COMPLEX LEARNING DIFFICULTIES AND DISABILITIES RESEARCH PROJECT (CLDD)

RARE CHROMOSOME DISORDERS

The term, 'rare chromosome disorders', refers to conditions which:

1. occur due to missing, duplicated or re-arranged chromosome material
2. have a low prevalence rate (thus not including chromosomal disorders such as Down syndrome).

Chromosomes are structures found in the nuclei of cells in human bodies. Each chromosome contains thousands of genes which determine how we grow and develop. A typically developing person will have 23 pairs of chromosomes with one member of each pair being inherited from each parent, giving a total of 46 individual chromosomes. Two of these are the sex chromosomes which determine whether we are female (XX) or male (XY). The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22. The arms of a chromosome are called 'p' (shorter arm) and 'q' (long arm) (see Figure 1); these arms are separated into numerical regions, which in turn are divided into bands and sub-bands.

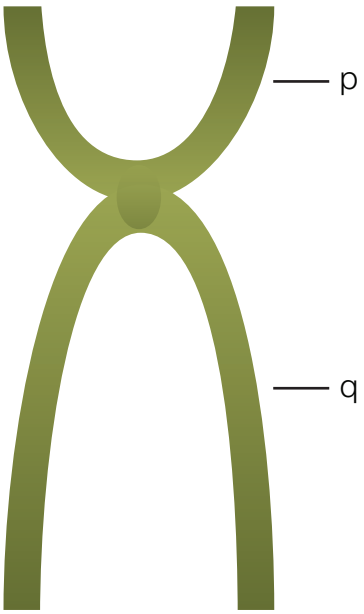

Figure 1. Diagram of a chromosome

Individually, rare chromosome disorders are extremely uncommon, with some being actually unique; however, collectively rare chromosome disorders make up at least one in every 200 live births, with babies either having symptoms from birth or early childhood, or being carriers of a chromosomal abnormality and experiencing the effects when they try to reproduce in later life (Searle and Hultén, 2009). Recent advances in technology and medical expertise has meant that chromosomes can be viewed at ever increasing magnifications, which is resulting in the detection of more complex defects. Therefore the prevalence rate is set to increase.

The amount of chromosome material which can be duplicated, re-arranged or missing can vary a huge amount, meaning that it may be difficult to identify two people with the same condition. Furthermore, even when people are identified as having a similar condition, the way in which it affects each person may still vary a great deal (Searle and Hultén, 2009). If enough children are born with the same chromosome disorder and present a similar pattern of characteristics it may be called a syndrome.

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The vast majority of carriers of a rearranged abnormality will not experience any symptoms, but might have problems in reproduction. For those with missing or duplicated chromosome material, the effects will vary, but symptoms could include physical and/or health problems, learning disability and maybe challenging behaviour. The combination and severity of symptoms will vary depending on which parts of chromosomes are involved and the way in which they are different. According to Unique, a support group for those affected by rare chromosome disorders, generally speaking a loss of a part of a chromosome is more serious than the presence of an extra copy of the same part, and defects of chromosomes 1 to 22 are far more serious than those of sex chromosomes X and Y. In general, most people with any loss or gain of chromosomes 1 to 22 will experience some degree of learning disability and developmental delay due to the number of genes located across these chromosomes which are responsible for typical brain development.

Karyotypes

The description of a person's chromosomal make-up is called their karyotype. As a way of gaining an accurate idea of where the abnormality lies, a standardised code has been devised to describe a person's karyotype. This is called the International System for Human Cytogenetic Nomenclature (ISCN). This can be very complicated to understand, but is explained briefly here. The ISCN code is generally written in the format 'number of chromosomes in a person's cell [comma] sex chromosomes'. For example, a typical female karyotype is 46,XX. Any breakpoints on the chromosome can then be described according to the numerical region/band/sub-band they occur at. For example, the karyotype ISCN code of a child with 1p36 deletion syndrome will look like:

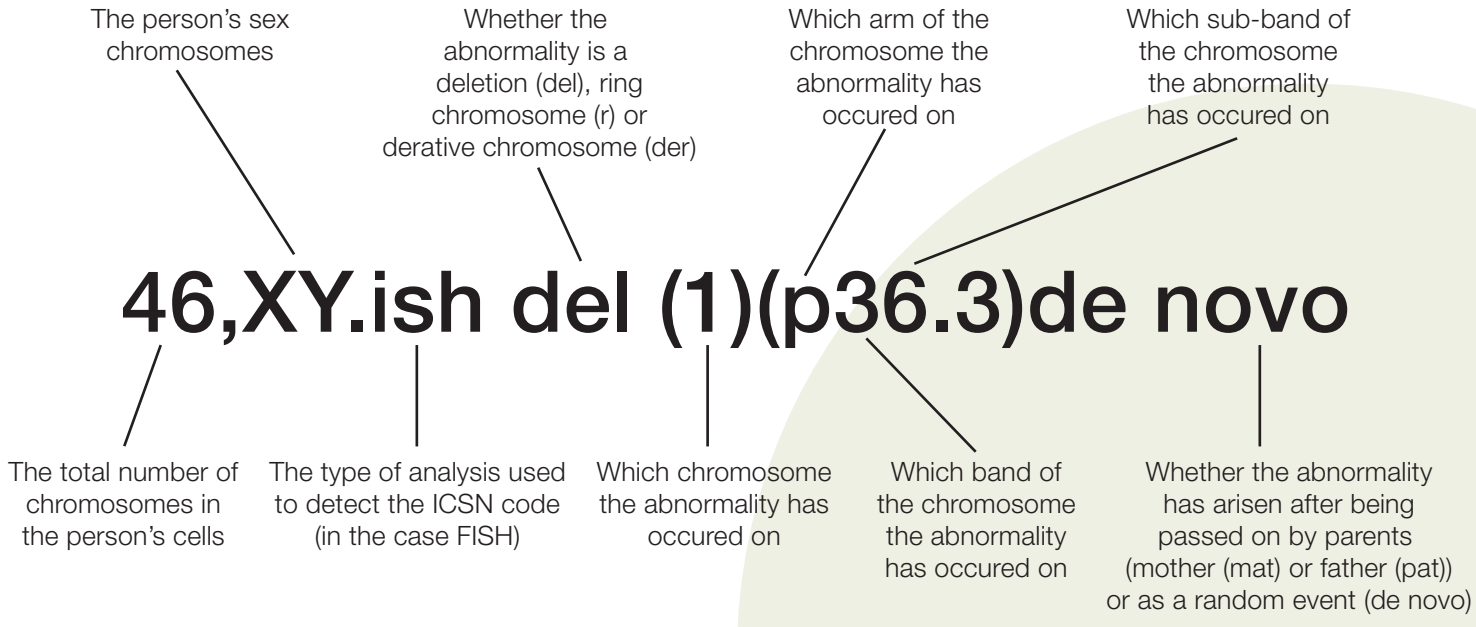

Figure 2. Diagram explaining the ISCN code (example adapted from Unique, 2008).

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Below some of the more common chromosomal disorders are described; however, it is impossible to cover all possible chromosomal disorders here as there are so many, with more being discovered all the time. You can obtain more information from the rare chromosome support group, Unique (www.rarechromo.org) by looking at their disorders leaflets on the website. There you will find information on the biological cause of each disorder, and the potential impact it could have for the student in terms of health, learning, behaviour and communication development.

1p36 deletion syndrome (also known as monosomy 1p36)

A deletion occurs when there is a loss of material from one chromosome because of either one break (a terminal deletion) or two breaks (an interstitial deletion). 1p36 deletion syndrome affects 1 in 5,000 live births and is thus classed as one of the more common deletion disorders (Unique, 2008). It is thought to be more common in females (65% of cases diagnosed). Symptoms found to be common among children with this diagnosis are: seizures; developmental delay; learning disability (to a varying extent); hypotonia or floppiness (in babies, but could persist into adulthood); difficulties with feeding; heart problems; impairments in hearing and vision, including photosensitivity; and distinctive facial features (eg small head, large rounded forehead, eyes set well into their sockets with flat eyebrows). As with most disorders, not all students with this deletion will have all of these features. Students with 1p36 deletion syndrome are often friendly and placid, but can be known to have outbursts of anger or self-harming, perhaps due to frustrations around communication. Some students are tactile defensive and may display challenging behaviours around particular objects they find unpleasant to touch. Some students may also be particularly shy and find social interaction difficult, displaying gaze avoidance.

According to Unique (2008) parents find that the key to their children's progression is control of their seizures. Effective learning strategies have been found to include the use of music, lights (with specialist advice) and tactile resources, with an emphasis on visual learning. As with most students, patience, repetition and lots of encouragement are required. Unique have found that, for some students, a touch screen computer has been successful in supporting their engagement and learning. Students with 1p36 deletion syndrome have particular strengths in communicating emotion through facial expression, vocal noises, gestures and body movements; imitation; and memory for faces and places. Difficulties have been found to be in speech, with delayed or absent speech reported for the majority of students. Signing is successful for some, but may be difficult for others due to poor fine motor skills. Speech and language therapy is recommended for all students to help them develop a means of communication.

Cri du chat syndrome

Cri du chat syndrome (CdCS) is a relatively rare chromosome disorder affecting approximately 1 in 15,000–50,000 live births (Cerruti Mainardi, 2006), and it is estimated that females outnumber males by 2 to 1. The syndrome is caused by a deletion from the 'p' arm of chromosome 5, so is also referred to as 5p deletion syndrome or '5p'. It is characterised by a high-pitched 'cat-like' cry in infants (Cri du chat translates as 'cry of the cat'), and physical features such as microcephaly (small head), hypotonia, low birth weight, and round, full face and wide-set eyes. For two thirds of those affected, their cry will persist into adulthood. Speech and language development is usually delayed, but augmentative communication approaches can be successful. Most will have intellectual disability to a varying degree and may display

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display hyperactivity, aggressive and oppositional behaviours, as well as sleep problems. Students with CdCS tend to be very friendly and outgoing, and will integrate well into social situations; however, it is important to be aware of possible underdeveloped social skills within the community and their potentially poor concept of danger.

22q13 deletion syndrome

Also known as Phelan-McDermid syndrome, 22q13 deletion occurs when there is a small part of one of the q arms missing at band 13 from chromosome 22. The rate of incidence is not known, but there are 500 identified cases, and it is thought to be the second most common deletion (after 1p36 deletion) leading to a clinically significant chromosomal disorder (Phelan, 2008). However, it is thought to be under-diagnosed, due to lack of clinical recognition and the overlap in characteristics it has with other disorders such as fragile X syndrome, ASD, and Williams syndrome. Every person will be affected differently by 22q13 deletion, but the most common features associated are hypotonia, global developmental delay, absent or severely delayed speech, normal to advanced growth (Phelan et al, 2001), and physical traits such as long eye-lashes, puffy eyes, prominent ears, large hands, pointed chin, full cheeks and bulbous nose (Phelan, 2008). Behaviours are often similar to that of an autistic profile, with poor eye contact, decreased socialisation, some tactile defensiveness and hand-flapping (Phelan, 2008). The majority of students with 22q13 deletion tend to chew or mouth non-food items and grind their teeth. Often giving them an object such as a rubber tube is successful in redirecting the sensory need from inappropriate objects.

Students with 22q13 deletion frequently experience some degree of learning disability and will benefit from extra support or special education. They often have more advanced perceptive language than expressive language, so speech and language therapy should be directed towards improving verbal and nonverbal communication, such as sign language (Phelan, 2008). However, poor fine motor skills from hypotonia might make sign language difficult to master for some students. Computer touch screens, voice based systems, and the picture exchange communication system (PECS) may be more successful supports for increasing communication skills. Adaptive sports, music therapy and sensory integration have been shown to increase the student's awareness and consequently improve their desire to communicate (Phelan, 2008).

Idic15 syndrome

Idic (isodicentric) 15 syndrome occurs when there is a small extra piece of chromosome duplicated to create another chromosome 15, making 47 chromosomes in total rather than 46. It may also be referred to as chromosome 15q duplication syndrome, which also covers interstitial duplication 15 (int dup 15). It is estimated to occur at an incidence rate of 1 in 30,000 live births, and evenly between males and females (Unique, 2005a). Diagnoses are often received quite late as there are no obvious physical features other than low muscle tone and maybe seizures. Delays in reaching motor milestones, such as walking, tend to prompt a chromosomal test. Other characteristics common to Idic15 syndrome are absent or delayed speech, autistic like behaviours and poor motor skills, as well as seizures, ‘button’ nose, high palate and strabismus (squint) (Cleary, 2006).

All children with a duplication of chromosome 15 will experience learning disability, from moderate to

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severe and even profound (Unique, 2005a). Unique reports that children tend to have good memories, enjoy looking and listening to books, and enjoy music. Hypotonia may prevent students from holding a pencil and writing, so a keyboard and touch screen computers are suggested as an alternative in the classroom. Students may also find focus and attention difficult; for this, a calm, quiet and structured learning environment is recommended (Unique, 2005a). Unique has found that students tend to have better receptive language (understanding of communication from others) than expressive (communicating to others), and often benefit from sign language, PECS or computer-based approaches to communicate.

Students with Idic15 syndrome are often happy, sociable and enthusiastic when young, but may display tantrums, anxiety and bursts of aggression as they grow up (Unique, 2005a). Students may also have poor sensory integration resulting in, for example, tactile defensiveness, oral hypersensitivity, hypersensitivity to noise, or under-responsiveness (hyposensitivity) to pain-causing stimuli. To stimulate the vestibular and proprioceptive senses, students may benefit from weighted blankets, hiking, wearing backpacks, deep pressure massage and rolling games. An occupational therapist can provide personalised advice for each student.

Jacobsen syndrome

Jacobsen syndrome, or 11q terminal deletion disorder, is caused when the end, or terminus, of the q arm of chromosome 11 is missing, usually from band 2, or sub-bands 3 or 4 (11q23/11q24). It occurs at an incidence rate of around 1 in every 100,000 live births, and equally between girls and boys. As with all chromosomal disorders, its impact will be different for every person; however, it is thought that students with less chromosomal material missing may be less affected.

Typically, students are small in stature and have quite distinctive facial features, including low set ears; pointed forehead; wide set eyes with drooping or hooded eyelids; small jaw; and microcephaly. Eyelids are often surgically operated on to provide less of an impairment to vision (Unique, 2005b).

Students with this syndrome will usually have mild to moderate learning disability. They might also have particular difficulties with attention span, especially in an unstructured learning environment. Receptive language is usually better than expressive language, but generally speech develops well, albeit with slight delay. In terms of behaviour, students with Jacobsen syndrome may have a tendency towards attention-seeking and compulsive behaviour, (Unique, 2005b). Many also display poor sleep patterns and low muscle tone, but will generally overcome hypotonia as they develop. Unfortunately, the majority will have a bleeding disorder known as Paris-Trousseau syndrome (Grossfeld et al, 2004). This is an impairment in the platelets' ability to clot, which makes students liable to bruise easily or bleed copiously if any blood is taken, and puts them at risk of internal bleeding; even something as seemingly minor as a nosebleed can cause heavy blood loss (Unique, 2005b).

DiGeorge syndrome (information adapted from maxappeal.org.uk)

DiGeorge syndrome is one of five disorders caused by a deletion of a small piece of chromosome 22 (22q11.2), affecting around 1 in 4,000 live births – again one of the more common chromosome disorders. Low calcium levels (hypocalcaemia), poor immunity, cleft palate and congenital heart

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problems separate it from other disorders associated with 22q11.2. Any facial characteristics tend to be quite subtle, but generally speaking there might be smaller facial features (eyes, chin, ears, mouth), with a long philtrum and possibly a prominent nose bridge. Students may have hypotonia also extending to facial muscles, poor motor skills and lack of co-ordination. Many students will have learning disability and developmental delay to some degree, and may experience communication problems. These often arise from either comprehension difficulties, abnormalities of the palate which affect speech imitation, or persistent ear problems such as infections which make it difficult for them to hear.

In school, the strengths of students with DiGeorge syndrome are often: numerical calculations; rote memory; spelling and written language; decoding words and basic reading. Areas of difficulty may be: comprehension; complex maths concepts such as time, money, shape, colour and size; and abstract concepts such as reasoning and problem solving. They may also be disorganised in their thinking and become obsessed with one topic or idea.

Socially, students with DiGeorge may struggle with peers, display immature or inappropriate behaviours, hyperactivity, impulsiveness or exhibit mood swings. They may also have a particularly low self-esteem and confidence, which may be noticeable in the classroom setting. It is advised that Ritalin not be prescribed to any children with DiGeorge syndrome who also have ADD/ADHD as they tend to have an adverse reaction.

In the classroom, it is recommended that students with DiGeorge syndrome are: taught with concrete, practical examples which incorporate opportunities to practice; given structure due to their disorganised nature; and provided with access to computer-based learning. It is important that staff focus on direct instruction rather than discovery learning, and are aware of the student's tendency to think literally. Creative projects have also been found to be beneficial for students with DiGeorge syndrome.

Sex chromosome disorders

This is an umbrella term for disorders where there are too many sex chromosomes. Each of these disorders is gender-specific. The presence of a Y chromosome makes the disorder male-specific, whilst the absence of a Y chromosome makes the disorder female-specific. The most common are sex chromosome trisomies which are either boys with XXY, XYY or girls with XXX. All these have a current prevalence rate of 1 in 1,000 births. Students with these disorders generally show only subtle physical features, and most achieve within age-related norms at school, perhaps with mild learning difficulties. There are also much rarer sex chromosome abnormalities, including monosomy X: girls with only a single X chromosome; tetrasomies: boys with XXYY, XXXY, or XYYY, and girls with XXXX; and pentasomies: boys with XXXXY and girls with XXXXX.

Useful websites

www.rarechromo.org
Is the website of Unique.

www.genesareus.org
Is an educational resource for those affected by genetic disorders, funded by the organisation who campaign as Jeans for Genes.

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