be a result of having the syndrome. This guide focuses on features that have been identified in a number of individuals with DYRK1A syndrome and are most likely associated with the loss or disruption of the DYRK1A gene.

How many people have this condition?

DYRK1A syndrome is a rare condition. It was first described in the medical literature in 2008. As of August 2022, 600 families of individuals with DYRK1A syndrome had connected with the DYRK1A Syndrome International Association: http://dyrk1a.org. In the past, many individuals with DYRK1A syndrome will have been undiagnosed, but with the increasing use of the latest 'gene sequencing' and 'array' technology, many more people will receive an accurate diagnosis. A large research study in the United Kingdom, which aims to identify the genetic causes of developmental delay in children, has identified *DYRK1A* as being one of the 10 most frequent genes involved (Deciphering Developmental Disorders Study, 2017). Overall DYRK1A syndrome accounts for between 0.1-0.5% of individuals diagnosed with intellectual disability and / or autism (Morison, 2022).

Was the diagnosis helpful?

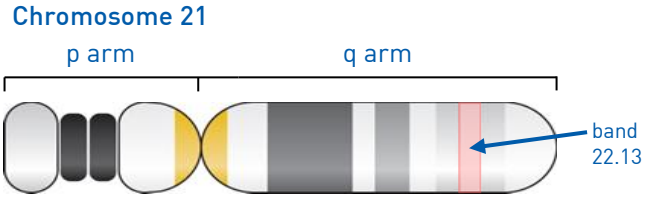
"Definitely. It was almost like a jigsaw puzzle being completed."

"Even though we started therapies before a formal diagnosis, it has been very helpful in terms of connecting with other families and knowing what to expect, what aspects of his life can we improve on and what aspects we should accept."

"The initial information given to us by the hospital's pediatrician was not supportive at all and gave a very negative outlook to our daughter's condition, life expectancy and quality of life."

What is 21q22.13 deletion syndrome and how is it related to DYRK1A syndrome?

21q22.13 is the way that geneticists refer to a specific small region (or "band") on the 'q arm' of chromosome 21. The gene *DYRK1A* is located within region/band 22.13 as shown in the image below.



Sometimes deletions occur that remove a segment of DNA from a chromosome. Such deletions can remove a single gene (or part of it), or a number of genes, depending on their size. A deletion of 21q22.13 can remove a single copy of the *DYRK1A* gene along with one or more neighbouring genes. For this reason, the 21q22.13 deletion syndrome has features that overlap with DYRK1A syndrome. Deletions of 21q22.13 are often quite large and involve a number of genes.

We all have two copies of chromosome 21. *DYRK1A* gene sequence variants and deletions usually occur on only one of these chromosome copies. A second unaffected chromosome 21 is also usually present.

About 13% of individuals reported to date (2022) with DYRK1A syndrome have a deletion of genetic material that includes part or all of the *DYRK1A* gene. Broadly speaking, children with a 21q22.13 deletion have the same types of difficulties as are found in children with a *DYRK1A* gene sequence variant. So far, there is no evidence that children with a 21q22.13 deletion are more severely affected than those with a *DYRK1A* sequence variant. However, it is possible that larger deletions involving other neighbouring genes could contribute to more severe symptoms and features. Unique also publishes a guide to '21q deletions'.

Why did this happen?

When children are conceived the genetic material (DNA) is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and random changes occur in the genetic code of all children, that are not seen in the DNA of their parents. This happens naturally and is not due to the parents' diet, environment or lifestyle. Most of these DNA changes have no obvious effect. But in rare instances these random DNA changes can lead to health issues or affect development. When such a random change disrupts the function of the *DYRK1A* gene then a child will have DYRK1A syndrome. In almost all people identified so far (2022) with DYRK1A syndrome, the genetic change was a random (or "*de novo*") change. Very rarely, one parent may have a chromosomal rearrangement

that led to *DYRK1A* syndrome in their child, or one parent may also have the same change (or variant) in some of their egg or sperm cells and passed it on to their child (this is known as germline mosaicism). However, it is important to recognize that no one should be blamed for variants in their DNA and no parent is at fault when a new DNA change occurs in their child.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. In almost everyone reported with DYRK1A syndrome so far (2022) the genetic alteration has been found to be "*de novo*", which means neither parent was found to have the same *DYRK1A* gene change as their child, and neither parent was found to have a chromosomal rearrangement that might have resulted in *DYRK1A* deletion in their child. Therefore, the chance of having another child with DYRK1A syndrome is usually less than 1%.

One reason why there is some residual chance of recurrence is due to a rare phenomenon called germline mosaicism. This is when a parent carries a genetic change, but it is limited to a few egg or sperm cells. The genetic change would not, therefore, be detected in the parents' blood test. Unique publishes a short general guide to mosaicism.

Parental genetic testing has been reported in the medical literature for about 100 individuals with DYRK1A syndrome and parental mosaicism for a *DYRK1A* variant has been reported twice (Blackburn 2019; Courraud 2021).

In another family where two siblings had DYRK1A syndrome, due to identical 21q22.13 deletions, the mother was found to be a carrier of a balanced chromosomal rearrangement (Ji 2015). This is when a piece of chromosome is relocated, usually onto a different chromosome, but no DNA is lost. When a child is conceived, the change in the parent's chromosome(s) can lead to a deletion in one or more of the child's chromosomes. This parent therefore had a high probability of having further children with DYRK1A syndrome. Again, this is very rare and has only been reported once so far (2022) in the medical literature. Unique publishes a separate guide to balanced translocations.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chances of having further children with DYRK1A syndrome.

❝ Every milestone is a wonderful achievement to be celebrated and never to be forgotten or taken for granted. When I was pregnant I once said: I don't think a second child can ever be as exciting as a firstborn, because you know every milestone will be surpassed by an even greater one. So we were given a child where every single milestone is simply awe inspiring and momentous. ❞

Why are there differences in the range of features seen in children with DYRK1 syndrome?

The DNA changes causing DYRK1A syndrome all lead to the loss of function of one copy of the *DYRK1A* gene. We all have two copies of chromosome 21 and so two copies of this gene. The second copy is assumed to be fully functional. The range of features seen in each person with DYRK1A syndrome does not seem to relate to the type of *DYRK1A* sequence variant (Earl 2017), and even individuals who share the same *DYRK1A* variant can have a different spectrum of characteristics (Fenster 2022). However, the *DYRK1A* gene is only one of many thousand genes, and there will also be effects from variants that are present in each individual's other genes. It is variants in our genes that make every one of us unique individuals.

Development

Growth

There is some evidence to suggest that babies with DYRK1A syndrome are often born slightly below the standard size range and as they grow, their height measurement remains slightly under that expected for their age, as does their weight (Fenster 2022, Unique). But this is not the case for all children with DYRK1A syndrome, some have height and weight measurements within the expected range. While head circumference can be within the expected range at birth, it is likely to be smaller than expected and most children have a small head circumference when they get older (this is called progressive microcephaly).

Skeletal

Of 74 individuals with DYRK1A syndrome involved in a research project (Fenster 2022), about half were reported to have at least one anomaly affecting their hands, feet, spine or other parts of their skeleton. Four individuals had curvature of the spine (scoliosis) and two had rounding of the upper back (kyphosis). Eleven had a sunken breastbone (pectus excavatum), although for two of these individuals this was noted as mild. Many had anomalies of the hands and/or feet, including five individuals with a high foot arch (cavovarus), four with two or more toes joined together (partial syndactyly), two with a big toe angled inwards (hallux valgus), and three with one or more curved or bent fingers (camptodactyly/clinodactyly). In many individuals, anomalies of the hands, feet or spine were noted but had not been specified.

Feeding

Parents are likely to need support as feeding difficulties can be an issue at first. Some babies will suck weakly and some need high energy milks to encourage weight gain. Many babies readily bring feeds back (this is known as gastro-oesophageal reflux or sometimes just reflux for short) and need careful positioning for feeding and while sleeping. Some babies are helped by medicines for reflux.

38 individuals with DYRK1A syndrome were described in a research study (Morison 2022) where 35 individuals were found to have a history of feeding or swallowing difficulty, and 16 children required a nasogastric tube (NGT) or percutaneous endoscopic gastrostomy tube (PEG/G-tube) during infancy. Five individuals had difficulty moving food around in their mouth, three had a habit of over-stuffing their mouth, and three tended to pocket food in their mouth. Oral aversion, in which children avoid all food or food of certain types or textures, was reported in 10 of the 38 individuals, and 15 took nutritional supplements because of their limited diet. A history of drooling was reported for 15 individuals, and this persisted in 8 of them. Of the 19 individuals who were over 8 years old, 10 continued to have some feeding difficulty. Many children can be affected by constipation (32 of 63 individuals reported in the Fenster (2022) study; of these 32, two were also reported as affected by diarrhoea). In a more detailed report of 24 individuals with DYRK1A syndrome (12 males and 12 females: Fenster 2022), who ranged in age between 2 to 24 years, gastro-oesophageal reflux was found to be common, and had been identified in about 2 in 3 individuals.

Moving and walking

Babies with DYRK1A syndrome are usually quite late to become mobile. All children have delayed motor development and some may need physiotherapy but most will be able to walk. Some children may have an unusual gait when walking because of stiffness, or balance issues (known as ataxia).

A study of 32 individuals with DYRK1A syndrome (Courraud 2021), found that 28 individuals learned to walk between the age of 15 months to 3 years (average of 22 months) and four did not walk until after 3 years. The same study found that 10 of 44 individuals had overactive or overresponsive bodily reflexes (hyperreflexia), and six had ataxia (balance or coordination problems). Poor muscle tone (hypotonia) was found in about half of the people with DYRK1A syndrome in two different research studies (Courraud 2021 and Fenster 2022). Hypertonia (stiff muscles) was also found in about 62% of people with DYRK1A syndrome during a detailed study of 24 participants (Fenster 2022). 15 individuals were found to have hypertonia, 5 of whom also had hypotonia. A less detailed review that included 60 people with DYRK1A syndrome found fewer people were reported to have hypertonia (35%) but this may be because the study was not as detailed.

Speech and communication

Children with DYRK1A syndrome typically experience delay in communicating and learning to use words. The eventual range of achievement is very broad, but most children will not develop meaningful speech within the expected range. Those who do develop speech may achieve single words, short phrases or basic sentences and others will use signing, gestures and vocal noises to express their needs. Some parents report good understanding of spoken language (receptive language skills).

A detailed assessment of speech and language abilities in a group of 38 individuals with DYRK1A syndrome, ranging in age from 19 months to 25 years, has been reported (Morison 2022). 18 individuals were found to be minimally verbal, using fewer than 30 words, 12 used more than 30 words as single words or short phrases, and 8 (all aged 7 years or older) had conversational speech. Children who were able to combine words, usually started to do so after the age of 4 years.

Children in this study also used alternative communication methods. 89% of children used gestures and signs in the first two years of life. The use of signs decreased from 75% using sign at 3-5 years to 43% using sign at 16 years and older. As children got older their use of Augmentative and Alternative Communication (AAC) systems increased. AAC can include drawing and pointing to pictures, as well as use of technology such as using an app to communicate and/or using a computer or other device that uses a "voice" to generate speech. Within the group, social motivation (the motivation to engage with other people) was found to be close to the range expected in the general population.

Assessment of the 20 least verbal participants in this study showed that socially-motivated communications were a relative strength, with all using some method of greeting, and most saying farewell and able to communicate to seek comfort. Communication of requests for food or objects was good, although 14 individuals were not able to communicate specific requests like going to the toilet. Some challenging behaviours (e.g. tantrums) or stereotypic behaviour like hand-flapping were reported to occur when the individual did not like something.

For 18 people in this study who were verbal, 17 struggled to pronounce words correctly as children (this is known as childhood apraxia of speech) and their articulation of words / speech was unclear (this is called dysarthria). Both childhood apraxia and dysarthria were observed in 14 of the 18 individuals. It was also found that eight of the 18 participants had limited upper lip movement and difficulties rounding their lips, and 12 had difficulties coordinating movement of their tongue. Caregivers were able to better understand the individuals speech.

This study also found that the best communicators were older than 8 years, suggesting that speech and language skills may continue to improve into adolescence. The researchers suggested that speech therapy which specifically targets apraxia and dysarthria could improve communication for children who are using words.

Learning

All individuals with DYRK1A syndrome have at least moderate learning disability and require specialist support with learning.

❝ Some 'professionals' gave their opinions on her future capabilities and have been completely wrong. She is a determined young girl and will not be stopped.

We were told that she will never sit or walk, she now does both completely independently.” - 2½ years

“He is very vocal but non-verbal at this stage and does not respond to signing either. His non-verbal communication is very good and he does show many signs of understanding us.” - 21 months

Autism

Children with DYRK1A syndrome typically tend to have behaviour in keeping with their overall degree of developmental delay, and most have a happy disposition. Many children with DYRK1A syndrome show features of autism, and DYRK1A syndrome accounts for up to 5 autism diagnoses per 1000.

A detailed study of autism reported findings from 61 individuals with DYRK1A syndrome, including individuals with small changes in the gene, with large deletions of all or part of the gene, and with other chromosomal rearrangements (translocations, inversions) affecting the *DYRK1A* gene (Earl 2017). No significant differences were noted between the occurrence of various clinical features, including autism, between people with the different genetic changes.

This study noted that whilst autism had been previously diagnosed in about 43% of people with DYRK1A syndrome, about 69% of individuals showed features of autism spectrum disorder (ASD), such as repetitive behaviours, limited eye contact, or limited social engagement. Anxious behaviours were identified in about 27% of individuals, and hyperactivity in about 33%. When a proper (“gold standard”) assessment of autism was carried out, about 73% of people with DYRK1A syndrome were diagnosed with ASD. The researchers suggest that many people with DYRK1A syndrome have not been formally assessed for ASD, and noted that there could be difficulties recognising ASD within the spectrum of other features of DYRK1A syndrome unless a professional ASD assessment was conducted.

“Most of what she does to/with us is fantastic. Since she was able to, she would smile in such a manner that it was infectious. She will hardly ever complain for the sake of it. She is a relatively quiet girl but also loves her cuddles and will squeeze into our arms when she feels it’s time for some attention.” - 2½ years

“She has a very dry sense of humour, and makes us laugh a lot. She doesn’t talk a lot, but when she does, she sparkles and lights up a room. She loves being outdoors and getting messy.” - 10 years

Medical concerns

The following medical concerns have been found in children with either a 21q22.13 deletion including *DYRK1A* or a *DYRK1A* sequence variant. They are not found in all children so not all children with DYRK1A syndrome will be affected.

Muscle tone Low muscle tone (hypotonia) is usually obvious in the new-born period and may persist throughout childhood. This is likely to contribute to feeding difficulties and delay in reaching motor milestones. Although nearly all children do learn to walk, some children may experience loss of previously achieved motor milestones as they grow older, although there is no evidence that DYRK1A syndrome is a progressive condition. Hypotonia has been described in about half of people with DYRK1A syndrome, and stiff muscles (hypertonia) in around one third to two-thirds of people with DYRK1A syndrome (see also the section above on "Moving and walking").

Feeding difficulties Feeding difficulties are fairly common in new-born babies. Some babies may require temporarily feeding by nasogastric tube (NG tube: a tube that passes through the nose down the oesophagus and into the stomach) or gastrostomy tube (G tube: a tube that passes through the abdominal wall into the stomach). In some children, feeding difficulties may persist (see also the section above on "Feeding").

"He has severe sensory issues. Due to his oral aversion and subsequent feeding difficulties, we had a Mic-Key placed at 15 months. He lost his oral intake 2 weeks afterwards and has taken nothing by mouth ever since. We struggled with severe and unexplained vomiting from 16-21 months, but after a blended diet was introduced, the vomiting gradually eased up." - 21 months

"Severe reflux treated with a special diet and two forms of medication."
- 2½ years

Eyes and eyesight A wide range of eye and sight anomalies has been reported in individuals with DYRK1A syndrome. A study of 145 individuals (Méjécase 2021) reported that 90 individuals (62%) with DYRK1A syndrome had an ocular (vision or eye) anomaly, although no relevant information was available for 28 of these people. About half of those with ocular issues had more than one vision or eye-related anomaly. The most common conditions were "refractive errors", seen in about one third of the 90 individuals with eye problems; this includes short or long-sightedness (myopia and hypermetropia) and a slight alteration in eye shape that can lead to blurry vision (astigmatism). 19 of the 90 individuals were found to have a strabismus (squint). Anomalies of the optic nerve were also present in 18 people; these included underdevelopment (hypoplasia) of the optic nerve (in 12 people). There was no significant difference between the vision-related features observed in individuals with DYRK1A sequence variants compared to those with large deletions.

Seizures Quite a few children with DYRK1A syndrome experience seizures, although these may be rare or occasional, they may warrant further investigation (e.g. by EEG or brain MRI). Reports in the medical literature differ slightly in the proportion of people with DYRK1A syndrome who have epilepsy. These

differences may be due to small study sizes and/or incomplete information. In a review of the medical literature (Fenster 2022) seizures were reported in 50% of people with DYRK1A syndrome (45 out of 90 people). In the researchers more detailed study of 24 people with DYRK1A syndrome, seizure activity was found in 14 individuals (about 60%). The most common types of seizure were grand mal (loss of consciousness followed by jerking of limbs) and drop attacks (when muscles go floppy, causing a fall if standing). Other seizure types often observed were tonic seizures (when muscles stiffen, which may cause a fall) and absence seizures (when the individual appears blank and does not respond to, or is not aware of, what is going on around them). Where the medication was identified, Levetiracetam was reported as the best medication for seizure control. Febrile seizures (seizures occurring during a fever) were also reported in 16 out of 24 individuals (Fenster 2022). Overall, 21 of the 24 individuals studied had seizures, a similar finding to that of another study (Courraud 2021).

- **Heart** A detailed study of 24 individuals with DYRK1A syndrome (Fenster 2022) noted heart problems in 8; these included a hole between the upper chambers of the heart (atrial septal defect, in four people) and a narrowing of the valve between the heart and the lung arteries (pulmonary stenosis, in four people). Some individuals had more than one heart anomaly, for example one child had an atrial septal defect, pulmonary stenosis and narrowing of the aorta (coarctation). In a wider but less detailed review that described 60 individuals with DYRK1A syndrome (Fenster 2022), heart anomalies were reported in 1 in 5 people (20%). Another study (Morison 2022) reported heart problems that included atrial septal defects and ventricular septal defects in 9 of 38 individuals with DRYK1A syndrome (about 1 in 4 or 25%). In children for whom heart problems are suspected, these can be diagnosed using approaches like electrocardiogram (recording the electrical activity of the heart), echocardiogram (ultrasound scan of the heart), or chest X-ray.

“ Our daughter was born with pulmonary stenosis. She has undergone an operation to stretch the artery and now has normal flow through the heart chambers. She now sees the specialists once a year for a checkup. ” - 2½ years

- **Kidney, urinary tract and genitals** A study was carried out to investigate kidney, urinary tract and genital anomalies in 19 individuals (11 male) with DYRK1A syndrome (Blackburn 2019). The left kidney was absent in 2 individuals (1 boy and 1 girl), and 2 other individuals (1 boy and 1 girl) had kidney anomalies (the boy had echogenic foci on ultrasound, the anomalies in the girl were not specified). The boy with kidney echogenic foci also had hypospadias (the opening of the urinary tract is not in its usual position at the tip of the penis). Another boy had hypospadias together with very small penis and chordee (bend or twist in the penis). Another study (Courraud 2021) reported that, of 17 boys, one had hypospadias and another had a very small penis. Six boys out of the 28 total between the two studies had one or both testicles undescended. Another boy was

reported (Blackburn 2019) to have had genital anomalies, but these were not specified further. Of 53 individuals (28 male) between the two studies, 5 boys and one girl were reported to have had inguinal hernias (this is when abdominal organs, for example part of the intestine, protrude through a weak spot in the abdominal muscles, forming a visible lump). Undescended testicles, hypospadias, chordee, and inguinal hernia can be corrected by (usually simple) surgery.

- **Recurrent infections** A history of ear infections was reported for 20 of 38 individuals in one study (Morison 2022), and frequent urinary tract infections were reported for one girl and one adult male in a different study (Blackburn 2019) of 19 individuals with DYRK1A syndrome. Another study (Ji 2015) noted that 6 out of 14 individuals had an increased susceptibility to infections by non-common pathogens.

- **Hormones** Endocrine problems (growth hormone deficiency, hypothyroidism, precocious puberty) have been reported by families in the Unique group, and a study noted that 4 of 14 individuals with DYRK1A syndrome had endocrine issues (Ji 2015), which included growth hormone deficiency in one boy and one girl, hypothyroidism in one girl, and premature breast development in a 7-year-old girl. Unexpected hormone changes do not seem to be reported in other studies, but this may be due to incomplete information.

- **Brain** In some people with DYRK1A syndrome, magnetic resonance imaging (MRI) and/or computerised tomography (CT) scans of the brain have identified one or more anomalies, including enlarged fluid-filled cavities in the brain (dilated ventricles), thinning of the band of white matter connecting the two halves of the brain (corpus callosum hypoplasia), and reduction in brain volume (cerebellar atrophy).

Management recommendations

At diagnosis

- EEG (measurement of brain's electrical activity), if seizures are suspected
- Brain imaging with MRI
- Vision (Ophthalmology) assessment
- Feeding management if necessary
- Consider heart and kidney ultrasound scans to rule out structural anomalies

After diagnosis

- Long term follow up by a developmental paediatrician
- Speech and language support as needed
- Physiotherapy and occupational therapy support as needed
- Regular eyesight checks may be recommended

Is there any research into new treatments for DYRK1A syndrome?

The genetic change causing DYRK1A syndrome affects development of the brain and other parts of the body before birth. Therefore, a complete cure is unlikely,

even in the future, since the brain has already formed by the time a diagnosis is made. However, research into improved treatments and managements for various features of DYRK1A syndrome, like autism, is ongoing.

In addition, although DYRK1A syndrome is a relatively rare condition, the gene *DYRK1A* is the subject of a lot of research because of its key role in brain function and aging (Arbones, 2019). DYRK1A is also one of the key genes that is duplicated in Down's syndrome.

The *DYRK1A* gene provides the instructions for cells to make a protein, also called DYRK1A which controls many different processes within the cells that make up the body. The DYRK1A protein has important roles in development of the brain, and also appears to have ongoing roles in function of the mature brain. With DYRK1A syndrome there is too little DYRK1A activity, but having too much DYRK1A activity (the opposite situation to DYRK1A syndrome) is associated with Alzheimer's disease, Parkinson's disease and dementia. For this reason, there is intensive research into DYRK1A and the other proteins that it interacts with to perform its functions. One avenue of research is to identify drugs that might alter the levels of DYRK1A activity; so far DYRK1A inhibitors have been identified, though not activators (it would be DYRK1A activators that might be predicted to have some benefit in DYRK1A syndrome, due to the lower amounts of DYRK1A and its ongoing role in the adult brain).

"People always remark on his serious facial expression, probably due to his mild dysmorphic features. Because we know him, we know this not to be true at all. He is an extremely friendly, gentle little soul and we love getting to know him better every day. Besides his problems, which are obviously numerous, he is in many ways such an easy child. He can entertain himself for hours and is happy to sit and play with his favourite toys. He has a wonderful sense of humour and loves 'talking' to us. He is extremely strong willed, which we love!" - 21 months

"We never did anything for charities before but now often take part for the charities or organisations that have helped us and our daughter. She has introduced us to a whole new world of people who we would never have met previously. She has managed to improve our quality of life in a way we would never have thought possible." - 2½ years

"Parenting a child with complex health needs, autism and a genetic disorder is the most challenging, rewarding, tiring and wonderful journey anyone can take. I am constantly amazed by our daughter's resilience, her ability to take all the challenges she faces in her stride. She is a wonderful, loving, joyful child who only wants people's patience and understanding, love and care to make her feel happy and secure. Our lives have changed beyond recognition, but my perspective on life has changed completely. She has taught me patience, compassion, all-consuming love - and it's been one hell of a roller coaster ride!" - 11 years

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Support and Information

Rare Chromosome Disorder Support Group,
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Websites and Facebook groups

Website: http://dyrk1a.org
Facebook DYRK1A gene changes
www.facebook.com/groups/dyrk1a

Unique lists external websites and webpages in order to be helpful to families looking for information and support. 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. The text was written by Dr Muriel Holder, Consultant in Clinical Genetics, Guy's Hospital, London, UK, and the guide was compiled by Unique. This guide was updated in 2023 by Dr Maria Jackson, University of Glasgow.

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