DEVELOPMENTAL REGRESSION IN CHILDREN WITH DOWN SYNDROME

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Submitted to the Department of Special Education
and the Faculty of the Graduate School of the
University of Kansas In partial fulfillment of the
requirements for the degree of Doctor of Philosophy

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ABSTRACT

This study presents in detail the data on a group of 20 participants, female and male, from 2 to 12 years old with Down syndrome (DS) who experienced developmental regression. This study took place at the Down syndrome clinic at Kennedy Krieger Institute, Baltimore, Maryland.

These 20 participants were divided into 4 groups according to their age at regression, comorbid condition, and the characteristics of their regression.

Using retrospective chart review, data showed that all 20 children lost communication, social skills, and play skills. Ten children lost some daily living skills, 8 participants had apparent motor skill changes, and 12 developed sleep disturbances. After regression 16 participants received a diagnosis of autism spectrum disorders or pervasive developmental disorders and only one received the diagnosis of stereotype movement disorder with loss.

With the onset of regression, data also showed that there was an emergence of maladaptive behaviors among participants. The most common maladaptive behaviors were stereotypy, developed in 13 cases; sensory problems in 11 participants; perseveration developed in 16 participants; and sleep disturbance in 12 cases. Other symptoms such as self-injury behaviors were developed by 9 participants, and mood swings in 8 participants. Behavior problems, Pica and psychotic like behavior were the least frequently observed.

For children older than 8 years, onset of mental health problems (mood swings, psychotic-like behavior and SIBs) was very frequent. Results were also compared to other regressive syndromes such as childhood disintegrative disorder, Rett syndrome, and regression in autism.

DEDICATION

This work is dedicated to my parents, Pilar and Pedro and to my husband Govert, the three pillars of my life, for their unconditional support throughout the years and through this endeavor. They have shown to me with their acts that hard work, perseverance, honesty, and open mind are essential qualities for a full life. Their examples have also helped me out to take on this journey that ends today with this work. Thank you!

I would also like to dedicate this work to the families of children with disabilities that I have work all these years, because no book can teach what you have taught me. Thank you!

ACKNOWLEDGMENTS

The work presented here is not only a dissertation but also a reflection of the support around me which made this all possible.

I am deeply grateful to my advisor Dr. Simpson who has given me the opportunity and space to grow as a person and as a researcher. He has walked with me through thick and thin and he has given me the confidence to face the struggles which a PhD comes with. Dr. Simpson has been an invaluable example of a nurturing academic advisor while maintaining high expectations of my work.

I owe my deepest gratitude as well to Dr. Capone, director of the Down syndrome clinic at Kennedy Krieger Institute, for his generosity with time and resources and the opportunity to make this work happen. Dr. Capone has been a continuous source of inspiration to work with families of children with Down syndrome. He has continuously shared with me his vast experience and knowledge of the field and he has given me his unconditional support to develop my own vision. I also like to acknowledge his wife Mary, and my and their friend Jill for their warmth and love and for opening their houses and hearts to me every time I was in Baltimore and now that I am finally graduating. They added to this journey a very special side!

My thanks go to the members of my committee, Dr. Wehmeyer, Dr. Harington, and Dr. Skrtic, for their support, their guidance and helpful suggestions.

I am also grateful for financial support from Foundation Focus Abengoa (Seville, Spain). Their "Ayuda de Investigación" is evidence for their commitment to enhance knowledge of the arts and sciences which benefit and strengthen our society.

To the families of children with Down syndrome of this study, for their time and willingness to share their stories so this study and others can be possible. And also for their

constant example of perseverance, love and care of their children with disability. Their example is an inspiration for myself personally and how I see my profession.

To my dearest professors from the department of Special Education at the University of Kansas: Deb Griswold, Chriss Walter- Thomas, Sean Smith, Earl Knowlton, Don Deshler, Steve Colson, Tom Skrtic, Michael Wehmeyer and Rud Turnbull. The knowledge you have shared, your experiences, your warmth, your progressive view on disability and teacher preparation made me come back again to pursue my PhD and feel the urge to share and create new knowledge wherever the future brings me.

Special acknowledgement to Sherrie Saathoff, the soul of the department and to Dona Goodwin, there is not enough space to describe what you have done for me and what you mean to me after all these years. I am glad that I have been telling you this for quite some time.

To my early mentors, Brenda Myles and Dolores Izuzquiza they were the first ones to encourage me to do my PhD and tickled my passion for the world of autism and disability. Thanks for opening my eyes to the importance of balance between research and practice.

Of course my friends have a big part in all this: Leticia, Osvaldo, Emily and Nazim, Andrew, Nina, Mark, Matt, Ed and Michelle, Ola, Bea, Sheila, Paul, Anna, Connie and Kevin, Alyson, Heather and Matt, Andrea and Femi, Sally and Dominic … through their jokes and encouragement, and sometimes with sentences like " shouldn't you be working on…" or also sometimes " ok.. now it is time for beer!" which helped me to get through.

To my family, my parents Pedro and Pilar, and my siblings and their spouses who really know how to keep me on track in the best old fashioned way!: Alfredo and Pachi, Curro, Perico and Yolanda, Jose and Ana, Fernando and Maria, my sister Alegria and her husband Javier.

To my family in law, John and Barry, Tinca and Gerald, Floris, Olaf, Jan and Ineke, who have walked with me through the entire process until the end. I have been blessed with them in my life and truly helped me when things looked ”uphill”.

Finally to my husband Govert, who fulfilled all possible roles. Who just knew when to push and when to help me to step back. He has been a solid support and a fundamental companion in every step of the way. I am sure I could not have done it without him. Thanks mi amor!

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Chapter I

INTRODUCTION

Background

John Langdon Down, an English physician, first characterized Down syndrome (DS) as a distinct form of intellectual disability in 1862 (Ward, 1999). It was not until almost 100 years later, however, that Jérôme Lejeune and colleagues (1959) discovered the extra chromosome 21 as the underlying cause of DS. This discovery established the chromosomal anomaly link to the disability.

Although autism spectrum disorders are one of the most common developmental disabilities today, affecting an average of 1 in every 110 children (CDC, 2009), DS is the most common genetic cause of moderate to severe intellectual disability worldwide (Moser, 1985). The presence of the extra chromosome affects the development of the central nervous system at different levels, leading to variation in the degree of cognitive and other neurological functions among persons with DS (Wisniewski et al., 1996).

Knowledge about DS has advanced rapidly in many areas, which in turn has resulted in better educational, medical, and family support. However, myths about personality and behavior traits in persons with DS are as prevalent today as in the past (Booth, 1985; Gothard 2002; Stores, Stores, Fellows, & Buckley 1998). Many people still incorrectly believe that persons with DS are always affectionate, have a great sense of humor, and are very sociable.

DS is a complex disability, and current estimates of the frequency of neurobehavioral and psychiatric comorbidity ranges between 18% and 38% (Gath, & Gumbley, 1986; Dykens, Shah, Sagun, Beck, & King, 2002; Meyers & Pueschel, 1991). These comorbid problems affect persons with DS with a range of intellectual abilities (Capone, Goyal, Ares, & Lanningan, 2006;

Dykens, Shah, Sagun, Beck, & King, 2002; Gath, & Gumbley, 1986; McCarthy & Boyd, 2001; Meyers & Pueschel, 1991; Howlin, Wing, & Gould, 1995).

Specific comorbid conditions frequently found in children and adults with DS include autistic spectrum (ASD) and stereotypic movement disorders (SMD) (Bregman & Volkmar 1988; Capone, 2002; Capone et al., 2005; Gath & Gumbley, 1986; Ghaziuddin, Tsai, & Ghaziuddin, 1992; Howlin, Wing, & Gould, 1995; Kent, Evans, & Sharp, 1998; Meyers & Pueschel, 1991; Rasmussen, Borjesson, Wentz, & Gillbeg, 2001); attention deficit disorder with hyperactivity (Gath & Gumbley, 1986; Maatta, Maatta, Taanila, Kaski, & Livanainen, 2006; Meyers & Pueschel, 1991; Nicham et al., 2003; Turner & Sloper, 1996). Oppositional defiant disorder and other maladaptive behaviors are also seen among individuals with DS (Coe et al., 1999; Collacott, Cooper, Branford, & McGrother, 1998; Dykens et al., 2002; Nicham et al., 2003; Turner & Sloper, 1996).

Conduct disorders and attention deficit, with or without hyperactivity, are the most common comorbid conditions that affect children with DS (Gath & Gumley, 1986; Howlin et al., 1995; Myers & Pueschel, 1991). Behavioral problems such as noncompliance, aggression, and hyperactivity are also commonly found in children with DS (Capone et al., 2006; Coe et al., 1999; Gath & Gumley, 1986; Meyers & Pueschel, 1991). In contrast, autism and mood disorders in children with DS are evident in less than 10% of cases (Coe et al., 1999; Gath & Gumley, 1986; Howlin et al., 1995; Myers & Pueschel, 1991).

Gath and Gumley (1986) found that 38 % of the 193 children with DS in their study had significant behavior disorders. Furthermore, 11% of the subjects with DS in their study had a conduct disorder or hyperkinetic conduct disorder. This occurrence was slightly greater than in the control group, which was integrated by children with similar degrees of verbal and motor

disability. In addition, Dykens et al. (2002) examined age-related changes in the maladaptive behaviors of 211 children and adolescents with DS between 4 and 19 years old. The children were recruited from family homes and residential placements specializing in the psychiatric management of people with DS. Externalizing behaviors were lower across both settings, while internalizing behaviors were much higher in the older groups, which encompassed ages 14 to 19 years old. Sixty-three percent of adolescents living in community-based residences showed significant withdrawal in comparison with 75% of adolescent clinic patients. Aggressive behaviors were found to reach their peak between the ages of 10-13 years and later declined significantly to be the lowest among adolescents. Also, rates of stubbornness and disobedience were between 79% and 74%, remaining consistent across all age groups. Problems with attention ranged between 71% and 79% across preadolescents groups, reaching their peak during ages 7 to 9 years old. By the age of 14 years, attention problems decreased to about 38%. Nicham et al. (2003) found similar results in their research on the presence of age-related changes in the spectrum of externalizing and internalizing problems. They noted that externalizing behaviors such as opposing and refusing, impulsiveness, inattention, and increased motor activity were significantly higher in the 5 to 10 year old group of children, whereas internalizing behaviors were more prevalent in adolescents and adults.

Autism spectrum disorders as a comorbid condition among children with DS have a prevalence rate between 5% and 10% of all cases, depending upon the criteria used (Capone et al., 2005; Ghaziunddin et al., 1992; Kent et al., 1999; Leshin, 2002; Lund, 1988). However, because DS encompasses intellectual disability and in many cases is severe, it is important to mention that despite the fact that the prevalence of autistic-like behavior increases when there is a more significant intellectual disability, persons with DS with the lowest intellectual level are, in

fact, sociable (Wing, 1981) and do not show signs of autism. Thus, it is difficult and somewhat controversial but important to distinguish if autistic-like behaviors reach a threshold of severity such that a comorbid diagnosis of ASD is warranted. Furthermore, children with DS do not typically lose developmental skills, so it is critical to determine if any history of developmental regression is present, and if so, when it occurred as this may lend support to the diagnosis of comorbid ASD.

Other research studies such as those conducted by Capone et al. (2005), Castillo et al. (2008), and Eisermann et al. (2003) have also found dual diagnosis of children with DS and Childhood Disintegrative Disorder (CDD) or developmental regression. Their research presented reports on children with DS who, after a period of expected cognitive, social, and motor development, suddenly started losing skills they had acquired after the age of three years. Subsequent evaluation of these children revealed comorbid autism. Other cases of children without DS found that developmental regression occurred later, between the ages of 7 to 10 years (Agarwal, Sitholey, & Mohan, 2005; Malhotra & Sight, 1993; Malhotra & Gupta, 1999). Some of these children with early or later onset of developmental regression also had a prior history of epilepsy, such as infantile spasms (Caplan & Austin, 2000; Goldberg-Stern et al., 2001; Stafstrom & Konkol, 1994; Tatsuno, Hayashi, Iwamoto, Suzuki, & Kuroki,1984). In those cases, the diagnosis was also DS with comorbid autism.

Given the prevalence of DS and its complexity, little research has been conducted on the various manifestations of co-occurring mental health and behavioral conditions among persons diagnosed with DS. Thus, a need exists for further research on comorbid conditions in DS to ensure accurate diagnosis as well as research on medical and educational interventions. Additional research is also important for adequate design and implementation of educational and

other medical treatments that may improve the quality of life for persons with DS and their families (Capone, 2004).

To advance our understanding of DS, this dissertation provided descriptive data on four groups of children with DS and developmental regression. From each group, a case study was written to exemplify the phenomenology of developmental regression in DS. It is mindful to recognize the differences between CDD and ASD as noted according to the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision (DSM-IV-TR) (American Psychiatric Association, 2000) (APA, 2000). It states that to diagnose CDD, the child must have normal development during the first two years of life with the onset of regression after the age of 2 years but no later than 10 years. In contrast, ASD onset occurs prior to 3 years of age, albeit without a pattern of normal development followed by regression. In this study, because participants had DS and experienced general delays in development, a more inclusive classification for developmental regression than the one found in the DSM-IV-TR (APA, 2000) was needed. Thus the term *developmental regression* was used. That term referred to "a more or less sudden loss of interest and attention towards others and the environment, loss of words, of communicative and imitative gestures, and of cognitive abilities occurring after a period of 'normal' or sometimes delayed development" (Bernabei, Cerquiglini, Cortesi, & D' Ardia, 2007, p.580). This loss of specific adaptive skills and emergence of maladaptive behaviors experienced by children with DS must have occurred between the ages of 2 and 12 years.

The background for the research questions presented in this project was based on a retrospective review of data obtained on each participant from a variety of sources as well as on the behavioral characteristics of CDD and core features of ASD. Questions about the loss of specific adaptive skills and the emergence of maladaptive behaviors was ascertained from

parents, teachers and other educational professional reports, as well as observations at the Down Syndrome Clinic at Kennedy Krieger Institute.

Purpose and Research Questions

The purpose of this research study was to characterize the phenomenology of developmental regression in children with DS between the ages of 2 and 12 years. To assess developmental regression, it was necessary to examine the development history of participants in the areas of language, social interaction, play, bowel and bladder control, and motor development. The emergence of new-onset behaviors or the intensification of preexisting behaviors accompanying developmental regression was also identified. These included, but were not limited to, sensory issues, stereotypic movement disorders, perseveration and atypical play, inattention, hyperactivity, and disruptive behaviors.

The following research questions were addressed:

1. Which adaptive skills were present and then lost during developmental regression?
2. Did participants lose the same skills?
3. Which maladaptive behaviors emerged after regression? Did participants experience the emergence of the same maladaptive behaviors?
4. Did regression occur at the same age?
5. If the age of onset varied, how did the regression itself vary?

Significance

In November 2007, a meeting was sponsored by the Centers of Disease Control and Prevention and the National Down Syndrome Society "to review the current knowledge, identify gaps, and develop priorities for future public health research related to Down Syndrome" (Rasmussen, Whitehead, Collier, & Frías, 2008, pp. 2998). One of the tasks assigned to all

participants, who were from different disciplinary backgrounds, was to indentify key public health research questions related to DS. Among the priority areas was an "improved understanding of comorbid conditions, including their prevalence, clinical variability, natural history, and optimal methods for evaluation and treatment" (Rasmussen, et al., 2008, p. 2998).

Dykens's (2007) review of psychiatric and behavioral disorders in persons with DS exposed the pressing need to research the evolution of psychiatric problems across development stages. This review proposed to examine continuous processes such as personality, regulation of mood, attention, and sociability through the life span.

In terms of a dual diagnosis of autism and DS, Dykens (2007) indicated that compared with children with ASD, those with DS are generally much older when they receive their comorbid diagnoses of autism because of the "syndrome overshadowing" factor. This factor reflects the understanding among certain professional that specific symptoms might be related to the child's intellectual disability and are not recognized as a comorbid condition.

Providing parents with an accurate diagnosis, which can then guide pharmaceutical and educational interventions for their child, is essential for the well-being of the child and family. It also gives clues about the child's prognosis. This present study extends the research into the area of comorbid conditions in DS, specifically in the area of developmental regression, in an effort to answer questions related to this important topic. Moreover, as Castillo et al. (2008) expressed, further study of this unique population may provide clues to understanding the more general phenomenon of regression in autism as well.

Definition of Terms.

Autistic-like behaviors: Behavior that is similar to those in children diagnosed with autism (e.g., stereotypical movement disorder, lack of eye contact, or echolalia). The child, however, does not present all of the criteria that would warrant a diagnosis of autistic disorder.

Autism Spectrum Disorders (ASD): A term commonly used to refer to pervasive developmental disorders (Volkmar & Weisner, 2009).

Atypical play or abnormal play: Type of play that a child exhibits that is not in accordance with the type of toy contact with.

Atypical sensory behavior: An atypical response or activity that the child is in (under-responsive or over-responsive) to a sensory stimulus because of the inability to process and organize the input from the senses adequately.

Atypical eye contact: The inability to establish and maintain appropriate eye contact with others during interactions.

Babbling: The talk typical of babies. It encompasses putting together consonants with vowels although no recognizable words are uttered.

Comorbid: Two or more disorders co-existing in one individual.

*Echolalia: "*Parrot like" repetition of verbal information stated by others. The information repeated can be something that the child just heard or something that he or she heard hours, days, or even months earlier.

EEG (Electroencephalogram): A test to detect problems in the electrical activity of the brain, usually suggestive of seizure activity.

Epilepsy: According to the National Institute of Neurological Disorders and Stroke (2010), epilepsy is a brain disorder in which clusters of nerve cells, or neurons, in the brain sometimes signal abnormally and result in seizures.

Epileptiform: Brain pathology resembling epilepsy.

Expressive language: Words or signs used to communicate.

Obsessive compulsive disorders: An anxiety disorder involving recurring thoughts and/ or compulsive actions.

Receptive language: Words or signs that an individual can comprehend.

Pica: The compulsion of eating nonedible items.

Seizure: An abrupt change in consciousness and/or behavior due to an abnormal electrochemical activity in the brain.

Social smile: The smile that a baby makes in response to a pleasant social interaction with an adult.

Motor stereotypy: Repetitive movement of hands, upper, or lower body, such as rocking or hand flapping.

Dissertation Organization

This research study is organized in five chapters. Chapter One is the introduction to the study. It presents the context of the topic, the statement of the problem, the research questions, and the significance of this study. Chapter Two provides a literature review. First, it introduces a review of the cytogenetic variations of DS and reviews the developmental characteristics of children with DS; second, it defines ASD and reviews current and past literature on DS with ASD. It also provides a definition of Childhood Disintegrative Disorder according to DSM-IV

(American Psychiatric Association, 2000) and reviews the available literature of CDD in autism and on developmental regression in DS. Finally, Chapter Two provides a review of the differences between regression and CDD and how regression affects neurotypical children and children with pre-existing autism. Chapter Three details the methodology used in the study, including design, setting, participants, procedures, data collection, and data analysis. Chapter Four presents the results of the study. Chapter Five provides a summary, discussion, conclusions, and limitations of the study as well as implications for professionals and families along with recommendations for further research. References and appendices are also included.

Chapter II

REVIEW OF THE LITERATURE

Overview of Characteristics of Down Syndrome

Cytogenetic Variations.

Down syndrome (DS) is the most common genetic cause of moderate to severe intellectual disability worldwide with a prevalence rate of 1 in 700 live births (Capone, Grados, Kaufmann, Bernad- Ripoll, & Jewell, 2005; Hassold, 1999; Moser, 1985; Steele & Stratford, 1995). This prevalence varies according the mother's age. Traditionally, women over age 35 have been considered most likely to have babies with DS.

There are three cytogenetic types of DS: trisomy 21, translocation, and mosaic. Each is determined by the structure arrangement of the extra chromosome

Trisomy 21. The most common form of DS is trisomy 21 (47, XX,+21), which occurs in approximately 92% to 95% of the cases of DS. This type of genetic variation is caused by the presence of an extra chromosome 21 in *all* cells when a non-disjunction during the meiotic phase occurs. When the disjunction does not occur, a gamete (sperm or egg cell) is produced with an extra copy of chromosome 21; thus, it has 24 chromosomes instead of 23. When combined with a normal gamete from the other parent, the embryo has 47 chromosomes, with three copies of chromosome 21. As the embryo develops, the extra chromosome is represented in every cell.

In 88% of cases, the extra copy of chromosome 21 stems from non-disjunction in the maternal gamete, and in 5% of the cases, from non-disjunction in the paternal gamete. Around 4% to 5% is due to mitotic errors that occur during the cell division after fertilization when the sperm and ovum are joined (Antonarakis, Avramopoulos, Blouin, Talbot, & Schinzel, 1993).

Translocation. The second type of cytogenetic variation in DS is translocation, which occurs in approximately 4% of cases. Translocation happens when an extra segment of chromosome 21 (as opposed to the whole chromosome) is joined to another chromosome either prior to or at conception (Mikkelsen, 1981; Pennrose, Ellis, & Delhanty, 1960). This attachment occurs most often in chromosome 14, expressed by 45,XX, t(14;21q), chromosome 21 45,XX, t(21q;21q) or in chromosomes 13 or 15.

Mosaic. The third cytogenetic variation is called mosaicism (Clarke, Edwards, & Smallpiece, 1961), which occurs in 1% of DS cases. In this cytogenetic variant, some cells have an extra 21 chromosome while others do not. The development of children and adults with this type of DS is closer to the normal range, due to the balancing effect of the normal cells. (Fishler & Koch, 1991; Selikowitz, 1997).

Developmental Characteristics of Children with Down syndrome

As Sigman (1999) argued, it is important to have a precise picture of the abilities associated with a particular syndrome. This will provide professionals with an understanding of the difficulties an individual is most likely to face, the extent to which these challenges can be mastered, and the need for developing alternative neurological functions to replace those damaged by the characteristics of a particular syndrome.

To arrive at a precise idea of the abilities associated with a particular syndrome, Sigman (1999) called for adopting a developmental framework. By identifying specific problems within a specific syndrome during different stages of development, it will help increase the understanding of how the genetic and neurobiological substrate of the syndrome affects a person. This is possible to the extent that psychological functions have been mapped out in specific brain regions.

The following section will review the developmental characteristics of children with DS, specifically the areas of cognitive and language development, joint attention, imitation and play, and emotion recognition.

Cognitive and language development characteristics of DS. Trisomy and translocation of chromosome 21 are assumed to be causes of DS intellectual disability. Nevertheless, researchers are still debating whether cognitive development in DS follows the same pattern as in neurotypical peers but at slower rate (Chapman & Hesketh, 2000) or if it is not only slower but also different (Morss, 1983; Sigman, 1999).

Although the cognitive development patterns in other conditions such as autism are clear, the question of developmental delay versus difference in DS remains unresolved (Sigman, 1999). The extent to which children with DS are seen as having developmental delays or different cognitive development varies with the age of the child, domains that are examined, and type of measures and instruments used in the process (Fidler, 2005). Furthermore, according to Carr (2002), some studies have shown that babies with DS aged 6 months were found to have a mean developmental quotient of 70 to 80. However as the children develop, data has shown a decline in intellectual quotient, with a mean of 40 by the age of 4 years (Carr,1985) and a mean of between 37 to 41 at 11 years old (Carr & Hewett, 1982). Nevertheless, as Carr (2002) explains, "differences *between* persons with DS are as striking as those found in any population" (p.176)

Still, there is general agreement among researchers that children and adolescents with DS manifest cognitive delay, deficits in expressive language, and verbal short term memory (Chapman & Hesketh, 2001; Kummin, 1996; Marder & Cholmain, 2006; Mundy, Sigman, & Yirmiya, 1988; Yoder & Warren, 2004), whereas the development of adaptive behavior skills is

more consistent with the patterns of development of neurotypical peers but acquired more slowly (Chapman & Hesketh, 2000; Jarrold, Baddeley, & Phillips, 2002).

Jarrold, Baddeley, and Hewes (1999) found relative strengths in visuospatial processing among individuals diagnosed with DS, and Fidler (2005) found strengths in visual memory and visual imitation areas, whereas spatial memory seemed to be the weakest areas for these children. Fidler, Hepburn, and Rogers (2006) also found poor motor coordination.

Visual processing is considered to be strength of individuals with DS (Kummin, 2003; Pueschel, Gallagher, Zartler, & Pezullo, 1987), because they are better able to remember what they see than what they hear. However, many children with DS have visual impairment. For example, research shows that about 50% of children with DS have strabismus, nearsightedness, farsightedness, and some type of muscle imbalance that causes problems with the extra ocular movement (Kummin, 2003).

Speech and language development. In terms of acquiring communication skills, children with DS usually demonstrate a delay compared to typical development. Many children with DS start communicating using signs during the first year of life (Kummin, 2003). Some researchers have pointed out that children with DS are ready to communicate and use a language system well before they are ready to speak (e.g., Kummin, 2003). Generally, their first words come between ages 1 and 2 years old (Buckley 2000; Buckley & Bird, 2001; Mundy et al., 1988). However, some researchers note that it may be delayed up to the age of 5 (Chamberlain & Strode, 1999; Kummin, 1996, 2003). Typically developing children normally reach the two- and three-word stage when they have an average vocabulary of 50 words at an average of 19 months to 2 years old. By comparison, children with DS do not use combinations of two words around the age of 3 (Chamberlain & Strode, 2000; Gillham, 1979; Kummin, 2003).

It is interesting to note that children with DS use nonverbal requests for objects or for assistance with objects less frequently than their peers without this disability (Mundy et al., 1988; Sigman, 1999). According to these authors, this might partially explain their expressive language delay. Conversely, Inverson, Longobardi, and Caselli (2003) found that even though children with DS have a smaller repertoire of gestures, no differences were found for overall usage when compared to typically developing peers.

Difficulty in producing speech could be due to low muscle tone and coordination in and around the face and body, hearing impairments, and sensory integration (Kummin, 2003). Low tone also affects the tongue and the lips, making speech sounds slurred and thicker. Some children with DS also have problems exhaling air and sustaining it long enough to say a whole sentence, which may result in shorter utterances (Kummin, 2003).

Hearing. Hearing impairments in this population are frequent. Many of these children develop middle-ear infections with fluctuating hearing loss, resulting in conductive hearing loss in 80% of the cases. In addition, difficulties with sensory integration translate into difficulties processing input from more than one sense (Kummin, 2003). This means that when information comes from different sources concurrently, such a picture, a verbal, and a physical prompt, the child has trouble integrating all the information necessary to understand the meaning of the stimuli and act upon them.

Joint attention. Joint attention is the ability to coordinate attention between people and objects, including the tendency to look in the direction where another person is looking or pointing (Frith 2003). For example, when a child sees a dog barking, he points it out and looks at his mom to check that she is also looking at the dog. Joint attention is important because it shows

that the child is not only interested in sharing his object of interest but also in the other person's perception of the object, in this example the mother's (Frith, 2003).

Sigman (1999) found that children with DS did not differ significantly from their typically developing peers in initiating or responding to joint attention. However, they used less advanced means, which is noted as they point without verbalization or utterances, and were less able to coordinate their attention with the attention of others.

Sigman (1999) also found that language gains in children with DS were associated with caregivers maintaining attention to child-selected toys and with more continuous joint attention. Caregivers redirecting attention away from child-selected toys and a greater frequency of joint attention episodes were negatively associated with children's language gains. The same researchers also found that when children with DS were able to initiate joint attention, they were less likely to request objects or assistance with objects. However, compared to typically developing children, children with DS focused their attention more frequently on people than on objects. Interestingly, children who showed more serious deficits in joint attention were less able to understand and use language and more likely to make smaller gains in language over time.

Franco and Wishart (1995) studied the interaction behaviors of 22 children with DS who were 21 to 47 months old. They found that if provided with a communicative context and opportunities to share their interest or information, these children produced pointing gestures for both declarative and imperative interactions. Furthermore, children with DS appeared to understand the need for checking if their partners were looking toward the object that they were pointing to. Children with DS produced more gestures when their mothers were their partners than when peers were fulfilling that role; however, they looked more often to their peers to ensure that they were looking at the same object. Franco and Wishart (1995) concluded that

children with DS show the same prototype of communicative awareness of people and use comparable gesture communication as do their peers.

Imitation and play. In normally developing toddlers, functional play, that is the ability to act on objects as their function denotes (e.g., pushing a toy fire fighter truck), emerges at approximately 14 months (Libby, Powell, Messer, & Jordan, 1997; Wright, Lewis, & Collis, 2006). However, symbolic play, that is, the ability to give to an object or situation a different use, as if it were something else (e.g., a using a spoon as an airplane), emerges later, around 20 months old in both typically development children and those with DS (Libby et al., 1997).

Imitation and pretend play in children with DS goes through the same developmental sequence as do typically developing children, and some researchers have suggested that their abilities in this area are more advanced compared to their language abilities (Fewell, Ogura, Notari-Syverson, & Wheeden, 1997; Hill & McCune-Nicholich, 1981; Motti, Cicchetti, & Stroufe, 1983; Shimada, 1990). Nevertheless, according to Wright et al. (2006), children with DS appear to have an attentional bias towards social stimuli and tend to rely more on social clues or imitative solutions when engaging in object search or play than their typically developing peers. Therefore, children with DS appear to imitate more than generate actions, based on weaker, pre-existing representations of the functional properties of an object, which potentially could reduce spontaneous functional play (Wright et al., 2006).

Emotion recognition. According to Kasari, Freeman, and Hughes (2001), on simple emotion recognition tasks (labeling and understanding of emotions from simple history based contexts), children with DS perform at a similar level than typically developing peers matched on a mental age of approximately 3 years. Yet, by the age of 4, children with DS perform worse than matched mental-age typically developing peers. Although the mental age of children with

DS increased over a two- year period, their ability to recognize and understand emotions did not. Thus, children with DS in this study often confused positive emotions for negative emotions (i.e., happy for angry), whereas children with non-specific causes of intellectual disability confused emotions of the same tone (i.e., sadness for anger). Similarly, Williams, Wishart, Picartin, and Willis (2005) found that children with DS, when compared to their neurotypical peers, had difficulties in processing emotional expressions, specifically fear, whereas there were no differences in the performance of children with other non-specific intellectual disabilities on the emotion-matching task. These deficits seem to be consistent with previous research using facial stimuli (Franco & Wishart, 1995; Kasari, Freeman, & Bass, 2003). Nevertheless, Kasari et al.'s (2003) study of empathy found that, compared to the other children, children with DS responded to distress in others by looking to them more and offering more comfort. However, in a hypothetical empathy situation, children with DS were less likely to feel the same emotion as the protagonist than were the typically developing children.

Motor Development. Research in motor development in people with DS across the lifespan is limited (Sacks and Buckley, 2003), and caution is necessary when interpreting results from limited research in these areas, due to small sample numbers, date of the studies, and types of comparison groups. Nonetheless, research generally indicates that the pattern of motor development of children with DS compared to typical children is delayed rather than different. Basic motor skills are attained in the same sequence but at older age (Sacks and Buckley, 2003). For example, in typically developing children, the average age for walking is 13 months, whereas for children with DS the average age is 26 months (Sacks and Buckley, 2003., Winders, 1997). It is important to note that children with DS might have genetically low muscle tone and

therefore balance might an area of particular difficulty compared with progress in general coordination and muscle strength (Sacks and Buckley, 2003).

That said, the majority of children with DS are able to improve their skills through practice and achieve the basic abilities needed to function on a day-to-day basis (Sacks and Buckley, 2003).

Comorbid Diagnoses in Individuals with DS and Regressive Syndromes

When referring to persons with DS, it is necessary to note that having an extra gene causes atypical structural and functional forms of the central nervous system. This translates into a variation in degrees of cognitive and other neurological abilities (Wisniewski et al., 1996). As discussed before, current estimates of the frequency of neurobehavioral and psychiatric comorbid conditions in DS ranges between 18% and 38% (Capone, Goyal, Ares, & Lanningan, 2006; Dykens, Shah, Sagun, Beck, & King, 2002; Gath & Gumbley, 1986; McCarthy & Boyd, 2001; Meyers & Pueschel, 1991). These statistics override the commonly held belief that behavioral problems in persons with DS are inherently linked to the severity of their cognitive impairment. The rate of these conditions in children with DS is lower than in those with other disabilities but higher than in the typical population (Capone et al., 2006; Coe et al., 1999; Dykens et al., 2002; Gath & Gumley, 1986; Meyers & Pueschel, 1991; Nicham et al., 2003; Stores et al., 1998; Turner & Sloper 1996). Additionally, there is often a distinction between conditions that have pre-pubertal or post-pubertal onset. This distinction is important because these two periods are considered biologically different, and each has a unique vulnerability to specific types of psychiatric disorders (Capone et al., 2006; Walker & Bollini, 2002). Most of the disorders observed in pre-pubertal children are manifest prior to the age of 7 (Capone, 2006) with marginal male overrepresentation (Gath & Gumley, 1986).

Using the classification of the *Diagnostic and Statistical Manual of Mental Disorders* DSM-IV-TR; American Psychiatric Association, 2000), this section discusses the diagnoses of autism and childhood disintegrative disorders or late onset of autism, including how those disorders are manifested in children with DS. These autism-related disabilities are included under the general umbrella of pervasive developmental disorders (PDD), which includes Rett's disorder.

Definition of Autism Spectrum Disorders and Autism Spectrum disorders in Children with DS

Autism is a lifelong developmental disability. Characteristics and symptoms of autism vary from mild to severe and affect 1 out of every 150 children (Centers for Disease Control and Prevention [CDC], 2007) when the total range of the spectrum is included. Unlike DS, autism does not have definitive biological markers (Frith, 2003); therefore, it is important to look at the symptoms, in this case behaviors, to be able diagnose it (Frith, 2003).

There is wide agreement among clinicians on the core symptoms of autism (Simpson & Myles, 1997). Following the diagnostic criteria of DSM-IV-TR (APA, 2000), behavioral symptoms of autism include a *qualitative impairment in communication;* that is, the use and understanding of words or the ability to initiate and maintain conversation with others; *qualitative impairment in social interaction* manifested by the inability to develop appropriate peer relationships, poor use of eye contact, and gestures or lack of understanding of social rules; and *a markedly restricted repertoire of activities and interest*. Behavioral signs also include repetitive behavioral anomalies, such as body rocking or dangling objects in front of their eyes (APA, 2000). Children with autism often lack the ability to engage in imaginative play, and frequently (Frith, 2003) they are not able to share their interests or experiences with their peers

or adults. Some children with autism demonstrate severe self-injurious behaviors (Cohen & Patterson, 1999).

In recent years there has been an increasing awareness of the psychiatric and mental health needs of all persons with developmental disabilities (Brereton, Tonge, & Einfeld, 2006; Cohen & Patterson, 1999; Dosen, 2007; Einfeld et al., 2006; Ghaziuddin, 2000; Sturmey, Lindsay, & Didden, 2007; Tsakanikos, Sturmey, Costello, Holt, & Bouras, 2007). Clinitians, Howlin et al. (1995) and Kent et al. (1999), among others, have directed the attention of health providers and school personnel to the risks of overlooking comorbid diagnosis of autism in children with DS.

Autism Spectrum Disorders in Children with DS

It is estimated that the prevalence of dual diagnosis of autism spectrum disorders and DS is between 5% to10% of all cases, depending upon the criteria used (Capone et al., 2005; Ghaziunddin et al., 1992; Kent et al., 1999; Leshin, 2002; Lund,1988).

An epidemiological survey (Ritvo et al., 1990) of autism associated with "rare diseases" conducted in Utah revealed that trisomy 21 was the most common rare disease associated with autism. The authors reported that 6 males out of 241 had a diagnosis of DS and autism.

Gillberg (1998) researched all major chromosomal disorders that had a comorbid diagnosis of autism, following DSM-III or International Classification of Diseases 10th Revision (IDC-10) criteria. He found that DS was one of the chromosomal disorders most reported in the research literature. Lund (1988) reported that 5 out of 44 persons with DS also had autism and 2 other people were functioning within the spectrum, even though they did not meet the full criteria for autism. Kent et al. (1999) arrived at similar findings, noting that 4 children with DS

out of a sample of 58 had autism and another 11 displayed marked obsessional and repetitive/ ritualistic behaviors.

Starr, Berument, Tomlins, Papanikolaou, and Rutter (2005) reported that out of 13 participants with DS who were functioning at a severe or profound level of cognitive functioning, 3 met the life time criteria for autism on the *Autism Diagnostic Interview-Revised* (ADI-R) (Lord, Rutter, & Le Couteur, 1994); 2 did meet the full criteria for the Pre-Linguistic Autism Diagnostic Observation Schedule. Of the 8 who remained, some did not meet the criteria for either instrument whereas others did show substantially impaired social and communicative functioning and some repetitive behavior. Capone et al. (2005), using the *Aberrant Behavior Checklist* (Aman, Singh, Stewart, & Field, 1985), found that in a cohort of 471 who visited the DS clinic during a 10-year period, 87 children with DS had an autistic-like condition. From those 87 children, 41 were diagnosed with autism spectrum disorders according to DSV-IV-TR guidelines, 26 had stereotyped movement disorder, 12 had a childhood disintegrative disorders, and 8 pervasive developmental disorder.

Carter, Capone, Gray, Cox, and Kaufmann (2007) examined specific behaviors which distinguished DS with autism phenotype from behavioral disorders in DS. Using the *Aberrant Behavior Checklist* and the *Autism Behavior Checklist*, they found that DS with autism presented a set of distinctive behaviors characterized by stereotypic behavior, anxiety, and social withdrawal.

A number of case studies of comorbid diagnoses of DS and autism are also reported in the literature (Rasmussen, Borjesson, Wentz, & Gillberg, 2001; Bregman & Volkmar, 1988; Ghaziuddin, 1997; Ghaziuddin et al., 1992; Howlin et al., 1995; Kent et al., 1999; Prasher & Clark, 1996; Wakabayashi, 1979). Bregman and Volkmar (1988) described the case of a 12-year-

old girl with DS functioning at a severely impairment range with barely any spoken words and severe deficits in her nonverbal and pragmatic use of language. Her level of sociability was particularly impaired with an inability to develop affectionate and reciprocal relationships. Her approach to others was only to satisfy an immediate need as no shared attention was present. She was not interested in her peers, nor did she seek out any contact with them or participate in any group activity. She avoided eye contact and engaged frequently in stereotypic and self-stimulatory behaviors, which included twirling objects, finger tapping, hand and finger waving, and repetitive vocalizations. Toys and other objects were explored through smell and oral manipulations.

Howlin et al. (1995) described four cases, in which the observed boys with DS presented certain special characteristics in their development that were noted in the first two or three years of life. These children had very poor social relationships and little evidence of shared attention or understanding of others' feelings. They did not use their parents' comfort in a typical manner, and relationships with peers were poor and mostly aggressive or resistant. While they had some language, it was poor and echolalic and rarely used for communication. Their nonverbal skills, gestures, and eye contact were infrequent and accompanied by stereotyped motor behaviors. Finally, their play lacked any type of imagination, and they all showed a powerful resistance to change and an insistence on routine. All four cases presented episodes of aggressive and destructive behaviors.

Ghaziuddin et al. (1992) and Ghaziunddin (1997) presented a total of six cases, five of male subjects and one of a female between the ages of 14 and 27 with dual diagnosis of Down syndrome with autism. Three were functioning at a severe level of intellectual disability, and the other three at a moderate level. All of them had very little speech, and the speech that they had

was echolalic most of the time with no intentional communication. Other autistic characteristics common in all six cases included avoidance of social interaction, impairment in nonverbal skills, and stereotyped movements. During these children's early years, as recalled by their parents, their play was repetitive, with no evidence of imaginative or symbolic skills. All six cases presented ritualistic and compulsive behavior. For example, participants frequently expended large amounts of time lining up objects or liked certain songs that had to be played for long periods of time on the same day. One of the cases reported was a participant who spent her day tying and untying objects. All of them also demonstrated an insistence on sameness. One of them needed to follow the same route to go to school each day; otherwise, he would not get off the bus. Three of them had strong sensory preferences, which included wanting to feel the texture of objects, especially the contours of furniture. Stopping them from doing so resulted in outbursts of distress.

Wing (1981) observed that the stereotyped and repetitive behaviors of children with dual diagnoses of DS and autism spectrum disorders were not simply those typically associated with severe intellectual disability, namely motor mannerism, stereotypes, and self-stimulatory behaviors. Instead, they were more complex and persistent.

It is important to emphasize here that even though the prevalence of autistic characteristics rises when there is impairment in the areas of socialization and communication accompanied with a severe intellectual disability, persons with the lowest intellectual level can in fact be sociable (Wing, 1981). Therefore, the cases described here present a series of behaviors that are not attributed only to low intellectual ability but a comorbid condition.

Childhood Disintegrative Disorder and Regression in Autism

Childhood disintegrative disorder is also known as Heller's syndrome or "dementia infantilis," named after the Viennese educator, Theodor Heller, who first described the condition in 1908. Since then, this regressive syndrome has been known by different names: Heller's dementia, Heller's syndrome, and disintegrative psychosis (Kurita, Osada & Miyke, 2004). Currently the DSM-IV-TR (APA, 2000) refers to this syndrome as childhood disintegrative disorder (CDD) within the category of pervasive developmental disorders.

The DSV-IV-TR (APA, 2000) criteria for CDD encompasses apparently typical development for at least the first two years of life marked by the presence of age-appropriate verbal and nonverbal communication, social relationships, play, and adaptive behavior, followed by a loss of previously acquired skills before the age of 10. ICD-10 (World Health Organization, 1992) also defines CDD by a significant loss of skills after the age of two in at least two of the following areas of development: language, social interaction and adaptive behavior, play, bowel or bladder control, and motor skills.

The prevalence of CDD. Within the neurotypical population, the prevalence of CDD is approximately 1.7 per 100,000 (Fombonne, 2002). There is agreement that among individuals diagnosed with autism, between 20% to 49% of them had a developmental regression (Bernabei, Cerquiglini, Cortesi, D' Aradia, 2007; Goldberg et al, 2003; Kurita, 1985; Kurita, Koyama, Setoya, Shimizu, & Osada, 2004; Rutter & Lord, 1987). As is the case with the overall prevalence of autism spectrum disorders, it is widely accepted that regression affects more male than females (Kurita, Koyama, & Osada, 2005; Volkmar, Koenig, & Sate, 2005; Kurita, Osada & Miyake, 2004). The gender ratio is approximately four males to one female (Volkmar, 1992).

Age of onset. As Volkmar, Koenig and State (2005) explain, the age of onset is especially

important for differentiating CDD from autism. This is because in some cases, autism is only recognized after 24 months. DSM- IV- TR (APA, 2000) defines 24 months of apparently normal development as one of the basis to differentiate between CDD and autism, and Heller's observations placed regression between the ages of three and five years (in Volkmar, Koenig and State, 2005). Most of the reports published suggest that the onset was between three and four years old (Fombonne, 2002), although there are others that place regression later, between five and ten years of age (Bray, Kehle, Theodore, & Brody, 2002; Agarwal, Sitholey, & Mohan, 2005; Malhotra & Singh, 1993; Volkmar, 1992).

Onset of regression in autism is different according to various studies. Some reports indicate that regression occurs between 10-30 months (Kurita, 1985) while others point towards 12-42 months (Tuchman & Rapin, 1997). Rogers (2004) explained that 50% of children with autism had regression between 12 and 24 months; in 30% of cases, it occurred later than this, and in 15%, it happened after their third birthday. It is important to note that research on ASD suggests that the emergence of autism during the first year occurs in 31% to 55% of all cases, and that in 75% to 88% of cases it appears in the first two years of life (Short & Shopler, 1988; Bernabei et al., 2007; Volkmar, Stier, & Cohen, 1985).

Characteristics of onset. As explained before and according to DSM-IV-TR (APA, 2000), the salient feature of CDD is the marked regression in multiple areas of functioning following a period of at least two years of apparently normal development. Between ages two and ten, the child loses previously acquired skills in two or more of the following areas: language, social interaction and adaptive behavior, play, bowel or bladder control, and motor skills. The loss of these skills is accompanied by the emergence of behavior similar to those seen in children with autism (APA, 2000). Volkmar, Koenig, and State (2005) provided a summary

of clinical features in a number of reported cases as well as other cases seen by the authors but not previously reported. In this summary, they found that in a number of reviewed cases from 1908 until 2004, speech deterioration and/or loss was present in 100% of the cases; 99.3% had social disturbance; 84.3% had problems with change and higher levels of stereotypy; 80.6% had a deterioration of self-help skills; and affective symptoms and anxiety was present in 77.6% of the cases in addition to over activity.

The onset can be abrupt (days or weeks) or gradual, lasting weeks or months, and in some cases premonitory signs such as high levels of anxiety and irritability are followed by speech loss and other skills (APA, 2000; Volkmar, Koenig, & State, 2005; Volkmar & Cohen, 1989; Kurita et al., 2004). For example, Palomo et al. (2008), analyzed the regression of a boy at age four using family home movies. The medical history for the first four years of the child's life did not reveal any significant health problems, although some family history of speech and language disorders existed but no member had pervasive developmental disorders. By 24 months, he could direct people's attention by pointing and showing as well as using conventional gestures such as blowing a kiss and waving. According to the authors, he showed clear interest in people. By 47 months, he spoke in fluent sentences and was seen playing appropriately with toys including pretend play. Nevertheless, his parents pointed out that between 38 and 42 months, their son went through a period of stress in different circumstances and started to display previously unseen behaviors. He slept less, was very active but slower at following directions, and on a couple of occasions, he smeared his feces. His parents also noticed less frequent eye contact. He was toilet trained by the age of three and a half. Just before his fourth birthday, his parents started noticing periods of intense anxiety and panic, including agitation for a couple of weeks. Within two months, his parents reported that he became completely socially withdrawn, did not

want to be touched, and loss his toilet skills. He would watch television in close proximity while jumping and flapping his hands, paced and wandered around the rooms aimlessly, and examined objects with the corner of his eye. After this period, his parents took him for all possible testing again, including neurological exams, EEG, head MRI, amino acid, and organic acid tests. All came back normal.

It is interesting to note in the literature that the authors mentioned that the child had experienced some sort of psychosocial stressor or a medical event before the onset of CDD. For example, Kurita et al. (2004) found that 80% of the participants of his study (8 out of 10) had a psychological event before their speech loss, which was a higher rate than in his group of participants with autism 12 out of 30. Also, Volkmar and Cohen (1989) found that 8 out of 10 participants suffered from stressful events before regression. These events were mainly classified as a death in the family, the birth of sibling, or marital discordance. Other researchers have identified the start of school, a febrile illness (Malhotra & Sight, 1993), or a geographical move as the stressor (Golberg et al., 2003). However, the relationship between stressful events and regressive syndrome has not been definitively established, although there has been speculation regarding this connection (Russo et al, 1996; Rapin & Katzman, 1998; Arnsten, 1999; Lainhart et al., 2002).

In autism, regression can be acute or gradual; however, there are no studies available to indicate which pattern is the most typical (Goldberg et al., 2003). In autism, this setback is characterized by speech loss but not by motor skill loss. Speech loss, according to Rogers (2004), occurs in children who had very limited verbal repertoire initially. Kurita (1985) also found that 93.8% of children with autism and speech loss only had one-word sentences to begin with. Of the 97 children with autism, 76 (78.3%) showed some developmental abnormalities, such as lack

of responsiveness especially towards strangers. Also, reports show that children with autism and speech loss have poorer intellectual development and poorer outcomes than those with autism without regression. This poor performance falls across areas such as social, behavioral, and intellectual development (Kurita el at 2004; Kobayashi & Murata, 1998), although there is no general agreement on this point.

Rett syndrome, also a Regressive Syndrome Less Common in DS.

Rett syndrome is a neurodevelopmental disorder that affects predominantly females. It is caused by mutations on the *MECP2* gene linked to the X chromosome (Amir et al, 1999). It is a rare disability that occurs approximately one time in every 10,000 to 15,000 births (NINDS, 2011).

The onset starts at around the 12-18 month after a period of relatively normal growth and development and is followed by a deceleration in head growth. The disorder is also commonly

marked by rapid regression with onset of midline hand stereotypes, ataxia, seizures, loss of language (receptive and expressive), and deterioration of fine motor and social skills (Moss & Howlin, 2009; Burd, Fisher, Kerbeshian, 1989).

This syndrome is a regressive condition. Rarely do cases of Rett's occur among children with DS (Leonard et al, 2004). Nevertheless establishing the similarities of various conditions that are associated with regression in DS, including Rett's disorder, CDD and regression in autism, may shade light on common neurological and genetic substrates that are associated with the phenomenon of regression among children and youth with AS.

Developmental Regression in Down Syndrome

The term CDD defined in DSM-IV-TR could not be strictly applied to the participants of this study because having DS typically implies generalized development delay. This circumstance made it necessary to find a definition that would be less restrictive.

The definition for regression. Used in this study, it is comprised from the definition given in the DSM- IV-TR (American Psychiatric Association, 2000) and the description given by parents as well as researchers. This definition is "regression is a more or less sudden loss of interest and attention towards others and the environment, loss of words, of communicative and imitative gestures, and of cognitive abilities occurring after a period of 'normal' or sometimes delayed development" (Bernabei & Camaioni, 2001; Bernabei et al., 2007; Kobayashi & Murata, 1998; Kurita, 1985; Shinnar et al., 2001).

To avoid confusions between terminologies from here to the end of this work, regression when referring to DS participants would be named developmental regression or regression.

Prevalence in DS. In terms of DS, there are no accurate estimates. In their research on DS and comorbid autism spectrum disorders, Capone et al. (2005) found that among their 87 subjects, 14% (12/87) had a diagnosis of CDD.

In DS, there is virtually no research specifically about CDD. Only Castillo et al. (2008) looked at difference in age of regression among children with autism, with and without DS. In their study, they found that the mean age of language loss in children with a dual diagnosis of autism and DS was 61.8 months (5.15 years old); the mean age of language loss in children with only autism was 19.7 months. The findings were similar when they looked at the regression of other skills (purposeful hand movements, motor skills, self-help skills, constructive or imaginative play, or social engagement and responsiveness). For the dual diagnosis group, the

mean age of language loss was 46.2 months, whereas for the group with autism alone, it was 19.5 months. Capone et al. (2005), Eisermann et al. (2003), and Wakabayashi (1979) presented reports on children with DS who, after a period of appropriate cognitive, social, and motor development, suddenly started losing their previously acquired skills before the age of three.

The characteristics of the late onset of regression in children with DS has not been studied using a large number of subjects. There are few reports on regression in children with DS wherein there were no injuries, sickness, or seizure disorder preceding regression. Wakabayashi (1979) described the case of a child with DS who uttered sounds and laughed when cuddled at the age of 5 months. He walked and was able to eat with a spoon around his second year. When he was around two and half years old, he began to lose interest in feeding himself, started to bang his head against the floor, and stopped walking. He also lost his bowel control at this time. By the age of 3, he started walking again but still refused to eat by himself, and he became hyperkinetic and started to flap his hands. Castillo et al. (2008) found that regression in children with autism and DS occurred on average much later on than was typically seen in children with autism alone.

Other research studies, such as those conducted by Capone et al., (2005) and Eisermann et al. (2003), presented reports on children with DS who, after a period of expected cognitive, social, and motor development, suddenly started losing their previously acquired skills before the age of three. Subsequent diagnoses of these children were DS with autism.

It is worth mentioning that Prasher (2002) wrote a letter to the editor of the Irish Journal of Psychological Medicine calling for professional attention about a disorder that also occurs in young adults with DS called "Young Adults with a Disintegrative Syndrome" (YADS) (p. 101). In his letter, he explained that in a health study conducted with 357 English patients with DS

who were monitored over a period of ten years, they found that there were a significant minority of young adults with a regressive/ disintegrative disorder. This group of young adults was between 15 and 30 years old, with a peak age of 22 when the disorder first appeared. The symptoms were a gradual but severe deterioration in functioning skills after a normal period of development for a person with DS. Some areas where regression occurred were cognition, language (receptive and expressive), mobility, and adaptive and social skills. As observed in children with autism and regression (Kurita et al., 2004), these young adults also suffered a mood change. Some of them became mute, withdrawn, and lost interest in previously preferred activities. Prasher (2002) also explains that despite the fact these changes occurred over a period of one to two years and some of the features resemble Alzheimer's disease, this could not be the case since the regression plateaued and no further deterioration was seen in these patients.

Regression and epilepsy in DS. Epilepsy is found to be one cause of regression in children (Tuchman, 2006). This topic has been studied to a certain extent in DS. It is estimated that the frequency of seizure disorders in children with DS is approximately 5% to 10% (Caplan & Austin, 2000; Goldberg-Stern et al., 2001; Pueschel, Louis & McNight, 1991; Stafstrom, Patxot, Gilmore, & Wisniewski, 1990).

Eisermann et al. (2003), in their study of the effects of delayed anticonvulsive treatment for children with DS who also had infantile spasms, reported that 7 of the 18 children in their sample showed clear developmental regression before the onset of spasms. They also found that the duration of the spasms was significantly associated with their tested developmental quotient and the level of autistic features. The shorter the spasms, the higher the level of development and the lower the autistic features.

Starr et al. (2005) described the case of a child with DS who, after developing infantile spasms, started to demonstrate deterioration in his social functioning. In this case, only social functioning seemed to have regressed.

Tastsuno et al. (1984), in their clinical data on eight cases of persons with DS with infantile spasms, found that one child presented a developmental regression, and by age eight he could not sit or stand alone. Stafstrom and Konkol (1994) also noted that until the infantile spasms began, the development of 12 children out of 17 seemed to be in the normal range according to DS parameters. After the spasms, 12 presented regressions, and among those, 8 eventually regained their previous developmental level and continued to expected levels of developmental progress. Finally, Goldberg-Stern et al. (2001) reported on seizure frequency and the characteristics of those seizures in children with DS. Out of nine children with infantile spasms, five had a loss of previously acquired skills and later experienced seizure remission without relapse and with partial restoration of the lost skills.

Other reports found that regression occurred later, between the ages of 7 and 10, and some of these children with early or later regression also had a type of epilepsy (Eisermann et al., 2003; Caplan & Austin, 2000; Goldberg-Stern et al., 2001; Stafstrom & Konkol, 1994; Tatsuno, Hayashi, Iwamoto, Suzuki, & Kuroki, 1984). In those cases, the diagnosis was also DS with autism.

In conclusion, it may be said that that the prevalence of seizures in children with DS is higher than in the population without disability; however, it is lower than in other types of intellectual disability (Caplan & Austin, 2000; Escofet et al., 1995; Goldberg-Stern, 2001; Pollack, Golden, Schmidt, Davis, and Leeds, 1978; Stafstrom et al., 1991). Infantile spasms seem to be one of the most common forms of epilepsy in children with DS (Eiserman et al., 2003;

Stafstrom & Kokol, 1994). However, the correlation between regression and infantile spasms in DS is unclear, and more research is needed on the outcomes of different forms of epilepsy in this population.

Conclusions

Reports of regression or CDD in children without DS are rare, because, even though the condition is fairly common, many of these individuals are simply diagnosed with autism as a comorbid condition, regardless of how they arrived to the "stage" of autism. In fact, Castillo et al. (2008) explained that many individuals with a dual diagnosis of autism and DS had a history of developmental regression. Research on regression in autism and neurotypical children is also uncommon due to the lack of accepted and shared diagnostic criteria, and the criteria available are based mostly on retrospective data (Bernabei, Cerquiglini, Cortesi, & D'Ardia, 2007).

Nevertheless, it is important to review regression in children with and without autism as it could help draw parallels on how this occurs in the DS population.

DS is a complex neurodevelopmental disability whose symptoms might be accompanied by comorbid conditions. These comorbid conditions can be difficult to identify, which in turn can negatively impact the quality of life of the child and their families. Therefore, there is an imperative need for research on comorbidities in DS as well as on evaluating the tools that will help to devise better and more accurate diagnosis. Thus, the purpose of this study is to better understand the diagnosis of comorbid conditions connected to DS, in particular developmental regression.

Chapter III

METHODS

The purpose of this research study was to characterize the phenomenology of developmental regression in children between the ages of 2 and 12 years who had a diagnosis of Down syndrome (DS). This chapter describes the methodology of the study. First, the setting and the rationale for inclusion criteria for the participants and the participant's selection procedures are discussed. The chapter also includes a description of the design of the study and research questions. There is also a discussion on data collection. Finally, a description of the data analysis method is presented, as well as information about participants' consent for research.

Setting and Participant's Inclusion Criteria

Setting

This study was conducted at the Down Syndrome Clinic at the Kennedy Krieger Institute (DS KKI) located in Baltimore, Maryland. KKI is one of the health divisions of Johns Hopkins Medical Institutions. This clinic has evaluated close to 2000 individuals and supports two satellites clinics in Maryland: the Holly Center in Salisbury and the Washington County Health Department in Hagerstown. The clinics meet at these satellites locations four times a year, thus allowing the clinic to serve more families and to accommodate those who are unable to travel to Baltimore.

The DSC offers diagnostic, follow-up evaluations, preventive medical screening and medical consultation, parent training, and ongoing therapy services. In addition to the main developmental pediatrician, the KKI clinic also consults as required with an occupational therapist, a physical therapist, a speech-language pathologist, a psychologist, a behavior

specialist, and various pediatric and adult medical specialists on an as-needed basis. Families who attend the DSC KKI primarily come from the Mid-Atlantic region of the United States, but individuals are seen from throughout the United States and around the world.

Participant Exclusion Criteria

Excluded from this study were individuals with DS and a primary DSM-IV Axis I diagnosis of oppositional defiant disorder, disruptive behavior disorder, adjustment disorder, intermittent explosive disorder, anxiety disorder, obsessive-compulsive disorder, depressive disorder, atypical or cyclothymic disorder made in accordance to the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (DSM-IV-TR; American Psychiatric Association, 2000).

Participant Inclusion Criteria

The participant recruitment process for this study was based on the following criteria:

Down syndrome and DSMIV Axis I diagnosis consisting of Autism/ PDD or Stereotypy movement disorder (SMD) with or without self-injury. Participants were individuals who carried a diagnosis of DS and autism /pervasive developmental disorder (PDD) or SMD after the onset of regression. According to the DSM-IV-TR, childhood disintegrative disorder or developmental regression falls within the umbrella of PDD. When developmental regression occurred, some participants received the diagnosis of autism or PDD based on specified loss of skills. Therefore, including children diagnosed with DS and autism or PDD and/or SMD increased the chance of finding all possible cases of regression. Accordingly, a comorbid condition of autism/PDD or SMD was one of the criteria for participation. Some individuals meeting these criteria also exhibited features of attention deficit disorder with hyperactivity (ADHD) impulse dyscontrol,

oppositional defiant disorder, disruptive behavior disorder, or anxiety and thus were not excluded from the study.

Diagnosis of comorbid condition before the age of 12. Individuals with DS who were potential participants for the study needed to have DS as well as one of the following diagnosed comorbid conditions: autism/PDD, late onset regression or SMD. This diagnosis must have been before the participant was 12 years old.

The primary reason 12 years was chosen as the maximum age to have been diagnosed with a comorbid condition was because in the United States, the average age of menarche is 12 years (Dahl, 2004). The changes experienced during puberty have the potential to influence participant's behavior and overshadow the findings for this study. Indeed, a strong body of evidence supports that "this developmental period shows a sharp increase in morbidity and mortality related to a wide range of types of behavioral and emotional problems" (Dahl, 2004, p.7).

No history of infantile spasms. Infantile spasms are frequent in DS and occur in 0.6 to 13 % of the cases, representing 4.5 to 47% of the seizures in this population (Stafstrom & Konkol, 1994; Eisermann et al., 2003; Goldberg-Stern et al., 2001). This type of epilepsy has been associated with loss of developmental milestones (Goldberg-Stern et al., 2001; Stafstrom & Konkol, 1994; Eisermann et al., 2003). For purposes of this study, the causes for developmental regression in each participant in this study could not be attributed to infantile spasms.

Fulfill the criteria for loss and emergence of maladaptive skills. Because not all parents and professionals defined developmental regression in the same manner, the criteria of loss and emergence of behaviors generally ensured similarities across cases. Participants needed to have at least two areas of loss and two maladaptive behaviors from the following list of behaviors:

1. *Loss of communication.* A definite period of loss of communicative use of language, words, signs, or a combination that had been previously used on a daily basis for a period of time.
2. *Loss of social interaction.* Loss of social interaction skills (e.g., waving, saying hello, goodbye, shared attention, social smile), and specifically that these skills were used for a definite period of time and then lost substantially or completely.
3. *Loss of play*. A definite period of loss of functional/imaginative play including skills that were previously used by the child and then completely lost completely or lost partially (e.g., peek-a-boo, hide and seek, doll play, cooking, cars, simple board games).

Emergence of maladaptive behaviors include the following:

1. *Sensory issues (hyper-hypo)*. Emergence of sensory integration problems (e.g., brushing teeth, combing hair, loud noises, lights, or food texture) before or after the onset of regression.
2. *Motor stereotypy*. Emergence of new body movements (e.g., rocking, flapping hands and/or fingers).
3. *Perseverative behaviors*. Emergence of new non-functional rituals and routines (e.g., stacking objects, repeating the same section of a video or song, organizing objects in equal manner repeatedly, or the need for closed doors).
4. *Atypical play*. Emergence of atypical play (e.g., spinning objects, fixation with only a part of a toy).

Additional documentation that supports developmental regression. Some of the participants came to the KKI DSC after regression had already occurred. At the time of the visit,

some parents brought reports from other clinicians, therapists, or school personnel stating that their son or daughter had experienced loss of a previously well-documented skill. Other parents came with no documents, although they could recount the regressive process in detail. As a method for validating developmental regression, every participant needed, in addition to parents' reports, alternative documentation from a professional whereby regression was identified, or when compared with other document, it was obvious that there was a loss of skills. For example, evaluations from IEPs from different years might be compared to the participant's developmental history. Additionally, parents were asked to bring other evaluations from before and after the occurrence of developmental regression. These evaluations could be from different professional disciplines and sources such as speech pathology, psychologists, physical therapists, or occupational therapists. These evaluation results were subsequently used to evaluate the loss of skills relative to the diagnosis criteria used in this study.

The regression represented by loss of cognitive and adaptive skills could not be directly related to illness or other medical causes such as a virus, head trauma or other accidents, seizure disorder, or pubertal changes.

Signed informed consent for research participation. Every participant needed to have a signed consent form that indicated that the participant's parent or legal guardian approved of participation in the research study.

Procedure: Pre-Selection Process and Selection of the Final Participants

The DSC KKI has an extensive database of its patients. Every patient has duplicate medical records, with one record located at the DSC, which includes the most important and updated information on each patient, including reports from all the visits to DSC KKI, log of

phone conversations, copies of email exchange with the family, tests that might have been performed on the child (e.g., MRIs, EEGs, sleep studies, blood work, or relevant school evaluations), and signed consent for research if the parents agreed to research participation. The second record is located at the KKI Department of Medical Records. This chart contains the same information as the one at DSC but might contain additional documentation (e.g., copies of a child's karyotype records, previous physician visits and hospital admissions information, or lab tests).

Every new patient, including the participants for this study, who comes to DSC has to answer an extensive intake form that probes for prenatal and postnatal medical concerns, developmental concerns, and behavioral concerns, as well as information regarding socialization, family demographics, early intervention, and educational programs (see appendix A). This intake is completed before the initial appointment is scheduled and forwarded to the DSC neurodevelopmental pediatrician (Dr. George T. Capone). The DSC also sends an envelope containing parent-rated behavioral questionnaires to the family for completion. The completed questionnaires are returned to Dr. Capone for analysis, including identification of parent and family primary concerns. Families are asked to bring any available documents, including prenatal and neonatal medical records, karyotype reports, and developmental assessments, as well as neurologic, psychiatric, or psychological evaluation reports that might provide additional evaluation insight.

During the initial visit, Dr. Capone conducts a 90 minute interview with the parents of the child, gathers or clarifies the information on the child about developmental milestones, medical history, levels of developmental functioning, behavior concerns, medications, and parents' main concerns. This information is found in every patient's chart in the initial evaluation form. During

the visit, the DSC's pediatrician assesses each patient, and if the case requires a diagnosis, one will be given along with a plan of action and scheduling of a follow-up appointment. It is during review of the intake form substantiated by this initial evaluation process that loss of skills are noted and tentatively substantiated. If the regression has occurred while the child is already a patient of the DSC KKI clinic, he or she will typically have several well-documented follow up visits during which this pertinent information is collected. On this form, in an area labeled "past diagnosis," the physician notes if any other diagnosis has been given to the patient. It is also in this same section that a diagnosis of regression can be found.

This researcher reviewed all the charts located at the DSC KKI of patients that were filed under the categories of autism or PDD and/or SMD. Two hundred potential participants were identified and shared information with Dr. Capone.

Selection of the Final Participants.

From the 200 charts located and reviewed, 40 charts (20 %) met the study inclusion criteria and were selected for further analysis (see Figure 1). All 40 pre-selected participants in this study had a diagnosis of DS and met the specific diagnostic criteria specified in the DSM-IV-TR for a comorbid condition of autism, PDD or SMD with or without self-injury. These diagnoses were based either on results from medical evaluations made by a developmental pediatrician and Director of the DSC KKI or results from other medical evaluations made by medical professionals who evaluated the participants prior to their visit to the DSC KKI. In the former cases, diagnoses were made formally by the Director of the DSC KKI or reviewed by him if the case was a referral from another clinic. Participants' comorbid conditions in this study were all diagnosed between the ages of 2 and 12 and could have been given before or after the regression.

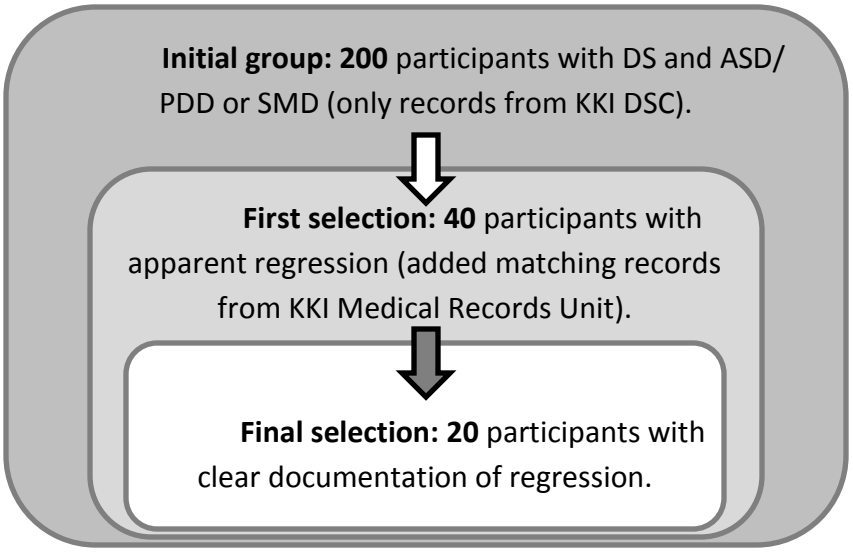


Figure 1: Diagram of participant selection process from initial group to final group.

The KKI Medical Records Unit charts on these 40 potential participants were reviewed by this researcher, from which 20 participants (11 males and 9 females) were selected for the study (see Table 1). The exclusion of 20 participants from the initial pool of 40 possible subjects was because developmental regression had not been clearly documented or there was missing data. The missing data on the rejected potential participants appeared to represent a significant threat to the integrity of the study. In some cases, the researcher could not establish the premorbid level of development function that the child had acquired prior to regression. In other cases, there was not enough detail on the characteristics of the participant's regression. Inaccuracy of events meant that among participant's documents, there was no clear agreement on when regression had occurred and the pattern that it followed. Thus, in these cases, accuracy of the data was compromised.

The 20 participants were divided into four groups according to their age at regression, characteristics of their regression and comorbid condition (see Table 1).

Table 1 *Summary of the Participants*

Participant/ Group	Gender	[1]Regression Onset (years)	Duration of Regression (months)	[2]ASD/PDD BEFORE Regression	ASD/PDD AFTER Regression
P01/ G1	F	1.3	9	no	yes
P02/ G1	F	2.2	18	no	yes
P03/ G1	M	2.3	17	no	[3]SMD with loss
P04/ G1	F	2.4	12	no	yes
P05/ G1	M	2.7	11	no	yes
P06/ G1	F	3.4	13	no	yes
P07/ G1	M	3.4	13	no	yes
P08/ G1	M	3.8	2	no	yes
P09/ G1	M	4.5	6	no	yes
P10/ G2	M	3.4	7	yes 15 month PDD suspicion	yes
P11/ G2	M	4.3	8	Yes, at 12 some PDD-like behaviors	yes
P12/G3	M	7.0	18	no, some [4]ADD	yes
P13/G3	F	7.0	36	no, had [5]ADHD/ perseveration	yes
P14/G3	M	7.0	6	no mild SMD/ADHD	yes
P15/G3	F	7.3	21	no	yes
P16/G3	M	7.4	12	no but ADHD, aggression, oppositional at 5y 4m	yes
P17/G4	M	9.0	6	yes, mild PDD/SMD	yes
P18/G4	F	9.0	8	no	yes
P19/G4	F	10.4	3	no	yes
P20/G4	M	11.0	8	no mild SMD	yes

1 Expressed In decimal years
2 ASD/PDD: Autism Spectrum Disorders/Pervasive Developmental Disorders
3 Stereotype movement disorder
4 Attention Deficit Disorder
5 Attention Deficit Hyperactivity Disorder

Group 1 (G1) was formed by 5 children (Participant 1- Participant 9 (P1-P9))whose age at regression was between 2-5 years old and had no signs of a comorbid condition predating regression. Group 2 (G2) was composed of 2 children (P10- P11) with regression between the ages of 2-5 years old with signs of autism or PDD before the onset of regression. Group 3 (G3) included 5 participants (P12-P16) whose regression occurred between the ages of 7-9. Four

participants had a diagnosis of either ADD/ ADHD or SMD. Group 4 (G4) was comprised of 4 children (P17- P20) with regression that occurred between the ages of 9-11 years old.

To summarize, the selection process of the participants who had a developmental regression was made identifying and reviewing all charts of children with dual diagnosis of DS with autism/PDD or SMD by looking at their initial evaluation and follow-up visit reports. Once all patients' charts were reviewed, all of those whose parents reported regression or other pediatrician diagnosed regression were separated. The second step was to review the charts of each participant located at the KKI Medical Records Unit and further narrow down the number of participants to those cases that fulfilled all criteria, including those related to regression. Participants were then grouped according to their age and regression characteristics.

Design of the Study

This study used a retrospective chart review process (Hess, 2004; Charlot, Fox, & Friedlander, 2002). Retrospective studies are a type of longitudinal analysis where the data used have been previously recorded for reasons other than research (Hess, 2004; Street & Ward, 2010). In health care, these types of studies are called *chart reviews* because the source of the data is medical (Hess, 2004).

The decision was made to use this methodology because developmental regression in children with DS is an unexplored area of research, and data for this study had to be reviewed retrospectively. That is, the loss of skills had already occurred and needed be traced back to its origins.

Retrospective cases series encompass the description of a group of cases with a new or unusual presentation; the event (in this case developmental regression) has already occurred. The

difference between prospective and retrospective studies, according to Hess (2004), is that in a prospective study the "baseline of the subjects is determined, the controlled intervention is applied and then the outcome is measured" (p. 1172). Hence, in retrospective studies, "The intervention, baseline state, and outcome are obtained from existing information that was recorded for reasons other than the study" (Hess, 2004, p. 1172).

The general methodology for retrospective studies research is the same as the methodology for a prospective study (Gearing, Mian, Barber, & Ickowicz, 2006; Hass 2004). That is, it mainly requires the formulation of research questions, development of hypotheses, a literature review, study design, collection of data, analysis of the data, explanation of results, and a written report.

Conducting retrospective research has several advantages. One is that it uses existing records and therefore can be inexpensive; a second advantage is that it allows a study of rare diseases or permits assessment of conditions where there is a long latency between exposure and disease. A third advantage is that because studies using retrospective methodologies cannot claim cause effect relationships, they have the potential to generate hypothesis that later can be tested prospectively (Gearing, Mian, Barber, & Ickowicz, 2006; Hass 2004; Wu & Ashton, 1997).

Relative to this study, the retrospective chart review process undertaken by this researcher involved using descriptive data on of the previously described 20 children along with four exploratory case series reports extracted from the aggregate group data available to this researcher (more detailed information about this process will be given later in the chapter). To describe how developmental regression occurred in these participants, it was necessary to review all available documents. Data on each participant came from multiple sources and had previously

been recorded for purposes other than this research. These records were sufficient to build the sequence of events before and after developmental regression had occurred.

Research Questions

Research questions addressed in this study are listed below.

1. Which adaptive skills were present and then lost during developmental regression?
2. Did participants lose the same skills?
3. Which maladaptive behaviors emerged after regression? Did participants experience the emergence of the same maladaptive behaviors?
4. Did regression occur at the same age?
5. If age of onset varied, how did regression vary?

Data Collection

The DSC KKI has collected data on children with DS since 1991 and holds all the data on this study's participants. Related to the developmental history of participants for this study, information came from two main sources: (a) personal interviews with the parents of the children and clinical information directly gathered by Dr. Capone, as a part of the evaluation and/or follow up protocol; and (b) historical data provided by the parents about their children, obtained through documents and parent's narrative reports. The information from the interviews was related to child developmental milestones, past clinical diagnoses and surgeries, parental concerns, notes from direct observations, and behavior rating scales.

It is important to explain the process of how Dr. Capone obtained the history and information from the patients because this information, in the form of clinical reports, is what this researcher used for this study. For the clinic, Dr. Capone obtains historical data and uses evaluation protocols to establish individual child baselines and identify each child's strengths

and weaknesses. Individual baselines are used to chart child progress and behavioral changes over time. This protocol includes the following information:

(a) KKI New Patient Evaluation Form (see appendix A) includes the queries asking families about children's symptoms that led a family to seek medical attention. This intake is sent to Dr. Capone at the DSC. Once the information is received at the DSC, further behavior questionnaires, described below, are sent to the family.

This form was used in this research to obtain the history of the patients: dates of birth, pregnancy, developmental milestones, family history of disability or other disorders, number of siblings, past diagnosis that the participant might have received, history of developmental regression, age at regression, presence of seizures, what skills were lost, parents' main concerns about their child's behaviors, sequence of symptoms that parents might have observed, any preceding illness to the loss, specific behaviors that the participant was evidencing, behavior disturbances (internalizing behaviors and/ or externalizing behaviors), repetitive behaviors, motor movements, general mood and mood changes, social behavior, sleep patterns, sensory preferences and sensory aversions, gross motor and fine motor levels, current expressive language and communication skills and previous skills in case the child had a loss, current receptive skills and previous also in case the child had a loss, ability to follow one and /or two steps requests, current/ previous play-social interaction skills, current self-help skills. This form was also used to extract information on other medical conditions that the child had, including tests and findings. This was important in order to rule out alternatives explanations for the onset of regression such as seizures.

(b) *Behavior questionnaires packet for children 2-13*. A package of eight questionnaires was sent by the DSC to the parents or tutors of the child. From this package, data from the

Aberrant Behavior Checklist (ABC) (Aman, Singh, Stewart, & Field, 1985) was used in this study. The ABC has 58 items that allowed parents to report the severity of behaviors on five subscales: irritability, lethargy/ social withdrawal, stereotypy, hyperactivity, and inappropriate speech. Items in this checklist are scored from 0 (not a problem) to 3 (severely problematic).

The primary reason for selecting this checklist was because it has previously been successfully applied on a population with DS with good results (Aman, Singh, Stewart, Field, 1985b). It has also been used in children with dual diagnosis of intellectual disability and psychiatric disorders, such as autism, and again obtained good results (Rojahn & Helsel, 1991). Second, because cross-sectional data from DSC KKI was available on a clinic sample of 305 children with DS, DS+ASD, DS + DBD, all children whose parents answered this checklist were between the ages of 2 and 13 years. Each ABC scale (hyperactivity, irritability, stereotype, lethargy, and speech) was analyzed across the whole study population and according to the DSM-IV-TR (APA, 2000) diagnostic groupings.

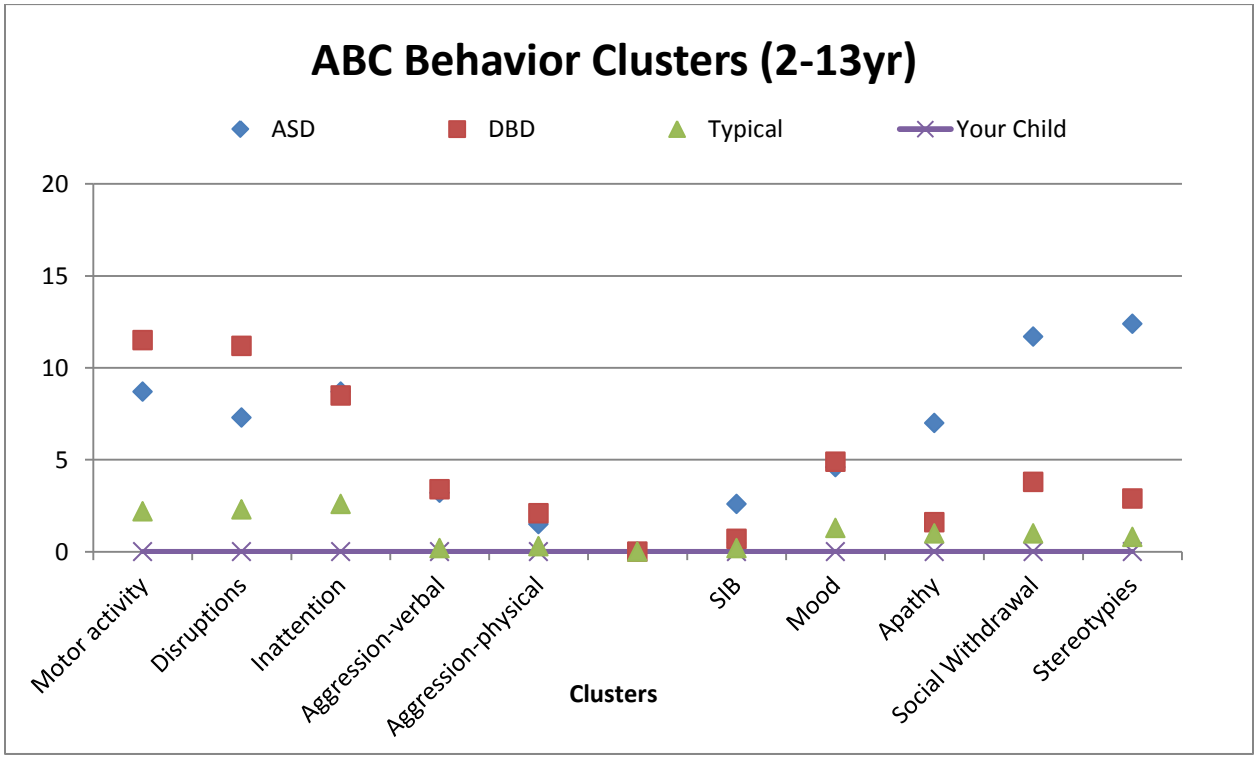
For the DSC purposes, once a family answers the ABC, the checklist was sent back to DSC and scored by the main pediatrician. Before the first interview with the parents, the information from the ABC was used to pre-identify parents' main and secondary behavior problem concerns; later, its use was to aid in identifying a possible diagnosis. The scores from the ABC subscales include hyperactivity, irritability, stereotypy, lethargy, and speech (Aman, Singh, Stewart, & Field, 1985) for each patient between the ages of 2-13 years old that are transferred to a computerized scoring form that updates ABC developmental progress (see appendix B and table 2 with figure). That is, the first ABC (Aman, Singh, Stewart, & Field, 1985) questionnaire establishes a baseline against which future questionnaires are compared.

This process is useful for monitoring behavioral changes over time, and it engages parents in both the art and science of clinical management and decision making.

Table 2 *Example of the Template, Table and Figure used for each Patient at the DSC-KKI*

ABC subscales 2-13yr	DS-ASD	DS-DBD	DS-Typical	Your Child XX
Hyperactive	**21.4**	**28.5**	**7.4**	**0**
Irritable	**13.2**	**14.9**	**3.3**	**0**
Stereotypies	**12.4**	**2.9**	**0.8**	**0**
Lethargy	**18.6**	**5.4**	**1.9**	**0**
Speech	**2.4**	**2.9**	**0.9**	**0**

Note. Cross sectional data on children from 2-13 years is shown for score comparison on children with DS+ASD, DS+ DBD and typical children.



For this study, the scores from the ABC (Aman, Singh, Stewart, & Field, 1985) subscales of the four case studies from this cohort of children were transferred into a rubric developed by the DS clinic staff for patient monitoring purposes (see appendix II and table 2). Each child's

scores from the ABC (Aman, Singh, Stewart, & Field, 1985) were routinely graphed and compared with the cross sectional data of the mentioned clinical sample of 305 children. This comparison provided a wider perspective for comparing the data with other groups of children with DS + ASD, DS+ DBD and Typical DS, and with subjects from the same group.

(c) During the *first visit,* the main pediatrician gathers new information and clarifies the information sent by the parents, observes the child and makes a diagnosis if needed, and together with the parents, crafts an action plan. This action plan can include treatment of underlying medical conditions (e.g., hypothyroidism, sleep disturbance, visual or hearing impairment), medication for specific target symptoms, referral to other specialists (e.g., occupational, physical and/or speech therapist) or to a behavioral clinic for functional behavior analysis, and creation of a management plan for implementation at home or school.

As previously explained, parents completed a "New Patient Evaluation Form" prior to their first visit. This form was discussed and revised during the first visit with the family and Dr. Capone. It became the first document used in this research to identify cases of regression because it asks explicitly for developmental regression.

(d) *Follow up visits* were scheduled according to the child's needs. At every visit, Dr. Capone completed a follow up report (see appendix C). In this form, the neurodevelopmental status of the child was noted in comparison with the last visit, as well as other new information that the parents or physicians found relevant.

For this study, the follow up reports were used to find participants. These were children who had been patients in the clinic for a long period of time and who, when first served by the clinic were free of autism symptoms, but later were diagnosed with ASD or with ASD with regression. This change of diagnosis noted on the follow up form. In addition, some patients had

initially visited with Dr. Capone, changed pediatricians, and later returned to the DSC. In some of these cases, the children had received a diagnosis at the original meeting with Dr. Capone. These diagnoses could also be found in the follow up form.

During the process of contacting the clinic, filing reports, and the first visit and follow up visits, families were encouraged to bring any document that they believed was relevant for Dr. Capone's understanding of their child's condition (e.g., IEPs, school reports, or psychological reports). In fact, parents of the participants for this study had often brought multiple school reports, such as IEPs and school multidisciplinary evaluations, as well as other medical data that made possible this study.

All of these reports are kept in the child's folder at the DSC KKI. Therefore, data from each of the 20 participants was extracted by this researcher from the extant files and summarized in a narrative format. This initial rubric contained all salient characteristics of each child's development month by month, annually, or by semester, depending on the availability of information along with a listing of the sources of the information from each evaluation or report. (See appendix D for an example).

After the narrative from each participant was finished, specific data was extracted by this researcher from all the participants and entered into a data base. Specifically, the data extracted from each participant's narrative chart included the following:

1. Gender.
2. Age at the time of developmental regression.
3. Length of the onset of regression.
4. Presence of ASD or PDD-NOS before regression and confirmation of autism symptoms before the onset of regression.

5. Presence of autism disorder or pervasive developmental disorders not otherwise specified after regression and confirmation of ASD symptoms after the onset of regression.
6. Stressors before or after regression.
7. Sleep disturbance before, during, or after regression, including information about falling sleep, staying asleep, or waking in the middle of the night and not being able to fall sleep again, or sleep apnea that the participant might have suffered before, during, or after regression.
8. Loss of communicative use of language of at least five different words or signs or a combination of words that were previously used in a daily basis for a period of time.
9. Loss of social interaction skills such as waving, saying hello, good-bye, social smiles, or shared attention.
10. Loss of functional/imaginative play such as peek-a-boo, hide and seek, doll play, pretend play, or simple board games.
11. Change in motor skills, such as walking, running, standing on one foot, holding things with hands, or throwing a ball, after regression.
12. Perseverative behaviors before, during, or after regression, which refers to the emergence of new routines such as staking objects, repeating the same section of a video or song, or the need for arranging the environment in a certain manner.
13. Loss of daily living skills (DLS), which is the loss of the capacity to perform activities of daily living that were mastering previous to regression, including eating independently, grooming, bathroom abilities, or dressing.
14. Emergence of sensory problems before, during, or after regression. This refers to the emergence of sensory integration problems such as over- or under-reaction to loud

noises, food texture, and brushing teeth or hair.

15. Emergence of stereotype movement disorders, such as rocking, flapping hands, flipping fingers in front of the eyes, or shaking the head.
16. Emergence of psychotic-like behaviors, such as hearing or viewing imaginary things.
17. Disruptive behaviors, which refers to the history of other maladaptive behaviors of the participants.
18. Pica, which is the emergence of the compulsion of eating non-edible items.
19. Self-injury behaviors (SIBS) such as head banging, skin picking, or pulling eye lashes.
20. Emotional liability (mood swings), which refers to sudden mood changes, specifically laughing and immediately after crying with no apparent motive, or sudden fear that some participants showed during the regressive phase.

Using the aforementioned information and data, the 20 participants were divided in four groups according to their age, characteristics of regression and comorbid conditions. From each group, one participant was selected as a representative case and a case study was written on that individual. These four cases were selected based on the researcher judgment and Dr. Capone's input regarding how an individual case was most representative of a particular group. It allowed a more detailed exposure of how regression occurs in children with DS. Briefly, the cases selected were as follows. The first case, from G1, is a girl whose onset of regression was at 3 years and 6 months of age with no apparent ASD symptom prior the onset. The second case, from G2 was a boy who did have ASD symptoms pre-dating the regression onset at the age of 4 years and 3 months. The third case, from G3, was a boy with some characteristics of ADHD and SMD predating also the onset of regression at the age of 7. The fourth case was that of a girl in G4 whose regression occurred at approximately 10 years and 5 months with no behavior

problems reported previous regression.

To build these four case studies (discussed in chapter 4) the same procedure was followed as with the other 16 participants. First, the documents in their folders were reviewed, and the most important data was summarized in a word document. However, the summary was extended further than with the other participants, as a more detailed narrative of their development through the years was written. The structure of the case is as follows:

- Summary introduction of the case.
- Date when the participant first came to DSC KKI.
- Main complaints that were exposed by the parents at the time of the visit or at subsequent visits.
- Place in family that the participant occupies in his or her family among siblings.
- Family history for intellectual disability.
- Pregnancy and birth history.
- Developmental history by age, sequentially organized.

Data Analysis

After the entire history of the participants was summarized and added into the database, the data from the 20 participants was analyzed. Due to the sample size and the nature of the research methodology, it was not possible to use parametric statistics. Analysis of the data was done using a variety of methods including simple descriptive statistics and case study procedures.

To begin the analysis, the 20 participants were analyzed as a group. This focused on how many children presented loss of adaptive skills, specifically loss of communication, play, social motor, and daily living skills, and how many presented with the emergence of maladaptive skills,

specifically SMD, hyper- or hypo- sensory problems, perseveration, behavior difficulties, PICA, self-injurious behaviors (SIBS), mood swings, and psychotic-like behavior. The data looked to differentiate among participants based on whether their symptoms came after regression or were present before the onset.

The second stage was analyzing the data by groups. From reading each participant's file, it became evident that there were certain patterns of behavior before and after regression that could be related to the age of regression and vice versa. Therefore, data was organized by groups and analyzed.

Participants were separated in four groups according to their age when regression occurred, characteristics of their regression and comorbid condition. The four groups identified are as follows:

1. G1: formed by 5 children (P1- P9) whose age at regression was between 2-5 years old and had no signs of a comorbid condition predating regression.
2. G2: formed by 2 children (P10- P11) with regression between the ages of 2-5 years old with signs of autism or PDD before the onset of regression.
3. G3: formed by 5 participants (P12- P16) whose regression occurred between the ages of 7-9 years old. Four participants had a diagnosis of either ADD/ ADHD or SMD.
4. G4: Formed by 4 (P17- P20) children with regression that occurred between the ages of 9-11 years old.

In addition, two rounds of participant groupings were made to verify the existence of those four groups mentioned and to verify that participants were added to the same group as previously had been done in the study. Once the groups were established, they were shown to the DSC

KKI's primary pediatrician in order to discuss the inclusion of each participant in each group, and discussion ensued until consensus was reached.

The analysis for the entire group (as was also done for each of the four groups) focused on how many children presented loss of adaptive skills, specifically loss of communication, play, social, daily living skills and change or decline in motor skills, before or after the onset of regression, and how many children presented with the emergence of maladaptive skills, specifically stereotypy, hyper- hypo sensory, perseveration, behavior difficulties, PICA, SIBS, mood swings, and psychotic-like behavior, again differentiating if those symptoms came after regression or were present before the onset.

From each group, one participant was selected for a specific case study in order to exemplify in more detail how regression occurred.

Consent

The data for this study were collected in previous years at DSC KKI. All parents or guardians of the participants signed an informed consent giving permission for their children's data to be used for research purposes. This consent form was reviewed and approved by the Joint Committee on Clinical Investigation at Johns Hopkins Medical Institutions. The researcher of this study also successfully passed all the research requirements for Johns Hopkins University and the University of Kansas.

Chapter IV

DATA ANALYSIS AND RESULTS

This chapter presents the data analysis and discussion for 20 participants and four case samples selected from among the 20 participants. Participants were divided into four groups related to their age at regression and diagnostic characteristics (see Table 3): Group 1 (G1) was formed by 5 children (Participant 1- Participant 9 (P1-P9))whose age at regression was between 2-5 years old and had no signs of a comorbid condition predating regression. Group 2 (G2) was composed of 2 children (P10- P11) with regression between the ages of 2-5 years old with signs of autism or PDD before the onset of regression. Group 3 (G3) included 5 participants (P12-P16) whose regression occurred between the ages of 7-9. Four participants had a diagnosis of either ADD/ ADHD or SMD. Group 4 (G4) was comprised of 4 children (P17-P20) with regression that occurred between the ages of 9-11 years old

The presentation of the data in this chapter is divided in two parts. The first part contains the presentation of the entire group's data; the second part presents the data from each group. Following each set of data, there is a case study that best exemplifies the regression that occurred for each group. The presentation of group data unfolds in the following sequence: (a) generic information on the participants (Table 3); (b) data about loss of skills (Table 4); and (c) data on emergence of maladaptive behaviors (Table 5 and Table 6).

Whole Group Data Analysis

Data in Table 3 presents descriptive participant information, specifically (a) gender; (b) age of the participant at the time of the onset of regression; (c) duration of the regression (defined as the time lapse between the first symptoms and the partial or complete loss of skills); (d) symptoms or diagnosis of autism (ASD) or pervasive developmental regression (PDD) before

regression (did participants have ASD or PDD or symptoms of these diagnoses before the onset of regression?); (e) symptoms or diagnosis of ASD or PDD after regression (participants

Table 3 *Information on the Participants on Timing of the Onset, ASD, Stressors, and Sleep.*

Participant/ GROUP	Gender	[1]Regression Onset (approx.)	Duration of Regression in Months (approx.)	[2]ASD /PDD BFORE Regression	ASD/PDD AFTER Regression	Stressors BEFORE Regression	Sleep Disturbance
P01/ G1	F	1.3	9	no	yes	hospitalization	no
P02/G1	F	2.2	18	no	yes	no	no
P03/G1	M	2.3	17	no	[3]SMD with loss	surgery and moving	no
P04/G1	F	2.4	12	no	yes	no	no
P05/G1	M	2.7	11	no	yes	no	no
P06/G1	F	3.4	13	no	yes	no	yes during
P07/G1	M	3.4	13	no	yes	no	yes after
P08/G1	M	3.8	2	no	yes	no	no
P09/G1	M	4.5	6	no	yes	physically abused	yes after
P10/G2	M	3.4	7	yes 15month PDD suspicion	yes	no	yes after
P11/G2	M	4.3	8	yes at 12 some PDD like behaviors	yes	no	yes before
P12/G3	M	7.0	18	no, had [4]ADD	yes	no	yes during
P13/G3	F	7.0	36	no, had [5]ADHD, perseveration	yes	no	yes after
P14/G3	M	7.0	6	no, had SMD and ADHD	yes	no	yes during
P15/G3	F	7.3	21	no	yes	no	yes during
P16/G3	M	7.4	12	no but ADHD, aggression, oppositional at 5y4m	yes	Traumatic EEG	yes after
P17/G4	M	9.0	6	yes mild PDD/ SMD	yes	no	yes after
P18/G4	F	9.0	8	no	yes	no	yes before sleep apnea then not being able to sleep
P19/G4	F	10.4	3	no some humming	yes	sister out friends get very upset	yes during
P20/G4	M	11.0	8	no but mild SMD	yes	Viral Infection	yes during

1 Expressed In decimal years
2 ASD/PDD: Autism Spectrum Disorders/Pervasive Developmental Disorders
3 Stereotype movement disorder
4 Attention Deficit Disorder
5 Attention Deficit Hyperactivity Disorder

received a diagnosis of ASD or PDD after the onset of regression); (f) presence of any psychosocial stress episode before regression (defined as any parent-identified stressful events experienced by children); and (d) sleep disturbance or anomaly (defined as sleep problems that disrupted a child's normal sleep patterns, including difficulty in falling into sleep in timely manner, waking up and not returning to sleep prior to the completion of the normal sleep cycle, waking up after being asleep and roaming around the house, and sleep apnea).

The gender distribution of the participants was 12 boys and 8 girls. The range of age of developmental regression onset was from 1 year and 5 months to 11 years (mean 5.4 years).

The average length of the regression onset for the entire data set (see Figure 2) was 12 months. However there was variability among the four groups. For G4, the older participants, the average length of regression was 6.25 months, whereas the mean length of regression for G3 (children with regression between the ages of 7-9) was 18.6 months, for G2 was 7.5 months, for G1 11.2 months (both G1 and G2 formed by younger participants with regression ages between 2 and 5 years old).

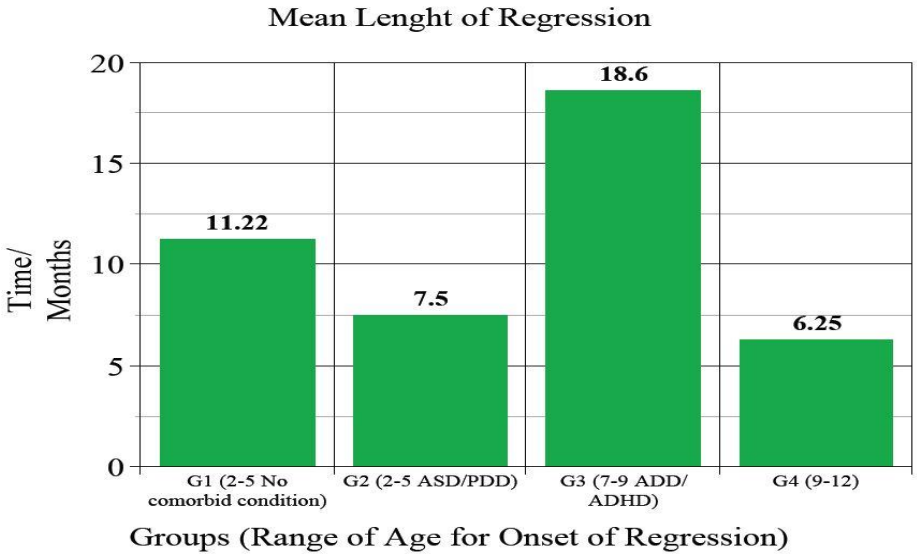


Figure 2. Data on mean length of regression for participants.

In terms of comorbidity predating developmental regression (see Figure 3), 60 % (12 out of 20) of the participants had no comorbid factors. Of those with comorbid characteristics, 15 % (3 out of 20) had some form of autism and 25 % (5 out of 20)had other behavioral problems. Among the 25 %, one participant had a previous diagnosis of ADHD and behavior disorders, one had ADD only, one had stereotype movement disorder (SMD), one had ADHD and perseverative behaviors, and one had SMD and ADHD. These participants belonged to the G3 group, except for one member that was from G4 who had a diagnosis of SMD.

After regression, all participants were diagnosed with ASD, except for one individual (P18 in Table 1) who was diagnosed with SMD with regression.

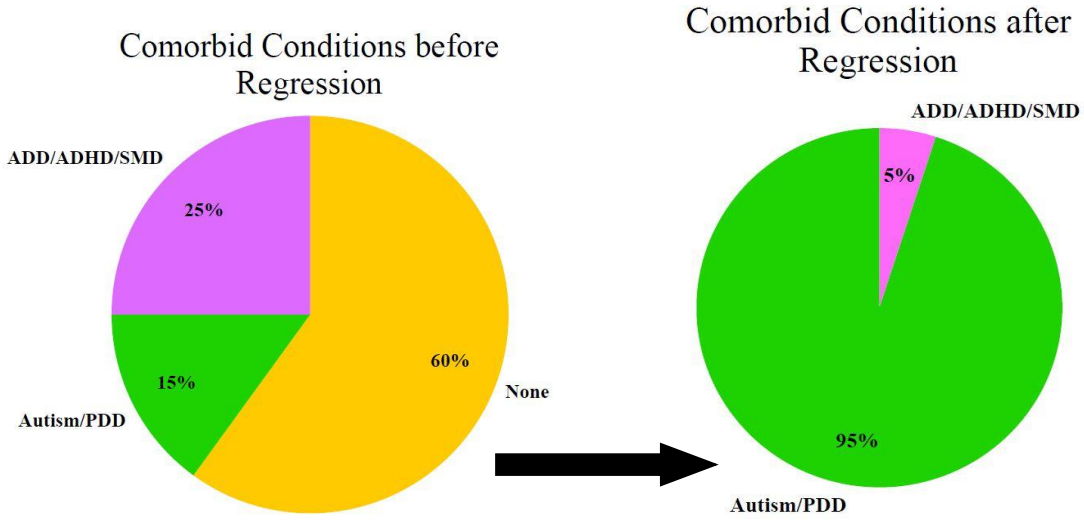


Figure 3: Change of comorbid conditions before and after regression for participants

As in other studies of this nature, parents were asked to identify stress factors (Volkmar & Cohen, 1989; Kurita, Kita, Miyake, 1992). These episodes were defined as times when thei ndividual with DS encountered unique or special stress. Six participants (30% of the sample) had some stress episodes prior to displaying patterns of regression. Participant 9 was reported to have been physically abused, and P16 reportedly experienced a traumatic EEG examination. In both

cases, these events occurred just prior to the onset of regression.

Finally, sleep disturbance (See Figure 4) was frequently mentioned by parents as an issue for their child. Among the 20 participants, 14 had sleeping problems. Of this number, 2 (10%) had sleep disturbance before the onset of regression, 6 (30%) had sleep disturbance after regression, and 6 (30%) had sleep disturbance while regression was occurring. The other 6 (30%) were not reported as having sleep disturbances.

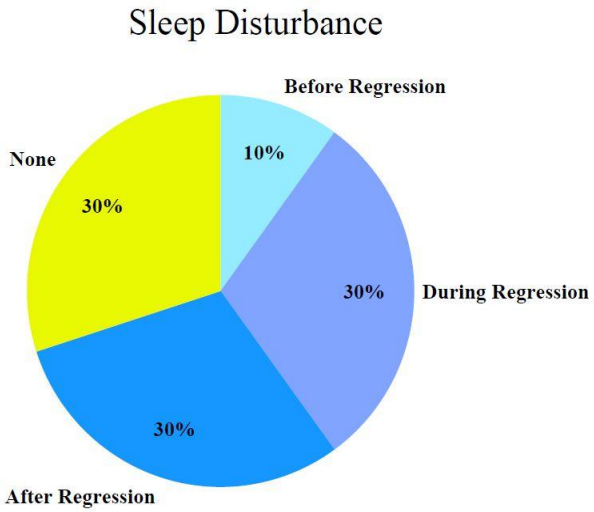


Figure 4: Comparison of sleep disturbance before and after regression among all participants

Loss of Adaptive Skills

Data on loss of skills is presented in Table 4. In addition to data about participants' group, gender, and age at regression, it shows loss of communication skills (e.g., use of signs, words, or a combination of these); loss of social skills behaviors (e.g., waving, saying "hello" and "goodbye," shared attention, social smiles, looking at the speaker); loss of play abilities (e.g., imaginative or pretended play, parallel play, group play); change in motor skills (e.g., running, jumping, walking, climbing stairs, swallowing); and loss of daily living skills (e.g., toileting, using fork or spoon, dressing and undressing, self-feeding).

Table 4 *Information on Participants' Loss of Skills*

Participant/ Group	Gender	[1]Regression Onset (approx.)	Loss Communication Skills	Loss Social Skills	Loss Play	Change in Motor Skills	Loss Daily Living Skills
P01/G1	F	1.3	yes	yes	yes	no	yes fork drink from cup
P02/G1	F	2.2	yes	yes	yes	hand coordination	yes potty
P03/G1	M	2.3	yes	yes	yes	yes, cautious, slow walking	yes potty, feeding
P04/G1	F	2.4	yes	yes	yes	no	no
P05/G1	M	2.7	yes	yes	yes	no	no
P06/G1	F	3.4	yes	yes	yes	no	no
P07/G1	M	3.4	yes	yes	yes	no	?
P08/G1	M	3.8	yes	yes	yes	no	no
P09/G1	M	4.5	yes	yes	yes	no	yes potty
P10/G2	M	3.4	yes	yes	yes	running jumping	yes
P11/G2	M	4.3	yes	yes	yes	no	?
P12/G3	M	7.0	yes	yes	yes	no	no
P13/G3	F	7.0	yes	yes	?	oral	yes feeding, potty dressing
P14/G3	M	7.0	yes	yes	yes	no	?
P15/G3	F	7.3	yes	yes	yes	fine motor	no
P16/G3	M	7.4	yes	yes	yes	no	?
P17/G4	M	9.0	yes	yes	yes	no	Yes toileting and make sandwich
P18/G4	F	9.0	yes	yes	yes	oral and slowed walk	yes fork spoon knife
P19/G4	F	10.4	yes	yes	yes	slowed walking	yes
P20/G4	M	11.0	yes	yes	yes	oral	yes feeding, potty

1 Expressed in decimal years.

All participants suffered from a loss of communication, social, and play skills (see Figure 5), except for P13 whose loss of play skills could not be verified. In contrast, apparent motor skills loss and/or change in walking patterns was experienced by only 40% (8 out of 20) of the participants. The apparent loss of oral motor skills was more often encountered among participants from G3 and G4. Slow walking, described as a child slowing his or pace as if he or she would be unable to walk faster as the child had previously been able to do, was found in three participants (P3, P18, and P19). Participant 3 was also described as exhibiting "cautious walking," which meant that the child had lost confidence in walking.

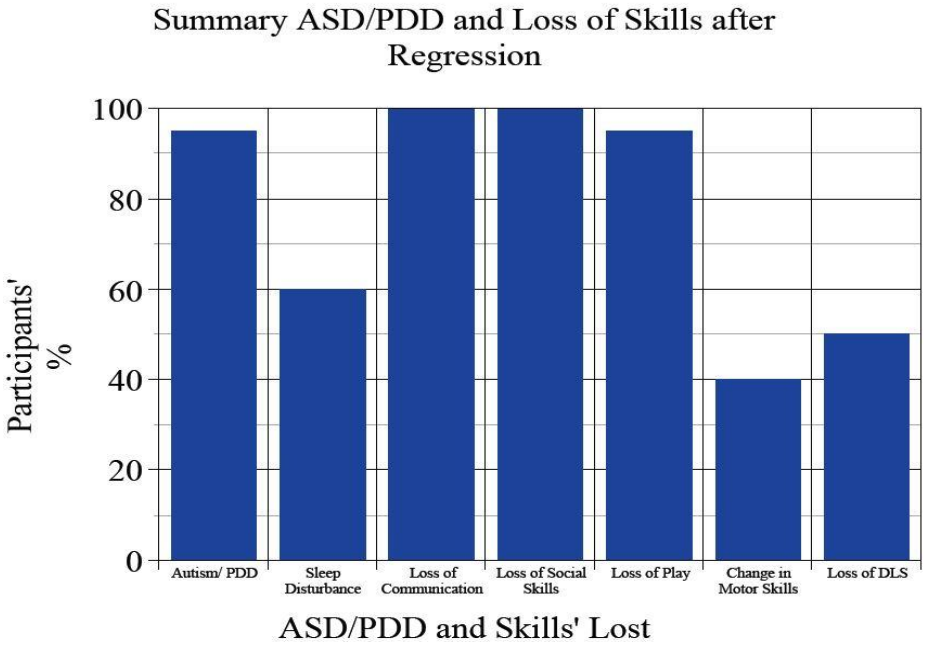


Figure 5: Summary of ASD/ PDD and loss of skills after regression.

In terms of daily living skills, 50 % (10 out of 20) of participants had a loss. The most commonly reported loss among participants was toileting and feeding skills. Three participants (P3, P13, and P20) had lost both abilities. Potty abilities in G1 and G2 meant the loss of the ability use the potty and the need to go back to the use of diapers, whereas for participants in G4, the loss of toileting skills meant the loss of the ability to follow the potty routine (e.g., pull down and up pants/underwear, washing hands, flushing, etc.). In four participants, the loss of daily living skills was not detailed as a specific type of loss.

Emergence of Maladaptive Behaviors

Parallel to the onset of regression and loss of skills was the emergence of maladaptive behaviors (these types of behavior will be introduced in Table 5 and Table 6). In some cases, the behaviors, even though they were present previously, were reported as worsening after the onset of regression

Table 5 *Emergence of Sensory Problems Perseverative Behavior and Disruptive Behavior*

Participant /Group	Gender	Regression Onset (approx.)	Emergence Stereotypy	Emergence Sensory Problems	Emergence Perseverative Behavior	Emergence Disruptive Behavior
P01/G1	F	1.3	yes after	yes after with food and hands	yes after watch same video, taping chin with object	no
P02/G1	F	2.2	yes after	yes after food texture	yes after with strings, stare at light/shadows	no
P03/G1	M	2.3	yes after	yes after mouthing objects coughing, throat clearing	yes after, shaking objects, slamming doors	no
P04/G1	F	2.4	yes after	yes after mouthing, tactile aversions	yes after running circles around flashing toy	no
P05/G1	M	2.7	no	yes before with food textures and tactile after with mouthing and loud noises	yes after yo-yo strings and waiving sticks around	no
P06/G1	F	3.4	yes after	yes before with food/textures	yes after with crayons	no
P07/G1	M	3.4	yes after	Yes after mouthing, licking dislikes hair-cut, play-doh, nails cut	yes after with video games, slam furniture	no
P08/G1	M	3.8	yes after	yes after tactile defensiveness, hair cut or touch, food texture	yes after feeding routines	yes after
P09/G1	M	4.5	yes after	yes after licks, loud noises baby cry	yes, after strings in front of eyes, lights off, empty shelves, line up things	no
P10/G2	M	3.4	yes before	yes after loud noise, brushing teeth, trim nails	yes, after regression: walking certain parts house	no
P11/G2	M	4.3	yes before	yes before loud noises later with food textures cutting/brushing hair brushing teeth	yes after, door closing	no
P12/G3	M	7.0	yes after	yes before food textures	yes before line up objects, running dangle objects	yes after
P13/G3	F	7.0	yes after	yes before food, hair and nail cut, brush teeth	yes, after flushing hand toilette, dangle objects	yes before
P14/G3	M	7.0	yes before	yes before haircut, loud noises brushing teeth	yes before chewing on fingers while jumping and humming	yes before
P15/G3	F	7.3	yes after	yes after with food, brushing hair and teeth	yes, after pick up scraps shaking clothes on hanger	no
P16/G3	M	7.4	yes after	yes after hair, nail trimming	yes after tapping chin, straightening blankets	yes before
P17/G4	M	9.0	yes before	yes before mouthing, throaty noises	yes after, card in hand and flipping it	yes before
P18/G4	F	9.0	yes after	yes after mouthing, throaty noises, loud noises	yes, after lines up toys	no
P19/G4	F	10.4	no	?	?	no
P20/G4	M	11.0	yes before	yes before mouthing, food textures	yes before flushing things in toilette	yes before

Table 5 presents participants' data for, gender, age of regression, the emergence of stereotypy (repetitive nonfunctional motor movements such as head and hand shaking, body rocking with and without humming, tongue clucking, shaking arms, flipping fingers in front of the eye, etc., in this case without self-injury), sensory integration problems (sensitivity with brushing teeth, combing and cutting hair, loud noises, lights, food texture), perseverance or perseverative behavior (meaning emergence of new strong routines like stacking or lining up objects, watching repeatedly the same section of a video, need for closed doors, constant dangling of objects, staring at lights or fans etc.), and disruptive behaviors such as oppositional, resistant, or hyperactive.

Data on stereotypy shows (see Figure 6) that all but two participant had some sort of stereotypy movement, but the appearance of this behavior varies among participants. Thirteen participants (65%) showed this behavior only after the onset of regression, five (25%) had some type of stereotypy predating their regression, and two participant (10%) did not develop any stereotypies.

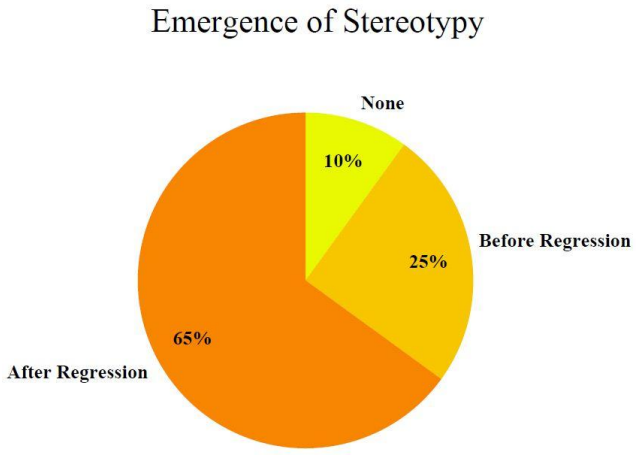


Figure 6: Emergence of stereotypy among participants before and after regression.

All participants in G1 had the emergence of stereotypy after the onset of regression

except for P5. In the other groups, the children who had some type of stereotyped behavior are the ones that had a previous diagnosis of SMD or ASD-like behaviors, (Participants 10, 11, 14, and 20). Participant 19 did not have a previous diagnosis of SMD or autistic-like behaviors; besides occasional humming, there were no other behaviors that could qualify her as having ASD or SMD.

The most frequent behaviors found were guttural noises, hand shaking on each side of the body or in front of the chest, bruxism, rocking, head shaking, and extension of legs and arms.

Sensory problems (see Figure 7) were present in eight participants before regression; however, for 11 participants, sensory problems came after regression. Only one participant, P19, had no documented evidence regarding when sensory problems started or if she had any. The most frequent problems reported among participants with sensory problems predating regression were food texture, excessive chewing on objects, and tactile defensiveness. For the eleven participants whose sensory problems came after the onset of regression, the most frequent problems were with loud noises, food texture, excessive object mouthing, and cutting and brushing hair.

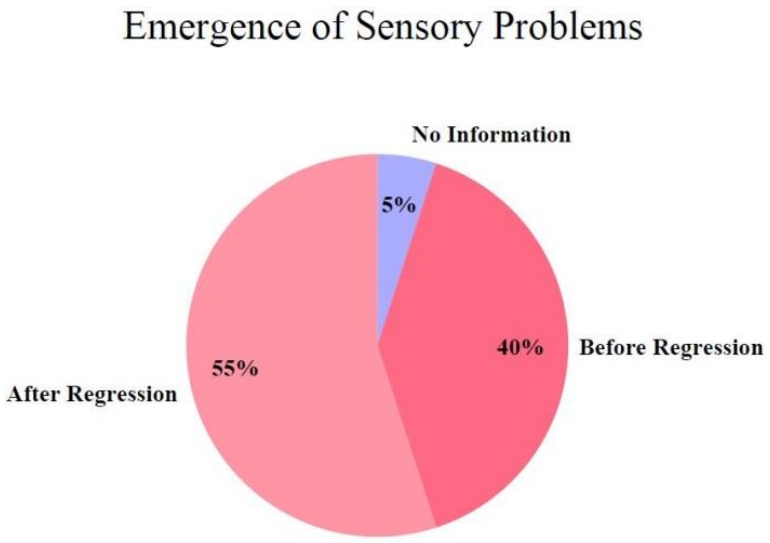


Figure 7: Emergence of sensory problems among participants before and after regression

It is important to note that participants with previous sensory integration problems developed additional ones after regression. For example, in P11, previous regression had been limited to aversion to loud noises; after the onset of regression, he developed problems with food textures, excessively mouthing objects, not liking to have his hair cut or brushed, and not wanting to have his teeth brushed. Similar changes occurred with P5; before regression, he was sensitive to certain food textures and avoided touching certain surfaces and materials with his hands. After regression, he developed problems with loud noises and would mouth and chew objects excessively.

Perseverative behaviors (see Figure 8) appeared before regression in 4 participants and after the onset in 14 other cases. Behaviors varied across participants, but the most commonly observed included dangling and twirling strings or objects (e.g., yo-yo string, cardboard, sticks), lining up objects, slamming doors or slamming into furniture, and watching the same videos continuously.

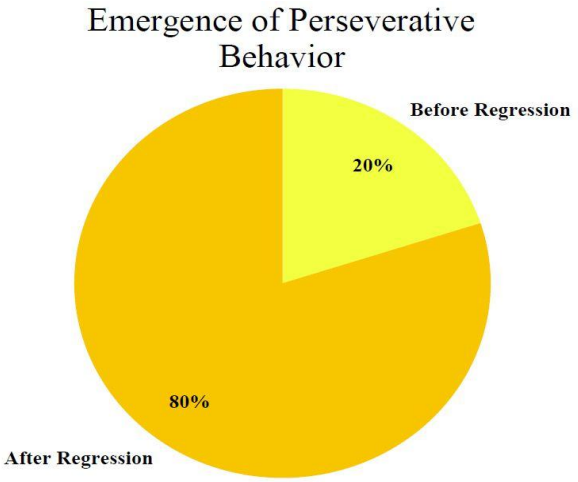


Figure 8: Emergence of perseverative behaviors among participants before and after regression.

For example, P9 would spend significant amount of time lining up objects and dangling

and twirling objects in front of his eyes. He needed to have light off and videos or books out of the shelves. Another example occurred with P15, who liked to line up objects, pick up scraps, dangle objects, and shake clothes from hangers.

Disruptive behavior (see Figure 9) (e.g., aggressive, oppositional, hyperactive, resistant, or ADHD) was a symptom reported by some parents and professionals. Two participants developed some type of maladaptive behavior after regression, whereas 6 participants (or 30% of the cases), had behavior problems prior to regression (Participants 11, 13, 14, 16, 17, and 20). In G3, all but one participant had a diagnosis of behavior disorder before the onset of regression. In the other 12 cases (60%), parents and professionals did not notice significant change on their child behavior.

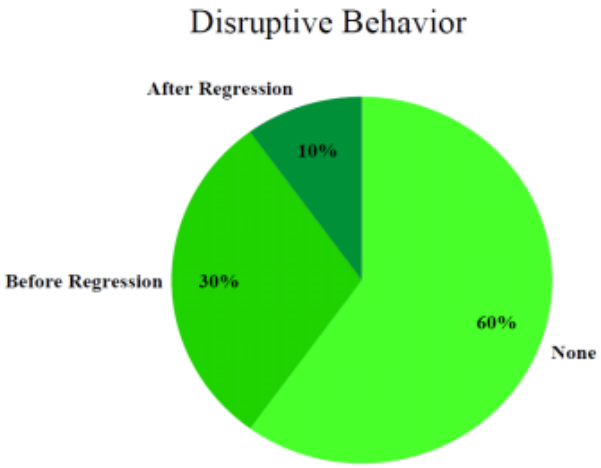


Figure 9: Emergence of disruptive behavior among participants before and after regression.

The second data table (see Table 6) shows emergence of maladaptive behaviors and includes information beyond gender and age of regression, such as emergence of Pica behaviors (compulsive behavior towards eating non edible items), SIB (self-injury behavior), mood swings (e.g., movement from crying to laughing with no apparent reason), and psychotic-like behavior (e.g., hearing voices or seeing things, catatonia).

In terms of Pica data, only 5 of the participants (25 %) did have Pica, all of which occurred after regression. All groups had at least one member with PICA except the older group, G4, that did not present this symptom among its members.

Self-injurious behavior (SIB) (see Figure 10) was another behavior often mentioned by parents. SIBs were present in a total of 13 participants (65%). Nine participants (45%) had this behavior emerge after the regression onset, and 4 participants (20%) had it before regression. The most common behaviors recorded for both groups (i.e., pre and post-regression) were head banging and head hitting, chewing on fingers, and poking eyes or pulling eye lashes.

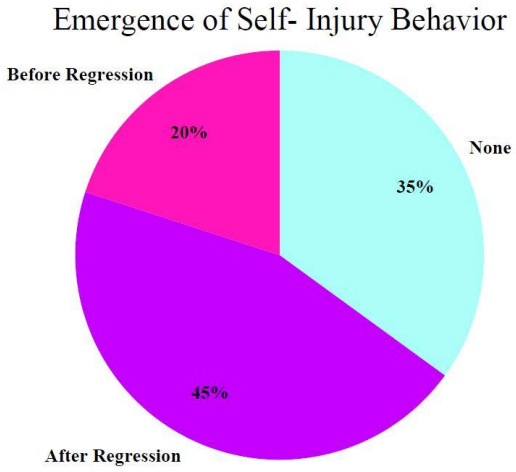


Figure 10: Emergence of self- injury behavior among participants before and after regression.

SIB by groups:

- G1 had only three children with SIBs and the three of them after regression.
- G 2 had both children with SIB, both before regression and both the same behavior, head banging.
- G3 had five members, and four had SIB, two before regression and two after regression.
- G4had three members who developed SIB and only after the onset.

Table 6 *Data on Pica, Self Injurious Behavior, Mood Swings, Psychotic- Like Behavior*

Participant/ Group	Gender	Regression Onset (approx.)	Pica	Self-Injurious Behavior (SIB)	Mood Swing	Psychotic-like Behavior
P01/G1	F	1.3	no	yes after head bang	no	no
P02/G1	F	2.2	no	no	no	no
P03/G1	M	2.3	no	no	no	no
P04/G1	F	2.4	no	no	no	no
P05/G1	M	2.7	no	no	no	no
P06/G1	F	3.4	no	yes after	no	no
P07/G1	M	3.4	yes after eat feces	no	sudden fearfulness	no
P08/G1	M	3.8	no	yes after chew on fingers pocks eyes	no	no
P09/G1	M	4.5	yes after eat feces	yes after hits head pulls hair	no	no
P10/G2	M	3.4	no	yes before head banging	no	no
P11/G2	M	4.3	yes after, sand and glue	yes before head banging	cry/laugh.	no
P12/G3	M	7.0	no	yes before	no	no
P13/G3	F	7.0	yes after sand, feces, leafs, dirt, grass, soap	yes after soap in eyes	sudden fear/ happy to sad	yes talk hand, hallucinations
P14/G3	M	7.0	no	yes before chew on fingers	no	no
P15/G3	F	7.3	no	yes after pulls eye lashes	cry/laugh	no
P16/G3	M	7.4	yes after	no	no	no
P17/G4	M	9.0	no	yes after chew on fingers poke eyes	cry/laugh, fear,	yes hallucinations
P18/G4	F	9.0	no	yes after picking nipples, taps her eye lid	cry/laugh, clinching hands	yes stare at hand
P19/G4	F	10.4	no	no	cry/laugh, clinching hands	lethargic out of touch
P20/G4	M	11.0	no	yes after head banging	cry/laugh, scream, fear	yes catatonic

Emergence of mood swings (see Figure 11), which are defined as switching from one state to another without an apparent trigger, was also present in 8 children (40%). This mood swing was often movement from laughing to crying or from stable to sudden fear. When parents and professionals explained these symptoms, they mentioned that they could not generally find the cause or triggers for these reactions. Looking at the data by groups, G1 and G2 each had 2

participants with mood swings and G3 had 2 out of 5 participants with mood swings. However, in G4, all 4 participants had mood swing, all after regression.

Psychotic-like behaviors (see Figure 10) after regression were present in 5 children, and 4 of these children belonged to G4 while the other participant was from G3. Therefore, these behaviors were absent in the younger groups (G1 and G2). Participant 11 and P15 were reported to have had several episodes of hallucination, P7 and 19 had similar behavior but parents described it differently: P7 had catatonic-like behavior and P19 had lethargy. In the last two cases, both cases parents said that their children seemed out of reach. The behaviors for P13 were slightly different after regression; at that point, she started having hallucinations, seeing ghosts, and talking to invisible people. Parents and teachers' reports noted that, according to the participant, she had a good and a bad hand that she would talk to, and once she tried to flush the bad hand down the toilet.

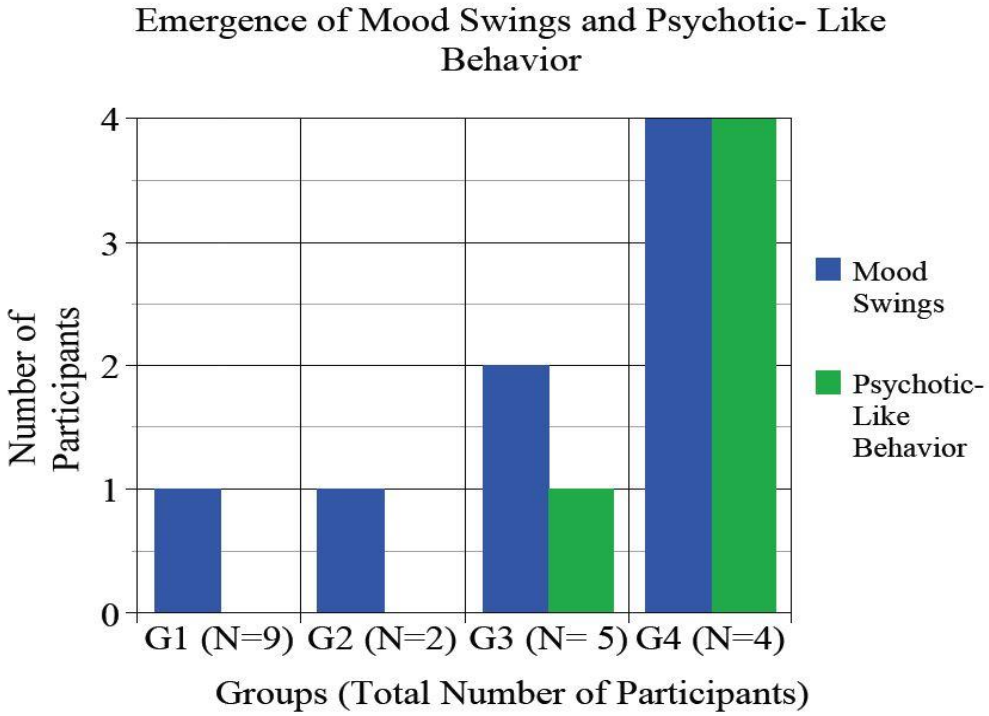


Figure 11: Emergence of mood swings and psychotic- like behavior before and after regression.

Summary of group data

To sum up, data from the 20 participants (see Figure 12) shows that after regression, 85 % of the children (or 17 participants) that did not have autism as a comorbid condition were diagnosed with ASD/PDD. The only participant that did not develop autism was diagnosed with SMD. Sleep disturbance was common among the participants. About 70 % (14 participants out of 20) had sleep issues, and those occurred more often during and after regression than before regression. All children in G2, G3, and G4 had some type of sleep disturbance.

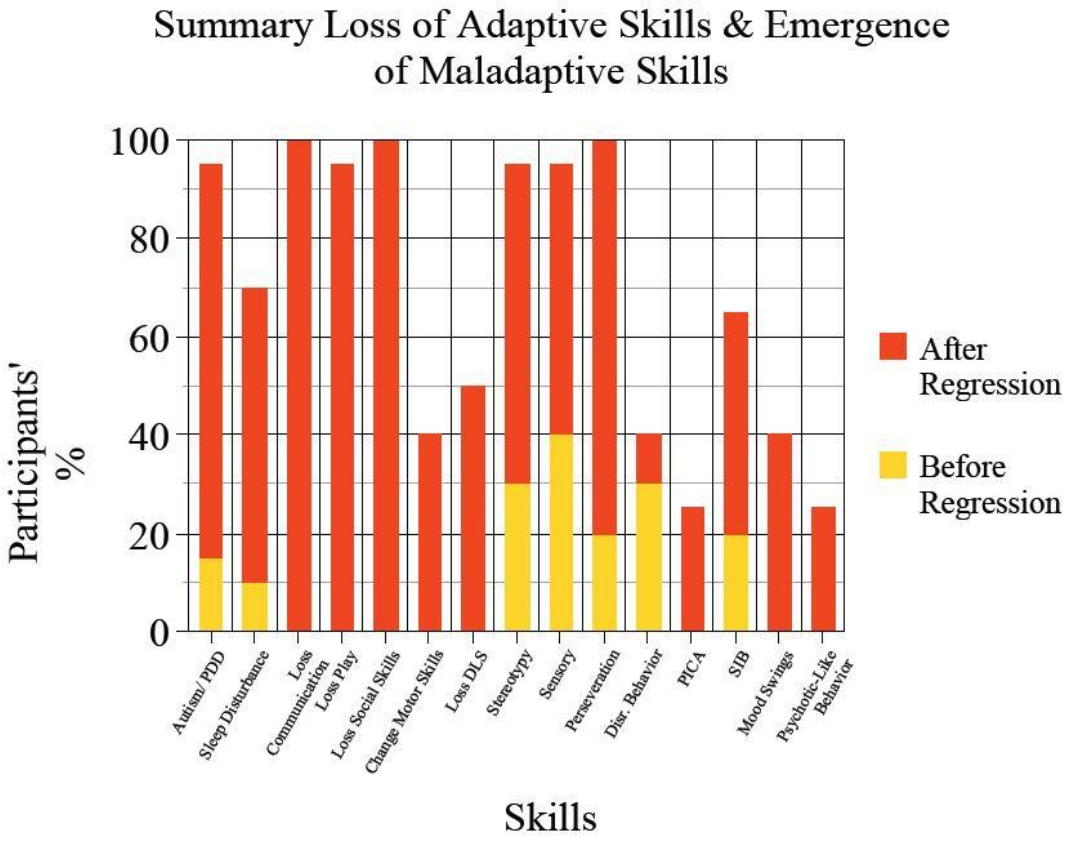


Figure 12: Summary of loss of adaptive skills and emergence of maladaptive skills.

In terms of loss of skills, communication and social were lost by 100% of the participants (20 out of 20 participants). For play skills, all but one participant whose data for this skill could not be found had lost this skill.

The loss apparent loss or change in motor skills and daily living skills was less common

among participants of this sample. As Figure 11 reveals, 40% had some changes in their motor skills (apparent loss or decline) and 50% (10 participants out of 20) lost daily living skills.

Emergence of maladaptive skills such as stereotipy and sensory problems occurred in 65% (13 participants out of 20) and 55% (11 participants out of 20) of the sample, respectively. The most common sensory problems that developed were to certain food textures, excessive mouthing, tactile defensiveness, and having hair combed or trimmed or nails trimmed. Perseveration emerged in 80% of the cases (or 16 participants out of 20), whereas behavior problems only in 10% (or 2 participants) of the cases. As earlier noted, Pica was not frequent among the groups, with only 5 participants developing this behavior after regression. Self-injury was present in 60% (or 12 out of 20) of the participants, but 40% (8 participants)developed those after regression. The most common problems were head banging/hitting, chewing on fingers, and picking on the eye area. Finally, mood swings and psychotic-like behavior were relatively uncommon in the younger groups compared to the older group G4, where all participants developed sudden mood swings (crying and laughing) and hallucinations as well as catatonic/ lethargic like behavior.

Individual Group Data and Representation of Each Group with a Case Study

In this section, each group will be analyzed individually and a case sample for each group will be discussed in detail. These four case studies are examples of a type of regression. The first case study represents G1, a girl with DS who went through developmental regression at around the age of 3 years and 5 months with no comorbid conditions. The second case study represents G2, a boy with DS whose regression happened close to the age of 4 years and 3 months. These two participants had developed autism symptoms previous to the onset of

regression. The third case represents G3, a boy with DS who went through developmental regression at about the age of 7 years and had preexisting behavior problems. The fourth case study represents G4, a girl with DS that went through developmental regression at the age of 10 years and 8 months with no preexisting conditions.

Group 1 Results

G1 is represented by 9 children (P1- P9), 5 boys and 4 girls whose regression occurred between the ages of 2-5 (except for P1 whose regression was noted at the age of 1 year and 3 months). This group of participants did not have a comorbid diagnosis (see Tables 3, 4, 5, 6, and Figure 13) before the onset of regression. The average age at the start of the regression was 2.9 years. None of the children had a comorbid condition before the onset of regression and all children but one were diagnosed with ASD after regression occurred. Participant 3 was diagnosed with SMD.

Stress episodes right before the onset were only noted by three of the nine parents. For P1, the parents recalled she had to be hospitalized, P3 had surgery and moved to another city, and for P9, the main informant explained that he was physically abused for a period of time, and it was right after that abuse that the child started to lose eye contact, words, and would not play anymore.

Sleep disturbance in G1 was not common, with only two children showing problems with sleep after regression. For P7 the problem was waking up several times in the middle of the night, for P9 the reported problem was also awaking in the middle of the night and not being able to go back to sleep, and for P6, her parents noticed sleep problems during her regression but no further details were given.

All nine participants in G1 lost communication, social skills, and play, but only two had

an apparent lost motor skills: P2 lost hand coordination, and P3 lost the ability to walk normally. He developed a “cautious” walking style.

The loss of daily living skills was obvious in four of the nine cases of G1. The loss was mainly toileting and feeding skills. For P7, the loss could not be corroborated.

All nine participants developed maladaptive behaviors after their regression. Perseverative behaviors were reported for all but one child, P 5, who developed stereotypy. Sensory problems were also very common among the children of this group. Seven participants developed sensory problems after their regression and two before. The problems identified by parents were avoidance of certain food textures, tactile defensiveness, avoidance of loud noises, excessive mouthing, and extreme dislike of hair brushing or cutting and nail trimming.

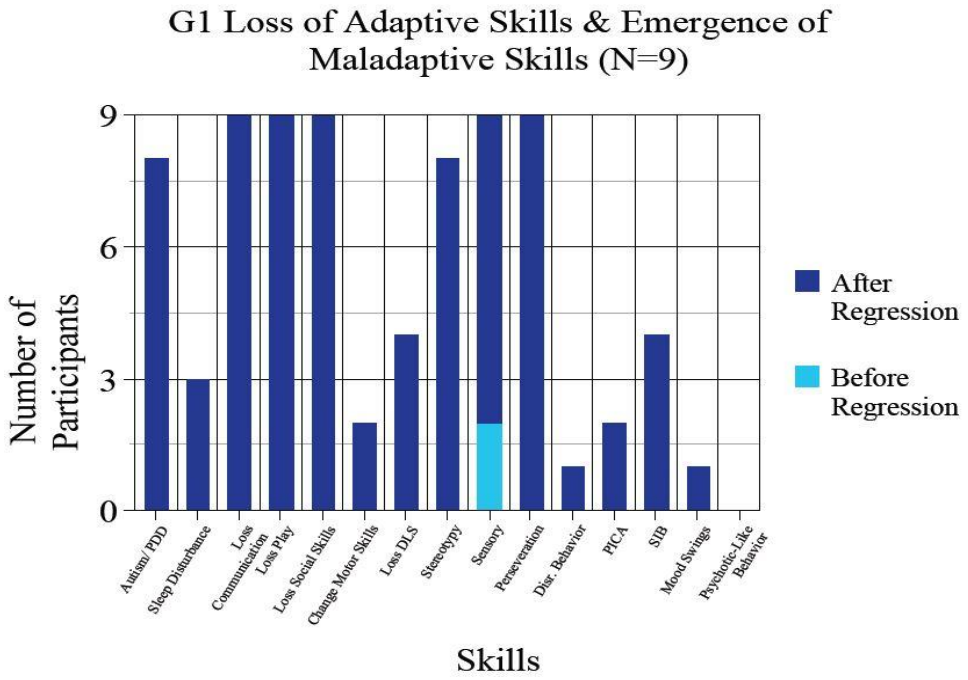


Figure 13: G1 summary of loss of adaptive skills and emergence of maladaptive skills.

Behavior problems, however, were absent in this group, except for one participant who developed some behavior problems after his regression. Parents pointed out that he became much

more resistant to leaving the house, as he would knock things off of the table, hitting and kicking others.

Mood swings and psychotic-like behavior were not common among the participants of G1 group. Only one participant (P7) had sudden fear, and neither parents nor teachers could identify what triggered it. The same Pica behavior was present only in two children (P7 and P9), and self-injury behavior was developed in three of the nine participants.

Case 1 Analysis: A Girl with Developmental Regression at the Age of 3 Years and 5 Months.

Summary introduction of the case.

This case presents a girl, SP, with DS with symptoms of developmental regression occurring at around the age of 3 years and 5 months with no apparent previous symptoms of autism.

SP came to the DSC KKI at the age of 4 years and 8 month. Parent's complaints at the time of the visit were loss of language and communication and emergence of autistic-like behaviors. She apparently developed normally until the age of 3 years. At that time, she had 25 words, 10 signs, and pretend play. Around the age of 3 years and 4 months, she started losing skills. First, she lost spoken language and then comprehension, she began flapping hands, and then she stopped playing with toys and would use objects in a preservative pattern. She also began having sleep problems and no longer would spontaneously sign or speak, pull mom's clothes, or attempt to gesture. She would grind teeth and moan when watching videos, and when left alone, she would sit and shake her hands in front of her eyes.

Developmental history by age.

SP is the oldest of three siblings. Her siblings are twins, a boy and a girl aged 22 months at the time of SP's evaluation. Her sister had a heart condition and developmental delay, and her brother was diagnosed with autism. The parents were reported to be healthy and did not have any other family members with disability.

Pregnancy and birth history.

The mother reported that during pregnancy she had low amniotic fluid and reduced umbilical blood flow. During delivery, SP was hypotonic, cyanotic, and had poor respiratory efforts. She was placed in NICU for five days because she had difficulties maintaining her body temperature.

7 months old. Brain stem auditory evoked response showed normal hearing in left ear and a mild loss for higher frequencies in her right ear. During an evaluation at Children's Hospital, she was described as very engaging, in no apparent distress, and doing extremely well in her educational setting, where she was making steady progress.

12 months old. According to the report from the pediatrician at the Children's Medical Center, SP began sitting at 10 months of age. At 12 months, she was able to bring her hands to the mid line, clap, and roll purposefully towards where she wanted to go. In terms of pre-language, she demonstrated some babbling. SP was enrolled in an early intervention program where she received physical therapy once a month and special education services twice a month.

Her diet included cereals, fruits, yogurt, some table foods, and some baby foods, but she was not interested in drinking from a zippy cup. Her parents at that point did not post any concern and were pleased with the development of their daughter.

18 months old. According to a Children's Hospital pediatrician, SP was able to crawl and

pulled to stand although could not cruise. SP continued to babble and could say “mama” and “dada” specifically. She would also point to two body parts and wave bye. Myopia was discovered during the visit that required glasses; and her thyroid function was reported to be within the normal limits. Her pediatrician concluded that SP was exhibiting very good progress. At this point, SP was receiving support from the toddler and infant services of her area; these comprehensive services included physical, occupational, and speech and language services as well as a special education teacher.

24 months old. In one of the follow-up visits to the Children’s Medical Center, it was reported that SP was a picky eater but would eat a fairly balanced diet. She was beginning to walk, cruise well, and used her fingers to feed herself. Her parents remarked that she had around 10 to 20 words, and her doctor found her very interactive and cooperative.

A month later, SP had an evaluation for her Individualized Family Services Plan (IFSP) from her home state. According to the report, SP had made progress in all areas during the school year. Specifically, on the Mullen Scales of Early Learning, her test scores were found to be at 14 month level. This scale measures SP’s ability to understand, remember, combine words, and use spoken language. Generally speaking, this scale looks at how the child communicates.

In a non-specified developmental test, SP was evaluated in different areas with the following results:

1. Receptive communication skills were at the 21 month level. SP would follow one-step directions and enjoyed action songs.
2. Expressive language skills were at 15 month level, and she was able to incorporate signs. SP had the ability to point to pictures appropriately in books. Her teachers also agreed that she made good progress in both areas during the school year. She

demonstrated 10-15 words/signs that she used to express herself.

3. Gross motor skills were found at 13 month level, and it was pointed out by teachers that these skills had also improved greatly. She demonstrated planning motor skills for climb or riding on toys.
4. Fine motor skills were at 14 month level. She had a partial pincer grasp and increasing hand strength. She seemed interested in playing with toys and using her both hands to manipulate them.
5. Adaptive skills were at 12-15 month level for dressing; she was able to undress and help with brushing hair. For feeding, she appeared to be at 9-11 month level. She would not use utensils or drink from a cup.
6. Social-emotional skills were at 16-19 months. It was observed that SP enjoyed the company of her peers and demonstrated pretend play skills.
7. Cognitive skills were at 18 month level. SP had improved her cognitive and play skills. She seemed interested in playing with toys and engaged in pretend play. She demonstrated object permanence and was able to put simple shapes into a puzzle.

Concerns raised at this point were her unwillingness to drink from cup, problems with self-feeding, and her need to improve oral motor skills.

30 months old. SP went with her parents for her follow-up visit with her pediatrician at Children's Medical Center. No major concerns were posted, except that her diet continued to be difficult. In other matters, her doctor also agreed with her parents that SP was doing well. Her vocabulary expanded to 15-20 words and 10 signs.

Two months later, at the age of 32 months, she was evaluated using Mullen Scales of Early Learning. Her scores were as follows:

1. Receptive Language: 12-15 month level
2. Expressive Language: 12-15 month level
3. Gross Motor: 15 month level
4. Fine Motor: 14 months level
5. Problem Solving : 13 month level

36 months old. Her pediatrician and parents noted that she was beginning to run and could kick and throw a ball. SP also knew all the hand motions of at least 15 music song games, and her vocabulary was also reported to be improving. SP was also attending music therapy classes.

She had two new born siblings. Parents concern's at this point were her oral motor and feeding skills and that she had a somewhat stubborn streak. Mom also reported that SP was having some sleeping problems.

3 years and 9 months old. SP attended to the preschool education program two hours and a half daily, five days a week. She also received occupational, physical, speech, and language therapy, as well as art, music, and physical education along with her two classmates.

A school report on SP pointed to some characteristics that were not seen before. SP would sometimes briefly play with a few toys when they were presented to her but she rarely would initiate play or interaction of any sort. They also noticed that SP would grind her teeth and liked to shake objects in front of her eyes. She liked to sit in a chair, and when left alone, she would sit and stare off to the space, shaking her hands, and sometimes vocalize. She also liked to take of her shoes and socks to dangle gently in front of her eyes.

According to classroom teachers, her most attentive time was during circle time, but she inconsistently followed hand songs. Teachers also reported that she would avoid eye contact

when it was initiated by others but less often if it was during circle time. She also required one-on-one adult assistance to participate in daily routines plus constant verbal and physical cues.

SP was also evaluated at this point at her school. This evaluation included scores on the *Mullen Scales of Early Learning* (Mullen, 1995) are shown below.

- Fine motor: 13 month level (previously at 14 month level).

  SP had some radial digital grasp on blocks when placed in the container, but she did not attempt to stack the blocks. She had difficulties picking up pennies from the table, and if they were dropped on the floor, she would not look for them. She did not attend to demonstrations or to materials, and when she would handle materials she would attempt to use them stereotypically as she would do in the classroom.

- Expressive language: 10 month level (previously 12-15 month level).

  SP was able to make vocalizations, play with sounds, and did some voluntary babbling. She was able to produce multiple consonant vocalizations but lacking intent for communication. She would use inconsistently gestures in songs.

- Receptive Language: 10 month level (previously 12-15 month level).

  According to the report, this scale measured SP's ability to follow directions and recall what she has heard, express knowledge, organize auditory information, and understand verbal-spatial concepts. SP enjoyed self-mirror interactions and attended to words and movements. She could recognize familiar names including her own. However, she was not able to identify objects, give a toy on request, comprehend questions, point to body parts, or follow simple novel directions.

- Visual receptive: 6 month level.

  This test measured SP's ability to match objects and pictures, recall what she has

seen, and organize visual information. Given numerous opportunities to answer, SP would track a moving bull's eye and looked at different objects. Nevertheless, she would stare at her hand often and would not look at a dropped spoon or other materials. SP did not pull a cord to obtain a disc although she did look for a fully hidden ring under a wash cloth.

The Brigance Diagnostic Inventory of Early Development (Brigance, 1992) was administered, and her scores were as follows. No further details were given.

1. Self Help Eating: 12 months
2. Self Help Dressing: 18 months
3. Self Help Toileting: below 12 months
4. Self Help Bathing and grooming: 18 months.
5. Pre-speech Receptive Language: 15 months
6. Pre-speech Gesture: scattered abilities to 12 months
7. Pre-speech Vocalizations: 7 months
8. Social Emotional Play and Behavior: isolated skills
9. Social Emotional Work Related Skills/ Behaviors: 12 months.

4 years old. At her pediatrician's office, SP's parents addressed the issue of stereotypies and other autistic-like behaviors that had been noticed in the past months, which were occurring at the same time that SP's gross motor skills were developing, as she could go up and down the stairs. Her fine motor skills were also improving despite her need for a lot of repetition. It was noted also by the doctor that her social skills were very good. During the medical examination, SP was active and engaging. Her thyroid functions were reported as normal. At this point, SP was attending preschool with three other children in her classroom.

4 years and 6 months old. SP came to KKI-DSC for an evaluation. At this point, SP's expressive language (signed or spoken) was absent and only with prompting she would say "beep," "mama," "dad," and "bye." In terms of receptive language, her parents stated that previously she could understand many words, but it now seemed that she had forgotten them except for "more," "all done," and "eat." She did follow one-step spoken directions.

In the motor skills area, it was reported that she could finger feed and was just starting to use a spoon. For food intake, she would reject vegetables and some fruit because of their textures.

Behaviorally, SP displayed self-stimulatory behaviors such as twirling and dangling objects, hand flapping while watching TV, and turning head sideways. The doctor noticed bruxism and moaning noises, and that she showed little interest in games or toys and perseverative play with crayons. Her attention was atypical and easy distractible with little eye contact. Her parents, at the time of the visit, filled out the Autism Behavior Checklist resulting in a score of 99 and the Guilliam Autism Rating Scale resulting in a score of 82, which placed her below average of probability for autism.

On the Aberrant Behavior Checklist, (see Table 7, Table 8 and Figure 14), she had a total punctuations of 126, with high scores in all subscales (hyperactivity 43 over 48; irritability 28 over possible 45; stereotypy 21 over 21; lethargy 28 over 28;) except for the inappropriate speech subscale with a higher score (6 over 21) when compared to the respective groups of children with ASD (2.4), DBD (2.9) and Typical (0.9).

Table 7 *ABC Scales for Participant SP*

ABC subscales 3-13yr	ASD	DBD*	Typical	SP	Maximum Score
Hyperactive	**21.4**	**28.5**	**7.4**	**43**	**48**
Irritable	**13.2**	**14.9**	**3.3**	**28**	**45**
Stereotypy	**12.4**	**2.9**	**0.8**	**21**	**21**
Lethargy	**18.6**	**5.4**	**1.9**	**28**	**48**
Inappropriate Speech	**2.4**	**2.9**	**0.9**	**6**	**21**
Total	**68**	**54.6**	**14.3**	**126**	**183**

Note: Comparison is made typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr). Notice her overall high scores.
*DBD: Disruptive behavior disorder

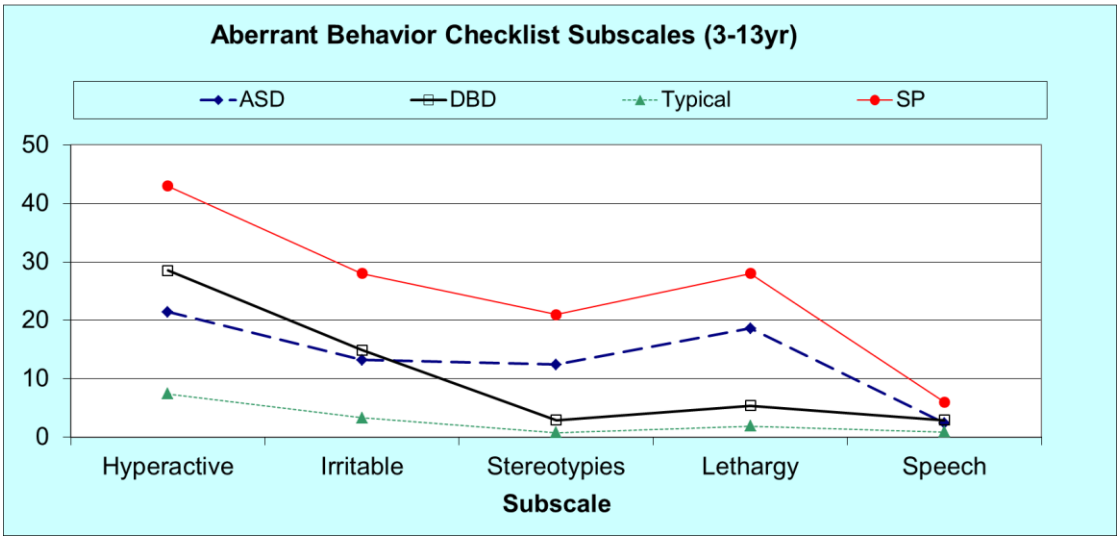


Figure 14: ABC subscales graph for participant SP: comparsion is made with typical child with DS and children with DS+ASD or DS+DBD. All data collected thorugh the DSC fomr 1995- 2000 (N=305 children ages 3-13).

A cluster analysis evidenced higher scores in motor activity, disruption, inattention, withdraw, and self–injury. However, self-injury concerns were not found in the records of the meeting with doctors or teachers, but SP scored high, 7 out of 9 possible points, and therefore it was assumed that those developed after regression. Scores in the ABC scales (see Table 7, Table

8 and Figure 14) were considerably higher when compared with her peers from the groups of DS and Autism (DS+ASD) and DS and behavior disorders (DS+DBD). The only score similar to her peers in the DS+ ASD group is on the apathy cluster and on the physical aggression with the DS= DBD group.

At this point, the pediatrician diagnosed her with ASD based on her social and communicative impairments, self -stimulatory behaviors, and restricted interests. An EEG was performed, and no alterations were found.

Table 8 *ABC Derived Behavioral Clusters for Participant SP: Comparison is made of Typical Children with DS and DS+ASD or DS+DBD*

ABC clusters 3-13yr	ASD	DBD	Typical	SP	Maximum Score
Motor activity	8.7	11.5	2.2	16	21
Disruptions	7.3	11.2	2.3	16	18
Inattention	8.7	8.5	2.6	15	15
Aggression-verbal	3.2	3.4	0.2	6	9
Aggression-physical	1.5	2.1	0.3	3	6
SIB	2.6	0.7	0.2	7	9
Mood	4.6	4.9	1.3	6	15
Apathy	7	1.6	1	8	21
Social Withdrawal	11.7	3.8	1	20	27
Stereotypy	12.4	2.9	0.8	21	21

Note: Notice that clusters are separated in two groups, externalizing behaviors and internalizing behaviors.

This case represents an example of regression for G1, formed by 5 children (P1-P9) whose age at regression was between 2-5 years old and had no signs of a comorbid condition predating regression. This case of early developmental regression explains the process of a girl with DS (see Table 9) who developed apparently normal until the age of 3 years. By 2 years she had between 10 to 15 words and was seen as cooperative. She enjoyed being with peers and

Table 9 Summary of SP Development through Time and Evidence of Cognitive Decline

Age							
7 months	12 months	18 months	24 months	30- 32 Months	3 years	3y 9months	4 y 6months
Engaging Doing extremely well in her educational setting No distress	Sits Brought hands to middle line Claps Rolled purposefully Babbling	Crawled Pulled to stand Babble "mama/dada" purposefully Pointed two body parts Waived bye Doing good progress	Problems: Picky eater/ wouldn't drink from cup and problems with self-feeding Started walking Cruised Used all fingers to self-feed 10-20 words Dr. found very interactive and cooperative skills	Vocabulary: 15-20 words, 10 signs Dr.: Doing well Picky eater	Started running Kicked-threw ball Hand motion for 15 music games Improving vocabulary Problems: oral motor feeding, and "stubborn streak", sleeping problems	Brief play with toys, would not initiate play with toys and would not interact with others. Grinds teeth Shook objects in-front eyes. Sit chair and stared off space, shook hands. Liked to take off shoes and socks and dangle in front of eyes. Would inconsistently followed hand-songs Avoided eye contact. Needed assistance for daily activities	Expressive language signed and spoken was gone. Receptive language could only understand "more, all done and eat" Could follow one step direction. Motor skills were doing fine. Food sensory SMD, no eye contact **Dx: ASD**
			IFSP: lots of progress Mullen: 14 m/lvel **Non disclosed test:** **Receptive Lang.** 21 m/lvel. Follow 1-step direction and enjoyed action songs **Expressive Lang.**:15 m/lvel incorporated signs, pointed pictures appropriately in books 10-15 words. **Gross Motor:**13 m/lvel **Fine Motor**: 14 m/lvel **Adaptive skills**: 12-15 m/lvel undressed and helped with brushing hair, feeding 9-11 m/lvel **Social emotional Skills**: 16-19 m/lvel: enjoyed other kids and showed pretended play **Cognitive Skills**: 18 m/lvel object permanent stage.	Mullen Scales **Receptive**: 12-15 m/lvel **Expressiv**e: 12-15 m/lvel **Gross Mottor**: 15 m/lvel		Mullen Scales: **Receptive Lang:** 10 m/lvel. **Expressive Lang.:** 10 m/lvel. **Fine Motor:** 13 m/lvel. **Visual Receptive:** 6 m/lvel.	

demonstrated pretend play skills. SP could do hand motions for at least 15 songs, climb,

and ride on toys. However, SP, as like the other participants in her group, started losing skills, first spoken language and then comprehension, began flapping hands, stopped playing with toys, and would use objects in a preservative pattern. She also lost interest in others. SP began having sleep problems and no longer would spontaneously sign or speak. This emergence of maladaptive behaviors was also observed in the other participants who formed the group. Like the majority of the children in her group, she did not develop PICA, SIB, mood swings, or psychotic-like behavior.

Group 2 Results

Group 2 is represented by two participants (P10- P11) (see Tables 3, 4, 5, 6, and Figure 15), both male whose ages at regression were 3.4 and 4.3 years respectively. The mean duration of their regression was 7.5 months. These participants did have ASD/PDD before their onset of regression.

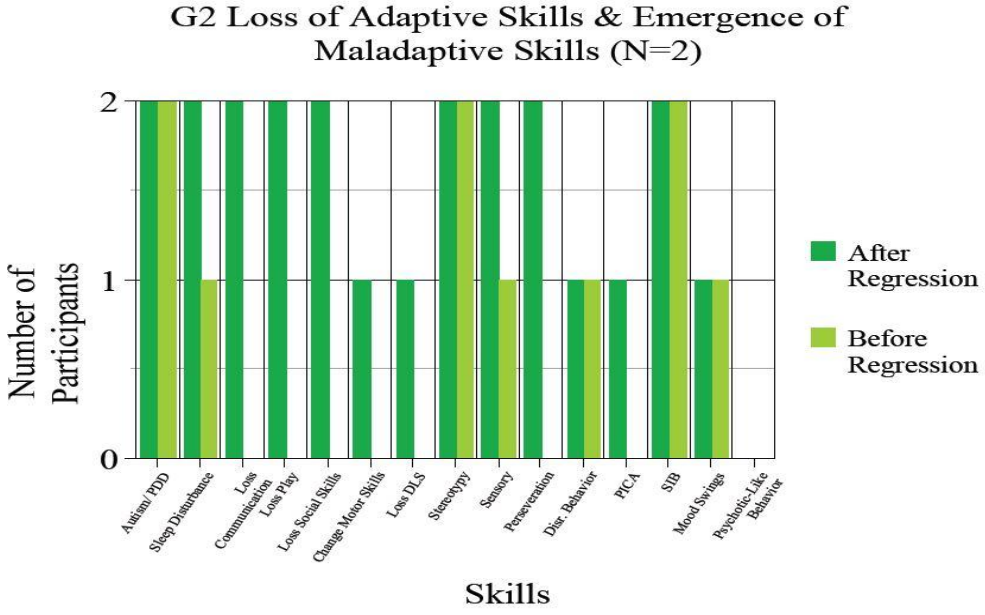


Figure 15: G2 summary of loss of adaptive skills and emergence of maladaptive skills after regression.

It is important to note that while the two children might not represent "a group" per se

since there are not enough members, it was necessary to mention them apart from G1, because they did have a comorbid condition before the onset of regression, and the characteristics of their regression are somewhat different from the participants in G1.

Neither of the two children had stressors before regression, and both had a loss of communication, social skills, and play; after regression both had sleep disorders although P11 had sleep problems before regression. Only P10 had a change of motor skills level, and after regression, he no longer could run or jump. Loss of daily living skills was experienced also by P10. Because they had ASD/ PDD previous regression, both had stereotypy. Sensory problems such as brushing teeth, trim nails and loud noises for P 10 came after regression. For P 11 problems were noticed after regression.

Both participants had developed certain perseverative behaviors after regression; P10 would only walk in certain parts of the house, and P11 would want to have doors closed. However, as per disruptive behavior, only P11 had developed problems before regression occurred.

SIBS after regression were experienced by both participants, but only P11 had Pica and mood swings. None developed psychotic like behaviors.

Case 2 Analysis: A Boy with Developmental Regression Occurring Around the Age of 4 Years and 3 Months.

Summary introduction of the case.

CJ came to DSC at KKI at the age of 6 years and 3 months with a recent episode of developmental regression. His behavior at the time was characterized as aggressive, and he lacked communication skills. He engaged in stereotypical and self-stimulatory behavior, including head shaking, humming, grinding teeth, and hand flapping.

At around the age of 4 years, he lost most of his speech skills. Although he had some echolalia, before regression he had expression of 250 words combinations of signing and talking. Receptively, he knew his name and body parts and could follow simple verbal instructions consistently; however, he no longer pointed to any body parts or spoke. His behavior worsened until 4.5 years when he was described as totally out of control. Gradually, his behavior improved somewhat then worsened again at the time he came to the DSC KKI. He would show aggressive behavior towards his siblings and occasionally towards parents and teachers.

Developmental history.

CJ is the older of two siblings, both reported to be healthy and doing well. Furthermore, according to his parents, there is no history of intellectual disability or other disability in any side of the family.

Pregnancy and birth history.

According to CJ's mother, pregnancy lasted 38 weeks, and CJ was not very active in uterus. There was a premature labor noted at 30 weeks that responded well to medication. She also was diagnosed with placenta previa, although there were no episodes of bleeding, and he was delivered through C-section.

CJ remained in the hospital for three days as an echocardiogram showed some irregularities; he developed hyperbilirubinemia requiring phototherapy and required oxygen for the first three weeks of life.

As an infant, he had some problems with feeding and was described as fussy baby, with some irregular sleeping patterns.

4 months old. His parents went for a pediatric follow-up at the local university medical center and found that CJ was doing well; no particular concerns were noted. However, between 6

and 9 months, his parents noticed that he would like to stare at ceiling fans and lights.

12 months old. CJ's mother reported that he would rock back and forth and did some mild head banging. He learned how to operate music books with his chin, and he would play them constantly. Mom also noticed that CJ liked one-on-one attention but avoided larger groups. He did not manifest separation anxiety if he was left on his own.

18 months old. CJ's physical and occupational therapist reported that he had made significant gains in his gross motor skills. He could crawl all around the house and stairs and could pull up himself and cruise along the furniture. He also had a wide variety of grasping appropriate to the size and shape of the object and was starting to place pieces in a hole. Scribbling had improved nicely, showing some preference for the right hand.

In terms of food, he was eating a variety of easily chewed table food and was finger feeding independently.

3 years and 1 month old. CJ's preschool teacher, using the Sequenced Inventory of Communication Development, evaluated his receptive language age, placing him in a 24 month level, and his expressive language age, placing him in a 20 month level.

At the same time, the Department for Students Personnel of the city public schools also evaluated his skills and developmental level using Bayley Scales and Vineland parent and teachers scales. For the evaluations, CJ wore his glasses, but according to the psychologist, his behavior interfered throughout all evaluation. He frequently ignored directions, threw the test materials, and verbally refused to cooperate. He did demonstrated pre-academic skills such as matching colors, counting to three, and attending to a story. After the evaluation, CJ's mother was asked about his adaptive behaviors at home. She explained that CJ had demonstrated some of those skills in the past, but that now he seemed to get bored and wanted something new. She

also was concern with his level of stubbornness and need for perfection.

On the Bayley Scales, his developmental age was 22 months. At the Vineland Adaptive Behavior Scale-Parent Form, his composite was at the 22 month level. Specifically, the results are as follows (no more detail was given):

- Communication: 21 months
- Daily living: 23months
- Socialization: 22 months
- Motor skills: 21 months

3 years and 3 months old. CJ's classroom teacher, with input from the speech and language pathologist, occupational therapist, and the physical therapist, filled a non-disclosed scale and their findings placed CJ at the following levers:

- Fine motor at 20-23 month level. CJ placed pegs in a pegboard, imitated vertical, horizontal and circular strokes, and unscrewed lids. He was also able to build eight cube towers and completed three pieces of foam board.
- Cognition at 20-23 month level. CJ was able to imitate movements, activate objects, match objects, sort, put together three piece puzzles, and count his fingers.
- Language at 20-23 month level. CJ would imitate new sounds, words, names, and names of objects with pictures. He also had the ability of pointing to named pictures and would use one to two word sentences using words, gestures, and signs.
- Social/emotional at 24-27 month level. CJ could independently choose the toys that he wanted to play with and play with them. His play was solitary although

near to other children, and he could play pretending.

- Feeding/oral motor 20-24 month level. CJ drank from a cup, used a straw, spoon, and fork.
- Gross/Motor 22 month level. CJ could walk on uneven surfaces. He would jump and walk up and down the stairs holding to the railing.

Behavioral. Teachers noted in class that he had a tendency to be very stubborn and a perfectionist, and he would not try things if they were too hard or were not highly motivating for him.

3 years and 11 months old. CJ's mother reported to the classroom teacher that CJ had approximately 250 words and around 120 signs. She wrote down all words and sentences that he would most often use and noticed that he communicated at times if he wanted to read a book or get a drink.

In her report, she mentioned that CJ had problems with mouthing (although when contingencies were in place, there were less mouthing) and some strong food texture avoidances for the past year. CJ's mother explained that he used to eat a large variety of foods except crunchy or hard to chew foods, and he did not tolerate red juices due to reflux. Like past teacher observations, CJ was defined as stubborn and difficult to motivate at times although he had improved for the past months.

4 years and 6 months old. CJ fell and hit his head and seemed to have a one brief seizure without loss of consciousness but the entire episode did not last more than a minute. An EEG was done shortly after with normal results.

4 years and 8 months old. CJ was brought by his parents to the University Medical Center for a behavioral evaluation. His parents' concerns at this point were impulsivity, mouthing,

obsessive door closing, PICA (mostly sand and glue), and stereotypic behavior (head shaking, hand clapping, and arm flailing). The parents also noticed plateau and regression especially in language signed and spoke.

During the visit, the clinician noticed as well as the parents that CJ did not display any functional language and displayed frequently stereotypic movements including hand clapping and head shaking. He also had some screaming that tended to escalate until re-directed.

Two months later, at the age of 4 years and 11 months the Department for Students Personnel of CJ's city public schools again assessed his developmental level using Bayley Scales for Infant Development second edition and Vineland Adaptive Behavior Sales. On the Bayley Scales, his developmental age was at the 18 month level. For Vineland, his scores were as follows:

Vineland Adaptive Behavior Scales-Interview parent:

- Communication: 14 month level (previously 21 month level)
- Daily living skills: 19 month level (previously 23 month level)
- Socialization: 10 month level (previously 22 month level)
- Motor skills: 21 month level (previously 21 month level)
- Adaptive behavior composite: 16 month level (previously 22 month level)

Vineland Adaptive Behavior Scales -Classroom:

- Communication: 14 month level
- Daily living skills: 16 month level
- Socialization: 15 month level
- Motor skills: 20 month level
- Adaptive behavior: 16 month level

During the assessment, the clinician observed that CJ did not use any words during one-on-one testing. He did not respond when asked to point to body parts or pictures of common objects. According to this clinician, these skills were reportedly present when CJ was assessed two years previously, and the clinician concluded that this loss of skills was consistent with CJ's parent's reports.

CJ was also evaluated for autism using the Childhood Autism Rating Scale and the Autism Behavior Checklist. The results of both instruments given indicated CJ's behavior was in the non-autistic range and that he was acting out just to get attention, since his parents had a new baby and had just moved into a new house.

6 years old. CJ's classroom teacher reported that CJ displayed many autistic-like behaviors such as hand flapping, finger clapping, waiving arms, shaking head, and making loud noise. She also reported that he would not participate willingly nor spontaneously join in classroom activities unless made to do so, as he preferred to sit alone. She also noticed that CJ had some avoidance behaviors such as shaking his head "no" or closing his eyes, as well as some mood swings, from sad to laughing for no apparent reason.

The teacher talked to CJ's past teachers and stated that apparently CJ had lost many skills that he had mastered before. She reported that she only had heard three words from him: "no," "bye," and "car," and he displayed very limited spontaneous signs.

6 years and 3 months old. CJ was brought to KKI to the DSC. Mom's primary concerns included behavior and communication skills. He engaged in stereotypical and self-stimulatory behavior including head shaking, humming, grinding teeth, and flapping hands. Lately, he had also displayed some aggression towards his siblings. Mom also elaborated on his loss of previously mastered skills at around age of 3 years and 4 months when he was functioning at 22

month level. Shortly after, he stopped signing, speaking, and was no longer able to communicate, and his behavior gradually worsened.

It terms of sensory problems, CJ liked to mouth rubber objects, an activity that had increased the last 9 months. He disliked loud noises, crowded places, haircuts, or having his teeth brushed. Clothing of rough texture did not bother him or the noise of the vacuum or the blender. Mom observed also that he was no longer interested in ceiling fans or dangling objects in front of his eyes. He had strong food preferences, but he was expanding to meats and vegetables; nevertheless, he did not like crunchy textures.

CJ's mother described his mood as content and happy although he was also distractible and impulsive. His sleep was reported to be somewhat disturbed.

Thyroid studies were reported to be normal. He continued having a mild loss in the left ear and needed prescription glasses that would correct his farsightedness.

During their visit to the DSC, the parents completed the Aberrant Behavior Checklist (see Tables 10 & 11 and Figure 16). He scored a total of 69 points, with the higher scores in hyperactivity, stereotypies, and lethargy. This score did not differ significantly with those scores found in children with DS + ASD without regression.

On the Autism Behavior Checklist, his score was 100, placing him with in the category of autism. No words or signs were observed, and there was no interaction during the visit. His attention was atypical, and CJ also had a number of self- stimulatory behaviors, such as rocking, shaking his head back and forth, and hand flapping. CJ would also moan and presented bruxism.

The pediatrician's diagnosis was ASD based upon the deficits in social reciprocal interaction, lack of intentional communication, and preoccupation with repetitive and stereotype behaviors.

Table 10 *ABC Scales for Participant CJ*

ABC subscales 3-13yr	*ASD*	*DBD**	*Typical*	*CJ*	*Maximum Score*
Hyperactive	**21.4**	**28.5**	**7.4**	**24**	**48**
Irritable	**13.2**	**14.9**	**3.3**	**10**	**45**
Stereotypies	**12.4**	**2.9**	**0.8**	**14**	**21**
Lethargy	**18.6**	**5.4**	**1.9**	**21**	**48**
Inappropriate Speech	**2.4**	**2.9**	**0.9**	**0**	**21**
Total	**68**	**54.6**	**14.3**	**69**	**183**

Note: Comparison is made typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr). Notice her overall high scores.
*DBD: Disruptive behavior disorder

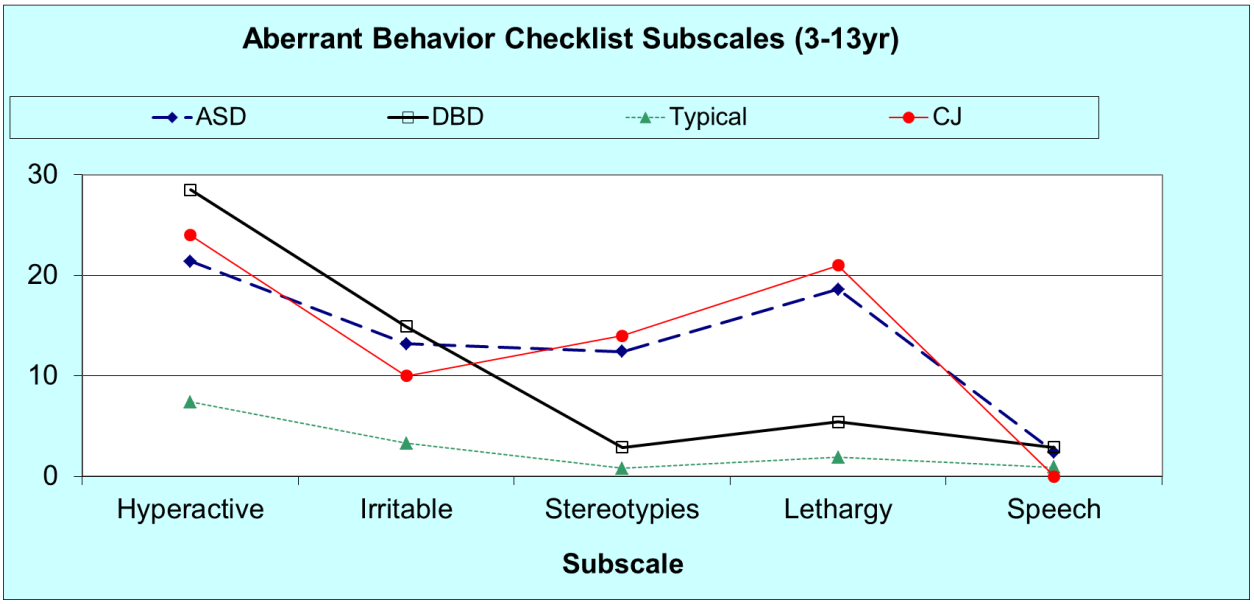


Figure 16: ABC subscales graph for participant CC: comparison is made typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr).

Table 11 *ABC Derived Behavioral Clusters for Participant CJ: Comparison is made of Typical Children with DS and DS+ASD OR DS+ DBD*

ABC clusters 3-13yr	ASD	DBD	Typical	CJ	Maximum Score
Motor activity	**8.7**	**11.5**	**2.2**	**7**	**21**
Disruptions	**7.3**	**11.2**	**2.3**	**9**	**18**
Inattention	**8.7**	**8.5**	**2.6**	**10**	**15**
Aggression-verbal	**3.2**	**3.4**	**0.2**	**0**	**9**
Aggression-physical	**1.5**	**2.1**	**0.3**	**3**	**6**
SIB	**2.6**	**0.7**	**0.2**	**2**	**9**
Mood	**4.6**	**4.9**	**1.3**	**2**	**15**
Apathy	**7**	**1.6**	**1**	**8**	**21**
Social Withdrawal	**11.7**	**3.8**	**1**	**13**	**27**
Stereotypy	**12.4**	**2.9**	**0.8**	**14**	**21**

Note: Notice that clusters are separated in two groups, externalizing behaviors and internalizing behaviors.

A comparison among testing (see Table 12) provides evidence of the decline of CJ's abilities over time. At the age of 3 years and 1 month on Bayley Infant Developmental scales, his developmental had been 51 points, compared to 30 points at age 4 years and 11 months.

At the same ages, his score followed this trend. According to his scores at the Vineland Parent Interview, his communication skills appeared to be at the 21 month level at the age of 3 years and 1 month, whereas at the age of 4 years and 11 months, it fell to the 14 month level. Socialization also fell from the 22 month level to a 10 month level, and adaptive behavior went from the 22 to the 16 month level. The only skill with no change was motor skills.

From the teacher's perspective, there were also substantial changes in CJ's abilities when compared over time. Furthermore, the scores on the Vineland Teacher's interview at the age of 4 years and 11 months were in concordance with his parent's answers. His socialization score, however, was the only place where his parents and teacher had differences for the testing at the

age of 4 years and 11 months. His parent's interview scores placed CJ at the 10 month level, whereas the teacher's interview score placed him at the 15 month level.

Table 12 *Summary of CJ's Available Testing's Scores through the Years and Evidence of Cognitive Decline*

SKILL	$3^{1/12}$ y/o	$3^{3/12}$ y/o	$4^{11/12}$ y/o	$6^{3/12}$ y/o
Words/ signs spoken	250	?	None	None
IQ/DQ	**Bayley Developmental age:** 51 DQ	Teachers evaluation of developmental age: 55 DQ	**Bayley Developmental Age**: 30 DQ	**Rosseti Scales**: 20 DQ
Communication	**Vineland Parent Interview** 21 month level	?	**Vineland Parent Interview**14 month level	**Rossetti Scales:** *Receptive* scattered 0-9 month level *Expressive* solid 0-3 month level
Daily Living skills	**Vineland Parent Interview**23 month level	?	**Vineland Parent Interview**19 month level	
Socialization	**Vineland Parent Interview**22 month level	24-27 month level	**Vineland Parent Interview**10 month level	
Motor Skills	**Vineland Parent Interview**21 month level	*Fine motor* 22 month level *Gross motor* 22 month level	**Vineland Parent Interview**21 month level	
Adaptive Behavior	**Vineland Parent Interview**22 month level		**Vineland Parent Interview**16 month level	
Communication			**Vineland Teacher Interview**14 month level	
Daily Living skills			**Vineland Teacher Interview**16 month level	
Socialization			**Vineland Teacher Interview**15 month level	
Motor Skills			**Vineland Teacher Interview**20 month level	
Adaptive Behavior			**Vineland Teacher Interview**16 month level	

At the age of 6 years and 3 months, CJ was evaluated using the Rossetti Infant Toddler Language scale, which placed his communication abilities between the 0-9 month level for receptive skills and at the 0-3 month level for expressive skills. This test, however, is designed

for infants from 0 to 3 years of age.

This case represents an example of regression for G2. This case is an example of developmental regression at around the age of 3 years and 5 months in a child with DS with unstable development, autism-like behaviors, and behavioral problems. Before regression, CJ expressively had a communication capacity of about 250 words, that is, a combination of signing and talking paired with echolalia. By the age of 4 years and 8 months, he developed PICA and the need to have the doors closed, and by the age of 6, he was given the diagnosis of autism and no longer speaks. Both cases for this group, P 10 and P 11, represent a type of developmental regression in children with DS and ASD symptoms at around the age of 3 to 4 years. Both children lost communication, play, and social skills, and both developed perseverative behaviors after regression; however, none developed psychotic-like symptoms. SMD and SIBS were already present before the regression and continued after regression developed.

Group 3 Results

Group 3 is represented by 5 participants (P12- P16), 3 males and 2 females, whose mean age at the moment of regression was 7.1 years (see Table 3, 4, 5, 6 and Figure 17). The mean duration of the regression for this group was 18.6 months, and all but one, P15, had a diagnosis of ADHD, ADD, and/or SMD before their onset of regression. All children had a diagnosis of autism after regression, and all also experienced sleep disturbances during or after their regression. However, only one participant had stressors before the onset, P16, who suffered a traumatic EEG that was testing for staring spells. After that, parents noticed that he would not allow anyone touch his face and started losing skills. The entire group lost communication and social skills and all but one lost play skills, P13, whose information on loss of play skills could

not be found. In terms of motor skills, only two participants were reported to have an apparent loss. Participant13 semmed to have lost oral skills and P15 seemed to have lost fine motor skills, according to the reports. The same participant, P13, was also the only who also lost daily living skills, such as feeding, potty, and dressing. The data for two other participants (P14 and P16) could not be found in this area, and the other two did not have a loss.

In terms of emergence of maladaptive behaviors, stereotypy was present in four participants after regression occurred, and only one, P14, had stereotypy before regression. Sensory problems were also found in all children in this group. The most frequent problem found was refusal of certain food textures and brushing or cutting hair. Three participants manifested this problem before regression and two after the onset.

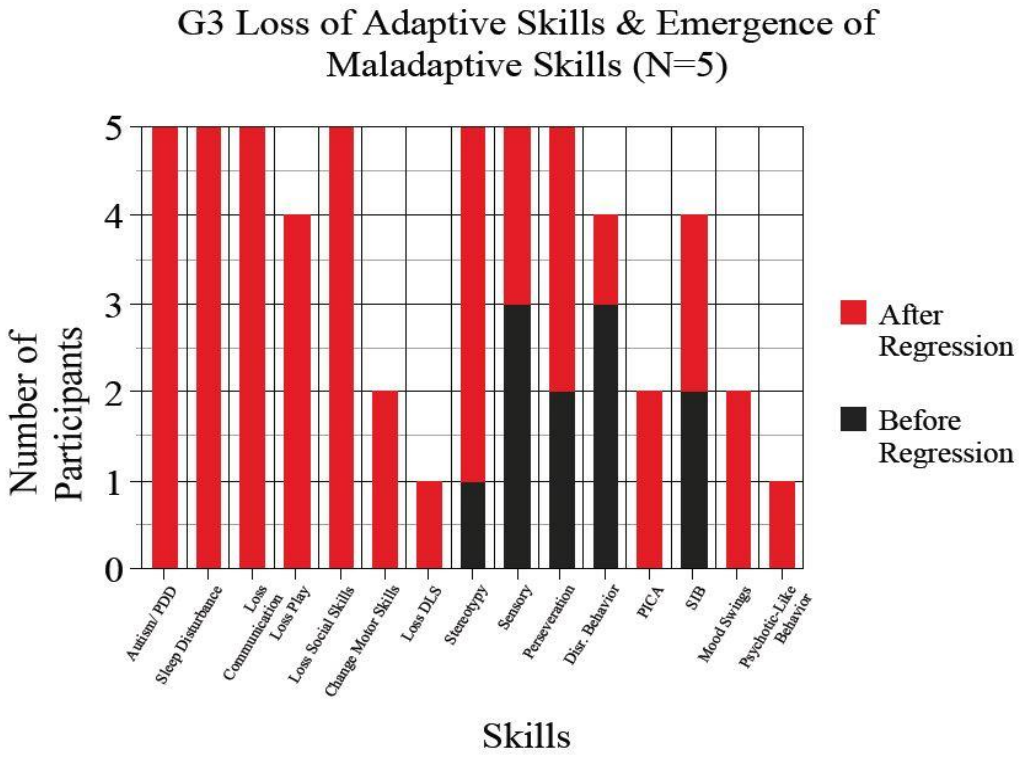


Figure 17: G3 summary of loss of adaptive skills and emergence of maladaptive skills before and after regression.

Perseverative behavior was developed in three cases after regression, while the other two

already had it before the onset. There was no common behavior in this group; they all had different preferences, such as straightening blankets, lining up objects, shaking cloths on hangers, or dangling objects.

Disruptive behaviors were experienced by four of the participants on this group, two before regression and two after regression. Pica was developed by only P13 (sand, feces, leaves, grass, dirt, and soap) and P16 (no detail was given).

Self-injurious behavior was also common in this group (in 4 participants out of the 5), unlike psychotic behavior, which was suffered only by one participant, P13, who also had mood swings. Participant 15, according to parents, also had some mood swings; she would switch from crying to laughing with no apparent trigger. This observation was frequently described by other parents or professionals in their children.

Case 3 Analysis: A Boy with Developmental Regression at the Age of 7 with a History of ADHD Like Behaviors.

Summary introduction of the case.

This case presents a boy with DS who came to the DSC at KKI with symptoms of developmental regression occurring at around the age of 7 years. Previous to his developmental regression, he had a history of ADHD-like behaviors with stereotypies and sensory problems.

TT first came to the DSC at KKI at the age of 4 years and 6 months. When TT was at the age of 3 and 9 months, he would engage in imaginative play. He could run and kick a ball and was starting to pedal. His expressive vocabulary consisted of a large vocabulary and small sentences. No behavioral issues were a concern, other than a short attention span present since the age of 2 years.

By 4 years, he was starting to adapt and participate in class activities; he would attend to

familiar stories and songs within the classroom but had problems when new activities were presented, and his answers could be inconsistent. TT could recognize the picture symbol from each one of his classmates and respond to it correctly. He could also point to pictures in books and greet his peers. TT was also more consistent than previously with using three word sentences spontaneously. Nevertheless, teachers were concern with his lack of compliance and some disruptive behaviors.

At 6 years, TT had already received the diagnosis of ADHD and stereotype movement disorder. Sensory integration problems were also observed. However, the school reported he was making progress in academics, self-help tasks, and attention.

By 7 years, teachers could not engage him. His eye contact was poorer, and he no longer would repeat phrases or words. Also, both his parents and teachers reported his spontaneous language decreased dramatically. His sensory problems became more acute as well as his stereotypies. He was restless and irritable. Six months later, he was diagnosed with a PDD-like regression.

Developmental history by age.

TT came to DSC at KKI at the age of 4 years and 6 months. The concerns presented at that time were his short attention span (since the age of two), lack of compliance with certain activities (especially fine motor tasks), and his habits of chewing and mouthing objects and sucking on fingers.

TT is the older sibling of three children, and his parents report the other two siblings do not have intellectual disabilities. Furthermore, there is no history of other disabilities among other family members.

Pregnancy and birth history.

The mother's pregnancy and delivery were reported to be normal, although because of pulmonary hypertension and jaundice shortly after delivery, TT remained in the hospital for two weeks. Other medical history includes myopia, multiple ear infections, and several replacements of tympanostpy tubes (PE-tubes). He also had sinus infections but no loud snoring or sleep apneas were reported. A tonsillectomy and adenoidectomy were also preformed previous to visiting KKI.

Toddler from 12-36 months.

TT walked at 28 month and attended a regular Pre- K class with 20 other students two mornings a week for three hours. He also attended to a special education preschool program five days a week in the afternoons with 11 other students. Other therapies included speech and occupational therapy privately one time a week for 50 minutes.

3 years and 9 months old. TT went to Children's Hospital for an assessment. His hearing was normal as well as his thyroid function. He was described as a picky eater but trying new textures. At that time, he also had myopia that was corrected with glasses.

For motor development, TT was able to run, dump objects from a container, throw and kick a ball, and was starting to pedal a tricycle. He would engage in imaginative play, and his expressive communication consisted of a large vocabulary and two to three word sentences. There were no behavioral complaints from school or home, although during the visit, the clinician noticed that TT had some issues controlling behavior.

4 years old. According to preschool reports, TT was just beginning to adapt and participate in class activities. TT preferred to be left alone with the activity that he chose, although with some resistance he could be redirected to a different one. It was also noted in the report that TT would attend to familiar stories and songs but would not attend to an unfamiliar

task. However, he would react positively to the use of pictures for activity transitions and would become engaged once he was familiar with the task. He would avoid situations or demands by "fleeing" the situation, and by avoiding eye contact with either the materials or the speaker. When inattentive, he would not answer to familiar questions.

In terms of preschool concepts, TT was able to hand a circle and a triangle to the teacher. He recognized the symbol of each one of his classmates and would hand it correctly to each classmate as well as pointing at pictures in a story book. When the teacher would ask him to write his name, he would make marks in a paper.

Socially, TT would greet familiar adults and peers with eye contact and a smile directed to them. He would also say "hi" to his peers. For playing skills, TT also expanded the variety of toys that he played with, from only dolls to plastic animals and cars, although his favorite game was housekeeping activities. Among his pretend play was "eating fake food." During recess, TT would use the playground, slides, cars, and sometimes the tricycle. At that time, it was noticed that he would not start interactions but did not mind having classmates playing with him or his toys.

For self-help skills, TT was able to take out his coat and place it near his cubby. He knew the place for his folder, and he would place it correctly. He still did not use the toilet but was interested in it.

His communication skills were developing slowly, and his attention for speech tasks was variable. He enjoyed circle time and usually would respond to "what" questions, and name objects using one word utterances, although two word utterances were emerging. He could identify body parts with 75% accuracy and name pictures of common objects and animals with 80% accuracy. TT was able to imitate signs and enjoyed signing songs; he also had good

understating of concepts such as “mine,” “up,” “down,” “by,” “little,” or “in.” It was noticed that he would place objects in his mouth frequently. TT would use signs to request basic needs such as “more,” “juice,” or “swing.”

According to the occupational therapist, his progress was slow due to his problems with inattention. TT was perceived as very self-directed in his play, and allowing hand on hand during intervention was challenging. One of TT’s preferences was the sensory table. Once TT adjusted the textures, the length of the time he was engaged before he needed to wash his hands increased. The therapist noticed progress in his pincer grasp, drinking from open cup, and putting his coat on.

TT’s special education teacher noted progress but she was concerned with his behavior and his noncompliance. TT would refuse to participate in activities, especially those of high demand like fine motor skills, by dropping on the floor and verbally refusing the request. He would also use inappropriate laughing.

4 years and 3 months old. TT had a new sibling and no adjustment problems were reported.

4 years and 6 months old. TT came to DSC at KKI for an evaluation. Parent’s concerns when they came to the clinic were related to TT’s short attention span, his lack of compliance, and his habits of chewing and mouthing objects as well as sucking his fingers. These behaviors, according to parents and school teachers, were impacting his learning. Nevertheless, according to his parents, TT’s overall progress was good. He had approximately 100 words and no signs. He would speak in one to two word sentences, although two to three word sentences were emerging, and he was more willing to speak. Receptively, he had around 100 words; he would point to three or four body parts, and he would follow one step direction. His parents pointed out

that his comprehensive language skills were better than his receptive skills.

At this point, TT would feed himself, undress, and would cooperate with dressing. According to parents, he was not interested in potty training. His sensory aversions were having his hair cut, brushing teeth, and loud noises. When the vacuum cleaner was on, he would scream, chews his fingers, grind his teeth, and did humming noises. Parents also noticed that when he did humming noises, he would be "like in another world." He often would also jump and flap his hands while chewing. TT did not have problems going to sleep until recently, when his parents found him to be more resistant. The DSC pediatrician at KKI noted in his report that TT had "ADHD like symptoms with stereotypies, oral-sensory seeking and negative responses to aversive sensory stimuli." His parents answered the Aberrant Behavior Checklist (Aman, Singh, Stewart, & Field, 1985) at the time of the visit. His total score was 45 out of 183 points (see Table 13 & Figure 18).

Table 13 *ABC Scales for Participant TT and Age of 4 Years and 6 Months*

ABC subscales 3-13yr	ASD	DBD*	Typical	TT 1st	Maximum score
Hyperactive	21.4	28.5	7.4	35	48
Irritable	13.2	14.9	3.3	2	45
Stereotypy	12.4	2.9	0.8	5	21
Lethargy	18.6	5.4	1.9	3	48
Inappropriate Speech	2.4	2.9	0.9	0	21
Total	68	54.6	14.3	45	183

Note: Comparison is made typical children with DS and subjects with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr). Notice her overall high scores.
*DBD: Disruptive behavior disorder

The highest punctuation was for the scale that measures hyperactivity where he scored 35 points out of a maximum of 48. The cluster analysis (see Table 14) reveled that motor activity and inattention were the items where TT scored higher. For motor activity, TT scored 17 out of

21 possible scores, and for inattention he scored 11 out of 15 possible points. However, his stereotypy was not significantly high, as he scored only 5 out of 21 possible points.

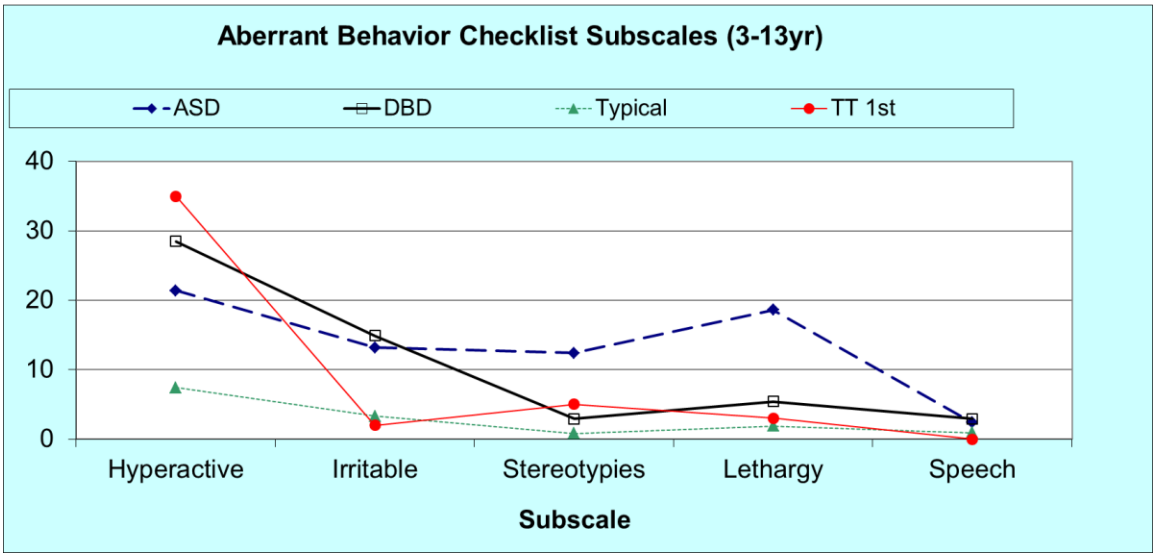


Figure 18: ABC subscales graph for participant TT at age 4 years and 6 months: comparison is made typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr).

Table 14 *ABC Derived Behavioral Clusters in Participant TT at the age of 4 Years and 6 Months: Comparison is made of Typical Children with DS and DS+ ASD or DS+DBD*

ABC clusters 3-13yr	ASD	DBD	Typical	TT 1st	Maximum Score
Motor activity	8.7	11.5	2.2	17	21
Disruptions	7.3	11.2	2.3	8	18
Inattention	8.7	8.5	2.6	11	15
Aggression-verbal	3.2	3.4	0.2	0	9
Aggression-physical	1.5	2.1	0.3	0	6
SIB	2.6	0.7	0.2	0	9
Mood	4.6	4.9	1.3	1	15
Apathy	7	1.6	1	1	21
Social Withdrawal	11.7	3.8	1	2	27
Stereotypy	12.4	2.9	0.8	5	21

Note: Notice that clusters are separated in two groups, externalizing behaviors and internalizing behaviors.

His overall progress in gross motor skills, according to the therapist, was good as he was

walking at a two and a half year old level. Also, his hearing evaluation and thyroid study were all within normal limits.

4 years and 9 months old. TT went back for a visit to the Children's Hospital for a follow-up. According to the clinician, TT improved slightly with broadening food intake and dressing skills. He was more consistent in using three word sentences and more spontaneous in his speech. At that point, he seemed interested in playing soccer and pedaling. It was also noticed that TT could be impulsive and distractible; he also showed some preservative behaviors and sensory preferences.

4 years and 10 months old. TT came back to the DSC at KKI still presenting symptoms of ADHD; he also would chew hands and objects and hum when tired. These behaviors worsened over the following four months to the point of becoming continuous. His eye contact was fleeting, and his behaviors were more disruptive. Medication was prescribed for his hyperactivity.

5 years and 8 months old. At a follow-up visit at KKI DS clinic, the pediatrician found TT had better attention, better communication and good eye contact. He still demonstrated some stimulating behavior but not as actively as in previous visits.

6 years and 2 months old. At the time of the follow-up visit at DSC at KKI, TT was found to be very restless. He was jumping and stimming with fingers in his mouth; however, his attention in school had improved. His speech was progressing, as it was more spontaneous; the same was true for his daily living skills. TT's sleep was not disturbed, and parents shared that TT was receiving sensory intervention at school. At that time, his thyroid function was tested and results came back normal.

6 years and 8 months old. TT came back for his scheduled follow-up visit at the DSC at

KKI. According to his mom, TT was vomiting daily before lunch, although his learning in school was progressing and he seemed interested in other kids. He would participate in circle time, and his comprehension seemed better. The pediatrician's observation was that TT was alert but not overactive, and he was also affectionate with no oppositional or disruptive behaviors.

7 years and 1 month old. The parents returned to the DSC at KKI because TT seemed to have more sensory issues, and for the past months, he had multiple ear and throat infections, making him feel very uncomfortable. Now his hand was in his mouth at all times. Teachers also noticed that they could not engage him, and his school progress seemed to be very poor. He was no longer repeating phrases and had very limited eye contact. His speech declined sharply, and he seemed very restless and irritable. The doctor's exam found TT much less responsive, distractible, and his activities and movements were less purposeful. His eye contact was very limited also, and his affect seemed blunted. His diagnosis was pervasive developmental-like disorder with regression. A month later, TT no longer repeated words and had sleep difficulties. At that time, a sleep study was performed, and snoring was present but no apparent apnea.

During the visit, the parents completed for the second time the Aberrant Behavior Checklist (Aman, Singh, Stewart, & Field, 1985). TT's total score on the checklist was 63. The hyperactivity, stereotypyes, and lethargy subscales were his highest scores (see Tables 15 & Figure 19). TT's score for hyperactivity was 19 out of a possible total of 48; for stereotype scale, his score was 13 out of 21, and for lethargy, his score was 28 out of 48. The cluster analysis (see Table 16) provided further evidences that stereotypy, inattention and social withdrawal were the items where TT scored highest in comparison with the other clusters.

Table 15 ABC Scales for participant TT at the age of 7 Years and 1 Month

ABC subscales 3-13yr	ASD	DBD*	Typical	TT 2nd	Maximum Score
Hyperactive/ADD	21.4	28.5	7.4	19	48
Irritable	13.2	14.9	3.3	3	45
Stereotypy	12.4	2.9	0.8	13	21
Lethargy	18.6	5.4	1.9	28	48
Inappropriate Speech	2.4	2.9	0.9	0	21
Total	68	54.6	14.3	63	183

* *Note:* Comparison is made typical children with DS and subjects with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr). Notice her overall high scores.
*DBD: Disruptive behavior disorder

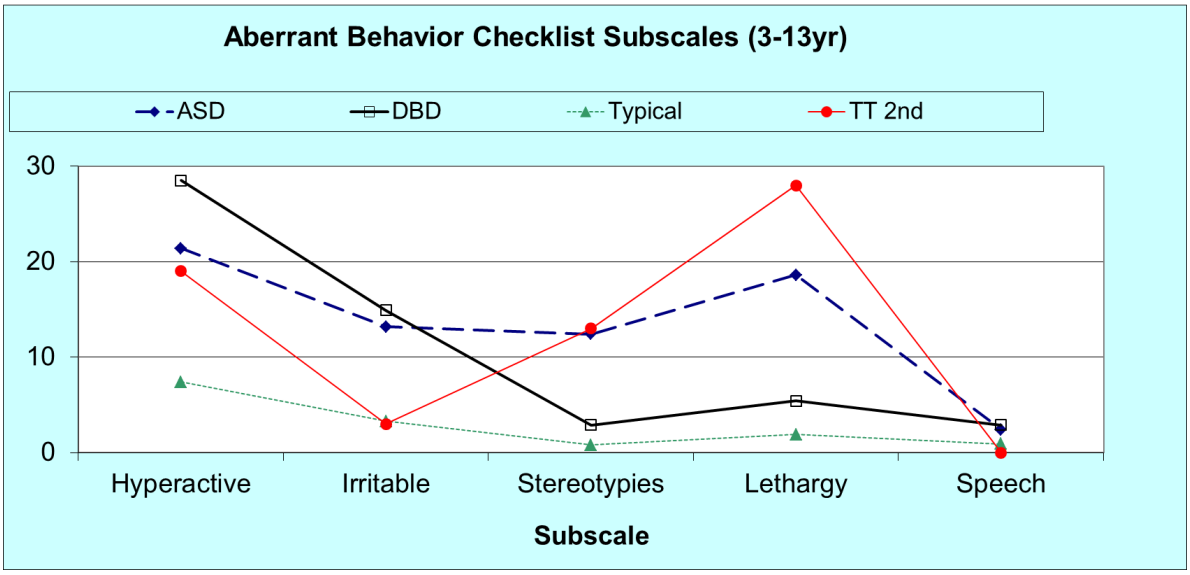


Figure 19: ABC subscales graph for participant TT at the age of 7 years and 1 month: comparison is made of typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr).

Table 16 *ABC Derived Behavioral Clusters in Participants TT at the Age of 7 Years and 1 Month: Comparison is made of Typical Children with DS and DS+ ASD or DS+ DBD*

ABC clusters 3-13yr	ASD	DBD	Typical	TT 2nd	Maximum Score
Motor activity	8.7	11.5	2.2	8	21
Disruptions	7.3	11.2	2.3	3	18
Inattention	8.7	8.5	2.6	10	15
Aggression-verbal	3.2	3.4	0.2	0	9
Aggression-physical	1.5	2.1	0.3	0	6
SIB	2.6	0.7	0.2	0	9
Mood	4.6	4.9	1.3	1	15
Apathy	7	1.6	1	6	21
Social Withdrawal	11.7	3.8	1	22	27
Stereotypy	12.4	2.9	0.8	13	21

Note: Notice that clusters are separated in two groups, externalizing behaviors and internalizing behaviors.

The hyperactivity scale refers to inattention, motor activity, and disruptive behavior. TT's high scores on the hyperactivity scale were due to the inattention cluster where he scored 10 out of a maximum punctuation of 15 (see Table 16), and to a lesser degree, his motor activity where he scored 8 out of a maximum score of 21. The lethargy subscale refers to internalizing behaviors such as apathy, low motivation, social indifference, and affective blunting. TT's total score in this scale was 28, and the clusters analysis for lethargy subscale indicated that higher scores were coming from social withdrawal (22 out of 27 points) and stereotypy with a score of 13 out of 21 possible points. These scores differ greatly from the scores obtained (see Table 14) when he first came to the DSC at KKI at the age of 4 years and 6 months.

Table 17 *Comparison of TT's Scores on the Aberrant Behavior Checklist first at Age 4 and 6 Months and second at the Age of 7 Years and 1 Month*

Cluster	SCORE 1st ABC (4.6 y/o)	SCORE 2nd ABC (7.1y/o)		Scales	SCORE 1st ABC (4.6 y/o)	SCORE 2nd ABC (7.1y/o)	
Motor activity	17/21	8/21	- 43%	Hyperactive/ ADD	35/48	19/48	-33%
Disruptions	8/18	3/18	-28%	Irritable	2/45	3/45	2%
Inattention	11/15	10/15	-7%	Stereotypy	5/21	13/21	+38%
Aggression-verbal	0/9	0/9		Lethargy	3/48	28/48	+52%
Aggression-physical	0/6	0/6		Inappropriate Speech	0/21	0/21	
SIB	0/9	0/9		Total	45/183	63/183	10%
Mood	1/15	1/15					
Apathy	1/21	6/21	+24%				
Social Withdrawal	2/27	22/27	+74%				
Stereotypy	5/21	13/21	+38%				

After developmental regression, TT's punctuations decreased significantly on the Hyperactivity/ADD scale (see Table 17). Cluster analysis indicated that the biggest decrease was in motor activity and disruption items whereas inattention remained almost the same. In contrast, on the scales of lethargy and stereotypy, TT's scores rose dramatically. Cluster analysis also indicated that TT was scoring higher on social withdrawal and stereotypes questions and lower in apathy. However, his scores were still higher than in his previous Aberrant Behavior Checklist (Aman, Singh, Stewart, & Field, 1985) scores at the age of 4 years and 6 months.

This case represents an example of regression for G3. This case represents an example of a child with DS with regression that occurred between the ages of 7 and 9 years. The participant was a boy with DS with a comorbid ADHD diagnosis prior to his developmental regression. His loss of skills was progressive after an unstable development, with further testing revealing that in addition to his previous diagnose with ADHD, after regression his scores on the ABC subscale

Hyperactive/ADD showed a 33% decrease on those symptoms, an increase of 52% on the lethargy subscale, and an increase of 38% on the stereotypy subscale. G3 is represented by 5 children, with regression ages between 7- 9 years and with a previous diagnosis of ADD/ADHD/SMD. This revealed a high incidence of developing autism-like symptoms, with loss mainly in communication, play, and social skills following the onset of regression. After regression, it was also noticed that all participants who did not have stereotypy, perseveration, and sensory problems did develop those. However, mood swings and psychotic-like behavior were not prominent among the children in this group. SIBS and behavior problems were experienced in all but one participant.

Group 4 Results

G4 is represented by two boys and two girls (P17- P20) (see Table 3, 4, 5, 6 and Figure 20) with regression that occurred between the ages of 9-11 years old. The mean age at regression for this group was 9.8 years, and the mean of the duration of the onset was 6.25 months. The two males of the group previous to their regression had SMD, and only P17 had also some mild autism. All of them fell in the category of autism spectrum disorders/PDD after the regressive onset, and only two parents from the group identified possible stressors that preceded the onset.

Sleep disturbance was a common characteristic in all children in this group. It mainly occurred during or after the regression; only one subject in this group had problems before regression (corrected sleep apnea).

As with the other three groups, all participants in this group lost communication, social skills and play, and all but one also suffered from a change in their motor skills; the aparent loss were mainly in oral motor skills and the change in the ability to walk with ease. Decline in some of their daily living skills was also observed by parents and professionals, specifically in the

areas of potty/toileting and feeding.

After regression, this group also experienced the emergence of maladaptive behaviors. Two participants (P17, and P20) had some stereotipy, and only one (P18) developed these symptoms after regression; the other two kept the symptoms after regression.

Sensory integration problems and disruptive behaviors were present in two participants, P17 and P20, out of the four that form this group, and only P18 developed sensory problems after regression. Interestingly, perseverative behavior was present in all children, but two had the symptoms before (for P17 it was a constant flipping of a card on his hand, and for P18 it was the need to continuously line up her toys), and two after the onset (P 20 liked to flush objects in the toilet, and for P 19, no details were given).

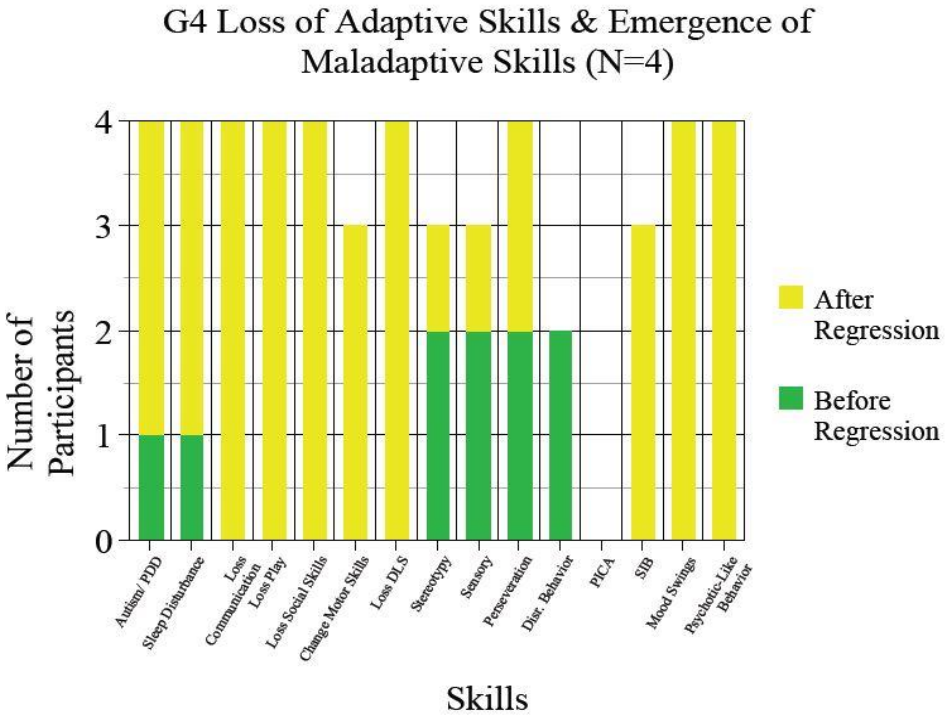


Figure 20: G4 summary of loss of adaptive skills and emergence of maladaptive skills before and after regression.

Pica was not present in any of the children on this group; however, SIBs, mood swings, and psychotic-like behavior were observed by all parents in their children after their regression. Only P19 did not have SIB. For SIBs, the behaviors described by parents were chewing on fingers, poking or touching the eyes, and head banging. For mood swings, as in other groups, these children experienced laughing and crying (or moving from happy to sad) in short periods of time without any apparent reason noted that could trigger such changes;

Psychotic-like behaviors were manifest differently among the participants on this group. P17 suffered from hallucinations, whereas P18 would spend most of the time staring at her hand. For P19 and P20, their behaviors were noted as catatonic and lethargic, as if they were out-of-touch.

Case 4 Analysis: A Female with Developmental Regression at the Age of 10 Years and 8 Months in a Girl with DS

Summary introduction of the case.

This case presents a girl (HK) with DS who came to the DSC KKI with symptoms of late developmental regression occurring at around the age of 10 years and 8 months.

At the age of 4 years and 8 months, she was administered a psychological evaluation that included the Stanford Binet Intelligence Scale 4th Edition (Thorndike, Hagen, & Sattler, 1986a). Her cognitive abilities were found to be at the borderline intellectual level (i.e., an intelligence quotient (IQ) between 71-84 (American Psychiatric Association, 2000).

At the age of 7 years and 10 months, she was re-evaluated by the school personnel in order to establish a current level of cognitive function using the Wechsler Intelligence Scale for Children Fourth edition (WISC-IV) (Wechsler, 2003). That test indicated that HK was again functioning at the borderline level.

At 8 years old, by school and parents' reports, HK would dress herself and work on the computer; her expressive language included three to four word sentences. By 10 years old, she was able to complete her homework within the time frame established by her parents, do all her assigned home care duties independently, and independently take care of her personal care activities. Soon after, by 10 years and 6 months, school personnel and her parents indicated that HK was having difficulties focusing and was not able to finish her homework in a timely manner. She also started having problems writing her name and letters, her eye contact was decreased, and she would laugh and cry for no apparent reason. She was observed to be working at a slower pace while dressing, and she needed assistance in cleaning her teeth. Her sleeping also was more irregular. Two months later, at 10 years and 8 months, HK was not answering to her name, was not able to hold a pencil, and it was impossible for her to follow previously mastered routines. Moreover, HK started to shake and twist her fingers, manifested increased guttural humming, and lacked awareness of her surroundings. Her teachers reported inappropriate sexual behaviors and an inability to use the bathroom properly.

Developmental history by age.

HK came to the DSC at KKI at the age of 10 years and 9 months. She had an older sibling who was reported to be in good health. HK's parents stated during their first visit to the DSC at KKI that there was no history of intellectual or mental disability in her family.

Pregnancy and birth history.

Based on interview information and medical records, HK's mother's pregnancy and birth were uneventful, although HK was delivered two weeks early. Her echocardiogram evaluation was negative, and no problems were reported at the nursery.

Toddler ages, from 0 to 36 months.

HK walked at 15 months. She was identified as a student with special needs by her county public school Infant and Toddler Program and received early intervention services beginning at age of 4 months. Services included speech and language, occupational, and physical therapy.

4 years old. HK attended the county preschool educational program five days a week for two hours and a half a day.

4 years and 8 months old. HK was administered the Stanford Binet Intelligence test 4th Edition (Thorndike, Hagen, & Sattler, 1986a) by a school district's licensed psychologist. HK was found to function in the mild to borderline range of cognitive functioning. A summary of her Stanford Binet scores follow (See also Table 1c):

- Verbal reasoning standard score: 65
- Abstract visual reasoning standard score: 64
- Short term memory standard score: 68
- Quantitative reasoning standard score: 72

The verbal reasoning, abstract visual reasoning, and short-term memory scores on the Stanford Binet Intelligence test 4th Edition (Thorndike, Hagen, & Sattler, 1986a) placed HK in the mildly impairment range. The quantitative reasoning score placed HK in the borderline range of abilities.

On the Vineland Adaptive Behavior Scales Classroom Edition (Sparrow, Cicchetti, & Balla, 2005), HK obtained a standard score of 62, which placed her in the mildly impaired range. On the Interview Edition, she obtained a standard score of 58, placing her in the mild to moderately impaired range.

7 years and 10 months old. While in second grade, HK was referred for a psychological re-evaluation to establish her current level of cognitive functioning. A classroom observation was also included as part of the evaluation.

The tests used in the evaluation were the WISC-IV (Wechsler, 2003) and Vineland Adaptive Behavior Scales (classroom and interview editions) (Sparrow, Cicchetti, & Ball, 2005). It is important to mention that the results on the WISC-IV (Wechsler, 2003), as indicated by the psychologist's report, were "interpreted informally to better present HK's cognitive levels" (p.3). HK demonstrated relative strengths in perceptual reasoning, visual motor integration, and coordination. She also demonstrated good ability for completing copy designs with blocks. According to the psychologist, her score was average for a 6 year old. HK also indentified the missing component of a matrix presented in a picture and was able to repeat a series of numbers presented to her orally but could not repeat two digits backwards. For matching skills, HK demonstrated the ability to match seven shapes with their corresponding mark. This skill was interpreted to be evidence of relatively good visual memory.

On the Vineland Adaptive Behavior scales (Sparrow, Cicchetti, & Ball, 2005), the interview edition was completed by her mother and the classroom edition by her classroom teacher. Her scores were in the mildly impairment range for communication and daily living skills, in the borderline range for motor skills, and in the low average range in the socialization domain. No numerical scores were provided in the written report.

Classroom observations made by a licensed psychologist indicated HK was "self-distracted*"*(p.2). Her visual ability appeared stronger than her motor skills. She was able to trace letters on paper and cut paper with a scissor. Her speech was at times unintelligible as she tended to run words together, although her verbal imitation skills were in good standing. The

psychologist notice that HK tended to learned better in group settings rather than one-on-one. She was also perceived by teachers and peers as very friendly. The psychologist concluded that her findings aligned with the previous evaluation at the age of 4 years and 8 months where HK's intellectual functioning was noted as being in the mildly impaired to borderline range. She also identified language as one area of need for more intervention for HK, specifically understanding and processing language and answering specific direct questions.

By the parent's report, at the age of 8, HK was able to dress herself, work on the computer, and had an expressive language level at three to four word sentences. She also demonstrated some preservative behaviors, oral humming, and some compulsive tendencies.

9 years and 6 months old. HK had an articulation evaluation by a certified speech pathologist. This report stated that HK presented hypotonia, which affected her oral motor strength and control, as well as dysarthria and apraxia of speech, which affected her intelligibility. Additional speech therapy was recommended for HK.

10 years and 4 months old. By parents' report during the fall of 2007, HK was able to pack and unpack her school bag, completed her homework in a reasonable time, and had no noted sleep problems. She also was able to independently dress and undress and brush her teeth. She would help in household routines and independently empty the dishwasher. She also started to get upset if her sibling would go out with friends instead of staying with her to play together at home.

10 years and 7 months old. Around January 2008, at the age of 10 years and 7 months, according to parent and school reports, HK started slowing down, taking a longer time to get dressed, and required assistance brushing her teeth. She seemed to be unable to focus and did not answer when her name was called, as if she was not aware of her surroundings. HK also started

to cry and laugh for no apparent reason and started having problems with sleeping (no sleep apnea was reported). She was unable to write letters or remember numbers and would not hold a pencil. Her eye contact also decreased dramatically, and at times she would cry while clinching her hands. Her self-stimulatory behaviors increased and new behaviors emerged, including shaking objects and twisting her fingers. Teachers also reported that HK was unable to use the toilet independently, engaged in inappropriate sexual stimulation behaviors, and failed to follow routines she had previously learned.

No infections, strep throat, fever, or other illnesses were reported before or during this general decline. HK parent's brought her to the neurologist where an electroencephalogram (EEG) test was performed. The results of the EEG fell within normal limits. A month later, in February 2008, a magnetic resonance image (MRI) was performed, and the results were found to be within normal limits.

10 years and 8 months old. In February 2008 at the age of 10 years and 8 months, HK's parents took her to a geneticist who made a diagnosis of pervasive developmental disorder (PDD) and referred HK to the DSC KKI for further evaluation. In March 2008, a psychiatrist diagnosed HK with possible depression and PDD; that physician also referred her to the DSC KKI for further study.

HK was seen at KKI in March 2008. At that time, HK received a diagnosis of late onset autism. Frontal lobe syndrome secondary to chronic sleep fragmentation, depression, and psychosis were ruled out. Her blood work also showed normal levels of thyroid hormone. Her vision was normal, and no onset of seizures was reported by parents. Her walk became slower, and some minimal loss in fine motor skills was noticed by her parents. No problems were reported in her chewing or swallowing ability. A medical history analysis did not show any

allergies, infections or recent or past hospitalizations, and her parents stated that HK was not taking any medication. Furthermore, sleep study reports done in May 2008 were found to be normal.

HK's parents completed the Aberrant Behavior Checklist (ABC) (Aman, Singh, Stewart, & Field, 1985) as part of the clinic intake process. Her total score was 42 (see Table 18, Figure 21, & Table 19). Lethargy and hyperactivity were her subscales with the highest scores. The lethargy subscale refers to internalizing behaviors such as apathy, low motivation, social indifference and affective blunting. Her total score in this scale was 16. Clusters analysis for lethargy subscale indicated higher scores in social withdrawal (7 out of 21 points) and apathy (9 out of 27 points). The hyperactivity scale refers to inattention, motor activity, and disruptive behavior. HK's relatively high scores on the hyperactivity scale were connected to the inattention cluster, where she scored 11 (see Table 19) out of a maximum punctuation of 15 and motor activity where she scored 1 out of a maximum punctuation of 21.

Table 18 *ABC Scales for Participant HK*

ABC subscales 3-13yr	ASD	DBD*	Typical	HK	Maximum Score
Hyperactive/ADD	**21.4**	**28.5**	**7.4**	**14**	**48**
Irritable	**13.2**	**14.9**	**3.3**	**3**	**45**
Stereotypy	**12.4**	**2.9**	**0.8**	**5**	**21**
Lethargy	**18.6**	**5.4**	**1.9**	**16**	**48**
Inappropriate Speech	**2.4**	**2.9**	**0.9**	**4**	**21**
Total	**68**	**54.6**	**14.3**	**42**	**183**

Note: Comparison is made typical children with DS and subjects with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr). Notice her overall high scores.
*DBD: Disruptive behavior disorder

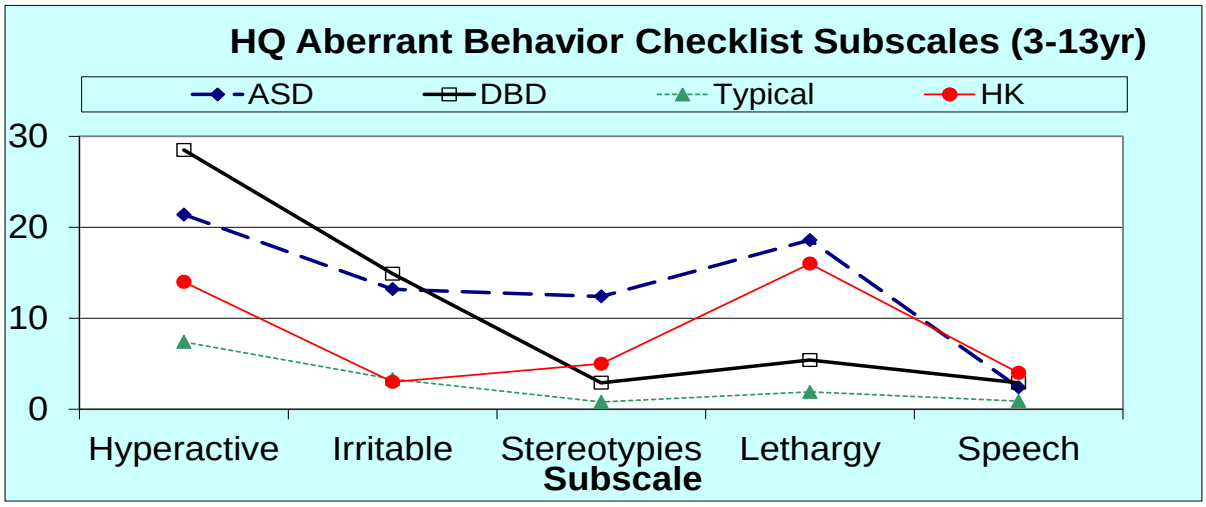


Figure 21: ABC subscales graph for Participant HK: comparison is made typical children with DS and children with a DS+ASD or DS+DBD. All data collected through the DSC from 1995-2000 (N= 305 children ages 3-13yr).

Table 19 *ABC Derived Behavioral Clusters for Participant HK: comparison made with Typical Children with DS, and DS+ASD or DS+DBD*

ABC clusters 3-13yr	ASD	DBD	Typical	HK	Maximum Score
Motor activity	**8.7**	**11.5**	**2.2**	**1**	**21**
Disruptions	**7.3**	**11.2**	**2.3**	**2**	**18**
Inattention	**8.7**	**8.5**	**2.6**	**11**	**15**
Aggression-verbal	**3.2**	**3.4**	**0.2**	**1**	**9**
Aggression-physical	**1.5**	**2.1**	**0.3**	**0**	**6**
SIB	**2.6**	**0.7**	**0.2**	**0**	**9**
Mood	**4.6**	**4.9**	**1.3**	**2**	**15**
Apathy	**7**	**1.6**	**1**	**7**	**21**
Social Withdrawal	**11.7**	**3.8**	**1**	**9**	**27**
Stereotypy	**12.4**	**2.9**	**0.8**	**5**	**21**

Note: Notice that clusters are separated in two groups, externalizing behaviors and internalizing behaviors.

In April 2008, at the age of 10 years and 10 months, HK was referred by her school team to the school district psychologist in order "to establish a current level of functioning and assist

in investigating extensive symptoms of cognitive regression" (p.1). It is important to note that the psychologist who did the evaluation was the same person who conducted previous assessments. For this evaluation, the psychologist used the Vineland Adaptive Behavior scales-Second Edition Teachers rating and a classroom observation (Sparrow, Cicchetti, & Balla, 2005). Results of the Vinland Adaptive Behavior Scale (Sparrow, Cicchetti, & Ball, 2005) are shown below and in Table 20:

- Communication standard score: 36
- Daily living skills standard score: 28
- Socialization standard score: 42

The report of the April 2008 assessment stated that HK was not able to respond to the tasks presented during testing. These were the same tasks that she was able perform three years before. The 2008 score placed her in the moderately impaired range. According to the report, this was a drop of approximately 30 points in HK's Vineland ratings when compared to her scores at the age of 7 years and 10 months.

The classroom observation report reflected the psychologist's concern with HK's performance level. She was unable to follow the small group reading activity even though she had "hand over hand" help. She was found to be frequently staring into space and was unable to locate her desk unless taken by the hand and guided to it. Reports also indicated that HK was moved from the classroom's highest academic reading group to the lowest, and the psychologist reported a significant drop in both her cognitive and adaptive behaviors skills.

Table 20 Summary of HK Tests Scores across Ages

Test	Age at testing	
	$4^{8/12}$	$10^{10/12}$
Binet Verbal Reasoning	65 standard score	
Binet Abstract Visual	64 standard score	
Binet Short Term Memory	68 standard score	
Binet Qualitative Reasoning	72 standard score	
Vineland Classroom Edition Communication		36 Standard score
Vineland Classroom Edition Daily Living		28 Standard score
Vineland Classroom Edition Socialization		42 Standard scores
Vineland Classroom Edition	62 standard score (Mild-Borderline Impairment)	(Mild impairment)

This case represents an example of regression for G4. This case presents a girl with DS who went through a period of developmental regression at the age of 10 years and 9 moths. Her functional level dropped from a borderline level of impairment to a moderately severe in a period of three months with no apparently premonitory factors that would foresee such a loss of skills from which she has not recovered to date. She lost all communication skills as well as her social and play skills, and she also developed sleeping problems and mood swings. Her motor and daily living abilities were affected, her walk slowed down, and she no longer was independent for basic grooming and toileting tasks or daily readiness for school (e.g., packing lunch, preparing her clothes, or back pack).

This participant was an example of the group of children that went through a developmental regression between the ages of 7 to 11 years. G4 represents the group with the oldest participants. As with HK, the regression of the other group members seemed more acute in certain areas, since they had more years of development before the onset. The loss of fundamental skills such as communication, socialization, and the emergence of psychotic-like

behaviors, SIBS, mood swings, and sleep disturbances made very obvious the cognitive decline in this group.

Summary

This chapter presented in detail the data on a group of 20 participants with DS who experienced developmental regression. These 20 participants were divided into groups according to their age at regression and the characteristics of their regression.

The results were 4 groups: G1, formed by 5 children (P1-P9) whose age at regression was between 2-5 years old (except for one who had 1.5 years at the time of regression)and had no signs of a comorbid condition predating regression; G2 formed by 2 children (P10- P11) with regression between the ages of 2-5 years old with signs of ASD/ PDD before the onset of regression; G3 formed by 5 participants (P12- P16) whose regression occurred between the ages of 7-9. Four participants had a diagnosis of either ADD/ ADHD or SMD; G4 formed by 4 children (P17- P20) with regression that occurred between the ages of 9-11 years old.

Data showed that all 20 children lost communication, social skills, and play skills, 10 children had a loss of daily living skills, and 8 participants had an apparent change of motor skills. Sixteen participants received a diagnosis of ASD/PDD after regression, one received the diagnosis of SMD with loss, and 3 had already shown autism symptoms predating their regression.

With the onset of regression, data also showed that there was an emergence of maladaptive behaviors among some participants, whereas in other participants those behaviors were present before their onset of regression. After regression, SMD developed in 13 cases and sensory problems in 11 participants. Perseveration developed also in 16 participants whereas behavior problems only developed in 2 participants, which was the symptom found least likely to

develop after regression among all participants. PICA and psychotic-like behavior were the second least frequently developed symptoms, affecting only 5 participants respectively. Finally, SIBs was developed by 9 participants, and mood swings were present after regression in 8 participants.

G1 was a fairly homogenous group. All 9 participants lost communication, social skills, and play, and only 2 lost motor skills and DLS as well; the two other participants lost DLS but not motor skills. Three developed sleep problems, and 8 received the diagnosis of ASD/PDD after regression, except for one participant, who was diagnosed after the onset as having SMD with loss.

The emergence of maladaptive behaviors was quite homogenous as well among the members of this group. All developed stereotypy and perseverative behaviors after regression, and all but one did not experience behavior problems after the onset. Only 2 participants had sensory integration problems previous to their regression, while the other 7 participants showed these problems after regression. Only one participant developed psychotic-like behavior or mood swings, and only 4 had SIBS and 2 had Pica.

Group 2 had only two members, and both had autism with stereotypy and SIBS predating the onset of regression. Both are boys and their profiles, along with G4, were the least homogenous except on their loss of skills, which were the same as the other groups. Both developed perseverative behavior after the regression, and neither had psychotic-like behavior.

G3 had 5 members, and 4 of them had ADHD/ADD or SMD as a comorbid condition before the onset. All received the diagnosis of autism after their regression and developed sleeping problems as well. The loss of communication, social skills, and play was present as was the case with the previous groups; only 2 lost motor skills and one also lost DLS. Stereotypy and

perseveration problems were present mainly after regression, whereas behavior and sensory problems were present in 3 participants before regression. Psychotic-like behavior, mood swings, and PICA were the least prominent, and only SIBS was present in 4 participants of this group, 2 before regression and 2 after the onset. Only one participant had emergence of PICA, SIBS, mood swings, and psychotic-like behavior simultaneously.

The final group, G4, was formed by 4 pre-adolescents, 2 with no previous condition, one with mild SMD and one with mild autism/PDD and SMD as well. All had developed sleeping problems with regression, and one had a corrected sleep apnea before the onset. The loss of the skills was across all areas in all 4 participants (communication, social, play, and DLS). Only one participant did not show signs motor skills decline. None had Pica, but 4 developed mood swings, psychotic like behaviors, and SIBS. Only one participant did not have SIBS. Furthermore, 3 had some preexisting SMD, sensory, and perseverative behaviors, but the difference was in the timing of the emergence of those behaviors. The only 2 participants that had behavior problems were those that had a comorbid condition before the regression, and the behavior problems predated the onset of regression. G4 and G1 were more homogenous than G2 and G3.

Chapter V

CONCLUSION AND DISCUSSION

This chapter presents a summary and findings of this research as well as a discussion of the results. There is also a discussion of the implications of this study for practitioners, limitations of the study, and suggestions for future lines of research.

Summary of the Study and Findings

Summary of the Study

The purpose of this research study was to characterize the phenomenology of developmental regression in a group of 20 children between the ages of 2 and 12 years who had a diagnosis of Down syndrome (DS). Using a retrospective chart review process (Hess, 2004; Charlot, Fox, & Friedlander, 2002), 200 cases from the Down Syndrome Clinic (DSC) at Kennedy Krieger Institute (KKI) were reviewed, but only 20 participants fulfilled the inclusion criteria and were selected for this study.

Twenty participants were divided into groups according to (a) their age at regression and (b) the characteristics of their regression. The division resulted in four groups. Group 1 (G1) was formed by 5 children (Participant 1 - Participant 9 (P1-P9)), whose age at regression was between 2 and 5 years old and had no signs of a comorbid condition predating regression (except for one who was 1.5 years at the time of regression). Group 2 (G2) was composed of 2 children (P10- P11) with regression between the ages of 2 and 5 years old with signs of autism or PDD before the onset of regression. Group 3 (G3) included 5 participants (P12-P16), whose regression occurred between the ages of 7 and 9. Four participants had a diagnosis of either ADD/ADHD or SMD. Group 4 (G4) was comprised of 4 (P17- P20) children with regression that occurred between the ages of 9 to 11 years old.

For each group, one participant was selected as a case sample who would exemplify how that individual's regression occurred. The first case, from G1, was a girl whose onset of regression was at 3 years and 6 months of age with no apparent ASD symptom prior the onset. The second case, from G2, was a boy who had ASD symptoms pre-dating the regression onset at the age of 4 years and 3 months. The third case, from G3, was a boy with some characteristics of ADHD and SMD that predated his onset of regression at the age of 7. The last case, from G4, was a girl whose regression occurred at the age of 10 years and 5 months, with no behavior problems reported prior to the onset of regression.

Each of the 20 participants' files was reviewed, summarized, and the data gathered on specific areas from each participant's narrative chart. That information included (a) gender; (b) age at the time of developmental regression; (c) length of the onset of regression; (d) comorbid diagnoses of DS and ASD or PDD before regression or after regression; (e) presence of stressors before the onset of regression; (f) sleep disturbance before, during, or after regression; (g) loss of communication; (h) loss of social skills; (i) loss of play; (j) change or apparent loss in motor skills; (k) perseverative behaviors before, during or after regression; (l) loss of daily living skills (DLS); (m) emergence of sensory problems before, during, or after regression; (n) emergence of stereotype movement disorders; (o) emergence of psychotic-like behaviors; (p) emergence of behavior disorder before or after regression; (q) emergence of the compulsion of eating non-edible items; (r) self-injury behaviors (SIBs); and (s) emotional liability

Summary of the Findings

Data from the 20 participants showed that all 20 children lost communication, social skills, and play skills, whereas 10 participants lost daily living skills and 8 had some change in their motor skills (see Table 4 in chapter 4). Twelve participants developed sleep problems

during or after regression, and 16 participants received the diagnosis of ASD/PDD after regression. One participant received the diagnosis of SMD with loss, and 3 had already showed autism symptoms predating their regression.

Parallel to the onset of regression, data showed that there was an emergence of maladaptive behaviors among some participants. After regression, 13 participants developed stereotypy and 11 children also developed sensory problems. Perseveration after regression was found in 16 participants, whereas the development of behavior problems was present in only 2 participants, which was the symptom least often found among all participants after regression. PICA and psychotic-like behavior were the second less frequent, affecting only 5 participants respectively. Finally, SIBs were developed by 9 children, and mood swings were present after regression in 8 participants.

In G1, all 9 participants lost communication, social skills, and play, and 8 received the diagnosis of ASD/PDD after regression. The single participant who did not receive the diagnosis of ASD/PDD was diagnosed after the onset as having SDM with loss. Only 2 participants had an apparent loss of motor skills and DLS, and another four lost DLS. Three had developed sleep problems, one during regression and the other 2 after regression. The emergence of maladaptive behaviors was quite homogenous as well among the members of this group. All developed stereotypy and perseverative behaviors after regression, and all but 1 did not experience behavior problems after the onset. Seven participants developed sensory integration problems after regression, and the remaining 2 had sensory problems previous to their regression. None had developed psychotic-like behavior or mood swings (except 1 participant) and only 4 had SIBs and 2 had PICA.

In G2, both cases had autism with stereotypy and SIBs predating the onset of regression between the ages of 3 and 5 years. Regression paths for the 2 participants from G2 were quite different from each other, which also happened for the participants from G4. Both children were the least homogenous except on their loss of skills, which were the same as the other groups. Both experienced loss of communication, social skills, and play, and 1 participant had a decline in his motor skills and DLS. Both also developed perseverative behavior after regression, while none had psychotic-like behavior or behavior difficulties. Before regression, they already had stereotypy symptoms as well as SIBs.

Children in G3 received the diagnosis of autism after their regression and developed sleeping problems as well. The loss of communication, social skills and play was present as with previous groups; only 2 had an apparent loss motor skills, and 1 lost DLS as well. Stereotypy and perseveration problems were present mainly after regression, whereas behavior and sensory problems were present in 3 participants before regression. Psychotic-like behavior, mood swings, and Pica were the least prominent problems, and only SIBs were present in 4 participants of this group, 2 before regression and 2 after the onset. Only 1 participant had emergence of PICA, SIBs, mood swings, and psychotic-like behavior simultaneously.

Participants in G4 had developed sleeping problems with regression, and 1 had a corrected sleep apnea before the onset. The loss of the skills was across all areas in all 4 participants (communication, social, play, DLS) as well as decline in their motor skills. One participant did not have a loss of skills or a change in his motor skills. None had PICA, but all 4 developed mood swings, psychotic-like behaviors, and SIBs. One participant did not have SIBs. Furthermore, all but one suffered from stereotypy, sensory, and perseverative behaviors, but the difference was in the timing of the emergence of those behaviors. The only 2 participants that

had behavior problems were those who had a comorbid condition before the regression, and the behavior problems predated the onset of regression.

Therefore, findings can be summarized as follows.

A. The core symptoms of regression in DS in this cohort:
    - Loss of communication, play skills, and social skills
    - Emergence of stereotypy, sensory problems, and perseverative behavior
B. Prominent symptoms of regression in this cohort:
    - Development of non- structural (physical) sleep problems
    - SIB's and DLS
    - For children older than 8 years, onset of mental health problems (mood swings, psychotic-like behavior and SIBs).
C. Infrequent symptoms that occurred in this cohort:
    - Change in motor skills
    - Emergence of disruptive behavior and PICA for children younger than 8 years old.

Discussion of Results

This section first discusses the questions identified in chapter 1 and compares with the findings with CDD and autism with regression conditions. Second, it includes a brief discussion of how developmental regression in DS is similar and different when compared to other regressive syndromes, such as those found in Rett Syndrome, childhood disintegrative disorder (CDD) and regression in autism.

Answer to the Research Questions

1. Which adaptive skills were present and then lost during developmental regression?

Pre-existing Adaptive Skills, and Comparison with CDD and Regression in Autism

All 20 participants had developed some level of communication (sign or language), social skills, and play, as well as motor and daily living skills (DLS). This level of development was different in each case. In CDD cases, children are reported to have age appropriate milestones of motor, language and adaptive skills prior to onset of regression (Malhotra & Gupta, 2002).

The participants in G1, G3, and G4 present similar development before regression than in the CDD cases. It must be noted that children in this study had DS and therefore by default they have an intellectual disability and not a neurotypical development. This suggests that the point of discussion for the diagnosis of CDD is if the children attained milestones and then lost them, instead of focusing on whether or not the development was normal or neurotypical before regression.

When comparing G2 type of regression (both participants had autism diagnosis before regression) with regression in children with autism, the type and age at onset might differ. Regression in autism, according to several researchers (Rogers, 2003; Rogers & DiLalla,1990; Landa, Holman, Garret- Mayer, 2007; Bernabei & Camaioni, 2001; Kobayashi & Murata, 1998; Luyster et al., 2005) might follow three patterns. However, only two would apply for this study: early milestone achievement followed by a developmental plateau or clear developmental loss of previous acquired skills. However, for the latter condition, research has found (Rogers, 20003) that development before regression in these cases might not have been completely neurotypical. Instead, those children were already demonstrating subtle developmental delays in social and communicative areas, which is what was observed in both children in G2.

Both patterns (development plateau and clear regression) ought to occur theoretically before 36 months. Otherwise, the child's disorder is classified as CDD rather than autism (Rogers, 2003). Children in G2 had regression at a later age than 36 months and had autism before regression. Therefore, one could hypothesize that instead of having a loss, the G2 participants reached a plateau. Having a regression age above 36 months combined with data from previous development shows that indeed the G2 participants experienced a regression and not just a halt in their development. In addition, the fact that they developed autism behaviors after the regression might reflect brain changes that are greater than what is typically seen in plateau cases. Nevertheless, because G2 had only two members, their type of regression cannot be generalized to other cases. These findings can only serve the purpose of exemplification.

Loss of Adaptive Skills: Communication, Social, and Play

Adaptive skills loss, which includes loss of communication, social, and play skills, were experienced by all participants. A change or decline in motor skills and DLS was less common, at 40% (or 8 participants out of 20) and 50 % (or 10 participants out of 20) respectively (DLS loss could not be confirmed in of the participants). This is similar to what other studies have found when looking at the type of loss in CDD, and it indicates comparable patterns of brain dysfunction for both CDD and DS with regression cases. Volkmar (1992) reviewed previous cases and studies on CDD and found that among other things, children exhibited loss or marked regression in language (expressive and receptive), communication skills, and problems with social interaction. Malhotra and Gupta (2002) found that participants with CDD (N=12) had age appropriate milestones for motor, language, adaptive, and sphincter control before the onset, and all had some

intellectual disability. During regression, 100% of the children lost speech as well as social skills. Loss of play skills was present in 75% of the cases, and bladder and bowel control losses affected 58% of the cases. They also compared their cohort with previous data from other studies (N=105) (Volkmar, Klin, Marans, & Cohen, 1997) and found that 100% of the children had a loss or deterioration of speech, 94% lost social skills, and 68% lost bladder or bowel control. No comparison data was available for play skills. Kurita, Kita, and Miyake (1992), had similar findings among their 18 participants with CDD; 100% lost speech and social skills. Zwaigenbaum et al. (2000) found a case of a child with CDD, who, upon the onset of regression, lost receptive and expressive play and feeding skills as well as interest in people and life around him.

Change in Motor Skills, Loss of DLS, and Increased Sleep Disturbance

Motor skills, when compared with other studies (Volkmar & Cohen, 1989; Evans-Jones, & Rosenbloom, 1978; Malhotra & Singh, 1993), were also less consistently affected. In this study, many children developed a "cautious walk," which was considered evidence of more of a change in mental status (a secondary change in higher cortical control functions) than a physical loss. According to Malhotra and Gupta (2002), "It is known that bladder and language skills have cortical control (via autonomic pathways for the latter), while motor skills are coordinated complex efforts arising out of inputs from the cerebral cortex, cerebellum and basal ganglia. Hence, it could be possible the children with CDD experience patchy cortical insult (involving cerebral hemispheres) rather than generalised insult to the brain" (p. 112). This could lead one to hypothesize that in children with DS, despite the fact they have hypotonia (generalize low tone muscle as one of the consequences of the trisomy 21), they also use different brain

systems to control gross motor and fine motor activity. Many gross motor functions are performed semi-automatically, falling under the control of basal ganglia, cerebellum, and sensory-motor cortex, while fine motor functions are more highly coordinated with prefrontal, frontal motor and sensory-motor areas, and as a consequence, are highly integrated with executive cognitive functions.

The loss or deterioration of DLS as found in CDD studies (Volkmar & Cohen, 1992; Volkmar, Klin, Marans, & Cohen, 1997; Kurita, Kita, & Miyake, 1992) was also present in this cohort, but changes were less frequent among participants. This was also found in some of the case studies, such as in Bray, Kehle, and Theodore (2002) and Malhotra and Singh (1993). The losses of DLS in this cohort were mainly constricted to the ability to use fork or spoon, which belongs to the fine motor skills area, and bowel control; this was in concordance with other studies (Palomo et al., 2008; Zwaigenbaum et al., 2000; Burd, Fisher, & Kerbeshian, 1988; Evans-Jones & Rosenbloom, 1978).

With the regression onset, there was also an increase in cases of sleep disturbance. It is known that children with DS are susceptible to obstruction of the upper airway during sleep caused by anatomical factors, such as having enlarged tonsils and adenoids and a relatively small mouth and upper airways passages (Stores & Stores, 1996). During regression and after regression, 12 participants suffered some type of alteration in their sleep patterns that was not related to an upper airways anatomical fault. This is an interesting change if researchers take into account that in ASD, sleep disturbance is a common problem that increases with the severity of the autism (Dickerson-Mayes & Calhoun, 2009; Schreck, Mulick, & Smith, 2003). Malhotra and Gupta (2002) also found in their study that sleep problems developed in 33% of their participants with CDD.

2. Did participants lose the same skills?

Loss of Adaptive Skills, Communication, Play, and Social Skills, by Groups and Comparison with DS Regression Literature

Loss of communication, play and social skills was suffered by all participants across groups. However, the loss of DLS and change in motor skills was less common among all participants, except for the motor skills changes that were observed in three participants from G4. Hyman et al. (2008) found in their study that among their 19 participants with DS and regression, 6 had a loss of language only, 3 lost language and other skills, and 10 lost other skills. In the Castillo et al. (2008) study of children with DS and regression, data showed that in their cohort of 12 children with regression 3 lost language skills only, 6 lost other skills only, and 3 lost both language and other skills.

In cases of regressive autism, reports also indicate that language only regression is less common than language loss with social and non-verbal communication losses (Goldberg, 2003). The differences between those studies and the present study come from the criteria followed to select participants; therefore, it cannot be assumed that their findings do not agree with the findings of this study.

Change in Motor Skills and DLS Loss by Groups

Change of motor skills occurred more often in G4, with 3 out of 4 participants. The most frequent apparent losses were oral, fine motor skills, and change in walking speed. In other studies like Prasher (2002), which was a health study conducted with 357 English patients with DS who were monitored over a period of ten years, a significant minority of young adults had a regressive/disintegrative disorder. This group of young adults was between 15 and 30 years old, with a peak of 22 years of age when the disorder

first appeared; the regression included, among other things, a change in motor skills. Cahalane (2009) also found in 5 participants with DS with regression between the ages of 12 and 16 years old a generalized slowing down of movements. G4, who is the oldest group in this research project, has a pattern that is more like the older cases of regression as presented by Cahalane (2009) and Prasher (2002). Apart from one case in G2, the changes in motor skills in G4 could elicit the idea that when regression occurs at an older age, the more likely the chances that the person will suffer from changes in motor abilities.

Loss of DLS was also more frequent in G4 and G1. In G1, 5 out of 9 participants had a loss of toileting or feeding skills or both. In G4, all participants lost DLS, specifically toileting and feeding skills. The same G2 participant who lost motor skills also lost DLS, but there was no information on what skill or skills. Only one G3 member had a loss of dressing, toileting, and feeding skills. Information on this skill for two participants could not be found. In terms of loss of skills, it can be assumed from the data that the most affected and homogenous in their skill loss were G4 and G1. This can also be because both groups did not have previous comorbid conditions, and therefore, their development was more clear and the loss more obvious and easy to identify. Furthermore, one could assume that better development before the loss meant the losses were more global.

3. Which maladaptive behaviors emerged after regression? Did participants experience the emergence of the same maladaptive behaviors?

The behaviors observed to emerge in this sample were varied as well as their frequency among groups. Studies on regression in DS do not discuss in detail the

emergence of maladaptive behaviors and are limited to the loss of skills as has been exposed (Castillo et al. 2008; Hyman, 2008). Therefore, the findings of this question will be compared to CDD studies as they share many of the regressive patterns.

Commonly Emerging Maladaptive Behaviors: Stereotypy, Perseveration, and Sensory Problems

The most frequent maladaptive behaviors encountered after regression and common across participants and groups were stereotypy, perseveration, and sensory dysfunction; to a lesser degree were SIBs and mood swing. The least frequent behaviors were disruptive behavior, Pica, and psychotic-like behavior. However, mood swings and psychotic like behavior, were present in all 4 children from G4, the older group.

The emergence of stereotypy, one of the core symptoms of autism and a prominent feature found in CDD cases (DSMIV-TR, APA 2000; Volkmar, Keoning & State, 2005; Kurita, Koyama, Setoya, Shimizu, & Osada, 2004; Hendry, 2000; Malhotra & Singh, 1993; Malhotra & Gupta, 2002), was especially evident in G1 and G3. In comparing G1 with CDD, Volkmar and Rutter (1995) also found that participants with CDD, independently of how they were diagnosed, showed more autistic symptoms than the autistic group. This was also observed through the scores on different autism scales, although not those that were recorded in this study as well as in the general practice in the DSC at KKI.

Stereotypy in the form of motor mannerisms was less frequent in G4, the oldest group. This is an interesting observation that reiterates findings in other studies (Capone et al., 2006) and observations made in the DS- KKI clinic, which is that stereotypic motor behaviors might become less frequent as developmental progress and maturation evolve

(Capone, 2009). Participants in G3 were also observed to have a decline in hyperactivity but an increase of stereotypy after regression (see Table 8e, TT participant) and an increased lethargy score. As Capone (2009) explains, "internalizing behaviors such as apathy, low motivation, social indifference, and affective blunting as captured on the ABC scale are often observed in individuals with stereotypy" (p.56). Furthermore, Capone points out that " The robust interaction between stereotype and lethargy suggest that the same circuits for regulation arousal, attention, motivation, social interest and motor control also function in the expression of intelligence and adaptive behavior" (Capone, 2009, p. 58). This suggests that with a decline in intelligent scores, there would be an expectation of a rise in stereotype and lethargy with lower scores on attention, motivation and interests in social relations for children with regression.

Perseverative behaviors after regression were found in 14 participants. By groups, G1 had all his members developing perseveration; both participants from G2 also developed perseveration. Behaviors were varied: some had a type of compulsion (watching same section of videos over and over, walking through certain parts of the house repetitively, or lining up toys) and some had more the need to shake and dangle objects. The development of perseverative behaviors in this cohort is a similar characteristic as is seen in CDD cases, where children after regression also adopted new behavioral routines (Zwaigenbaum et al., 2000; Agarwal, Sitholey & Mohan, 2005; Chmiel & Mattsson, 1975; Malhotra & Gupta 2002). Palomo et al. (2008), in their case study of a child who regressed at the age of 50 months, explained that the child liked to line up his toys and look at them using his peripheral vision. Evans-Jones and Rosenbloom (1978) described a child who developed a number of ritualistic behaviors

such as constantly flushing the toilet and playing with water faucets. Related to stereotypy, Lewis and Bodfish (1996) and Capone (2009) explained that stereotypy seldom occurs as an isolated phenomenon and is often associated with other types of repetitions such as perseveration, obsessive compulsive behavior, or motor oral tics.

Sensory problems were noticed in 11 participants and more frequently in G1 after regression than in the other groups. Mouthing objects, food texture, and tactile defensiveness were the most prominent issues among affected participants. Few studies in CDD have described or mention changes in the sensory system. It could be that sensory changes are not part of the symptomatology of CDD but are for regression in DS, although further research need to be done since the sample of this study is too small to generalize the findings. Other explanations for the lack of data on this issue could be that sensory integration has been overlooked for many years and only in the last decade has attention been paid to it, or that consequences from sensory integration problems were labeled as behavior problems without noticing the sensory issues behind the behavior. Few case studies found in the literature mention such changes. From the Palomo et al. (2008) study, it can be inferred that the boy in their case study developed sensory problems during regression, as he avoided being touched and liked to watch television close to the screen. Burd, Fisher and Kerbeshian (1988) also described the change in a child whose difficulties started at 4 years and 7 months, who began putting things in his mouth, rubbing things with his hands, and licking objects. In Malhotra and Gupta (2002), all 12 participants in their study developed eating problems; however, the research did not specify what type of eating problems. The researchers did have a different category for the number of children with loss of motor skills that included oral motor, and thus one

could assume that problems occurred because of food sensitiveness, as 10 children in the study developed food texture problems with the onset of regression.

Less Common Emerging Maladaptive Behaviors: SIBs and Mood Swings

Less common maladaptive behaviors among the children were SIBs and mood swings. These two maladaptive behaviors, along with psychotic-like behaviors, were developed in all G4 participants (except for P19, who was the only one not developing SIBs) and in a more scattered manner among the other groups. It might be that older children with DS with regression when compared to younger children with DS and regression from this cohort present a more global deterioration that affects more and different brain circuits in comparison with younger groups. This global deterioration was also described by Prasher (1999) and Cahalane (2009). However, this is a hypothesis that needs validation.

Self- injurious behavior was also found in other children from G1 and G3 after the onset of regression. This origins of this particular maladaptive behavior is difficult to determine, although it has been hypothesized that these children may require higher levels of sensory input to have their needs met. In CDD, as in regression in autism, self-injury is seldom reported. Palomo et al. (2008) described a child, who during the course of regression at around the age of 5 and before the loss of his abilities, started to pinch himself and bang his head.

Mood swing for G4 was characterized by swings between crying and laughing and fearful. If mood swing are included within the umbrella of anxiety, this behavior was widely reported in CDD cases across ages (Palomo et al., 2008; Argarwal, Sitholey, & Mohan, 2005; Chmiel & Mattsson, 1975; Evans-Jones & Rosembloom 1978; Kurita,

Koyama, Setoya, Shimizu, & Osada, 2004; Volkmar 2005; Kurita, Osada & Miyake, 2004; Kurita, Kita, & Miyake, 1992; Malhotra & Gupta 2002).

The Least Common Maladaptive Behavior: Psychotic-like Behavior, Disruptive Behavior, and Pica

Psychotic-like was one of the least common behaviors, along with BD and Pica, but it affected all of children from G4. Psychotic-like behavior was defined mainly by catatonic-like conduct, although hallucinations were also the symptom for two children. The descriptive term used "catatonic-like behavior" was the chosen one for parents when describing the aloof state of their child. This aloofness might not necessarily indicate a psychiatric disorder, but a symptom present in ASD that in older children in comparison with younger cases might not present hyperactivity but instead the lethargy symptoms as seen before. For example, Prasher (1999) described the changes in personality of a population of young adults with a disintegrative disorder as having changes in personality, mood, and behavior where they became mute and withdrawn, among other symptoms. The cases in this study are similar to those in Wing and Shah's (2000) study on catatonia in autism. In this study, 17% of the referrals (total of 506) of children 15 and over with autism had severe exacerbation of catatonic features. Agarwal, Sitholey, and Mohan (2005) described the case of a child of 8.8 years old with CDD onset who had hallucinations and extreme fear; Palomo et al. (2008) also describe in their case of boy who at 4 year and 5 months with the onset of CDD experienced intense anxiety and panic-like agitation.

Disruptive behaviors were developed in only two participants after regression (one from G1 and one from G3). Five children across G1, G2, and G3 showed Pica

behavior but none from G4. These behaviors were not frequent in G4, and in fact, Pica and disruptive behaviors are not part of the diagnostic criteria of the DSM-IV (APA, 2000) for CDD, although some reports have mentioned problems in these areas in CDD literature. Malhotra and Gupta (2002) found in their study that 5 children out 12 developed behavioral problems with the onset of CDD. In another study, Malhotra and Sight (1993) showed that 4 out of 5 cases, who were at an average of 3.76 years old at regression, had aggressive outbursts. Evans-Jones and Rosembloom (1978) describe behavior problems in 2of their 10 cases; regression for one child was at the age of 4, and in the other case was at 3 year of age. In other studies, problems with transitions and resistance to change have been mentioned (Volkmar, Koenig & State, 2005; Kurita, Koyama, Setoya, Shimizu, & Osada, 2004). In terms of Pica only, isolated case studies mention the appearance of this behavior with the onset of CDD (Evans-Jones & Rosembloom, 1978; Palomo et al., 2008).

4. Did regression occur at the same age?

The age of regression among the participants in the study varied. In fact, the separation of the groups was made because it was observed that the age when regression struck was different as well as its presentation. Additionally, variation occurred in the length of time between the start of the onset and the end of it.

The mean age at regression by groups ages were at 3.06 years old for G1 and G2, at 7.14 years old for G3, and at 9.85 years for G4. The ages at regression for G1 and G2 resemble those found by Castillo et al. (2008) in their study where children with DS and autism had an onset of regression and loss of other skills apart from language that occurred at 3.8 years old; in that same study, language regression in children with DS

was at around 5.15 years old, or 61.8 months. Hyman et al. (2008) also found in their study that children with DS and regression in their cohort had a variance in their age at regression. The average at age of regression for loss of language and other skills was at 3.6 years old and 2.7 years old when it was a loss other than language. However, in Hyman's (2008) study, 11 of the 19 participants with DS and regression related their losses to medical illness, with infantile spasms and other seizures the most frequent medical illnesses mentioned.

In other studies, regression occurred later, between the ages of 7 and 10; however, in these studies, the children with DS and regression also had epilepsy (Eisermann et al., 2003; Caplan & Austin, 2000; Goldberg-Stern et al., 2001; Stafstrom & Konkol, 1994; Tatsuno, Hayashi, Iwamoto, Suzuki, & Kuroki, 1984). According to Touchman (2006), "As a group epileptic encephalopathies are associated with regression or slowing down of cognitive, language or behavioral development; the hypothesis is that seizures or the interactial epileptiform are responsible for the deterioration […]" (p.107). Touchman did point out that it is difficult to determine which comes first, the epilepsy or the deterioration. In this study, having epilepsy or other epileptiform was an exclusion criterion for selecting the participants.

When looking at CDD cases, Matson and Mahan (2009) concluded in their review of the current status on CDD that skill loss appears to happen between about 2 and 8 years of age, with an average of onset at 3 to 4 years of age. Nevertheless, the incidence of epilepsy is at around 70% (Rapin, 1995; Kurita, Koyama, Setoya, Shimizu, & Osada, 2004; Malhotra & Gupta, 20002) and around 21% in autistic regression (Tuchman & Rapin, 1997).

5. If the age of onset varied, how did the regression itself vary?

As with other elements of this study, the results of this research need further validation and replication with other participants from other DS clinics. Research on childhood regression in DS is scarce, and although this phenomenon is frequently mentioned in papers, it is often based on observations and not conclusions drawn from research. Therefore, the answer to this question needs to be taken with a precaution: what is being observed in this study cannot be extrapolated or generalized to other cases, although it could be used as a guide to future research.

As the age for onset varied, so did the characteristics of regression.

The first variation found was the amount of time that elapsed between the evidence of the first symptoms to the completion of the regression. The shortest time span was for G4, who presented a mean time lapse of 6. 25 months, and the longest span was for G3, with a mean time lapse of 18.6 months. This could be because G3 development was more unstable and presented more behavioral difficulties before regression; therefore, the limits of when it started to when the full onset was established were less clear.

Second, there was variation in symptoms presentation among groups, although regression for G1 and G4, albeit their differences in presentations of the symptoms, was homogeneous. All G1 participants lost communication, social, and play skills, and all but one developed stereotypy and perseveration after regression. None developed psychotic-like behaviors. Pica, disruptive behavior, and mood swings were also infrequently found.

Sleep disturbance was only present in 3 out of the 9 children in G1, whereas all the children from the other groups were affected by sleeping problems. One discussion point could be that children with DS with other behavioral comorbidities such as ADHD/ADD

or ASD predating regression are more vulnerable to develop sleep disturbances than children with only DS before regression.

All the G4 participants lost play, communication, and social skills. Furthermore, it was the only group where all its members lost DLS, developed very similar mood swings (specifically the sudden change from laughing to crying), and also developed psychotic-like behavior (catatonic-like and hallucinations). Moreover, 3 out of the 4 participants in G4 had also a change in their motor skills, while motor skills change was a less common finding in G1, G2 and G3 or other types of regression such as CDD or autism with regression. Loss in G4 was observed to be more acute in general, affecting more areas of development along with greater development of mental health problems. It could be argued that the older the child is the faster and more global is the loss. Other reports on slightly older participants than in G4 include Cahalane (2009), who found that 5 participants in their young adolescent years (12 to 16 years old) with DS had a gradual but marked decline in daily living skills, social withdrawal, and a generalized slowing down of movements and speech. Some participants also lost speech. The regression was, in appearance, autistic-like with withdrawal from others and development of abnormalities of movement. In addition, Prasher (2002) described in his health study that the group of young adults was between 15 and 30 years old with a peak of 22 when the disorder first appeared. The regressive symptoms were gradual, with severe deterioration in functioning skills after a normal period of development for a person with DS. Some areas where regression occurred were cognition, language (receptive and expressive), mobility, and adaptive and social skills.

However, it was observed in the G3 participants, although it remains to be proven, that their ADD/ADHD lessened considerably after regression, whereas the autism symptoms gained enough strength to have the diagnosis of autism. Dykens et al. (2002) examined age-related changes in the maladaptive behaviors of 211 children and adolescents with DS between 4 and 19 years old and found problems with attention that ranged between 71% and 79% across preadolescents groups, reaching their peak during ages 7 to 9 years old. By the age of 14 years, attention problems decreased to about 38%. Nicham et al. (2003) found similar results in their research on the presence of age-related changes in the spectrum of externalizing and internalizing problems. They found that externalizing behaviors such as opposing and refusing, impulsiveness, inattention, and increased motor activity were significantly higher in the 5 to 10 year old group of children, whereas internalizing behaviors were more prevalent in adolescents and adults. Participants of G3 also lost play, social, and communication skills and developed stereotypy, sensory problems, and perseveration as did the other groups; however, as with G2, they were less homogenous in the presentation of the other symptoms. This could be because they had ADHD/ADD as comorbid conditions before regression, which might cause this variability among participants.

Finally, G2 was composed by only two children whose data was very heterogeneous; it might be better used as individual cases.

What Are the Similarities and Differences between DS with Regression and Rett Syndrome, CDD, and Regression in Autism? What Is Unique about the Occurrence of DS with Regression?

It is important and of interest to compare regression in DS with other regressive syndromes due to the striking similarity and difference that these regression syndromes share with DS (see Table 21). This could help researchers to better understand the origins of this phenomenon as well as consider possible interventions and future treatment for these children.

Table 21 compares general regression features among DS with regression, Rett Syndrome (RS), CDD, and ASD with regression that will be discussed subsequently.

Table 21 General Features of Regression by Condition

Condition	Genetic	Age onset	Type Onset	Gen -der	Possible co-occurren. seizures	Loss Communic, Social Play Skills	Loss DLS	Loss Motor	DB/ Anxiety	Sensr prob.	Stereotypy	Persever.
DS + Regress.	+	2-12yr	A/D	M/F	+	+	–	–	–/+#	+	+	+
RS	+	>18mo <36mo	A	F	++	+	+	+	–	+	+	+
CDD	?	3-10yr	A/D	M> F	++	+	+	–	++/++	–	+	+
ASD+ Regress.	?	<36mo	A/D	M> F	+	+*	+	–	–/++	+	+	+

DB: Disruptive behavior
RS: Ret Syndrome
A: Acute,
D: Delayed
– not frequently reported
++ more often reported
*in ASD regression in language only is also possible
frequently found in regressive cases older than 8 years old.

Regression in Rett Syndrome Compared with Regression in DS

Both Rett Syndrome and DS are genetically based. Rett Syndrome is caused by mutations on the X- linked *MECP*2 gene (Amir et al., 1999), and DS is caused by a full or partial trisomy in chromosome 21 and occasionally by translocation of chromosome 21 (Dykens, Hodapp, & Finucane, 2000). Nevertheless, the nature of the regression is significantly different in the two conditions. Rett Syndrome affects dominantly female children (Moss & Howlin, 2009). Normal development for children with Rett Syndrome lasts between 3 and 18 months, and after this period follows a rapid regression onset with midline hand stereotypes, decline on head growth, ataxia, seizures, loss of language (receptive and expressive), fine motor skills, and social skills. However, it is noted that a diagnosis of DS with Rett Syndrome as a comorbid condition is rare (Leonard et al., 2004). In DS, the onset of regression can occur at various ages and different stages of development, affects boys and girls equally, and the stereotypes are not reduced to the midline. Furthermore, the loss of motor skills in DS is more subtle and different in nature; those losses are not as prominent or frequent for the children in this study.

Regression in CDD Compared with Regression in DS

According to the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (APA, 2000) the criteria for CDD currently states "apparently typical development" (p.79) for at least the first two years of life followed by a loss of previously acquired skills before the age of 10. The areas of loss are two of more of the following: expressive or receptive language, social skills or adaptive behavior, bowel or bladder control, play and/or motor skills. With the onset, there is also a qualitative impairment in social interaction and in communication, and a restricted pattern of interests and stereotyped behavior.

The DSM- IV- TR (APA, 2000) defines CDD as following 24 months of apparently normal development. Most of the reports published suggest that the onset was between 3 and 4 years old (Fombonne, 2002; Volkmar, Koenig & State, 2005), although there are others that place regression later, between 5 and 10 years of age (Bray, Kehle, & Theodore, 2002; Agarwal, Sitholey, & Mohan, 2005; Malhotra & Singh, 1993; Volkmar, 1992). The onset could be abrupt or insidious with premonitory behaviors such as irritability and anxiety and increased frequency of EEG abnormalities and seizure disorder.

Regression in DS seems to be not significantly different from the current DSM-IV-TR criteria for CDD, but one caveat is important to the definition. DS encompasses a known genetic etiology and global developmental delays from birth. However, following DS standards of development, children in G1, G3, and G4 had an apparently typical development for toddlers with DS. As with CDD, all participants in this study lost communication, play, and social skills and developed the type of maladaptive behaviors also seen in CDD. The notable difference found was the higher frequency of sensory problems and sleep disturbance among children with DS. Also, the older group, G4, presented changes in motor skills, SIBs, and psychotic-like behavior seem more frequently when compared to CDD cases; however, this needs to be examined with a larger sample of participants.

The age of onset and the tempo of developmental regression in DS were also within the upper limits of age as previously described in CDD cases.

It has been mentioned in the literature that there is a higher rate of epilepsy in children with CDD. However, in this study having epilepsy was an exclusion criterion. Therefore, a need exists for future research to study children with DS with epilepsy to determine the frequency and characteristics of regression in such cases.

Regression in Autism

The onset of regression in autism is different according to various studies. Some reports indicate that regression occurs between 10 to 30 months (Kurita, 1985) while others point towards 12 to 42 months (Tuchman & Rapin, 1997). Rogers (2004) explained that 50% of children with autism had regression between 12 and 24 months; in 30% of cases, it occurred later than this, and in 15%, it happened after their third birthday. According to the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (American Psychological Association, 2000), the criteria for Autism/ PDD states that regression occurs prior to 36 months. In this study, the participants of G2, even though they had autism before the onset of regression, had an onset that came at a later age (3.4 and 4.3 years old respectively). This is close to what Castillo et al. (2008) found in their study, where the mean age of language loss in children with a dual diagnosis of autism and DS was 61.8 months (5.15 years old); and for regression of other skills (purposeful hand movements, motor skills, self-help skills, constructive or imaginative play, or social engagement and responsiveness), the mean age of other skill loss was 46.2 months (3.85 years old). In this study sample, only 5 out of the 20 subjects (25%) experienced regression prior to 36 months of age. Therefore, consistent with the findings of Castillo et al. (2008), regression in DS appears to occur at a somewhat later age than regression with autism.

The onset also can be abrupt (days or weeks) or gradual, lasting weeks or months, and in some cases there are some premonitory signs such as high levels of anxiety and irritability followed by speech loss and other skills (Volkmar, Koenig, & State, 2005; Volkmar & Cohen, 1989; Kurita et al., 2004). This is similar the findings in this study, which found that the G4 children regressed within 6 months, whereas in G3 the regression lasted a mean of 18.6 months.

Volkmar, Koenig, and State (2005) provided a summary of the clinical features of autism with regression from a number of reported cases from 1908 until 2004. Their findings revealed that speech deterioration and/or loss was present in 100% of the cases; 99.3% had social disturbance; 84.3% had problems with change and higher levels of stereotypy; 80.6% had a deterioration of self-help skills; and affective symptoms and anxiety was present in 77.6% of the cases in addition to other activity. Speech loss, according to Rogers (2004), occurs in children who had very limited verbal repertoire initially. Kurita (1985) also found that 93.8% of children with autism and speech loss only had one-word sentences to begin with. In this study, the level of development in the cohort was variable. However, G2 participants experienced similar symptoms as the ones exposed by Volkmar, Koenig, and State (2005). It should be noted that data in this study was only recorded in terms of presence or absence of behavior after the onset of regression, and there were only two participants in G2, so no firm conclusion can be reached. However, in general terms when comparing data on loss of skills from Volkmar, Koenig, and State's (2005) study with these study findings, it can be said that the areas of skill loss experienced by both groups are similar.

What Could Explain the Differences between DS and the Other Regressive Syndromes?

Capone (2009) explains that "the study of behavioral phenotypes in individuals with genetic conditions is necessarily concerned with the measurement of observable behavioral phenomena" (p. 51). This work shows that regression in DS shares many characteristics with other regressive syndromes such as CDD, autism, and in part with Rett Syndrome. However, as Sigman (1999) noted, in order to arrive at a precise understanding of the associated features of any particular syndrome, it is necessary to adopt a developmental framework. This seems to be the case when trying to understand the phenomenology of regression. Identifying early

behavioral markers, or so-called "red flags" for specific problems during different stages of development, can help to guide researcher's understanding of the neurobiological substrate of brain development in specific syndromes.

There are three points that would make the case of why regression in DS has its own character. The first point is the genetic component of DS and how dosage imbalance (amount of chromosome 21 that transferred to other cells) for the more than 300 genes on chromosome 21 impacts brain development and organization. It argues in favor of the observation that developmental process itself does not always result in a specific, pre-determined functional outcome, but rather that individual outcomes can differ, and hence their occurrence is probabilistic (Capone 2009).

The second point is the instability of cognitive growth of DS across the life span. One of the most consistent finding across studies is that the rate of cognitive development tends to slow and decline as children with DS get older (Carr, 1985; Carr 1994; Sigman & Ruskin 1999). Carr (1988) also found that significant decline in intelligence was present before the age four but found fewer declines among her participants between the ages of 4 to 11 years old. This advance-plateau pattern related to growth to chronological age and in adaptive development was also found in Dykens, Hodapp, and Evans' (2006) study. In their cohort, younger children from 1 to 7 years old showed significant age-related gains in adaptive behavior with little evidence of generalized decline. Older children from their group, however, leveled off in their development of adaptive behavior during middle childhood years. Furthermore, Fowler (1988) found also patterns of acceleration and deceleration in grammatical development in children with DS; plateaus were between the ages of 7.5 and 10.5 years old across levels of intellectual development. Other studies such as Miller (1992) found that expressive language weaknesses

increased as the mental age of children with DS grew older; Brown, Greer, Aylward, and Hurt (1990) showed that children with DS demonstrated deceleration in their social age as they get older.

The third point is that several studies have shown that persons with DS have higher risks of developing dementia or Alzheimer's disease, especially if they live pass their fortieth birthday (Hazlett, Hammer, Hooper, & Kamphaus, 2011). However, dementia is a progressive disorder, resulting in a steady deterioration of skills over time. The subjects with DS in this study did not continue to deteriorate following their initial episode of regression, making Alzheimer's dementia a highly improbable etiology. Instead, our findings suggest that DS subjects experiencing regression as an unstable developmental course due partially to neurobiological factors that make their brain more vulnerable to disconnection (Geschwind & Levitt). As Castillo et al. (2008) expressed, further study of this unique population may provide clues to understanding the more general phenomenon of regression in autism as well.

Implication for Practitioners and Parents

An implication of the findings of this study for educators who work with children with DS is the awareness of the fact that regression occurs among this population. It is important to recognize the symptoms as early as possible and not confuse them with attention seeking, oppositional behavior, or lack of motivation among others. The symptoms presented by these students represent serious behaviors that reflect a neurobiological disturbance and require immediate attention from medical and mental health professionals such as neurologists, developmental pediatricians, and experienced psychologists. Because teachers working with children with DS are among the professionals that spend the most time with these children, they may be the first ones to identify the signs of developmental regression, particularly as it affects

social, language, and adaptive skills. This indicates a call for open and frank communication with the children's parents that includes not only concerns about social, language, and adaptive skills but the possible significance of the child's maladaptive behaviors.

Parents also need to be aware of the possibility of a regressive episode in their child development and have an open and frank communication with their developmental pediatrician and family doctor. This communication has to be characterized by mutual respect and reciprocal listening. Many times parents turn to their child's physician with concerns about their child's behavior, and too often these concerns are labeled as overprotective. Only when the behaviors become highly dysfunctional or are clearly interfering with developmental progress are the parent's concerns taken seriously. Therefore, three-way communication between parents, medical staff, and teachers represents the best way possible to succeed in understanding and managing these cases.

Prognosis is another factor to be aware of when deciding on management and treatment. It has been observed in the DSC KKI clinic that children experiencing regression may have a very narrow and limited window for regaining skills (however, further studies are needed to prove this observation). Therefore, it is essential that once concerns about deterioration in social, language, or play skills become obvious, teachers should not wait for the abilities to return, but instead need to call this deterioration to the attention of the parents and start as soon as possible to re-teach the lost abilities. The process of readjusting developmental and academic expectations should not interfere with expecting the best from each child. Admittedly, this can be a difficult adjustment for teachers and parents to make in real practice.

Finally, professionals are in a unique position to help parents adjust to and cope with this new reality about their child. Keep in mind that the parents of most children with DS have

already rushed to engage their children in early intervention programs (sometimes at a high economic cost) in order to give their child every possible developmental advantage early in life. However, when regression strikes, many parents feel they are back to "step-one" again, trying to understand and cope with a condition that is new, unexpected, and frightening. This can be heartbreaking for many parents, and therefore, support from professionals is imperative.

Limitations of this Study

The primary limitation of this study relates to questions of reliability. Information, data, and diagnosis for this study were collected by a single experienced clinician, Dr. Capone, over a period of 15 years. This means that confirmation of regression and post-regression status from other medical personnel was not available. Nevertheless, to reduce the impact of this limitation, it was an inclusion criterion that all selected participants had documents from at least two different professionals stating a loss of skills.

The secondary limitation of this study is that when selecting children for the regression cohort, only this researcher read all files and selected the participants that were later shared with Dr. Capone. This round of selection was performed on two separate occasions and included blinding the subjects by name to look for consistency in symptoms that would qualify them for the study and eventual categorical grouping.

The third limitation is that the population sample was derived from a convenient clinical cohort with a referral bias towards individuals with high levels of maladaptive behavior. Because regression in DS is considered a rare event, it limits the generalization of the findings to other settings or to the larger populations of children with DS.

The fourth limitation is the use of historical data and the fact that this research required a retrospective design. Data on all subjects was gathered from many different sources, and

therefore, the quality of the data could be affected. This variance could not be controlled for except by selecting only those cases with data that could be organized chronologically and provided enough evidence from at least two sources to avoid inaccuracies.

Despite all of these limitations, it was important to pursue this research topic because of the need for better understanding of regression in children with DS and the paucity of studies on this topic. A better understanding of regression in DS will ultimately affect the quality of life for these children, their families, and provide much needed guidance to educators.

Suggestions for Future Research

This study, because of its characteristics and that it is just the second on the topic of regression in DS, has probably brought more questions than answers to the community. This means it is important to develop additional studies that will support or refute these findings on children with DS.

Educational and psychological research will be important because of the need to determine which interventions work best for this population. Currently, we are working with these children on the assumption that those research-based interventions that are successful for children with ASD might also work with the DS population. Prospective studies that follow the developmental course of high risk children with early signs of atypical development, so-called "red flags," would be valuable as would studies centered on the long-term outcome or prognosis of regression in children with DS.

In terms of medical research, it might prove informative to study the brain mechanisms that modulate developmental regression and the identification of possible environmental or medical conditions that can trigger regression. Ultimately, being able to predict those DS individuals at increased risk for regression and any similarities with CDD, autism, or Rett

Syndrome would be useful. Similarly, knowing which medications and other interventions could potentially prevent developmental deterioration once started or that are effective in treating and managing target symptoms would be a great asset.

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APPENDIX A. Kennedy Krieger Down Syndrome Clinic New Patient Evaluation Form

Kennedy Krieger Institute

Down Syndrome Clinic

New Patient Evaluation Form (Children - DD)

GENERAL INFORMATION/ *Información general*

CHILD'S AGE (YEARS & MONTHS)	Years:	Months:
Edad Hijo/a (años y meses)	*Años:*	*Meses:*

FAMILY NAMES/ *NOMBRES DE LOS FAMILIARES:*

Child's Name/ *Nombre de su hijo/a:*

Mother's Name/ *Nombre de la madre:*

Father's Name/ *Nombre del padre*:

CURRENT HOME ADDRESS*/ Dirección y Teléfono Familiar actual*:

Street/ *Calle y Nº:*

City/ *Ciudad*:

State/ *Estado*: Zip/ *Código postal:*

HOME PHONE NUMBER/ *Número de teléfono de la casa:*

PREFERRED DAYTIME PHONE NUMBER/ *Número de teléfono preferente para contactarles:*

PRIMARY PHYSICIAN ADDRESS & PHONE NUMBER/ *Dirección y Teléfono del médico de familia*:

.

Street/ *Calle y Nº:*

City/ *Ciudad*:

State/ *Estado*: Zip/ *Código postal*:

Phone Number/ *Número de teléfono*:

Psychiatrist or Neurologist Address & Phone Number/ *Dirección y Teléfono del Psiquiatra o Neurólogo*

Street/ *Calle y Nº*:

City/ *Ciudad*:

State/ *Estado:* Zip/ *Código postal*:

Phone Number/ *Número de teléfno*

PREVIOUS MEDICAL DIAGNOSES (IN ADDITION TO DOWN SYNDROME):
Diagnósticos que su hijo/a haya recibido de otros doctores

PRESENT CONCERNS/ *Qué preocupaciones tiene/n sobre su hijo/a?):*

1.

2.

BEHAVIORAL CONCERNS/ *Preocupaciones sobre el comportamiento de su hijo:*

At what age did you first become concerned about your child's behavior?
Qué edad tenía su hijo cuándo empezaron a preocuparse por su comportamiento?

Has your child ever received behavior management or medications for behavior problems?

Y or N

Ha recibido su hijo, en algún momento, intervención o tratamiento para cambiar su comportamientio? Si o No

Has your child been seen by a child psychiatrist or neurologist ? **Y or N**
Ha/n llevado a su hijo a algún psiquiatra o neurólogo? *Si o No*

Indicate if you were given a neurobehavioral diagnosis?
Indique que otros diagnósticos neurobiológicos ha recibido su hijo?

Are you interested in discussing medications as part of your child's treatment plan ?
Y or N
Tiene/n interés en hablar sobre posibles medicaciones como parte del tratamiento para su hijo?
Si o No

If medications were recommended would you want them prescribed, managed and adjusted by Dr Capone, your PCP, Psychiatrist or Neurologist?
Si medicaciones son recomendadas, querría/n que éstas fueran recetadas, seguidas y ajustadas por el Dr Capone, su médico de familia, el psiquiatra o neurólogo que visita actualmente a su hijo/a?

PRESENT CONCERNS/ PREOCUPACIONES PRESENTES O ACTUALES:

Onset or initial concern:
Cuándo empezaron los síntomas? Cuántos años tenía su hijo cuando empezaron los síntomas?

Sequence of symptom presentation:
Que síntomas notaron primero? Cómo se secuenciaron los síntomas?

Preceding illness or psychosocial stressors:

Tuvo su hijo/a alguna otra enfermedad antes de que aparecieran los síntomas? Tuvo su hijo algún episodio de estrés antes de que aparecieran los síntomas (Ej. muerte de un familiar cercano, operación, cambio de escuela etc…?

SYMPTOM CATEGORIES/ *CATEGORÍAS SINTÓMATICAS* :

BRIEFLY DESCRIBE ACTIVITY LEVEL (E.G. OVERACTIVE, RESTLESS, RUNS AWAY, UNDERACTIVE):

Describa brevemente el nivel de actividad de su hijo/a (Ej. Hiperactivo, inquieto, se escapa, sin actividad…)

BRIEFLY DESCRIBE CONDUCT (E.G. OPPOSITIONAL, RESISTANT, ARGUMENTIVE, TANTRUMS):

Describa brevemente el comportamiento de su hij/a (Ej. Es oposicional, resistente, tiene rabietas, se pelea…)

BRIEFLY DESCRIBE ANY OVERT BEHAVIORS (E.G. AGGRESSIVE, INJURY TO OTHERS OR SELF,

DISRUPTIVE, DESTRUCTION OF PROPERTY):

Describa brevemente cualquier comportamiento evidente que presente su hijo/a (Ej. Agresivo, daña a otros o a si mismo, daña la propiedad…)

SYMPTOM CATEGORIES (CONTINUED):

BRIEFLY DESCRIBE ANY REPETITIVE BEHAVIORS OR RITUALS (E.G. REPETITIVE MOTIONS, ROCKING, SHAKING, VOCALIZATIONS, NOISES, COMPLEX RITUALS, ODD BEHAVIORS):
Describa brevemente cualquier comportamiento repetitivo o ritual que haya observado en su hijo/l (Ej. movimientos repetitivos, mecerse, ruido, agitar los dedos delante de los ojos, etc..)

BRIEFLY DESCRIBE ANY MOTOR MOVEMENTS (E.G. SUDDEN JERKS, TICS, GRIMACING, TREMOR, SLOWING, CLUMSINESS):
Describa brevemente calquier movimiento motor que haya observado en su hijo/ (Ej.estirones repentinos, gestos faciales o corporales, temblores, torpeza motora…)

BRIEFLY DESCRIBE LEARNING & COGNITION (E.G. ODD-ATTENTION, DISTRACTIBILITY, FOCUS, ORGANIZATION, PROCESSING SPOKEN WORDS):
Describa brevemente el tipo de aprendizaje y cognición que tiene su hijo/a (Ej. Presta atención de manera inusual, se distrae con frecuencia, se centra en ciertas tareas ,organización de sus movimientos, comprensión de mensajes…)

BRIEFLY DESCRIBE MOOD (E.G. ANXIETY, IRRITABILITY, FEARFULNESS, SADNESS, CYCLIC FLUCTUATION):
Describa brevemente como es el estado de ánimo de su hijo (Ej. Ansioso, nervioso, triste, cambia de un estado de animo a otro con frecuencia, temeroso, irritable…)

BRIEFLY DESCRIBE SOCIAL BEHAVIOR (E.G. WITHDRAWN, ISOLATES SELF, APATHY, PLAY SKILLS, PEER INTERACTION):
Describe brevemente como es la conducta social de su hijo/a (Ej. Le gusta estar solo, esta ensimismado, apático, juega con companeras, tiene mucha imaginación cuando juega…)

BRIEFLY DESCRIBE SLEEP PATTERN (E.G. DURATION OF SLEEP, QUALITY OF SLEEP, AWAKENINGS, DAYTIME TIREDNESS)
Describe brevemente el patron de sueño de su hijo/a (Ej. Duerme toda la noche, se levanta y no se vuelve a dormir, está cansado si no ha dormido bien…)

COMMENTS ABOUT ANY OF THE ABOVE CONCERNS/
Otros comentarios sobre las preocupaciones mencionadas anteriormente:

SENSORY FUNCTION/ *Funcionamiento sensorial*

Sensory aversions (dislikes) - list
Liste aversiones sensoriales (No le gustan)

Sensory preferences (likes) - list
Liste las preferencias sensoriales , (si le gustan)

Auditory
(Auditorias)

Visual
(Visuales)

Touch
(Tacto)

Smell
(Olfato)

Oral
(Orales)

DEVELOPMENTAL SKILLS (DESCRIBE BRIEFLY)/ *Desarrollo de Habilidades (describa brevemente)*

How would you rate child's OVERALL progress? Choose one: Excellent/Good/Fair/Poor
Cómo describiría usted el progreso o desarrllo de su hijo/a (señale una): Excelente/ Bueno/ Normal/ Pobre

Has child experienced a period of DEVELOPMENTAL REGRESSION (LOSS) or PLATEAUING? (Y or N)
Ha notado si su hijo ha perdido habilidades o no aprende como lo hacía antes?: Si o No

If YES, what age did this start?
Si contesto "sí" *A qué edad comenzó*_____

What skills were lost? (Describe Briefly):
Qué Habilidades perdió o dejó de utilizar (ej. Lenguaje, socialización, capacidad de jugar con otros...)

Has child experienced NEW onset of seizures? (Y or N)

- **If YES, what age did this start?**

Nueva aparición de convulsiones o epilepsia? *Si o No* *A qué edad comenzaron?*

GROSS & FINE MOTOR SKILLS/ ***ACTUAL DESARROLLO MOTÓRICO GRUESO Y FINO***

Current GROSS motor level:
Desarrollo motórico grueso actual:

What age did child begin walking?
Cuándo empezó su hijo a caminar?

Current FINE motor level:
Desarrollo motórico fino Actual

Handedness (Left/Right/Both):
Con qué mano realiza su hijo/a la mayor parte de las tareas, con la derecha o con la izquierda, o con las dos?

CURRENT EXPRESSIVE LANGUAGE:

Number of WORDS SPOKEN SPONTANEOUSLY:
Número de palabras que pronuncia espontáneamente: espontáneamente:

- **Number of SIGNS USED SPONTANEOUSLY:**
  Número de signos o gestos que utiliza

Uses 1-2 word/sign phrase? (Y or N)
Hace frases de 1-2 palabras/signos? Si o No

- **Uses 2-3 word/sign phrases? (Y or N)**
  Hace frases de 2-3 palabras: Si o No

Uses gestures or points to picture to indicate wants/needs? (Y or N)
Utiliza gestos o señala en fotos/ dibujos para indicar sus necesidades o lo que quiere? Si o No

PREVIOUS EXPRESSIVE SKILLS (DESCRIBE BRIEFLY IF LOST)/
Habilidades expresivas previas, describa las que perdió o dejó de utiliza.

CURRENT RECEPTIVE LANGUAGE/ *Habilidades actuales de lenguage receptivo:*

Number of words understood:
Cuántas palabras entiende?

Number of signs understood:
Cuántos gestos entiende?

Follows simple 1-step SPOKEN directions? (Y or N)
Entiende y cumple una orden cuando se le da hablada?

Follows complex 2-step SPOKEN directions? (Y or N)
Entiende y cumple una ordenes de dos pasos cuando se le da hablada?

Understands when others use gestures or point to pictures? (Y or N)
Utiliza gestos o señala en fotos/ dibujos para indicar sus necesidades o lo que quiere? Si o No

PREVIOUS RECEPTIVE SKILLS (DESCRIBE BRIEFLY IF LOST):
Habilidades comprehension receptivas previas (Describa brevemente)

CURRENT SOCIAL-INTERACTION SKILLS (DESCRIBE BRIEFLY):
Habilidades de interacción social actuales (Describa brevemente)

Gets your attention:
Pide o busca su atención?

Plays with toys:
Juega con juguetes?

Initiates a request:
Inicia conversación, o pide cosas?

Shares toys with others:
Comparte los juguetes con otros?

Responds to a request:
Responde cuando se le pide o pregunta algo?

Plays with other children
Juega con otros niños?

PREVIOUS SOCIAL-INTERACTION SKILLS (DESCRIBE BRIEFLY IF LOST):
Habilidades sociales previas (Describa brevemente si fueron perdidas)

CURRENT SELF HELP (INDICATE IF INDEPENDENT OR NEEDS ASSISTANCE):
(Habilidades para la vida diaria, señale si su hijo realiza éstas actividades de manera independiente o con ayuda)

Feeding:

(Comer)

Toileting:

(cuando va al baño para orinar o defecar)

Dressing:

(Vestirse)

Bathing:

(Aseo, ej: bañarse, lavarse los dientes…)

Undressing:
(Desvestirse)

Preferred Foods (Please List):
Cuáles son los alimentos preferidos de su hijo/a?

Problems with chewing or swallowing foods or liquid? If yes, please describe briefly:
Tiene su hijo algún problema para masticar o tragar la comida o líquidos:

5. FAVORITE ACTIVITIES (DESCRIBE BRIEFLY)/ *Cuáles son las actividades favoritas de su hij/a*

1. Physical Exercise:
Ejercicio físico

2. Leisure
Ocio y tiempo libre

3.

4.

6. OTHER MEDICAL HISTORY (DESCRIBE BRIEFLY)

BRIEFLY DESCRIBE PREVIOUS HOSPITALIZATIONS (WHERE - WHY - WHEN)/
Describa brevemente otras hospitalizaciones (INDIQUE Lugar, Motivo y Cuándo):
1.

2.

3.

4.

BRIEFLY DESCRIBE PREVIOUS SURGERIES (WHERE - WHY - WHEN):
Describa brevemente Otras operaciones (Indique Lugar, Motivo Y Cuándo)
1.

2.

3.

4.

BRIEFLY LIST ANY CURRENT MEDICAL PROBLEMS (THOSE REQUIRING ANY TREATMENT):
Actualmente tiene su hijo/a alguna otra condición que requiera tratamiento u otros problemas de salud?
1.

2.

3.

4.

5.

6.

7.

LIST CURRENT MEDICATIONS (INCLUDE DOSE & TIMES):
Liste las medicaciones que su hijo/a esta tomando actualmente

LIST CURRENT NUTRITIONAL SUPPLEMENTS/SPECIAL DIET:
Liste complejos vitamínicos o dietas especiales que su hijo/a esta tomando actualmente

LIST ANY PAST MEDICATIONS (INCLUDE REASON FOR STOPPING):
Liste las medicaciones que su hijo/a ha tomado en el pasado

ENT CONCERNS

Has your child had any EAR INFECTIONS ? Y or N
Ha tenido su hijo Infecciones del oído? Si o No

If YES, how many in past 6 months?
Si su hijo Si ha tenido infecciones de oído, cuántas ha tenido en los últimos 6 meses?

Has your child had any SINUS INFECTIONS? Y or N
Ha tenido su hijo sinusitis? Si o No

If YES, how many in past 6 months?
Si su hijo Si ha tenido infecciones de oído, cuántas ha tenido en los últimos 6 meses?

Does your child SNORE LOUDLY when asleep? Y or N
(Cuándo su hijo duerme, nota que éste ronca a menudo?) Si o No

Does your child have SLEEP APNEA (pauses in breathing)? Y or N
Ha notado si su hijo tiene Apnea obstructiva del sueño o nota que su hijo deja de respirar cuando duerme? Si o No

Has your child ever had a SLEEP STUDY ? Y or N
Han estudiado el sueño de su hijo/a? Si o No

If YES, what were the results?
Si le realizaron un estudio del sueño, que resultados obtuvo?

Does your child have any ALLERGIES? If YES, please specify below:
Tiene su hijo/a algún tipo de ALERGIA? Si su hijo/a padece alergia specifique a continuación:

Medications:
Mediaciones

Environmental:
Ambientales

Foods:
Alimentos

MEDICAL CONSULTATIONS/ *Otras consultas medicas*

MEDICAL CONSULTANTS *(Consultas médicas)*	PHYSICIAN NAME *(Nombre del Doctor)*	FINDINGS *(Resultados)*	DATE OF LAST VISIT *(Fecha última visita)*
Dental *(Dentista)*			
Cardiology *(Cardiólogo)*			
Ophthalmology *(Oculista)*			
Ear-Nose-Throat *(Oído- Nariz-Garganta)*			
Gastrointestinal *(Estómago)*			
Endocrine *(Endocrino)*			
Neurologist *(Neurólogo)*			
Psychiatrist *(Psiquiatra)*			
Other *(Otro)*			

MEDICAL TESTING/ *Test Medicos*

MEDICAL TESTING	DATE	RESULTS	(PLEASE ATTACH COPY OF REPORT)
HEARING (Y OR N): *(Audición)*			
THYROID (Y OR N): *(Tiroides)*			
NECK FILM (Y OR N): *(Radiografia del cuello)*			
MRI OR CT (Y OR N): *(Resonancia magnética/Pruebas radiológicas)*			
EEG (Y OR N): *(Electroencefalograma)*			
OTHER *(Otros)*			

BIRTH HISTORY/ *Datos del Nacimiento*

PREGNANCY/ *Embarazo*

Mothers age *(Edad de la madre):* **Fathers age** (*Edad del padre*):

Length of (*Duración del embarazo*):

Special tests ***(Test especificos):*** **Ultrasound (***Ultrasonido*):

Triple screen (*Triple marcado*r):

Amniocentesis (*Amniocentesis*):

Problems during pregnancy (*Tuvo algún problema durante el embarazo?)*

LABOR & DELIVERY

Name of Birth Hospital *Nombre del hospital donde nació su hijo/a:*

Duration of Labor/ *Duracion del parto/ alumbramiento "alivio":*

Type of Delivery (e.g. vaginal, c-section) / *Tipo de parto (Ej. Vagina, cesarean, etc.):*

Apgar Scores *Calificación Apgar***:** **Weight/** *Peso:*

Please describe any problems in delivery room/ *Tuvo algún problema en la sala de de parto?*

NEWBORN PERIOD/ ***Periodo: Recién Nacido o neonato***

Length of Hospitalization/ *Cuántos días estuvo su hijo/a hospitalizado?*

Did you come home together? *Volvieron a casa juntos o su hijo permaneció hospitalizado?*

Results of Cardiac ECHO/Evaluation (If Known)/ *Resultados de las evaluaciones cardiacas (si las recuerda)*

Results of Chromosome Testing (e.g. Trisomy 21, translocation or mosaicism)/ *Resultados del test Cromosómico (Ej. Trismomia, mosaicimo o traslocación)*

Please describe any problems in NICU/Nursery/ *Tuvo su hijo/a algún problema en la* Unidad de Cuidados intensivos/ maternidad

10. CURRENT DAYCARE AND SCHOOL PROGRAM/
Guardería y/o Programa escolar al que atiende su hijo actualmente

Program Name Location Group/class size Type Of Services Frequency Of Services

Nombre del Programa Localización Grupo/ N^{O} de estudiantes Servicios que recive Con qué frecuencia:

1.

2.

3.

PLANS FOR NEXT YEAR (DESCRIBE BRIEFLY):
Planes para el año que viene (describa brevemente)

11. CURRENT SPECIALIZED OR PRIVATE PROGRAMS
Programa especializado o privado dónde atiende su hijo actualmente

Program Name **Location** **Group/class size** **Type of Services** **Frequency of Services**

Nombre del Programa *Localización* *Grupo/ N^{O} de estudiantes* *Servicios que recive* *Con qué frecuencia*

1.

2.

3.

PLANS FOR NEXT SCHOOL YEAR (DESCRIBE BRIEFLY):
Planes de escuela para año que viene (describa brevemente)

12. FAMILY/ *Familia*

Do you belong to a DS parent group in your area? **(Y or N)**
Pertenece/n a alguna asociación de Síndrome de Down? *Si o No*

Do you use on-line parent/info resources? **(Y or N)**
Busca y utiliza información en Internet? *Si o No*

Do you have childcare available? **(Y or N)**
Tiene acceso a un cuidador/a o "baby sitter" *Si o No*

MOTHER/*MADRE*:

Mother's Age:
Edad actual de la madre:

Highest Level of Education:
Estudios cursados:

Current Occupation:
En qué trabaja?

Any Health Problems?
Tiene algún problema de salud?

FATHER/PADRE

SIBLINGS/ *HERMANOS*

Siblings Name(s) & Age(s)/ *Nombre y edad de los hermanos/as*

HEALTH STATUS/ *ESTADO DE SALUD*

FAMILY HISTORY/ *HISTORIA FAMILIAR*

Is there a family history of major mental health disorders? This includes those affecting the child's Grandparents, Parents, Aunts, Uncles, Cousins, and Siblings. Please indicate relationship to child below:

Schizophrenia
Esquizofrenia

Bipolar Mood Disorder:
Trastorno bipolar

Obsessive Compulsive Disorder:
Trastorno obsesivo compulsivo

Severe Depression:
Depresión severa

Severe Anxiety:
Ansiedad Severa

Autism:
Autismo

ADHD:
Trastorno de la Atención con Hiperactividad

APPENDIX B. Aberrant Behavior Checklist Screening (3-13years old) Templates

ABERRANT BEHAVIOR CHECKLIST (3-13yr)	
Question:	Current Rating (0, 1, 2, or 3)
1 Excessively active at home or school	
2 Injures self	
3 Listless, sluggish, inactive	
4 Aggressive to other patients and staff	
5 Seeks isolation from others	
6 Meaningless, recurring body movements	
7 Boisterous (inappropriately noisy and rough)	
8 Screams inappropriately	
9 Talks excessively	
10 Temper tantrums	
11 Stereotyped, repetitive movements	
12 Preoccupied; stares into space	
13 Impulsive (acts without thinking)	
14 Irritable (“grizzly” or “whiny”)	
15 Restless, unable to sit still	
16 Withdrawn; prefers solitary activities	
17 Odd, bizarre in behavior	
18 Disobedient; difficult to control	
19 Yells at inappropriate times	
20 Fixed facial expression; lacks emotional reactivity	
21 Disturbs others	
22 Repetitive speech	
23 Does nothing but sit and watch others	
24 Uncooperative	
25 Depressed mood	
26 Resists any form of physical contact	
27 Moves or rolls head back and forth	
28 Does not pay attention to instructions	
29 Demands must be met immediately	
30 Isolates himself/herself from other residents	
31 Disrupts group activities	
32 Sits or stands in one position for a long time	
33 Talks to self loudly	
34 Cries over minor annoyances and hurts	
35 Repetitive hand, body, or head movements	

(Cont.) ABERRANT BEHAVIOR CHECKLIST (3-13yr)	
Question:	Current Rating (0, 1, 2, or 3)
36 Mood changes quickly	
37 Unresponsive to activities (does not react)	
38 Does not stay in seat during lesson period	
39 Will not sit still for any length of time	
40 Is difficult to reach or contact	
41 Cries and screams inappropriately	
42 Prefers to be alone	
43 Does not try to communicate by words or gestures	
44 Easily distractible	
45 Waves or shakes the extremities repeatedly	
46 Repeats a word or phrase over and over	
47 Stamps feet while banging objects or slamming doors	
48 Constantly runs or jumps around the room	
49 Rocks body back and forth	
50 Deliberately hurts himself/herself	
51 Pays no attention when spoken to	
52 Does physical violence to self	
53 Inactive, never moves spontaneously	
54 Tends to be excessively active	
55 Responds negatively to affection	
56 Deliberately ignores directions	
57 Throws temper tantrums when he/she does not get own way	
58 Shows few social reactions to others	

Source: Aman, M., Singh, N., Stewart, A., & Field, C. (1985). The aberrant behavior checklist: A behavior rating scale for the assessment of treatment effects. *American Journal of Mental Deficiency, 89*, 485-491.

NAME
DATE BL Q
3-13yr

Subscale I **Irritability**		Subscale II **Lethargy**		Subscale III **Stereotypy**		Subscale IV **Hyperactivity**		Subscale V **Speech**	
Question #	Score 0-3	Question #	Score 0-3	Question #	Score 0-3	Question #	Score 0-3	Question #	Score 0-3
2	0	3	0	6	0	1	0	9	0
4	0	5	0	11	0	7	0	22	0
8	0	12	0	17	0	13	0	33	0
10	0	16	0	27	0	15	0	46	0
14	0	20	0	35	0	18	0		
19	0	23	0	45	0	21	0		
25	0	26	0	49	0	24	0		
29	0	30	0			28	0		
34	0	32	0			31	0		
36	0	37	0			38	0		
41	0	40	0			39	0		
47	0	42	0			44	0		
50	0	43	0			48	0		
52	0	53	0			51	0		
57	0	55	0			54	0		
		58	0			56	0		
TOTAL	0	TOTAL	0	TOTAL	0	TOTAL	0	TOTAL	0

Cluster scores	Total	Maximum
Aggression (total)	0	24
Verbal	0	9
Physical	0	6
SIB	0	9
Disruptive (total)	0	18
Mood	0	15
Apathy	0	21
Withdrawal	0	27
Innattention	0	15
Motor activity	0	21

APPENDIX C. Kennedy Krieger Down Syndrome Clinic Follow- Up Form

KENNEDY KRIEGER CHILDREN'S HOSPITAL
Down Syndrome Clinic Mental Health Progress Note

DOE: NAME:

AGE:

Previous Diagnoses:

CONCERN INTERIM HISTORY

MEDICATIONS ROS

1. 4.

2. 5.

3. 6.

TARGET BEHAVIORS (improved - same - worse) SIDE EFFECTS

1.
2.
3.
4.

MENTAL STATUS EXAM PHYSICAL EXAM Wt_____ Ht_____ BMI_____

HR_____ BP_____

DIAGNOSES LABS

1.
2.
3.
4.
5.

RECOMMENDATIONS

1.

2.

3.

4.

5.

6.

_____ _____

xxxxxxxxxxxxxxxx, M.D.
Director, DSC

xxxxxxxxxxxx ,CRNP
Pediatric Nurse Practitioner, DSC

APPENDIX D. Example of Data Gathered from a Case

Name: x • **Group 1**
KKI #:
Regression/ Skills lost Developed well the first two years of life and at that point he knew the colors, words and songs. Then he started to plateau especially with speech. Began having unusual articulation, accentuates and of words. By age $2^{1/2}$ started to loose eye contact, developed sensory issues, became more resistant to therapies. Regression was in speech and sociability.

Developmental History:

1mos: *Association for Children with DS: Early intervention Summary:*

- Personal and social: she demonstrates awareness of people in the room by focusing inconsistently on their faces. He turned eyes when he heard voices.
- Cognitive: x appeared to listen and be aware of people in the room.

4 mos: *Dvision of Developmental and behavioral Pediatrics*

- started babbling
- and rolls to back since $3^{6/12}$mos.

5 mos: *NYC Early Intervention Program*:

- He makes good eye contact and grabs adult finger to rise himself. He was alert all session and willing to explore toys.

6 mos: *Kathy Franen Christian Ma,*

- X. Is alert to auditory stimulation and demonstrates consistent localization of sound to either side. He clearly differentiates his mom from other voices and searches actively to locate her when she calls. He still seems not to recognize specific words as yet. (expected in the next six mos)
- X is developing basic gestures such as raising her arms to be picked up and reaching for desired objects. At times he adds vocalization to gestures to emphasize or direct attention to his request (although not yet consistently).
- He maintains eye contact with faces of speakers and fixes his gaze upon items of his environment. His interest have shifted from strong patterns to familiar toys, faces and his mirror image; he also has begun to imitate clapping as well as hand opening during play. X appears to recognize when he succeeds in imitating simple gestures.
- X smiles readily and laughs in response to physical stimulation.
- Over the summer he past from cooing and gurgling vocal behaviors to somewhat more purposeful vocal play and seems to recognize the social impact of his responses upon his listeners.
- X. demonstrates a somewhat intense reaction to food for the first few bites with some oral motor movement problems.

Division of Developmental and Behavioral Pediatrics

- Gazes intently to toys
- Watched examiner scribble bangs objects together and transfers. Shakes rattles, reached out for the doll but did not grab it.

7 mos: *NYC Early Intervention Program*:

- Progress report where it is noted that X. has a great eye contact and tolerates being placed in a variety of positions.
- X. is developing his cognitive skills and he is able to play peek a boo by removing the cloth from his face and giving a good eye contact to the therapist.
- He is also able to find a object hidden under a cloth.
- X is able to bring his hands to middle line and bang rattles together.
- X is able to activate cause and effect toys functioning at 4-5 mos level.

8 mos: *NYC Early Intervention Program*:

- X still displays good eye contact and reaches out to grasp colored pegs.
- He also shows interest in knocking down stacks blocks while in a variety of therapeutic positions.
- Concern: fluid in his ears and his decreased in sounds production.

9 mos: *NYC Early Intervention Program*:

- His very social and appears to be comfortable with therapist and teacher's company.
- He focused his gaze on the faces of others around him and shows an interest in a variety of toys.
- He improved his ability to transfer from quadruped to sitting.

12 mos: *NYC Early Intervention Program*:

- He is starting to point spontaneously although inconsistently at pictures in a book and able to scribble with minimal prompting.

13 mos: *NYC Early Intervention Program*:

- Tolerates various textures when exploring with his hands. He also sits independently and is performing fine motor skills at 7-9 mos (HELP checklist)

14 mos: *NYC Early Intervention Program*:

- N continues to expand his verbal and sign vocabulary. He now signs: Ball, book, more, eat, music, and occasionally baby and block.
- He consistently says "zha" for shoe, and does so spontaneously.
- He is expanding his play skills and enjoys playing with a toy train that makes noises and has a light.
- He also pushes a car down the ramp with assistance putting the car on the ramp.
- According to the HELP checklist X is functioning in gross motor skills at 8 to 10 mos level. He is able to crawl functionally in a reasonable speed.
- He is in a phase where he only wants his mother to interact with him.

15 mos: *NYC Early Intervention Program*: (6/30/01)

- Moves from chair to chair and stand momentarily without falling.
- June has been the month of vocabulary expansion for X and consistently can sound mooand say "Ba" for ship. X's signs are expanding also, he signs Gorilla and car consistently.
- X does not like messy activities like finger paint.

16 mos: *NYC Early Intervention Program*:

- Continues expanding vocabulary he now signs Mama with prompts and started to make s soft "woo woo" sound for the bark of the dog.

- N is able to place a circle, triangle, and square and more into a puzzle when each is removed one at time. Hi is able to push a car to see it move and will say "gzsh" for "go" to see the car roll down a ramp.
- N is also able to place a ball in a basket from a sitting position.
- He is cruising from room to room and crawling stairs with stand by assistant.

17 mos: *NYC Early Intervention Program*:

- N continues to progress in all areas, especially in communication. He continues to accurately identify pictures of dogs and he makes "woo woo" gestures with his mouth without the sound. His sound for sheep has gotten more sophisticated.
- X is able to sign ice cream. His receptive skills are better then his expressive.

18 mos: *NYC Early Intervention Program*:

- OT: Difficulties with motor planning (transferring objects from one pot to another) but doing progress in all areas.
- His self feeding is getting better but still has issues with textures.

19 mos: *NYC Early Intervention Program*:

- Good imitation skills for signs and discrimination of visual. He signs for video, airplane. He is now able to sight read certain words such as fingers, ears, eyes and nose.

20 mos: *NYC Early Intervention Program*:

- Improving his sight word vocabulary, now also identifies: cow, dog sheep and pig by making the animal sounds when the sight reads the words. He also reads baby,
- He also gives the correct piece of puzzle when asked to give it to a therapist (dog, sheep, cow, horse, pig, duck) and is beginning to give Barn, and tractor.
- He says Ma for the writing "mom"

21 mos: *NYC Early Intervention Program*:

- Steady gains in all areas of language, speech and feeding skills.
- Frequent upper respiratory infections.
- N responds now to many routines directives (open, come, stand up, kick, throw, put in etc..) and is better able to discriminative locatives "in" and "under" although still inconsistently.
- He has a very large vocabulary of nouns and can find a named object among a group of items in or within a picture.
- N also recognizes fairly abstract illustrations and is very attentive to picture books.
- N communicates primarily in one word utterances but attempting to use word series. His spontaneous utterances are most often manual signs which is his preferred modality. In fact he imitates signs far more easily and his approximation of signs are closer than parallel attempts at spoken words.
- He does use spoken words at times but often responds to instructions to speak with a loud protest or attempts to flee.
- X still shows some tactile defensiveness to messy projects. At times he cries when ask to participate in such activities.
- He continues to mature in his exploration of the environment and he is easily able to entertain himself playing with his toys. He still loves music activities.

22mos: *NYC Early Intervention Program*:

- X is working on matching skills. He is consistently matching an elephant a lion, and frog when given two options to choose from. Now when giving a third option his accuracy falls dramatically.
- Teachers at this point are working on social skills by having X ply with assistance with peers. He shares interests with them but need assistance to turn take and stay focus on interactive play.

26 mos: *NYC Early Intervention Program*:

- His fine motor skills are at 20 mos level. He is able to spoon feed himself the majority of the time and can drink from cup.
- Tactile defensiveness is much less now.

IFSP *NYC Early Intervention Program*:

- X walks independent and use stairs with assistance.
- Can stack 4- 5 block tower and string beads.
- Enjoys variety of sensory play like foam or play doh.
- Motor planning still is a problem. And can't manipulate a fork but eat with spoon soft foods independently.
- He does not assist with dressing but does not resists, not potty trained and can remove his socks.
- His vocabulary with clarity consists in 15 words. His overall receptive vocabulary is much higher. He use signs and body language to make his needs known. His speech repertoire and accuracy is inconsistent with poor intelligible skills.
- He responds to name when called and follows with eye contact. X can also follow one step command consistently. He also consistently can point and label objects and can say mommy and daddy, wave bye bye.
- X also recognizes familiar faces.
- Identifies himself in the mirror, and is working with sequential toys (problem solving to combine fine motor skills).
- He loves loud toys and play with balls.
- X knows some colors, can point at them and also label some letters and say them aloud. He also can point to his body parts.
- Social emotional he is warm, affectionate, and outgoing to people he knows but takes his time with people that he does not know.
- Gets along with other children but he does not play with them, he prefers to observe them.
- No behavioral concerns and his attention span varies and is considered medium depending on the task and activities.

30 mos ($2^{5/12}$) *NYC Early Intervention Program*:

- **X** has made very significant strides in communication skills during the past months and he has become a more confident speaker. He is using one to four word sentences, most typically 2 word phrases) to describe objects, indicate possessions, negate, request, describe events and direct actions. However his speech is poor intelligibility.
- Oral feeding skills are really good.

32 mos ($2^{8/12}$) *NYC Early Intervention Program*:

- He has a great ability to acquire and retain new vocabulary.
- He is able to combine 3-4 word sentences to spontaneously request desired items and answer familiar "WH" questions. In 1 -2 word phrases.
- X has some difficulty executing the verbal communication skills that he has when group activities and requires verbal prompting to help him to join in during circle time.
- X interest in his peers and socializing have increased slightly over the past three mos. He recognizes all his peers and will at times spontaneously greet them. He engages in parallel and associative play with peers and will at times initiate such a play.
- He has some difficulty with transitioning independently.
- He also has problems with unstructured play time, X is easily distracted and has difficulty choosing play materials and following through on play schemes.

3 y/o: *Therapy and Learning center: Speech and language evaluation (*look Xerox) (Psychological eval had similar findings)

- Playful child whose skills vary widely depending upon the setting. In quieter 1:1 setting X will name and describes items, initiates songs and finger plays. 1:1 settings also he responds more consistently to verbal cues of adults. However in busier environments has more difficult attending to structured activities and transitioning.
- His ability to remain seated during circle time and tabletop activities has greatly improved since the beginning of the year.
- X verbal output is limited in classroom and is difficult for him to imitate modeled phrases in that environment without maximum adult sues. X also presents with decreased relatedness in 1:1 and group activities. Eye contact is generally limited and he requires
- Awareness of peers and their activity appears to be limited but it increases with adult facilitation. In larger group activities. X will leave the group and sit on his own.
- During formal eval. X had significant difficulty attending to presented stimulus and maintaining attention task. He appeared to have problems "getting organized" and to attend to task. He did produce spontaneous speech but mostly for label and describe.
- He tends to over stuff his mouth with food and needs to be remain to empty it before putting more.
- X informally evaluated was seen to produce up to 4 utterances but with decreased intelligibility.
- Preschool Language scale 3 (pls-3)
    - Auditory comprehension age equivalent : 1.4 (16 mos)
    - Expressive 1.6 (18 mos)
    - Total language score 1.5 (17 mos)
    - During administration of PLS-3 receptively:
        - X had difficulty using following directions
        - Noted that he had extensive receptive and expressive vocabulary.
        - It was noted also that his limited relatedness with others made it difficult for him to respond to simple questions and request.
        - X did follow simple instructions when visual cues were included
    - During administration of PLS-3 Expressively:
        - He will label pictures but not upon adult request.
        - He imitated simple words upon request and uses multiple words utterances in self directed activities while playing alone or with an adult. He was not

observed to use possessive pronouns (me mine yours..) use inflection in questions, or simple plural form.

- He had problems responding to directives and sometimes gave no response
- He uses his extensive expressive vocabulary to label and describe but needs maximum cues to use it for communicative intent in the classroom. his eye contact is very limited and sometimes needs max cues to establish even brief eye contact with communication partners.
- He prefers to play alone and needs adult for parallel play.

OT EVALUATION:

- Gross motor skills: 20-23 mo
- Fine motor skills: 16- 19mos
  - Builds towers of 3-4 blocks using both hands.
  - Has selective attending and is inconsistently complaint
  - He is distractible with short attention span and he requires re direction to remain engaged in structured table-top activities.
  - He continues to mouth/ licks objects during exploration.
  - Counts to 20 and labels colors and shapes
- Sensory: X. presents inconsistent eye contact, but can read sight words.
- Short attention span.
- Not toilette trained
- Finger feeds, drinks from cup and assist with dressing and undressing.
- Does not like to have his hair washed.

$3^{7/12}$: *McCarton Center: Williams report School Psyc.*

- Parents report normal development but losing skills: articulation, motor planning, spontaneous use of words he previously used and knew well, and interest in engaging with peers.
- Clintian observations:
  - Engaged with parents and fleet the table when small demands where posted. Was very active
  - Socialization: eye contact was intermittent with examiner and not sustained. And eye contact with parents was good.
  - Could imitate simple actions,
  - Several emotions where observed during session and responded well to social praise.
  - Attention/ activity level: attention was variable with high levels of distractibility.
  - Behavior: low tolerance frustration and self directed behavior. He liked to shake a string with beads and he frequently babbled to himself in a high pitch voice. Tensing, body posturing and spastic motor movements where observed. He would throw objects when done with them.
  - When given the opportunity to play with toys he engage very briefly with a few, he would lay over the table and moved a string of beads or shaking them. He moved actively about the room and enjoying dumping objects.

- Communication: ability to use language effectively to communicate was limited. He does not let the care giver know if he is thirsty or hungry. His parents report that his language has become more intelligibility in the last 6 to 9 mos. He will spontaneously label objects but not upon request and would respond to simple questions. He was observed to use "yes or no" in an appropriate manner.
- PDD dx (look Xerox 2)

GTC $3^{9/12}$ Fixates on yo yo strings, waves them around, specially when tired but can be re direct with some protest. May tense arms and stare at hands briefly. X Does not like fruit and brother screaming. Loves massage and scratching softly his face, strings and chew tubes. No SMD's. Also PDD.