WILLIAMS SYNDROME

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Williams syndrome is known by several names: Beuren's syndrome, Williams-Beuren syndrome, Fanconi-Schlesinger syndrome, Williams' elfin face syndrome, Williams-Barratt syndrome, and Williams' syndrome (Also known as . . . 2001). Williams syndrome (WS) affects 1 in 7500-20,000 births regardless of gender or race (Stromme, Bjornstad, and Ramstad 2002). It is typically diagnosed in infancy or in early childhood. Recently, there has been a great deal of research regarding all aspects of this

perplexing syndrome. Therefore, the scope of this paper will be an overview of the history, etiology, characteristics, and interventions surrounding Williams syndrome.

History

Williams syndrome is named after Dr. J.C.P. Williams, a cardiologist at the Greenlane Hospital in Auckland, New Zealand. Dr. Williams noticed that many of the children entering the hospital for repair of supravalvular aortic stenosis had other similar characteristics. All the children had common facial features, outgoing personalities, and varying degrees of mental retardation. He publicized his findings in a medical journal in 1961. Dr. Williams was offered a position at the Mayo Clinic in 1964. He accepted, but never showed up, although he did go to work in London. He later disappeared, leaving only his suitcase in a London luggage office, never to be heard from again (J.C.P. Williams, 2001).

Other noteworthy physicians that are associated with Williams syndrome are: Dr. Guido Fanconi, Dr. Bernard Schlesinger, Dr. Alois J. Beuren, and Sir Brian Gerald Barratt-Boyles. Dr. Guido Fanconi is known as the father of pediatrics. He practiced pediatrics in Zurich until 1929 where he became director of the Children's Hospital at the University of Zurich. He was one of the pioneers in applying scientific methodology to the investigation of clinical problems. Dr. Fanconi was instrumental in describing 17 conditions that bear his name, one of which is Fanconi-Schlesinger syndrome, a.k.a.

Williams syndrome (Guido Fanconi, 2001).

Dr. Bernard Schlesinger was a British pediatrician during the early 1900's. He was the first to photograph this group of children with similar facial features (Bernard Schlesinger, 2001). Dr. Alois J. Beuren was a German cardiologist during the early part of the twentieth century who also described children with surpaventricular aortic stenosis and similar facial features (Alois Beuren, 2001). Sir Brian Gerald Barratt-Boyles is a pioneering heart surgeon from Auckland, New Zealand. He is most noted for the development of cardiopulmonary bypass procedures during heart surgery, the human cadaveric aortic homograft for aortic valve replacement, and described children with heart conditions and other similarities (Vlietstra, n.d.). Sir Barratt-Boyles worked in Greenlane Hospital and was most likely aware of Dr. J.C.P. Williams' findings.

Etiology

Williams syndrome is considered to be a sporadic gene deletion of a submicroscopic contiguous area of chromosome 7q11.23. This deletion can occur sporadically or during crossover events within misaligned regions of the chromosome (Elcioglu, Mackie-Ogilvie, Daker, and Berry, 1998). The missing region is one to two megabases in length. Most of the time, this deletion includes the gene for elastin and as

many as 14 other genes (Hartz, Tiller, Bocchini, and McKusick 2004; What is Williams syndrome, n.d.). The elastin gene deletion is considered to be responsible for connective tissue and cardiovascular abnormalities. LIMK1 (lim kinase 1) has been linked to abnormal visuospatial constructive cognition. GTF2I (general transcription factor II, I) deletion is considered to negatively impact IQ (Morris, 2003). WBSCR14 gene has also been identified as missing. Researchers have discovered that the WBSCR14 gene encodes an 852-amino acid protein. This gene is expressed in many tissues, especially certain brain regions and the intestinal tract. Scientists have hypothesized that this particular gene deletion may account for some of the features of Williams syndrome (Hartz et al., 2003). It is not known what impact the remaining genes involved in a typical deletion have on the individual (Morris, 2003).

The diagnosis of Williams syndrome is based on clinical criteria, but it is confirmed by the contiguous gene deletion in the critical region of chromosome 7, which over 99% of people with Williams syndrome possess. This detection is done using fluorescent in situ hybridization (FISH). The FISH test is widely available. Real-time quantitative polymerase chain reaction (PCR) is another method that is considered to be as reliable as the FISH test. Heterozygosity testing can be used to detect a deletion in the critical area of chromosome 7, but it is usually used to determine the size of the deletion (Morris, 2003).

The typical genetic deletions of Williams syndrome are considered to be an autosomal dominant disorder that can be passed from one generation to the next.

Generally prenatal testing is not warranted because most cases of Williams syndrome are single occurrences within the family, but prenatal screening can be performed for pregnancies at 50% risk of Williams syndrome. Chorionic villus sampling can be done at 10-12 weeks of gestation with the FISH test used to detect the presence of critical region deletions (Morris, 2003).

Characteristics

Facial and Physical Features

Similar facial and physical features, personality traits, medical complications, visual system defects, and talents have generally characterized children with Williams syndrome. Most children look like members of their family but children with Williams syndrome look remarkably like each other. This resemblance can be attributed to classic elfin facial features. Typically seen features are a small upturned nose, wide mouth, full lips, widely spaced small teeth, and a small chin (What is Williams syndrome, 2002). (See appendix A for photographs of children with Williams syndrome). These features become more pronounced as the child ages. A stellate or lacy iris pattern is noted in 51% of children with lighter pigmented irises (Holmstrom, Almond, Temple, Taylor, and Baraitser, 1990). Esotropia, a form of strabismus, is found in a large portion of the Williams syndrome population. This frequency has led to the postulation that hereditary infantile esotropia is genetically linked to Williams syndrome (Kapp, von Noorden, and Jenkins, 1995; Kapp, Gunter, von Noorden, and Jenkins, 1995; Sugayama, Bertola,

Albano, Plaggert, Bechara, and Kim, 2000).

In addition to ophthalmologic abnormalities, Tarjan, Balaton, Balaton, Varbiro, and Vajo (2003) described typical dental anomalies in patients with Williams syndrome. They found dental aplasia in 90%, primary tooth reabsorption anomaly in 96%, and fan shaped front teeth positioning in the majority of patients. These dental abnormalities give the appearance of the small wide-spaced teeth typical in people with Williams syndrome (Hertzberg, Nakisbendi, Needleman, and Pober, 1994). Many children also have problems with malocclusion. All of the dental abnormalities are readily remedied with orthodontic treatment.

In addition to common facial features, most children exhibit similar physical features. Most infants are born overdue and at a lower birth weight than their siblings. They exhibit poor weight gain with many infants being labeled as 'failure to thrive.' Feeding problems have been linked to muscle hypotonicity, which contributes to poor suck/swallow abilities, and an overly sensitive gag reflex. Many infants have extended periods of colic and erratic sleep cycles that may be linked to infantile hypercalcemia. The hypotonicity of infancy is present in young children coupled with joint laxity. Joint laxity can progress to stiffness and contractures as the child ages. Physical therapy can be helpful to combat these physical problems (What is Williams syndrome, 2002). Adults with Williams syndrome tend to be smaller in stature and age faster than their peers. The mean adult height has been reported to be in the lower third percentile (Morris, 2003).

Personality Traits

Coupled with like appearances, people with Williams syndrome often have similar fractionated personality traits. Children with Williams syndrome have been described as being "extremely sociable, charming, outgoing, and highly concerned about the well-being of others" (Sullivan, and Tager-Flusber, 1999, p. 2). The hypersocial behavior included in this 'cocktail party' personality can be attributed to the great attraction to human faces and sincere empathy seen in people with Williams syndrome (Sullivan et al., 1999). This type of social behavior tends to be pervasive and difficult for parents to inhibit, especially with respect to interaction with strangers (Jones, Bellugi, Lai, Chiles, Lincoln, and Adolphs, 2000). The classic Williams syndrome personality is summed up as "instant connection, instant enthusiasm, instant empathy, little sense of boundary" (Levine, and Wharton, 2000, p. 5).

In contrast to typical overt happiness, many children with Williams syndrome also have behavioral and emotional disturbances. Williams syndrome is also characterized by anxiety, insecurity, hyperactivity, perservations, and inappropriate interpersonal behaviors. These children are also more likely to be labeled as 'psychiatrically disordered' than other children with mental retardation (Einfeld, Tonge, and Florio, 1997). Stewart, Einfeld, and Tonge (1997) suggest that there is now "sufficient evidence to include a disorder that might be called 'Williams Syndrome Behavior Disorder' in a future Diagnostic and Statistical Manual" (p. 8).

One aspect of the typical Williams syndrome personality is its expressive use of language. Language ability in people with Williams syndrome has been extensively studied. Jones et al. (2000) proposed that expressive linguistics by people with Williams syndrome is a part of their hypersocial nature. Language development in children with Williams syndrome is significantly delayed, then it becomes a strength when the child reaches school age (Jones et al., 2000). Although people with Williams syndrome have seemingly unaffected language abilities, certain aspects of word learning do not progress beyond the preschool stage (Grant et al., 1997). During the preschool period, many children with Williams syndrome can produce surprisingly complex words, but upon further investigation, they do not understand the meaning of the words used (Bellugi, Liclitenberger, Jones, Lai, and St. George, 2000). The classic language of a person with Williams syndrome is often described as 'unusual.' Many times they use rather complex, unexpected words partially incorrect in context. For example, one child explained the emptying of a glass as: "The glass needs to be evacuated." (p. 8). Overall, language ability for people with Williams syndrome far surpasses the language abilities of others with a similar IQ. They have been described as 'natural storytellers,' using sound effects and voice inflections to enhance their language (When words don't fail, 1995).

Medical Complications

As with common personality traits, people with Williams syndrome have classic medical conditions. (See Appendix B for a medical checklist devised to assist

pediatricians). The most commonly seen malady is supravalvar aortic stenosis with 80% of all children with Williams syndrome having a heart murmur (What is Williams syndrome, n.d.). The stenosis worsens as the child ages; therefore, it is highly recommended that a pediatric cardiologist follow all children with Williams syndrome periodically. Often the supravalvar aortic stenosis requires open-heart surgery for correction. Significant hypertension is often developed in the teenage years with 46% of Williams syndrome children being identified as having the disease (Reinhardt, Ahern, Lifton, Tamborlane, and Pober, 1999). Extraordinarily high blood pressures of 160/110 are not uncommon. All of these classic cardiovascular diseases, also referred to as 'elastin arteriopathy,' can be related to the deletion of the elastin gene on chromosome 7 (Morris, 2003). Coronary artery stenosis and severe biventricular outflow tract obstruction has been identified as predisposing individuals with Williams syndrome to sudden death (Bird et al., 1996).

In addition to cardiovascular problems, 15% of infants with Williams syndrome have been identified as having infantile hypercalcemia. Hypercalcemia generally occurs in the first years of life but may reoccur during puberty. Symptoms of hypercalcemia are often irritability, feeding intolerance, and constipation. The condition can be resolved with medical intervention and diet management during the acute phase. The etiology of infantile hypercalcemia remains a mystery because the genes that regulate calcium are outside of the deletion area of chromosome 7 (Cagle, Waguespack, Buckingham, Shankar, and DiMeglio, 2004).

Despite hypercalcemia being a problem in Williams syndrome, typical urinary system problems exhibited by people with Williams syndrome are not related to nephrocalcinosis. The typical urological problems presented are bladder diverticula, renal aplasia or hypoplasia, and recurrent urinary tract infections. These types of problems are associated with the deletion of the elastin gene. Because of the increased risk of urological problems in children with Williams syndrome, it is recommended that routine examination by a urologist be a part of routine medical management (Pankau, Partsch, Winter, Gosch, and Wessel, 1996).

In addition to the biological system problems, Williams syndrome is associated with other less common maladies. Associated with connective tissue abnormalities are hoarse voice, inguinal and umbilical hernias, and rectal prolapse. Hypothyroidism, early puberty, and an increased occurrence of diabetes mellitus are commonly seen endocrine abnormalities (Morris, 2003).

Visual System Defects

Along with classic medical conditions, Williams syndrome is associated with distinct visuo-motor and visual spatial deficiencies. Cognitive profile examinations show that the typical adult with Williams syndrome scores at a six to eight year age equivalent in areas such as reading, spelling, and arithmetic (Howlin, Davies, and Udwin, 1998). Bellugi, Lielitenberger, Jones, Lai, and St. George (Bellugi et al., 2000) describe numerous experiments that illustrate the severe visual processing deficiencies found with

Williams syndrome. They report that drawing ability results in poor cohesion and lacks overall organization. People with Williams syndrome seem to show a distinct local bias or a 'can't see the forest for the trees' situation. An example was given of a large 'D' made up of little 'Y's that subjects with Williams syndrome were asked to copy. The results were a drawing of random little 'Y's across the page with no recognizable global 'D' (Bellugi et al., 2000). This deficiency in the ability to visualize how different parts make up a larger object has been examined using brain-imaging systems. Scientists have linked this defect to the scarcity of tissue in a small portion of the brain's visual system. The lacking brain tissue has been attributed to "a shortage of neurons in part of the brain network that locates objects in space and discerns spatial relationships among objects." (Bower, 2004, p. 2) Further analysis using fMRI indicates weaker neural activity in that area of the brain which partially blocks visual information to the brain (Bower, 2004).

Talents

Regardless of the defects in the visual system, many people with Williams syndrome exhibit some surprising talents. The most notable talent is the love of music despite the common problem of hyperacusis. According to Don, Schellenberg, and Rourke (1999), "compared to normal (sic) children, the WS group expressed greater liking of music and a greater range of emotional responses to music." (p. 154). Additionally, Levitin, Cole, Chiles, Lai, Lincoln, and Bellugi (2004), found that "WS individuals . . . manifested interest in music at an earlier age, and spent more hours per

week listening to music" (p. 223). The incidence of music savants are rare in the Williams syndrome population, but members have shown a higher degree of absolute pitch, strong lyric memory, and ease of composing music (Reis, Schader, and Milne, 2003).

Interventions

Even with the difficulties people with Williams syndrome have to face, the affinity for language and music can be used as a basis for intervention strategies. These talents have led to a new model for special education instruction termed 'talent development.' Talent development has been used in a program designed specifically for people with Williams syndrome called "Music & Minds" (Tieso, 2002). In response to his own daughter's diagnosis of Williams syndrome, Dr. Howard Lenhoff was instrumental in the development of 'Williams Syndrome Music and Arts,' an annual music camp for people with Williams syndrome in Western Massachusetts (Scheiber, 1998). In addition to music, many of the participants of these unique camps involve drama. The use of drama enables students with Williams syndrome to utilize their language talents (Tieso, 2002).

Through these enrichment programs, many areas of weakness are addressed using music and language. Students are paired based on similar interests and taught strategies using music or drama. Frequent breaks and varied activities help students overcome their short attention spans and focus on the activity at hand. To address their emotional

hypersensitivity, instructors diffuse situations before they became pervasive and discuss the situation until the students are ready to move on. The great distress created by hyperacusis is overcome by focusing on song or dance during thunderstorms or periods of other loud noises. Role-playing, social stories, and redirecting the student's focus address the tendency toward perservation. Anxieties about changes in routine are addressed with a scheduling notebook. This intervention allows students with Williams syndrome to address their anxiety over daily events. Also, social stories are used to assist with the development of peer relationships (Tieso, 2002).

In addition to addressing social and behavioral issues, academic instruction was adapted to include music, language, and imitation. A scaffolding approach is used and is adapted to include each of the student's strengths. This approach includes providing clear goals and instructions for students while keeping the concepts simple. Instructions should avoid metaphors and idioms because many students with Williams syndrome take things literally. Students play musical instruments, sing, or act during instruction. Parents reported retention of math and money topics weeks after the program ends (Tieso, 2002).

Discussion

People with Williams syndrome present a unique picture of talents and troubles. This distinct syndrome has allowed researchers to examine the complexities of the human

mind and how the mind develops its humanity. The study of Williams syndrome has also led to innovative teaching techniques that can assist all students by focusing on their strengths rather than weaknesses. Programs designed to address the unique learning needs of individuals with Williams syndrome have brought to light that all people with mental retardation have potentials that have been untapped. Dr. Ursula Bellugi has summed up the mysterious condition known as Williams syndrome, by saying "people with Williams syndrome are smart and mentally retarded, gifted and inept at the same time." (1991 as cited in Finn, p. 1).

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