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Autism Spectrum Disorder Symptomatology in Verbal Children with Williams Syndrome

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AUTISM SPECTRUM DISORDER SYMPTOMATOLOGY IN VERBAL CHILDREN WITH WILLIAMS SYNDROME

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ABSTRACT
AUTISM SPECTRUM DISORDER SYMPTOMATOLOGY IN VERBAL CHILDREN WITH WILLIAMS SYNDROME

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Many genetic disorders of known etiology share behavioral characteristic with the autism spectrum disorders (ASD), including language delays, social difficulties, and unusual patterns of behavior. There exist tendencies to either over- or under-pathologize these similarities, resulting in both false diagnoses and diagnostic overshadowing. Recent findings in Williams syndrome (WS), a genetic disorder often contrasted with ASDs, have demonstrated a significant overlap between these two phenotypes in young children with limited language. Using a gold-standard autism diagnostic tool, the ADOS, the present study aimed to further characterize the nature of socio-communicative behaviors in verbal children with WS, both within WS and in comparison to children with Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and developmental conditions of mixed etiology (ME). Results indicated that approximately one-third of the children with WS met threshold for classification on the autism spectrum. There were a number of items on which the children classified "ASD" and those classified "non-spectrum" received different scores, such as conversation difficulties, quality of social overtures including integrated eye contact and facial expressions, and play behaviors. Consistent with previous studies, children with WS who have significant socio-communicative difficulties (i.e., those classified "ASD") demonstrate a behavioral

profile similar to that seen in children with Pervasive Developmental Disorder-Not Otherwise Specified. Implications for understanding the nature of the behavioral pattern in WS, and in genetic disorders in general, will be discussed.

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Acknowledgements

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Introduction

A substantial body of literature indicates that there are considerable behavioral similarities between autism spectrum disorders (ASDs) and numerous disorders with known genetic etiology. Williams syndrome (WS) has historically been contrasted with ASDs because people with Williams syndrome are generally highly sociable. However, behavioral overlap is considerable and further characterization of the social phenotype in WS is warranted. In addition, diagnostic overshadowing in this population is a potential risk that could be managed better with an increased understanding of the behavioral overlap. Given that language delays, socio-communicative difficulties, and restricted and repetitive behaviors are common among ASDs and genetic conditions, the implications of further investigations into behavioral overlap include increasing our understanding of the genetics of these behaviors in general. In addition, the locations of the genetic abnormalities of these disorders and their relation to behavioral similarities with the autism spectrum may point to additional genetic risk areas for further investigations into ASDs.

This Introduction will first provide a brief overview of the general features of ASDs, followed by a review of a number of genetic disorders of known etiology, with specific emphasis on their behavioral overlap with ASDs. Overlaps for people with WS will then be covered in depth, given the focus of this study. The implications of these findings for better understanding the behavioral phenotype in WS and other genetic conditions will be discussed, as will limitations and future directions in relation to the understanding of the genetics of socio-communicative behaviors in general, as well as

those of ASDs, will then be discussed. The rationale for the current study will then be presented.

Brief Review of ASD Symptomatology

In short, ASDs, which include the distinct diagnoses of Autistic Disorder (AD), Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), and Aspergers disorder, are characterized by qualitative impairments in communication and reciprocal social interactions, as well as the presence of restricted or stereotyped patterns of behavior, interests, or activities (APA, 2000). Although the nature and severity of these impairments varies between the individual diagnoses within the spectrum, difficulties in socio-communicative behavior are generally considered the hallmark feature (Kanner, 1943; Fein, Pennington, Markowitz, Braverman, & Waterhouse, 1986). This variability in phenotypic presentation makes for a fairly heterogeneous group of individuals classified on the spectrum.

Since first described by Kanner (1943), autism and the subsequently characterized related disorders (i.e., PDD-NOS and Aspergers syndrome) have become the focus of a large body of research, including investigations into the prevalence of the conditions. The earliest estimates of the rate of autistic disorder were 4-5 people per 10,000 (Lotter, 1966); although a thorough discussion of the explanatory reasons is beyond the scope of this paper, shifting conceptualizations of a broader spectrum, as well as growing awareness of ASDs, has contributed to an increase in this rate over time. The most recent reports estimate that 1 out of every 110 children in the United States has an ASD (ADDM, 2009).

Currently, ASDs are widely considered to be genetic in nature, such that heritability estimates for the disorders, as well as the broader spectrum of related behaviors, are among the highest of any neuropsychiatric disorder (Bishop et al., 2004). Strong support for the assertion of the genetic nature of ASDs originates from findings within families. For example, one landmark study demonstrated that monozygotc twins were 92% concordant for ASD, while dizygotc twins were 10% concordant (Bailey et al., 1995). The strongest risk factor for the development of an ASD is having a sibling who has previously been diagnosed with one (Fombonne, 2005; Lauritsen, Pedersen, & Mortensen, 2005).

Despite these findings that demonstrate the genetic nature of ASDs, as well as decades of research and increasingly sophisticated methods, the genetic underpinnings of ASDs are largely unknown. Various genetic loci and specific chromosomal aberrations have been implicated in ASDs; however, the vast majority of the findings are inconsistent and generally are not replicated from study to study. These findings are further complicated by the fact that when genetic abnormalities are detected in an ASD sample, they only account for 1-2% of the cases (see Abrahams & Geschwind, 2008 for a review). Although there are many possible explanations for this discrepancy across findings, the general consensus among many researchers is that given the wide variability in presentation, ASDs can best be conceptualized as multi-gene disorders (Zhao, et al., 2007; Ronald, Happe, Price, Baron-Cohen, & Plomin, 2006), with various paths contributing to the behavioral phenotype observed (Belmonte & Bourgeron, 2006; Happe, Ronald, & Plomin, 2006; Persico & Bourgeron, 2006).

Before proceeding to a discussion of genetic disorders of interest, two important concepts relevant to studying behavioral phenotypes need to be acknowledged. First, it is important to remember that these phenotypes are probabilistic; that is, individuals with a specific syndrome are considered to be more likely to exhibit characteristic traits than other individuals. While typically present, these traits are not necessarily universal within the disorder. Second, many genetic disorders have certain behavioral traits in common, making them less specific to a particular disorder per se and more broadly related to genetic or developmental disorders in general (Dykens & Hodapp, 2001).

Behavioral Phenotypes in Genetic Disorders of Interest

Down syndrome.

Individuals with Down syndrome (DS) have typically been described as charismatic (Gibbs & Thorpe, 1983; Wishart & Johnston, 1990), with strengths in social functioning relative to individuals with other forms of intellectual disability (Dykens & Kasari, 1997; Myers & Pueschel, 1991). However, some studies haven found inconsistencies in the presentation of this stereotyped personality in DS (Ghaziuddin, Tsai, & Ghaziuddin, 1992; Flynt & Yule, 1994), with reports of co-occurring ASDs ranging between 2% (Collacott, Cooper, & McGrother, 1992) and 10% (Paly & Hurley, 2002).

Commonly described behavioral features in individuals with DS that overlap with the autism spectrum include social isolation, poor eye contact, restricted interests, and repetitive behaviors (Ghaziuddin, 1997; Kent, Evans, Paul, & Sharp, 1999; Capone, Grados, Kaufmann, Bernad-Ripoll, & Jewell, 2005). Although many early studies used questionnaire methods to obtain reports of behavior, more recent studies have used

observational methods and expert clinical judgment to better understand the specific problematic behaviors. Descriptions of the behavioral presentation include difficulties in all areas affected in ASDs. Hepburn and colleagues (2008) found that many children with DS exhibited communication difficulties at a level consistent with ASDs; however, social interactive behaviors were relatively stronger, although still an area of concern, and therefore precluded a comorbid ASD diagnosis in the majority of children in the study. A similar study using parent report along with direct observation revealed that stereotyped behaviors, not socio-communicative deficits, generally differentiated those children with DS alone from those with DS and ASD (Hepburn & Maclean, 2009). In summary, it appears that communication difficulties and stereotyped or repetitive behaviors are quite common among children with DS and are typical components of the behavioral phenotype. Social reciprocity difficulties are also present in a proportion of the DS population, although to a lesser degree in comparison to both other behaviors and to ASDs. Nevertheless, significant behavioral overlap with the autism spectrum does exist in DS.

Fragile X Syndrome.

Fragile X syndrome (FXS) is considered the leading cause of genetically inherited intellectual disability (Hatton, Bailey, Hargett-Beck, Skinner, & Clark, 1999) and is associated with a number of behavioral characteristics similar to those seen in ASDs, particularly when compared to other genetic disorders (Oliver, Berg, Moss, Arron, & Burbidge, 2011). The first report of diagnostic overlap between these disorders indicated that 18.5% of males with FXS also met criteria for autistic disorder (Brown et al., 1982), although subsequent studies found estimates up to 30% (Bailey, Mesibov, Hatton, Clark,

Roberts, & Mayhew, 1998; Baumgardner, Reiss, Freund, & Abrams, 1995; Cohen, 1995; Rogers, Whener, & Hagerman, 2001; Turk & Graham, 1997). Similar rates were found when a broader ASD conceptualization, including autistic disorder and PDD-NOS, was used (Clifford, Dissanayake, Bui, Huggins, Taylor, & Loesch, 2007).

Although rates of comorbidity differ between studies depending on the inclusion of males only versus males and females (Mazzocco, Kates, Baumgarder, Freund, & Reiss, 1997) as well as the measures used, there is a general pattern of specific behaviors common in FXS that overlaps significantly with the autism spectrum. In fact, Clifford and colleagues (2007) found that when overall patterns of behavior and not simply diagnostic categories were used, approximately two-thirds of boys and one-fourth of girls with FXS demonstrated behavioral similarities with the autism spectrum. Atypical use of language, poor eye contact, social anxiety, and hand and finger mannerisms have all been reported in a variety of studies (Baumgardner et al., 1995; Kerby & Dawson, 1994; Lachiewicz, Spiridigliozzi, Gullion, Ransford, & Rao, 1994). Philofsky and colleagues (2004) have suggested that children with FXS and autism demonstrate a pattern of social interactive behaviors that are qualitatively different than those seen in FXS alone. Although children with FXS alone demonstrate social anxiety that may superficially mimic difficulties seen in ASDs, these behaviors are significantly improved when studied with caregivers and other familiar adults; however, children with FXS and ASD do not demonstrate this improvement and continue to struggle to interact typically (Roberts, Boccia, Bailey, Hatton, & Skinner, 2001). In addition, individuals with FXS and ASD have been differentiated from those with FXS alone using descriptions of parent-reported communicative behaviors (McDuffie et al., 2010) and reciprocal social interactions

(Kaufmann et al., 2004). McDuffie and colleagues reported differences in the use of gestures, play-related behaviors, and stereotyped language in the two groups, while Kaufmann and colleagues (2004) found that all behaviors related to reciprocal social interactions were problematic for the FXS and ASD group. It appears as though there are communication and social reciprocity difficulties present in a subset of individuals with FXS that warrant an additional diagnosis on the autism spectrum; however, careful consideration of the severity and pervasiveness of these difficulties is necessary. Regardless, given the high rate of ASDs and difficulties with socio-communicative behaviors in FXS in comparison to other genetic syndromes, it seems likely that the genetic regions associated with FXS will continue to be areas of interest in terms of understanding both socio-communicative difficulties and ASDs.

Rett Syndrome.

Rett syndrome (RS) is a genetic disorder involving a known mutation of the MECP2 gene of the X chromosome (Amir, van den Veyber, Wan, Tran, Francke, & Zoghbi, 1999), characterized by an early period (up to 18 months of age) of typical development, followed by the gradual loss of language and motor skills (Nomura & Segawa, 2005) and the development of behaviors similar to those seen in the autism spectrum. In fact, before the identification of RS as a separate disorder, many with RS were considered to have autism (Olsson, 1987; Olsson & Rett, 1987; Witt Engerstrom & Gillberg, 1987). Stereotyped and repetitive hand movements, generally midline hand wringing, are present (Hagberg, 1995). Typically, regression in RS involves the loss of language, as well as skills in socialization and appropriate play (Charman et al., 2002). The cumulative effects of these changes are such that individuals with RS often

demonstrate a pattern of difficulties in the ability to relate to others socially (Mount, Charman, Hastings, Reilly, & Cass, 2003). Given these behavioral similarities, RS is currently considered one of the pervasive developmental disorders (APA, 2000). While there is debate regarding the appropriateness of this classification (Rutter, 1994; Tsai, 1992), further discussion of this is beyond the scope of this review. Nevertheless, given the behavioral presentation of individuals with RS and the similarity to behaviors associated with ASDs, the genetic origin of the disorder is informative in terms of further investigations pertaining to communication difficulties as well as repetitive and social behaviors.

Tuberous Sclerosis Complex.

Tuberous sclerosis complex (TSC) is a genetic disorder that is often linked with ASDs (Smalley, Tanguay, Smith, & Guiterrez, 1992); in fact, TSC is considered one of the most commonly associated medical conditions with ASDs (Rutter, Bailey, Bolton, & Le Couter, 1994), with approximately 3-4% of children with autism also having TSC (Gillberg, 1992). Although the earliest descriptions of TSC included symptoms commonly observed in children with ASDs such as stereotyped movements, social isolation, and behavioral difficulties (Critchley & Earl, 1932), systematic investigations into this phenomenon did not begin until many years later. Reports of the prevalence of comorbid autism in TSC range from approximately 25% (Curatolo, Verdicchia, & Bombardieri, 2002; Gillberg, Gillberg, & Ahlsen, 1994) up to 50% (Hunt & Dennis, 1987); however, when the broader conceptualization of ASD is used, rates have been reported as high as 86% (Gillberg, Gillberg, & Ahlsen, 1994). The wide variability in these estimates may be related to the use of discrepant methodologies for diagnosis and

outdated diagnostic criteria, as well as selection biases. A small subset of studies has attempted to address the selection bias issue by including participants with TSC who have average cognitive abilities. While the rates were considerably less, the results of these studies continued to demonstrate an overall higher rate of ASD in individuals with TSC and average intelligence than in individuals without TSC and average intelligence (Prather & de Vries, 2004; de Vries, Hunt, & Bolton, 2007), indicating that behavioral overlap with the autism spectrum is common in TSC regardless of cognitive functioning.

In terms of behavioral similarities, Smalley and colleagues (1992) found that individuals with TSC were reported to demonstrate difficulties in the communication and reciprocal social interaction domains that were similar to those typically described in classic autism. However, the children with TSC did not engage in the same amount of repetitive behaviors or have the stereotyped interests that are part of the diagnostic criteria; therefore, these behaviors were more indicative of an PDD-NOS diagnosis than one of classic autism. Using a direct observation method, Jeste and colleagues (2008) found that virtually all children with TSC demonstrated significant deficits in play skills when measured across four different age points. In addition, a substantial portion of children demonstrated significant difficulties in communication and reciprocal social interactions at all time points. The nature and severity of these difficulties were such that the percentages of children classified on the autism spectrum ranged from 46% to 66%. TSC clearly represents a genetic disorder with considerable socio-communicative difficulties and overlap with the autism spectrum in terms of behavioral similarities and comorbidity.

Angelman syndrome.

Angelman syndrome (AS) is a genetic disorder frequently associated with ASDs, although little is know in regard to the rates of comorbidity due in part to the high incidence of intellectual disability within the syndrome (Petit et al., 1996; Steffenberg, Gillberg, Seffenberg, & Kylerman, 1996). For example, Trillingsgaard & Ostergaard (2004) and Peters and colleagues (2004) found that over half of individuals with AS demonstrate socio-communicative difficulties consistent with a diagnosis on the autism spectrum. However, in both studies, the individuals with more profound intellectual disability were also the individuals who were most likely to also be diagnosed with an ASD.

Despite this potentially confounding factor, there remains considerable behavioral overlap between AS and ASDs regardless of intellectual functioning. Parents of individuals with AS reported high rates of delays particularly in expressive language, as well as failure to develop appropriate imitation skills. In addition, stereotyped behaviors such as hand flapping and mouthing of objects were commonly reported, although repetitive use of objects was not (Walz, 2007). One study using direct observation (Peters et al., 2004) reported that even the participants with AS who did not meet criteria for an ASD demonstrated stereotyped hand and body movements, as well as deficits in play skills and in language development. When compared to individuals with idiopathic autism, those with AS and autism demonstrated relatively fewer difficulties in the areas of reciprocal social smiling, directing facial expressions towards others, sharing enjoyment in interactions with others, response to name, and unusual or repetitive behaviors (Trillingsgaard & Ostergaard, 2004), suggesting a pattern of socio-communicative difficulties with AS that differs from that seen in classic autism. It

appears as though individuals with AS appear to have verbal and socio-communicative difficulties and some stereotyped behaviors that overlap with the autism spectrum, while lacking the aloofness and repetitive behaviors commonly reported in ASDs. Nevertheless, the behavioral presentation across the disorders is quite similar and AS continues to serve as a disorder of interest in relation to further understanding socio-communicative behaviors and the genetic basis of ASDs.

Smith-Magenis Syndrome.

Smith-Magenis syndrome (SMS) is a genetic disorder with characteristic physical features (see Greenberg et al., 1996 for a review), as well as a behavioral profile that includes features similar to those often seen in ASDs. Currently, no systematic studies have been published regarding the prevalence of ASDs in SMS; the majority of reports of comorbidity are in the form of case reports (Vostanis, Harrington, Prendergast, & Farndon, 1994). However, a limited number of studies describing the behavioral phenotype of the disorder do exist. One of the most striking and fairly ubiquitous features of SMS is self-injurious behavior (Dykens & Smith, 1998; Finucane, Dirrigl, & Simon, 2001), which is commonly reported in ASDs but are not part of the core symptoms (APA, 2000). In addition, a distinct pattern of repetitive behavior is also characteristic of SMS, including self-hugs and "lick and flip" stereotypies when turning pages (Dykens & Smith, 1998). The presence of these behaviors is likely to raise concerns regarding a comorbid diagnosis on the autism spectrum; however, children with SMS do not consistently demonstrate difficulties in communication and social reciprocity that are core symptoms of autism. Reports of social awareness, appropriate eye contact, seeking out social interactions with others, and typical eye contact, as well as descriptions such as

"loving," "eager to please," and "enjoying, seeking, and interacting with adults" (Udwin, 2002) in SMS are inconsistent with ASDs and point to the need for further investigation of the behavioral patterns present. For example, it may be that the genetics of SMS relate more to the underpinnings of repetitive behaviors but not broad socio-communicative difficulties.

Specific Chromosomal Locations.

Given that heritability estimates in ASDs are approximately 90% (Bailey et al., 1995; Le Couteur, et al., 1996), the genetics of autism have been a topic of much research in the past decade. Despite the advent of more sophisticated technology and countless investigations, the specific genetics of ASDs are widely unknown; however, using population genome scans, a variety of chromosomal locations have been implicated as association areas. For the purposes of the present review, 15q11-q13 disorders and 22q11.2 deletion syndrome will be discussed as they represent the chromosomal locations most strongly associated with ASDs.

15q11-q13 Disorders.

Deletions within the 15q11-q13 region lead to the occurrence of two known neurodevelopmental disorders with behavioral characteristics that overlap with the autism spectrum. One of these disorders, Angelman syndrome (AS) has been previously discussed in this review; Prader-Willi syndrome (PWS) is also associated with an increased risk for ASDs, although to a lesser degree (Descheemaeker et al., 2002). Duplications within this region, particularly those stemming from maternal inheritance, have been associated with a general developmental disorder that includes severe intellectual impairment and language delays (Bolton et al., 2001; Boyar, et al., 2001;

Browne et al., 1997). Difficulties with social interactions, poor joint attention difficulties, hand flapping, and rigidity in the use of language have also been reported (Cook et al., 1997). Relatively fewer reports of documented cases of comorbid ASDs were reported (Bolton et al., 2001), leading researchers to continue investigating this link between socio-communicative behaviors in individuals with 15q11-q13 deletions and potential ASDs.

Given the rarity of these deletions, most reports are limited to case studies. Kwasnicka-Crawford and colleagues (2007), using gold-standard diagnostic measures, described the behavioral presentation of a young girl with duplication in the 15q11-q13 region. Poor eye contact, difficulties with reciprocal social interactions, a lack of social play, and repetitive behaviors were cited as behaviors that overlapped considerably with the autism spectrum, such that a comorbid diagnosis was made. Pagnamenta and colleagues (2009) reported on a family with three children diagnosed with autism who subsequently were found to have a deletion at 15q13.3. All three of the children met criteria for autism using the same widely accepted measurements, demonstrating severe language delays, limited to absent social communication, and ritualistic and repetitive behaviors. Although duplications in the 15q11-q13 region are not universally associated with ASDs, there does seem to be a link between the genetic abnormality and behaviors similar to those seen on the autism spectrum. In contrast, tripilication in this area is more consistently associated with ASDs, as various reports have described “autistic features” in one or more subjects (Dennis, Veltman, Thompson, Craig, Bolton, & Thomas, 2006; Schinzel, et al., 1994; Vialard et al., 2003). These studies are also limited by small

sample sizes and as of yet do not use gold-standard measures or provide specific examples of behaviors present that overlap with the autism spectrum.

22q11.2 Deletion Syndrome.

Similarly to many of the genetic disorders already discussed, there is wide variability in the phenotypic presentation of individuals with 22q11.2 Deletion Syndrome (22q11.2DS), including mild intellectual disability, language delays, and learning disabilities (McDonald-McGinn et al., 1999; McDonald-McGinn et al., 2001). Behavioral issues, including attention and mood difficulties, have also been reported (Arnold, Siegel-Bartlet, Cytrynbaum, Teshima, & Schachar, 2001). Reports of social skills deficits, including withdrawn and shy behaviors, difficulty initiating interactions, and a narrow variety of facial expressions, have also been reported (Gerdes et al., 1999; Niklasson, Rasmussen, Oskarsdottir, & Gillberg, 2001, 2002; Swillen et al., 1999), indicating that there may be a possibility for a link between the deletion and difficulties in socio-communicative behaviors. Although these reports of increased frequency of ASD-like traits in individuals with 22q11.2DS exist, there have also been conflicting reports of a low rate of co-occuring ASDs (Kozma, 1998; Ogilvie, Moore, Daker, Palferman, & Docherty, 2000). Many of these studies relied on small sample sizes and used simple questionnaire methods to determine the rate of ASDs; when more sophisticated methods are used with larger samples, results indicate that there is an increased rate of ASDs in individuals with 22q11.2DS (Fine et al., 2005; Vorstman et al., 2006). It is worth noting that even those individuals with 22q11.2DS who do not carry a comorbid ASD diagnosis do not demonstrate entirely typical behavior in terms of socio-communicative difficulties. Based on parent report, Vorstman and colleagues (2006) found that among 60 children

with 22q11.2DS, few were reported to have typical socio-communicative behavior. Half of the children met criteria for an ASD; despite the lack of a diagnosis, the other half were described as having significant difficulties in all areas implicated in ASDs. Although these studies did not include a direct observation of the child, the presence of parent-reported difficulties is such that continued research in this area is warranted.

In summary, a number of genetic syndromes present with socio-communicate difficulties and other behavioral similarities with the autism spectrum; however, the presence of these behaviors is not universally associated with a comorbid ASD diagnosis (see Table 1 for a review). The wide variability in phenotypic presentation points to the importance of these disorders in our understanding of socio-communicative behaviors in general, as well as in relation to the triad of features present in ASDs. This variability also indicates the need for continued studies using empirically validated measurement instruments intended to better characterize the behavioral phenotype present. Williams syndrome (WS), an additional disorder not yet discussed, is an example of a disorder with known genetic etiology that has long been the subject of comparison to ASDs. It has also been relatively well characterized in terms of socio-communicative difficulties using gold-standard measures.

Socio-communicative Behavior and ASD Overlap in WS

WS is a neurodevelopmental disorder of genetic origin, stemming from a hemizygous deletion of approximately 25 genes on chromosome 7q11.23 (Ewart et al., 1993; Hillier, et al., 2003). In addition to a variety of common physical features, individuals with WS often demonstrate characteristic cognitive and behavioral phenotypes. Briefly, there is some degree of developmental delay present in the majority

of individuals with WS (Greer, Brown, Pai, Choudry, & Klein, 1997; Mervis et al., 2000; Udwin & Yule, 1991), with relatively stronger language, after a period of early delays, than would be expected given developmental level (Gosch, Städing, & Pankau, 1994; Mervis & Bertrand, 1997; Mervis & Robinson, 2000; Udwin & Yule, 1990) and a pervasive difficulty with visuospatial tasks like pattern construction (MacDonald & Roy, 1988; Mervis, Robinson, & Pani, 1999) and drawing abilities (Wang, Doherty, Rourke, & Bellugi, 1995).

The characteristic personality profile associated with WS includes high levels of sociability, friendliness, and empathy (Dilts, Morris, & Leonard, 1990; Gosch & Pankau, 1997; Klein-Tasman & Mervis, 2003; Tomc, Williamson, & Pauli, 1990). Individuals with WS have been described as being less hesitant to interact with strangers than other children with developmental delays (Mervis et al., 2003), as well as overly friendly and affectionate (Tomc, et al., 1990). The presence of these personality traits would not logically lead one to consider difficulties with social interaction in individuals with WS. In fact, conceptualizations of the disorder have sometimes included a direct contrast to ASDs (Rapin & Tuchman, 2008). However, over the course of decades of research on WS and its behavioral manifestations, a pattern of deficits in individual social skills and functioning has become evident, such that a stark contrast to ASD may not provide an accurate characterization of the behavioral profile seen in WS. In order to further discuss this overlap, the following sections will summarize the literature on WS in the areas impaired in ASDs: repetitive behavior, verbal and nonverbal communication, and reciprocal social interactions.

Repetitive behavior and preoccupations in WS.

Repetitive behavior and preoccupations or obsessions are common in WS, with some reports as high as 86% of individuals with disorder demonstrating some form of these behaviors (Davies, Udwin, & Howlin, 1998; Rodgers, Riby, Janes, Connolly, & McConachie, 2012). Many adults with WS have obsessive interests, many of which appear to be related to anxiety-provoking topics such as natural disasters or anticipation of upcoming events such as birthdays or holidays. Highly routinized behavior and more obsessive-compulsive checking behaviors are not as common, but have been reported in some portion of the population (Davies et al., 1998). Compulsive greetings, watching spinning objects, and obsessive needs to locate the sources of sounds have also all been reported (Semel & Rosner, 2003). Some have suggested that there is a relation between these behaviors and sensory processing abnormalities, problem behaviors, and adaptive behavior (Semel & Rosner, 2003; John & Mervis, 2010; Riby, Janes, & Rodgers, 2013). Although no studies have explicitly examined the causal relations between these factors and repetitive behavior, it is clear that repetitive behaviors and preoccupations are part of the typical behavioral presentation in WS.

Verbal communication in WS.

Early reports of language skills in WS pointed to a relative sparing of abilities in relation to overall cognitive ability (Bellugi, Marks, Bihrle, & Sabo, 1988; Bellugi, Wang, & Jernigan, 1994). However, further investigation revealed that these abilities are present after a period of early delays. Masataka (2001) found delays in WS across all early language abilities measured, including the onset of canonical babbling and first words. A longitudinal study of language development in young children with WS and DS, as well typically developing children, found that at 18 months of age the children in

the WS and DS groups produced less sophisticated babbling patterns and a lower number of syllables per babble, as well as fewer consonant sounds per observational session (Velleman et al, 2006 as cited in Mervis & Becerra, 2007). Difficulty segmenting words within the verbal stream has also been described in toddlers with WS, which may limit the ability to acquire expressive vocabulary (Nazzi, Paterson, & Karmiloff-Smith, 2003). In fact, parental report of the average age of acquisition of a 10-word expressive vocabulary in WS falls below the 5th percentile; age of 50- and 100-word acquisition also falls below the 5th percentile (Mervis, Robinson, Rowe, Becerra, & Klein-Tasman, 2003b). The average age at which the children in this study met the 100-word vocabulary milestone was 40.9 months, while the majority of typically developing children meet this milestone at 18 months (Fenson et al, 2007). These findings are consistent with an overall pattern of delayed acquisition of language in WS.

While the majority of individuals with WS do eventually gain basic language skills, as the demands of language use become more complicated, patterns of strengths and weaknesses in this area become evident. Gosch and colleagues (1994) described the vocabulary abilities of a group of children with WS as similar to those of children with nonspecific developmental disabilities and found that the groups performed similarly across the majority of measures of language comprehension and production in terms of both words and sentences. Similarly, the receptive vocabulary of children with WS has been described as similar to other children of the same chronological age with developmental delay, specifically those with DS (Klein & Mervis, 1999); however, impairments become more obvious when the tasks become more complicated than simply identifying a spoken word. Mervis and John (2008) demonstrated a relative strength in

concrete vocabulary when compared to relational vocabulary in WS. Overall, despite an early delay in expressive vocabulary acquisition, once children with WS begin to use single words, the overall growth pattern of subsequent vocabulary acquisition is generally similar to what is seen in typically developing children (Mervis, 2004), although at a delayed rate. Although these linguistic challenges may not be as pronounced as those evident in other aspects of cognitive functioning in WS, there does appear to be considerable difficulties in language development and use in WS.

Additional language difficulties in WS have been reported in the area of pragmatics, or the use of language in social situations. Although parents reported that their children with WS had stronger pragmatic skills than children with ASDs (Philofsky et al., 2007), their skills in these areas were weak in comparison to typically developing children and children with DS or specific language impairment (SLI). Of particular relevance to the overlap with the autism spectrum are the difficulties reported in the inappropriate initiation of conversation and use of stereotyped conversation in WS (Laws & Bishop, 2004).

An overall pattern of delayed achievement of early language-related milestones, such as babbling, use of single words, and vocabulary development, coupled with difficulties related to the appropriate use of language paints a picture of atypical language development in WS similar to the pattern seen in ASDs.

Nonverbal communication in WS.

As described above, language studies in WS point to a delay in the acquisition of first words and early vocabulary development. Often times, children with language delays compensate for these delays by employing an effective communicative strategy –

the use of nonverbal communication such as gestures and eye contact. However, children with WS have demonstrated a delay in this behavior as well. Singer Harris and colleagues (1997) compared a large sample of young children with WS and DS on a parent completed measure of early language skills and use of gestures and found a difference between the groups in gesture use. In this study, the children with DS and WS were equally delayed in language use, but the children with DS demonstrated a compensatory pointing mechanism, while those with WS did not. This finding was replicated in a subsequent study using both parent questionnaire and direct observation of the child in numerous conditions (Laing et al., 2002). Across these varied behavioral observations, children with WS produced fewer pointing behaviors than the control group. These findings persisted even when the researchers modified the interaction to allow for more pointing opportunities. In addition, these opportunities allowed for the examination of the comprehension of pointing by looking at how often the child followed the point of the examiner or produced a pointing gesture in response the examiner's point. Similar results were found in this condition, such that children with WS followed points less often than controls. Previous research has found that typically developing children follow a pattern in which comprehension of referential pointing begins at about 10 months of age and that this comprehension precedes the production of pointing (Butterworth & Grover, 1990). Another interesting observation from the Liang and colleagues study (2002) is the fact that the children with WS do not exhibit the same pattern. In fact, these children were delayed in both the production and comprehension of pointing gestures.

An aspect of social communication that is separate from spoken language use is eye gaze, which is also reported to follow an abnormal developmental trajectory in WS.

Although they did not use a systematic observation or coding procedure, and did not include a contrast group, Jones et al. (2000) reported anecdotal evidence that children with WS demonstrate an intense interest in the faces of other people, so much so that the task at hand is often ignored. More controlled studies have elaborated on this observation and have found differences in the gaze behaviors of young children with WS. Mervis and colleagues (2003a) compared the behaviors of a single child with WS, age 10 months, during play sessions with her mother and a stranger to the behaviors of both chronological and developmental age matched control infants. The child with WS was reported to spend double the amount of time looking both her mother and the experimenter when compared to the controls. The quality of her gaze towards the examiner was also rated as "extremely intense" 78% of the time, whereas the gaze behaviors of the control children were never described in this way. Within the same report, a larger group of older children with WS (8 to 43 months) was compared to children of the same age range with developmental delays of other etiology during an appointment with a doctor, considered to be the stranger in this setting. The children with WS demonstrated abnormal gaze behaviors, once again manifested as "extended and intense looking," a description that was never used for any of the control children.

In sum, both verbal and nonverbal communication is delayed in WS, which is similar to the overall characterization of communication development in ASDs (APA, 2000). As the following review will summarize, social impairments have also been reported in WS.

Reciprocal social interactions and ASD overlap in WS.

Considering the typical behavioral phenotype observed in WS (i.e., outgoing personality, gregariousness, a friendly and approaching demeanor; see Mervis & Klein-Tasman, 2000 for a review), one would not intuitively expect to see difficulties in social interactions. However, upon further examination, a profile of delays in back and forth-social interactions, such as difficulties with joint attention and social referencing behaviors even in early childhood, is evident (Laing et al., 2002). While young children with WS are responsive to verbal and nonverbal displays of emotionality in others, it appears as though they do not use this information in socially meaningful ways (Fidler, Hepburn, Most, Philofsky, & Rogers, 2007). That is, while they are able to pick up on the feelings and the reactions to environmental stimuli of those around them, this ability does not necessarily translate to an improvement in the quality of social interactions. These difficulties with early precursors to more sophisticated social overtures point to the potential for an overlap with the autism spectrum in WS. In order to further investigate these difficulties, measures typically used to diagnose ASDs have recently been used in WS.

In order to increase the reliability of ASD diagnoses, gold-standard measures have been developed and include a standardized semi-structured interview, the Autism Diagnostic Interview-Revised, or ADI-R (Rutter, LeCouteur, & Lord, 2003). This interview asks parents or caregivers to describe the individual's behavior in the 4-5 year old period, as well as current behavior. A clinician-administered semi-structured play observation, the Autism Diagnostic Observation Schedule, or ADOS (Lord, Rutter, DiLavore, & Risi, 1999), is meant to specifically capture the socio-communicative behaviors indicative of ASDs and has been shown to be able to differentiate individuals

with ASDs from those with other developmental difficulties, particularly language delays (Noterdaeme, Sitter, Mildenberger, & Amorosa, 2000; Noterdaeme, Mildenberger, Sitter, & Amorosa, 2002; Bishop & Norbury, 2002). Using these measures, various reports have been published further characterizing the specific socio-communicative difficulties present in WS. To date, only one study using the ADI-R in coordination with the ADOS has been published (Tordjman et al., 2012) and describes behavioral patterns in a small sample of individuals with WS. Relatively more studies have been completed using the ADOS to describe socio-communicative behavior in children with WS.

One such study found that the profile of abnormalities that children with WS demonstrate as measured by the ADOS is different from the profile seen in ASDs in both severity and type (Lincoln, Searcy, Jones, & Lord, 2007). The children with WS demonstrated problems in the communication and social interaction domain, including restricted use of gesture and pointing, initiating joint attention, and showing. Despite these difficulties, the children with WS did not show delays in other areas related to social functioning such as shared enjoyment, vocalizations and facial expressions directed to others, response to joint attention, quality of social interactions, and unusual eye contact. The key difference in this area between individuals with ASD and WS is that although the attempts may not be typical, the latter still make "social overtures and efforts to gain and sustain the attention of others" (p. 323).

Using the same methodology, Klein-Tasman and colleagues (2007) were able to find evidence for a pattern of socio-communicative difficulties in WS such that approximately half of the young children included exhibited abnormalities in their use of various social interactive behaviors, including both initiation and response to joint

attention, integrating gaze with communicative behaviors, and reciprocal social smiling. These children also demonstrated difficulties with the socio-communicative behaviors mentioned in the previous section, eye gaze and pointing behaviors. In addition, abnormalities in play behavior and repetitive and restricted interests were also observed in numerous children. As the author suggests, the finding of a greater degree of difficulty in this particular population when compared to the group of participants with WS previously described in the Lincoln et al (2007) paper is most likely due to the higher level of language abilities in the latter group. When administering the ADOS, placing fewer language demands on an individual may result in an underestimate of existing difficulties (Klein-Tasman, Risi, & Lord, 2006); this finding may provide one explanation as to why the two groups performed differently.

While the previous investigations provided estimates of the performance of children with WS as compared to children diagnosed with autism, subsequent research has furthered the findings by adding comparison groups of children diagnosed with PDD-NOS and those with other developmental disabilities that do not fall on the autism spectrum. Comparisons of the entire group of children with WS to the control groups have yielded an interesting behavioral profile; the children with WS, regardless of ASD diagnosis, demonstrated more difficulties in social interaction than the children with developmental delay of mixed etiology (ME), indicating a level of social difficulties above and beyond what would be expected from developmental delay alone (Klein-Tasman, Phillips, Lord, Mervis, & Gallo, 2009).

Summary and Rationale for the Present Study

While not suggesting that the majority of individuals with WS demonstrate behavioral difficulties indicative of an ASD, these studies demonstrate the nature of socio-communicative difficulties present in WS. This general behavioral phenotype, while significantly variable, includes traits and difficulties that overlap significantly with the autism spectrum, such that one study found that approximately half of a sample of young children with WS behaved similarly to those with PDD-NOS (Klein-Tasman et al., 2009). Although there is a growing literature describing socio-communicative difficulties in WS and potential overlap with the autism spectrum, there are several caveats to be mentioned. Firstly, studies that replicate findings related to the behavioral phenotypes need to be completed with random samples of individuals with WS of various ages and language levels. In addition, comparison groups need to be carefully chosen in order to make conclusions related to the specificity of these behaviors in WS as opposed to genetic syndromes in general. Nevertheless, a pattern of difficulties in socio-communicative behavior within WS has emerged and warrants a continued line of research. Findings demonstrating the overlap between conditions of known etiology and ASDs underscore the necessity of continuing to further characterize their phenotypes and prevent either over- or under-diagnosing ASDs.

Past research has described socio-communicative overlap between WS and the autism spectrum using gold-standard instruments in young children with limited or absent spoken language (Klein-Tasman et al., 2006, 2009; Lincoln et al., 2007). However, given the limited language abilities in these children and the developmental pattern of later language and gestural development in Williams syndrome, the role that further language development plays in the pattern of behavioral similarities between WS and ASDs in

unknown. It is possible that, as children with WS make gains in terms of language development, their behavioral profile becomes such that this overlap is less pronounced or is no longer evident. Conversely, it may be possible that social communication difficulties remain despite language development. Therefore, the current study will use the same instrument, the ADOS, to further characterize the socio-communicative behavior in older children with WS with more advanced language.

Research Questions

Primary Aim: To investigate the nature of socio-communicative difficulties seen in a sample of verbal children with WS, including exploratory comparisons to groups of children with Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) and developmental conditions of mixed etiology (ME).

Research Questions:

A. What is the overall pattern of socio-communicative behavior in the sample?
    i. Are there socio-communicative behaviors that are more or less problematic for children with WS?
    ii. Does socio-communicative behavior relate to intellectual functioning?
    iii. Does socio-communicative behavior relate to gender?
B. Is there a different behavioral pattern in children with WS who receive an ADOS classification of "ASD" or "autism" in comparison to those who are classified "non-spectrum?"
C. How does the socio-communicative behavior in the WS sample compare to the behavior of a group of children with PDD-NOS?

D. How does the socio-communicative behavior in the WS sample compare to the behavior of a group of children with developmental conditions of mixed etiology who do not have ASDs (ME group)?

Method

Participants

The study include a group of children with WS, a group of children with PDD-NOS, and a group of children with non-ASD developmental conditions of mixed etiology.

All children with WS were evaluated either in the Child Neurodevelopment Research Lab (CNRL) at the University of Wisconsin-Milwaukee (UWM) or as part of a longitudinal study of the Williams syndrome phenotype at the University of Louisville. Children with PPD-NOS or ME were evaluated at either of these two sites or by C. Lord's group, presently at Cornell University. All children with PDD-NOS and ME were evaluated under the supervision of an experienced clinician trained in the use of the ADOS and DSM-IV criteria were used to determine ASD classification. Children in the ME group had non-ASD neurodevelopmental disorders such as intellectual disability, Down syndrome, cerebral palsy, or other known genetic disorders (e.g., neurofibromatosis, Treacher Collins syndrome).

In the WS group, 34 children were administered the Module 2 of the ADOS (18 males, 16 females). These children ranged in age from 3 to 7 years old (M = 5.39 years, SD = 1.11 years) and were representative of the cognitive profile within WS (i.e., cognitive level ranging from impaired to average; M = 59.93, SD = 13.02). The performance of these children was compared to the performance of a group of 34 children

with PDD-NOS (24 males,10 females). These children ranged in age from 3 to 8 years old (M = 4.92 years, SD = 1.22 years). The two groups did not differ significantly in age ($t(66) = 1.67$, $p = .10$). Scores on an intellectual functioning measure were available for all the children with WS and for 19 of the children with PDD-NOS; the two groups did differ in overall intellectual functioning ($t(51) = -5.60$, $p < .001$). The performance of the children with WS was also compared to a group of 38 ME children (25 males, 13 female). These children ranged in age from 3 to 8 years old (M = 4.78 years, SD = 1.49 years). The two groups did not differ significantly in age ($t(70) = 1.97$, $p = .06$). Scores on an intellectual functioning measure were available for 29 of the ME children; the two groups did differ in terms of overall intellectual functioning ($t(61) = -7.70$, $p < .001$).

In the WS group, 50 were administered Module 3 of the ADOS (23 male, 27 female). These children ranged in age from 5 to 15 years old (M = 10.05 years, SD = 2.55 years) and were representative of the cognitive profile within WS (M = 65.20, SD = 12.13). The performance of these children was compared to the performance of a group of 40 children with PDD-NOS (32 males, 8 females). These children ranged in age from 5 to 14 years old (M = 9.01 years, SD = 2.69 years). The two groups did not differ significant in terms of age ($t(88) = 1.89$, $p = .06$). Scores on an intellectual functioning measure were available for all the children with WS and for 38 of the children with PDD-NOS; the WS group had significantly weaker overall intellectual functioning ($t(86) = -9.03$, $p < .001$). The performance of the children with WS was also compared to a group of 74 ME children (51 males, 23 females). These children ranged in age from 5 to 14 years old (M = 9.20 years, SD = 2.38 years). The two groups did not differ significantly in age ($t(122) = 1.91$, $p = .06$). Scores on an intellectual functioning measure were

available for all the children with WS and for 69 of the ME children; the WS group had significantly weaker overall intellectual functioning ($t(117) = -7.86$, $p < .001$).

Materials

Autism Diagnostic Observation Schedule (ADOS), Module 2 and 3

The ADOS (Lord et al., 1999) is a structured play observation administered by a trained examiner designed to elicit communication and reciprocal social interactions through a series of activities. Module 2 is administered to individuals with phrase speech, while Module 3 is administered to individuals with fluent speech. Communicative overtures, reciprocal social interactions, and restricted and repetitive behaviors are coded according to descriptions provided, with higher ratings indicating more impaired functioning. Typically, behaviors that appear to be consistent with typically developing individuals are given a code of 0, while behaviors that are considered mildly abnormal are scored 1, and more severe impairments receive codes of 2 or 3. A subset of the items, which were previously determined to be most likely to distinguish between individuals with ASDs and those without, are then included in the total scoring algorithm. Two cutoff totals are provided in communication (COM) and reciprocal social interaction (RSI) domains, as well as for the total score (TOT), consistent with an "ASD" classification or an "autism" classification. Recently reported revised algorithms (Gotham, Risi, Pickles, & Lord, 2007; Gotham et al., 2008) use the same methodology, although they differ in the items used to determine scores and the domains included. Specifically, there is a social affect domain (SA) and a social affect plus restricted interests and repetitive behaviors domain (SA + RRB). Given recent studies demonstrating the utility of this revised algorithm, the present study will report performance in terms of new algorithm

scores. In addition, recently published severity ratings (Gotham, Pickles, & Lord, 2009) are available to compute the degree to which individuals are impaired by autism spectrum symptomatology.

Differential Ability Scales (DAS), 1st and 2nd Editions

The DAS and DAS-II are measures of cognitive functioning intended for use with children ages 2 ½ to 17 years of age. Versions for younger (Early Years, ages 2:6 through 8:11) and older children (School Age, ages 7:1 through 17:11) are available and include a verbal and nonverbal domain; the DAS-I includes a spatial component for older children, while the DAS-II also includes a spatial component for younger children. Domain scores are reported as standard scores. All versions yield a General Conceptual Ability score (GCA), which is similar to an IQ score (i.e., standard score with a mean of 100 and standard deviation of 15). Both the DAS and the DAS-II are ideal for use with intellectually disabled populations given their low floors. Specifically, domain and GCA standard scores are normed as low as 30.

Hypotheses

It is hypothesized that the majority of verbal children with WS will demonstrate few socio-communicative difficulties and that there will not be many items on which more than half of the sample demonstrates significant impairment. It is also expected that intellectual functioning, but not gender, will be related to behavioral patterns, particularly in terms of severity of impairment. Specifically, it is expected that the children with WS with lower intellectual functioning will also be the children who are more severely affected by behavioral symptoms overlapping with the autism spectrum. It is hypothesized that there will be items that differentiate children who are classified on the

autism spectrum from those who are not and that these items will mostly be classified as nonverbal communication skills. Finally, it is hypothesized that the WS group and the ME group will demonstrate different behavioral patterns and the WS and PDD-NOS group will demonstrate similar behavioral patterns on the ADOS.

Results

In order to account for the number of comparisons being made between groups (i.e., when differences at the item level are being examined), a $p < .01$ alpha level was used. When fewer comparisons were made (i.e., when algorithm or severity score differences were being examined), a $p < .05$ alpha level was used.

Research Question A: What is the pattern of socio-communicative behavior in the sample of children with WS?

Of the 34 children with WS who were administered Module 2 of the ADOS, 25 (74%) were classified "non-spectrum" on the SA domain. The remaining 9 children (26%) were classified on the autism spectrum (6 "ASD" and 3 "autism"). When the RRB domain was combined with the SA domain, 26 of the children (76%) were classified" non-spectrum," while the remaining 8 children (24%) were classified on the autism spectrum (1 "ASD" and 7 "autism").

Of the 50 children with WS who were administered Module 3 of the ADOS, 35 (70%) were classified "non-spectrum" on the SA domain. The remaining 15 children (30%) were classified on the autism spectrum (10 "ASD" and 5 "autism"). When the RRB domain was combined with the SA domain, 33 of the children (66%) were classified "non-spectrum," while the remaining 17 children (34%) were classified on the autism spectrum (10 "ASD" and 7 "autism").

Research Question Ai: Are there socio-communicative behaviors that are more or less problematic for children with WS?

See Figures 1 and 2 for frequencies of endorsement for items on which more than half of the WS sample demonstrated some degree of difficulty (score of 1, 2, or 3). The imagination/creativity item was the only item frequently rated as problematic across both module 2 and 3, with 65% of the module 2 children and 60% of the module 3 children receiving a score of 1 or 2. On Module 2, there were 2 items on which more than half the sample received a "1"; these items were imagination/creativity (n = 19) and unusually repetitive interests or stereotyped behaviors (n = 18). When codes of "2" or "3" were also included, more than half of the sample demonstrated some degree of difficulty on the following items: conversation (n = 18), gestures (n = 17), conversation (n = 22), unusual sensory interest in play material/person (n = 22), hand and finger and other complex mannerisms (n = 20), and unusually repetitive interests or stereotyped behaviors (n = 25). There were no Module 2 items on which more than half the sample received a code of "2" or "3". On Module 3, there were 4 items on which more than half he sample received a "1"; these items were speech abnormalities associated with autism (n = 32), facial expressions directed to others (n = 30), insight (n = 26), and imagination/ creativity (n = 29). When codes of "2" or "3" were also included, more than half the sample demonstrated some degree of difficulty on the following items: speech abnormalities associated with autism (n = 33), empathy/comments on others' emotions (n = 31), insight (n = 45), and imagination/creativity (n = 30). On the insight item, an additional fourteen children received a code of "2" and 5 children received a code of "3," for a total of nineteen children earning codes indicative of significant impairment on this item. Taken

together, 45 children (90%) received codes on the insight item that indicated some degree of difficulty.

See Figures 3 and 4 for frequencies of endorsement for items on which more than 75% of the sample received a code of "0," suggesting behaviors that are less commonly seen as problematic in WS. In module 2 (n = 34), the unusual eye contact (n = 27), shared enjoyment in interaction (n = 28), response to name (n = 33), spontaneous initiation of joint attention (n = 29), response to joint attention (n = 32), self-injurious behavior (n = 33), and overactivity (n = 28) items were rated typical (i.e., code = 0) in more than 75% of the participants. In module 3 (n = 50), the immediate echolalia (n = 49), asks for information (n = 38), gestures (n = 41), unusual eye contact (n = 39), shared enjoyment in interaction (n = 40), amount of reciprocal social communication (n = 43), unusual sensory interests (n = 39), hand, finger, and other complex mannerisms (n = 43), self-injurious behavior (n = 49), excessive interest in or references to unusual or highly specific topics or objects of repetitive behaviors (n = 41), compulsions or rituals (n = 40), tantrums, aggression, negative or disruptive behavior (n = 45), and anxiety (n = 44) items were rated typical (i.e., code = 0) in more than 75% of the participants.

Research Question Aii: Does socio-communicative behavior relate to intellectual functioning?

On Module 2, there was no difference in overall intellectual functioning between those children with WS who met the cutoff and those who did not ($t(32) = 1.70$, $p = .10$). Clusters scores were available for 33 of the children; there were no differences in verbal ($t(31) = 1.03$, $p = .31$) or nonverbal ($t(31) = .44$, $p = .66$) cluster scores between the groups. However, there was a modestly significant correlation between severity of

impairment and overall IQ ($r(32) = -.37$, $p = .03$), but not for verbal ($r(31) = -.28$, $p = .12$) or nonverbal ($r(31) = -.13$, $p = .46$) cluster scores.

On Module 3, there was no difference in overall intellectual functioning between those children with WS who met the cutoff and those who did not ($t(48) = .52$, $p = .60$). Cluster scores were available for 47 of the children; there were no differences in verbal ($t(45) = .06$, $p = .95$) or nonverbal ($t(45) = -.35$, $p = .73$) cluster scores between the two groups. In addition, there was no significant correlation between severity of impairment and overall IQ ($r(48) = -.07$, $p = -.65$), verbal IQ ($r(45) = -.02$, $p = .88$), or nonverbal IQ ($r(45) = .07$, $p = .65$).

Research Question Aiii: Are there gender differences in sociocommunicative behavior?

On Module 2, neither gender was more likely to be classified on the autism spectrum ($\chi^2(1, N = 34) = 2.04$, $p = .15$) and the severity of impairment did not differ between males and females ($t(32) = .33$, $p = .74$). On Module 3, females were more likely to be classified on the autism spectrum than were males ($\chi^2(1, N = 50) = 5.24$, $p = .02$); however, the severity of impairment did not differ between males and females ($t(48) = -1.85$, $p = .07$).

Research Question B: Is there a different behavioral pattern in children with WS who receive an ADOS classification of "ASD" or "autism" in comparison to those who are classified "non-spectrum?"

Previous reports have indicated that children with WS who meet the cutoff for an ASD classification differ significantly from those children with WS who do not meet the cutoff. (Klein-Tasman et al., 2007). See Table 2 for results of Mann-Whitney test

comparisons of Module 2 ADOS items that were different in children classified "ASD" or "autism" and those classified "non-spectrum." Children who were classified ASD had significantly higher scores on the following items: amount of social overtures/maintenance of attention, speech abnormalities associated with autism, stereotyped/ idiosyncratic use of words or phrases, conversation, facial expressions directed towards others, quality of social overtures, quality of social response, overall quality of rapport, and functional play with objects.

See Table 3 for results of Mann-Whitney test comparisons of Module 3 ADOS items that differed significantly by ADOS classification. Children who received as ASD classification ("ASD" or "autism") had significantly greater abnormality on the following items: overall level of non-echoed language, speech abnormalities associated with autism, offers information, reporting of events, conversation, unusual eye contact, facial expressions directed towards others, shared enjoyment in interactions, insight, quality of social overtures, quality of social response, amount of reciprocal social communication, overall quality of rapport, hand, finger, and other complex mannerisms, and tantrum, aggression, negative or disruptive behavior.

Research Question C: How does the overall pattern of socio-communicative behavior in the WS sample compare to the behavior of a group of children with PDD-NOS?

For the children who were administered module 2, the group with WS had significantly lower SA algorithm scores than the PDD-NOS (WS group M = 3.74, SD = 2.69; PDD-NOS group M = 7.88, SD = 3.52; $t(66) = -5.46$, $p < .001$) and significantly lower total algorithm scores than the PDD-NOS group (WS group M = 6.47, SD = 4.21;

PDD-NOS group M = 12.09, SD = 4.56; $t(66) = -5.28$, $p < .001$). The WS group also had significantly lower severity scores (WS group M = 3.06, SD = 1.97; PDD-NOS group M = 6.15, SD = 1.64; $t(66) = -7.04$, $p < .001$).

For children who were administered module 3, the group with WS had significantly lower SA algorithm scores than the PDD-NOS group (WS group M = 3.30, SD = 2.89; PDD-NOS group M = 6.95, SD = 3.94; $t(88) = -5.07$, $p < .001$) and significantly lower total algorithm scores than the PDD-NOS group (WS group M = 4.40, SD = 3.38; PDD-NOS group M = 9.57, SD = 4.74; $t(88) = -6.04$, $p < .001$). The WS group also had significantly lower severity scores (WS group M = 2.74, SD = 2.05; PDD-NOS group M = 5.58, SD = 2.57; $t(88) = -5.82$, $p < .001$).

See Table 4 for results of Mann-Whitney comparisons for items that were significantly different between the WS and the PDD-NOS groups on module 2. The items that were different between the two groups were amount of social overtures, speech abnormalities associated with autism, immediate echolalia, stereotyped/idiosyncratic use of language, conversation, pointing, gestures, unusual eye contact, response to name, spontaneous initiation of joint attention, quality of social overtures, quality of social response, amount of reciprocal social communication, overall quality of rapport, and overactivity. In contrast, the majority of the play and restricted and repetitive behaviors, as well as the problem behavior items, were not different between the two groups.

See Table 5 for results of Mann-Whitney comparisons for items that were significantly different between the WS and the PDD-NOS groups on module 3. The items that were different between the two groups were speech abnormalities associated with autism, immediate echolalia, stereotyped/idiosyncratic use of language, asks for

information, reporting of events, conversation, gestures, unusual eye contact, shared enjoyment in interaction, empathy/comments on others' emotions, quality of social overtures, quality of social response, amount of reciprocal social communication, overall quality of rapport, imagination/creativity, unusual sensory interest in play material/person, excessive interest in or references to unusual or highly specific topics or objects or repetitive behaviors, compulsions or rituals, and overactivity/agitation. In contrast, there were a few items in the play and restricted and repetitive behavior domains that were not different between the two groups; these similarities were less pronounced than they were in module 2.

Given previous studies indicating different patterns of results depending on ADOS classification (Klein-Tasman et al, 2009), the children with WS in each module group were split into subgroups based on ADOS classification (i.e., non-spectrum and spectrum) and then compared to the PDD-NOS group separately. On both module 2 and 3, the children with WS who were classified non-spectrum (WS NS) had significantly lower algorithm and severity scores than the PDD-NOS group (see Table 6). These groups also differed on a number of individual items. See Table 7 for results of Mann-Whitney comparisons of items in module 2 and Table 8 for module 3 comparisons. Across both module 2 and 3, the children with WS who were classified autism spectrum (WS ASD) did not differ significantly from the children with PDD-NOS in terms of algorithm and severity scores. In addition, these two groups did not differ on the majority of ADOS items. Children in the WS ASD group had a higher score on the hand and finger and other complex mannerisms item in module 2 and received lower scores on the stereotyped or idiosyncratic use of language and asking for information items on module

3 than did the PDD-NOS group. See Table 9 for module 2 comparisons and Table 10 for module 3 comparisons.

Research Question D: How does the socio-communicative behavior in the WS sample compare to the behavior of a group of children with developmental conditions of mixed etiology (ME group)?

For the children who were administered module 2, the group with WS and the ME groups did not differ significantly in terms of overall SA algorithm score (WS group M = 3.74, SD = 2.69; ME group M = 3.55, SD = 2.26; $t(70) = .31$, $p = .76$), total algorithm score (WS group M = 6.47, SD = 4.21; ME group M = 5.50, SD = 2.74; $t(70) = 1.17$, $p = .25$), or severity of impairment (WS group M = 3.06, SD = 1.97; ME group M = 2.89, SD = 1.62; $t(70) = .39$, $p = .70$).

For children who were administered module 3, the group with WS and the ME group did not differ significantly in terms of overall SA algorithm score (WS group M = 3.30, SD = 2.89; ME group M = 3.72, SD = 2.55; $t(122) = -.85$, $p = .40$), total algorithm score (WS group M = 4.40, SD = 3.38; ME group M = 4.58, SD = 2.90; $t(122) = -.32$, $p = .75$), or severity of impairment (WS group M = 2.74, SD = 2.05; ME group M = 2.64, SD = 1.71; $t(122) = .31$, $p = .76$).

See Table 11 for results of Mann-Whitney comparisons for items that were significantly different between the WS and the ME groups on module 2. The items that were different between the two groups were conversation and hand and finger and other complex mannerisms; on the conversation item, the WS group had lower scores than the ME group, while the ME group had lower scores on the mannerisms item.

See Table 12 for results of Mann-Whitney comparisons for items that were significantly different between the WS and the ME groups on module 3. The items that were different between the two groups were asks for information, facial expressions directed to others, and overall quality of rapport. For the asking for information and the overall quality of rapport items, the WS had lower scores; for the directed facial expressions item, the ME group had lower scores.

Again, the children with WS in each module group were split into subgroups based on ADOS classification (i.e., non-spectrum and spectrum) and then compared to the ME group separately. On module 2, the children with WS who were classified non-spectrum (WS NS) had significantly lower social affect algorithm and severity scores than the ME group, while the children with WS who were classified on the autism spectrum (WS ASD) had significantly higher scores than the ME group in terms of social affect, total algorithm, and severity scores (see Table 6). Again, there were a number of items that were different across groups. See Table 13 for item analysis results between the WS NS and ME groups in module 2 and Table 14 for module 3. The WS NS group had significantly lower scores than the ME group, indicating less abnormality, on the conversation, quality of social response, and overall quality of rapport items. The WS ASD group had significantly higher scores than the ME group, indicating greater abnormality, on the facial expressions directed to others, shared enjoyment in interaction, quality of social overtures, functional play with objects, unusual sensory interest in play material/person, hand, finger, and other complex mannerisms, and unusually repetitive interests or stereotyped behaviors items.

On module 3, the children with WS who were classified non-spectrum (WS NS) had significantly lower algorithm and severity scores than the ME group, while the children with WS who were classified autism spectrum (WS ASD) had significantly higher scores than the ME group. In addition, there were a number of items on which the two groups differed from one another; see Tables 15 and 16 for results of Mann-Whitney comparisons in modules 2 and 3, respectively. The WS NS group had significantly lower scores than the ME group on the asks for information, unusual eye contact, quality of social response, overall quality of rapport, and overactivity/agitation items. The WS ASD group had significantly lower scores than the ME group on the asks for information item. The WS ASD group had significantly higher scores than the ME group on the offers information, conversation, facial expressions directed to others, shared enjoyment in interaction, insight, and quality of social overtures items.

Discussion

The present study examined the performance of verbal children with WS on an autism diagnostic measure, the ADOS, both in terms of the overall pattern of socio-communicative behavior within the group and in exploratory comparisons to a group of children with PDD-NOS and a group of children with non-ASD developmental conditions (ME group). As was hypothesized, the majority of children with WS were not classified on the autism spectrum using the ADOS, although an elevated rate of ASD difficulties was indeed observed. There were a few items that were often endorsed as mildly to moderately problematic for children with WS; however, as was expected in light of the predicted low rates of ASD classification, the majority of items were not rated as problematic in more than half of the sample. Gender was not related to overall

classification or severity of impairment, while intellectual functioning and ASD symptomatology were somewhat related. Specifically, significant relations between intellectual functioning and symptom severity were observed in children who completed module 2 of the ADOS, but not in those who completed module 3. This suggests that as language development continues, there is less of a relation between cognitive abilities and socio-communicative difficulties in WS. In addition, there were a number of items that appeared to differentiate between those children with WS who met the threshold for classification on the autism spectrum and those who did not, including more pronounced speech abnormalities and difficulties with sustained conversation, fewer directed facial expressions, less shared enjoyment in interactions, and poorer quality of social overtures, social responses, and general rapport.

Exploratory comparisons to children with PDD-NOS diagnoses and a ME group comprised of children with other developmental conditions were also conducted. Research with younger children with WS with less well-developed language indicated socio-communicative functioning similar, on average, to a group of children with PDD-NOS. In contrast, in the current study, the children with WS demonstrated significantly fewer socio-communicative difficulties, on average, than the PDD-NOS group. Across modules, children with WS were less likely to be classified on the autism spectrum, had lower algorithm and severity of impairment scores, and different scores across many ADOS items. However, a different pattern emerged once the group of children with WS was divided into those classified non-spectrum and those meeting cutoff for an ASD classification and then compared separately to the PDD-NOS group and to a group of children with developmental conditions without ASD (ME group). Specifically, the

children with WS who were classified non-spectrum continued to show significantly fewer socio-communicative difficulties and repetitive behaviors than the PDD-NOS group, with levels similar to the children in the ME group, while the WS children who met cutoff for an ASD classification demonstrated more impairments than the ME group and generally did not differ from the PDD-NOS group in their difficulties. This suggests that there are some verbal children with WS who have significant socio-communicative difficulties above and beyond what would be expected in developmental conditions more generally, and present with behavioral profiles similar to that seen in children with PDD-NOS.

Overall Pattern of Performance within the WS Group

Approximately two-thirds to three-fourths of the children who were administered module 2 or 3 of the ADOS were classified "non-spectrum," suggesting that the majority of verbal children with WS do not demonstrate difficulties that overlap significantly with the autism spectrum. In light of previous findings reporting significant socio-communicative difficulties, restricted and repetitive behaviors, and abnormalities in play behavior in children with WS with limited language (Laing et al., 2002; Klein-Tasman et al., 2007), these results suggests that as children with WS gain skills in terms of expressive language, behavioral similarities to the autism spectrum become less pronounced. This difference is particularly striking when compared to the rate of difficulty in Klein-Tasman and colleagues' (2007) report (i.e., approximately half of the children were classified on the autism spectrum). However, given what is known about developmental patterns in WS, this finding is perhaps not unexpected. Many of the behaviors that were rated as problematic in these younger children with little language

are part of the typical WS behavioral profile. In the Klein-Tasman et al study (2007), more than half the children received codes indicative of lack of pointing; however, young children with WS show abnormalities in the development of this behavior, pointing less often than other children (Singer Harris, 1997) and delays in the comprehension of the pointing of others (Laing et al., 2002). Many children in the Klein-Tasman et al. study also showed unusual eye contact, which is another behavior previously known to be atypical in children with WS (Jones et al., 2000; Mervis et al., 2003a). These components of nonverbal communication are commonly used when language has not yet fully developed. However, as language development continues and individuals become more able to express themselves using spoken language, reliance on gesture use to communicate decreases (Nicoladis, Mayberry, & Genesee, 1999) and a preference for spoken language over gesture use emerges (Capirci, Iverson, Pizzuto, & Volterra, 1996). Therefore, it logically follows that as children with WS gain language skills, this deviance from the typical pattern of development may no longer be as striking.

It is also possible that the behaviors identified as problematic for younger children with WS are not necessarily present throughout the lifetime, but that the developmental trajectory of these behaviors follows a different course than they do in typical development, resulting in a greater overlap with the autism spectrum in younger children. As was previously mentioned, children with WS demonstrate an atypical pattern of development in terms of the emergence of pointing behaviors. Since children with WS begin to point *after* learning to speak (while the opposite pattern is true in typical development), they often do not use pointing as a method of nonverbal communication. Children with WS also have difficulty understanding the pointing of others (Singer Harris

et al., 1997; Laing et al., 2002). Comprehension of pointing precedes production in typical development; however, in WS, these skills emerge at the same time (Laing et al., 2002). It seems possible that the higher rates of item endorsement in younger children with WS could therefore be related to these types of differences in the sequence of developmental processes.

The only gender difference that emerged was in module 3; in this group, females were more likely to be classified on the autism spectrum. One possible interpretation of this finding lies in the different expectations for boys versus girls in terms of social interactions. It may be that when girls demonstrate socio-communicative difficulties, it is more striking, which could then result in higher scores. Severity was not related to gender in either group.

Consideration of intellectual functioning revealed a developmental pattern to relations between cognitive abilities and ASD symptomatology. In the current study, there was no difference in intellectual functioning between children with WS who were classified on the autism spectrum and those classified non-spectrum. However, severity and intellectual functioning were mildly related for module 2, such that children who demonstrated more severe behavioral difficulties were also the children who had lower intellectual functioning. In contrast, there was no significant relation between severity and intellectual functioning for children who were administered module 3. This is strikingly different from the robust relations between ADOS performance and developmental level observed in younger children with less language (Klein-Tasman et al., 2007). In the Module 1 study, the children with weaker cognitive abilities were more likely to be classified on autism spectrum. In the current study with older children with

more language, children with GCA scores at or below 50 were equally likely to be classified non-spectrum or ASD spectrum.

Klein-Tasman and colleagues (2007) found that the children in their study who were more likely to be classified on the autism spectrum were also the children in the sample who demonstrated more language difficulties; the same is not true in the current study, again suggesting that the development of language abilities in WS has a substantial impact on the behavioral profile observed. There is evidence suggesting that after a period of early delays the language development of most children with WS follows a path that is similar to what is seen in typical development (Mervis, 2004). Although continued language difficulties do remain (i.e., problems with relational vocabulary, conversation difficulties), the majority of individuals with WS are able to use language to communicate. As these verbal abilities develop and there is less reliance on nonverbal communication, the majority of individuals with WS demonstrate a more typical pattern of socio-communicative behavior. However, higher scores in the WS sample on items such as speech abnormalities associated with autism (i.e., tone, intonation, inflection), stereotyped or idiosyncratic use of language, difficulties with conversation (including not asking for information or struggling to report events), and not linking of language with nonverbal behaviors are consistent with difficulties reported elsewhere in the literature. Individuals with WS across age and language levels do demonstrate some behavioral similarities that overlap with the autism spectrum, suggesting that there are significant socio-communicative difficulties in WS.

Consistent difficulties were also observed across modules in terms of play abnormalities. Difficulties on items related to play behavior were commonly observed in

Klein-Tasman and colleagues' (2007) study of younger, nonverbal children. In the present study with older children with more language, more than half of the participants in both modules 2 and 3 demonstrated some degree of difficulty with items related to play. Hence, play appears to be an area of frequent difficulty in children with WS.

In the domain of repetitive behaviors, in comparison to the present study, previous reports of younger children with WS and less developed language revealed more items that were problematic for the majority of children (Klein-Tasman et al., 2007; Lincoln et al., 2007), including more prevalent repetitive behaviors and unusual sensory interests. Although repetitive behaviors continue to be common for children who completed module 2 of the ADOS, these were less common for the children who completed module 3. It is possible that repetitive behaviors may decrease in their prominence as language abilities increase in individuals with WS. In the older children with more advanced language included in the present study, fewer difficulties overall were reported. Additionally, for most items that are present in module 1 of the ADOS and remain in modules 2 and 3, the rates of difficulty are generally lower, suggesting again that the majority of the difficulties overlapping with the autism spectrum become less common in children with WS as they gain language skills. The high percentage of children receiving a code of 0 on the gestures and eye contact items in the present study illustrates this difference very well. Additionally, many items on which the majority of children did not demonstrate difficulty (e.g., unusual eye contact, shared enjoyment in interaction, initiation of and response to joint attention,) were related to social responsiveness, which is consistent with the generally sociable nature of individuals with WS.

Differences Between WS Children with and without Socio-Communicative Difficulties

In order to investigate the differences between children with WS who were classified "non-spectrum" and those who met the threshold for an ASD classification ("ASD" or "autism"), the larger groups were divided into smaller subgroups based on ADOS performance. The examination of differences between these two groups is crucial in order to better understand what types of behaviors are common in the WS behavioral profile and what types of behaviors are indicative of the presence of more significant socio-communicative difficulties. Previous studies have shown that children with WS who also meet the cutoff for an ASD classification on the ADOS demonstrate difficulty on items such as directed vocalizations and facial expressions, the use of eye contact and gestures during communication, and the spontaneous initiation of joint attention. The quality of their social overtures was also rated as poorer and their play was less developed than would be expected (Klein-Tasman et al., 2007). As presented in Tables 2 and 3, there were a number of items in each module on which children who met the threshold for ASD classification (WS ASD) and those who did not (WS NS) differed. A number of these items were consistently different across groups in both module 2 and 3 (i.e., speech abnormalities associated with autism, conversation, unusual eye contact, directed facial expressions, shared enjoyment in interaction, quality of social overtures and social response, amount of reciprocal social communication, overall quality of rapport, and hand and finger and other complex mannerisms). This suggests that there are clear differences between children in each group, such that these behaviors should be considered with additional weight when there is a question of a comorbid ASD diagnosis

for a child with WS. Specifically, special attention would need to be paid to the types of behaviors endorsed. If a child is receiving the majority of higher ratings on items that are commonly endorsed in all children with WS, regardless of overall ADOS classification, the difficulties present would be better characterized as part of the WS behavioral phenotype rather than indicative of an additional diagnosis on the autism spectrum. Conversely, a child receiving higher scores on items commonly associated with ADOS classification on the autism spectrum more likely presents the potential for a dual diagnosis.

In addition, many of the items that were reported to be different between the groups in the report of module 1 performance (Klein-Tasman et al., 2007) were the same items that remained different in the present study. Unusual eye contact, abnormalities in the direction of facial expressions, a lack of coordination of language with nonverbal communicative overtures, and poor overall quality of social overtures were behaviors that differentiated children meeting ASD classification and those who did not across modules 1, 2, and 3, suggesting that they continue to be problematic even as children gain communication skills. The presence of speech abnormalities associated with autism, which is similar to the module 1 item related to the intonation of vocalizations, was also an item that differentiated the groups, indicating that odd or irregular speech quality across levels of language in WS appears to be present in children with more pronounced socio-communicative difficulties.

Exploratory Comparison to a PDD-NOS Group and a ME Group

Previous studies using the same methodology demonstrated socio-communicative difficulties in WS at a level suggesting more impairment in this area than is seen in

children with developmental delay alone, but consistently less difficulties than a group of children with autism. The performance of the children with WS was in fact most similar to a group of children with PDD-NOS (Klein-Tasman et al., 2009). Given these results, there was no reason to expect that verbal children with WS would demonstrate impairments similar children with autism; therefore, the current study compared the behavior of verbal children with WS to the behavior of children with developmental conditions of ME and with PDD-NOS, but not to children with autism. The groups were matched in terms of age but not on intellectual functioning. In fact, the ME and PDD-NOS groups included a good number of children with very strong intellectual functioning, in the high average to very superior range. This is an important caveat to consider when interpreting the present data, as it is possible that the group differences that were observed could be related to these group differences in intellectual functioning; however, cognitive abilities were not strongly related to symptom severity in the WS group, providing rationale for comparison to a non-IQ matched group. On average, children with WS received lower algorithm and severity scores than children with PDD-NOS; the two groups also differed on a number of individual ADOS items, such that the children with WS had lower scores than the children diagnosed with an ASD. However, children with WS did not differ from a ME group in terms of algorithm or severity scores and there were considerably fewer items on which the two groups received significantly different ratings. On these items, children with WS sometimes received lower scores than ME children and sometimes received higher scores. These findings indicate that, although there are some items on which they differ, verbal children with WS and children with non-ASD developmental conditions generally demonstrate similar levels of socio-

communicative difficulties, while on average children with WS typically show fewer difficulties than children with PDD-NOS.

In Klein-Tasman and colleagues' study (2009), the group of children with WS who met the cutoff for an autism spectrum classification demonstrated a pattern of difficulties that was similar to that seen in children with PDD-NOS, whereas the children who were classified non-spectrum continued to differ significantly from this group. This suggests that when children with WS have socio-communicative difficulties that are consistent with an ASD classification on the ADOS, the behavioral pattern is different from what is seen in developmental delay alone and is in fact more similar to what is seen in PDD-NOS. In order to further explore this, the children in this study with WS who were classified non-spectrum (WS NS) and those who were classified on the autism spectrum (WS ASD) were then compared to children with developmental conditions of ME and PDD-NOS separately. Both the WS NS and WS ASD subgroups demonstrated significantly different patterns of behavior in comparison to the ME group. Specifically, the WS NS group showed fewer impairments than the ME group, while the WS ASD group showed more impairments than the ME group. Consistent with the findings in the younger children, the WS NS children differed significantly from the PDD-NOS group, with fewer difficulties, while the WS ASD children did not, again suggesting that when children with WS demonstrate significant impairment in socio-communicative behaviors, their profile is similar to those with PDD-NOS.

Repetitive Behavior and Play Abnormalities

As a whole, the children with WS in the present study presented with a number of behaviors that would be classified as repetitive or restricted in nature. Among the

commonly endorsed items in module 2 were unusual sensory interests, hand, finger, and other complex mannerisms, and repetitive interests or stereotyped behaviors. In addition, more than half of the children in both module 2 and 3 were rated as having difficulty using imagination or creativity in their play. The ratings of these types of difficulties are not different between the WS non-spectrum group and the WS ASD spectrum group and were similar to those seen in PDD-NOS, suggesting that they are common within WS in general, regardless of socio-communicative impairment. Similar difficulties have been reported in younger, nonverbal children with WS using the same measure (Klein-Tasman et al., 2007) as well as in other reports using different methodologies (Davies et al., 1998; Riby et al., 2012, 2013).

However, an interesting pattern emerges when the repetitive behavior and play of children with WS are compared to children with PDD-NOS and developmental delay of ME. Previous studies with younger children have reported repetitive behaviors and play abnormalities in WS that are similar to those seen in PDD-NOS. In module 2, the same pattern emerged; that is, the children with WS demonstrated the same amount of repetitive behaviors as the PDD-NOS group. This similarity remained even when the children in the WS group were split into WS NS and WS ASD, further suggesting that these repetitive patterns of behavior are present in WS in general. In comparison to a ME group, only the children in the WS ASD demonstrated more repetitive behaviors. This finding is further evidence that children with WS present with a number of repetitive behaviors and/or stereotyped interests. In module 3, these similarities did not remain; children with WS demonstrated fewer repetitive behaviors than the PDD-NOS group, and their behavior was similar to the ME group. These results suggest that as children with

WS age and gain fluid language skills, the nature of the repetitive behaviors they demonstrate changes.

Conceptualization of Socio-communicative Difficulties in Williams Syndrome

Another potential angle to consider when thinking about the nature of the behavioral overlap with ASDs in WS is to explore behavioral phenotypes within the autism spectrum itself. Wing and Gould (1979) suggested three social subtypes in ASDs: the aloof, the passive, and the active-but-odd subtypes. The aloof subtype is characteristic of the majority of individuals with classic autism. With the exception of situations in which they are seeking contact to have their needs met, these individuals actively reject social contact with peers and adults. Typically nonverbal, these individuals do not compensate for lack of language using other social overtures such as eye contact, gestures, or facial expressions. When language is present, it is generally repetitive in nature and is marked by atypical intonation, pronoun reversal, and the use of neologisms. Pretend play and joint attention and rarely observed and activity is generally limited to repetitive behaviors. This subtype typically presents with many associated features of autism, such as toe walking and odd gait, sensory sensitivities, and behavioral difficulties. The second subtype, the passive subtype, is also characterized by a lack of seeking interactions with others; however, these individuals are typically responsive to the advances of others and can be engaged in activities. While still repetitive, language skills in this group are generally more typical. Play skills frequently include imitative actions, but not imaginative or pretend play. The last subtype, the active-but-odd subtype, is not as easily called to mind as the other two. Individuals within this group may actually seek out interactions with others and appear to be quite socially motivated and interested;

however, they lack the skills necessary to have meaningful reciprocal social interactions. Language is generally at a level allowing for conversation; however, these are typically one-sided and may revolve around interests of the affected individual. Stereotypical speech abnormalities, such as repetitive language and odd intonation, are common. Understanding of typical social conventions is delayed if not absent, such that approach behaviors are often inappropriate. The validity of these three social subtypes has been demonstrated in numerous studies using various methods and in individuals of a wide range of ages (Beglinger & Smith, 2005;.Borden & Ollendick, 1994; Castelloe & Dawson, 1993; O'Brien, 1996; Prior et al., 1998; Waterhouse et al., 1996), as well as in comparison to alternative subtyping methods (Sevin et al., 1995).

Descriptions of the active-but-odd subtype within the autism spectrum are similar in some ways to descriptions of the behavioral phenotype of WS. For example, individuals with WS often do seek out interactions with others; in fact, they have been described as less reserved towards strangers and more willing to approach others (Gosch & Pankau, 1997; Klein-Tasman & Mervis, 2003). However, reports of conversations difficulties (Stojanovik, 2006; Stojanovik, Perkins, & Howard, 2001), deficits in social skills (Mervis, Klein-Tasman, & Mastin, 2001), and a limited comprehension of the more nuanced aspect of social interactions, such as subtle humor (Sullivan, Winner, & Tager-Flusberg, 2003), have also been reported. Individuals with WS have difficulty establishing and maintaining friendships (Einfeld, Tonge, & Florio, 1997; Udwin & Yule, 1991). Using parent and teacher report, Klein-Tasman and colleagues (2011) found that although children with WS were not reported to have significant difficulties in prosocial behaviors, they were reported to have elevated levels of atypical behavior in terms of

reciprocal social interactions. More specifically, difficulties with seeking out social interactions and initiating conversations were not reported, but a "poor understanding of socially-relevant information" (p. 8) was. It appears as though the typical behavioral phenotype of individuals with WS overlaps considerably with the active-but-odd subtype of ASDs. This profile represents the typical behavioral phenotype expected in individuals with WS; it is not universally associated with a comorbid diagnosis on the autism spectrum.

In this study, the children with WS who had significant socio-communicative difficulties (WS ASD group) appeared to struggle with items that appear to be consistent with what would be expected in this active-but-odd subtype profile. Language abnormalities, such as odd intonation, stereotyped use of words or phrases, echolalia, and conversational difficulties were elevated in this group. Items related to the appropriate use of eye contact and directed facial expressions, as well as overall quality of social overtures and rapport also received higher scores in this group. These behaviors may translate to social interactions that are awkward or unnatural in come way. Some play difficulties and repetitive behavior were also reported, but did not reach the threshold for significance. Other items reflecting social responsiveness (i.e., asking for information from others, response to name and joint attention, empathy, amount of reciprocal social communication) were not different between the two groups, suggesting that this is not an area of difficulty per se. Taken together, these difficulties seem to point to a pattern of overtures and interactions that are present, but odd in some manner, consistent with the active-but-odd subtype. Again, this does not suggest that children with WS have an ASD

that is best characterized using this subtype label; however, it does seem plausible that the more subtle difficulties present in WS are best compared to this subtype.

Limitations and Future Directions

The present study represents the first report of the socio-communicative behavior of verbal children with WS using a gold-standard autism diagnostic instrument, the ADOS. The results obtained are important in understanding the nature of the behavioral profile in WS. However, there are limitations in the study design that point to areas for improvement in future research in this domain.

Firstly, the children with WS in the current study did not all undergo an extensive autism diagnostic evaluation; therefore, parent interview information and final diagnosis were not available for all participants. This information would be helpful in future investigations in order to explore any similarities and differences between children with WS who were diagnosed with an ASD and those who were not. As the present study found a relatively small number of children exceeding the ASD cutoff, future investigations will need to include more children in order to have a more substantial sample size in a WS ASD group.

In addition, the children in the PDD-NOS group were seen as part of diagnostic evaluations and not as part of research evaluations. While this may not appear to be an obvious limitation, the fact that these children were seen for their first diagnostic evaluation at a later age than is typical suggests that the symptoms they exhibit may be less severe or impairing than is common in PDD-NOS in general. Therefore, it may be possible that the comparisons made between the WS and the PDD-NOS groups do no accurately reflect the true similarities and/or differences that exist between these groups

as they naturally occur. An additional limitation within this PDD-NOS group is that cognitive data was available for only a subset of these children (n = 19), limiting the exploration of the role of cognitive functioning. Future investigations using children who were initially diagnosed with PDD-NOS at younger ages and therefore have perhaps more obvious or problematic symptoms would allow for a more precise comparison as they would be a more representative sample of the behaviors present in PDD-NOS in general.

Finally, the lack of IQ match among the groups is a highly significant limitation, such that interpretation of the group comparison results of the current study must be tentative at best. Future studies that include comparison groups that are matched to the WS group on intellectual functioning would allow for a more precise identification of the patterns of socio-communicative strengths and weaknesses in WS regardless of cognitive abilities. Due to availability, the present study examined the differences in behavioral profiles without matching for IQ. The pool of ME and PDD-NOS participants available were fairly high functioning, which was a result of the nature of the clinic in which they were seen, as discussed above. Therefore, it was very difficult to match the children based on IQ and attempts to do so resulted in very small group sizes. However, given that there were relatively few aspects of overall ADOS performance related to intellectual functioning, it seemed reasonable to compare the groups without matching for IQ as a preliminary endeavor. However, there may nevertheless be some behaviors that are more or less tied to intellectual functioning (i.e., some items may have more relations to IQ than others) and having matched groups would allow for more definitive comparisons. For example, it may be possible that repetitive patterns of behavior are more closely

linked to IQ than nonverbal communicative overtures and being able to compare children in these areas independent of IQ would reveal different patterns of behavior. The group comparison findings in this study should be interpreted with great caution.

Summary and Conclusions

Given that less than half of the children in the sample demonstrated significant socio-communicative difficulties overlapping with the autism spectrum, it appears that the socio-communicative overlap between WS and ASDs documented in previous studies is less pronounced as children with WS become more verbal. Verbal children with WS are not demonstrating as significant impairment in socio-communicative abilities on the ADOS as their younger counterparts with less developed language, despite reports of conversational difficulties (Stojanovik, 2006; Stojanovik et al., 2001), struggles with making and maintaining friendships (Udwin & Yule, 1991), and both parent and teacher reported difficulties with reciprocal social interactions (Klein-Tasman, Li-Barber, Magargee, 2010. However, close to 1/3 of children with WS do demonstrate significantly impaired socio-communicative abilities, such that a substantial minority of verbal children with WS shows behavior during the ADOS that is consistent with an ASD. Furthermore, when children with WS are experiencing significant impairments in socio-communicative behavior, their behavioral profile is similar to what is typically seen in children with PDD-NOS. It seems as though the behavioral difficulties that are present point to subtle overlaps within the ASD phenotype. Careful consideration of the type and severity of impairments seen are important to keep in mind when considering an ASD diagnosis in a child with WS.

Past reports of the socio-communicative behaviors of young, minimally verbal children with WS described significant difficulties. However, using the same methodology in older children with WS who have begun to develop language, it seems as though these difficulties decrease. The nonverbal communicative behaviors that are generally delayed in WS (i.e., pointing, other gestures, effective use of eye contact, initiation of joint attention) appear to be influencing the profile in younger children much more than they do in older children. However, other significant impairments do exist and there remain a proportion of individuals with WS with considerable social difficulties. These findings illustrate the need for further investigations of behavioral profiles in children with genetic disorders using standardized measurement instruments. In addition, the results highlight the importance of careful consideration of typical phenotypic presentation in all genetic conditions in order to accurately understand the needs of the affected individual.

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Table 1
Summary of Behavioral Phenotypes in Genetic Disorders of Interest

Genetic Disorder	**Reported rates of comorbid ASD**	**Behavioral Overlap with Autism Spectrum**	**Features Associated with Autism Spectrum**	**Notable limitations to interpretation/ areas for future research**
Down syndrome	1 – 18%	Social isolation, poor use of eye contact, restricted interests, pre-occupation with parts of objects, hand & finger mannerisms, complex body mannerisms, lack of awareness of surroundings	Behavioral difficulties; intellectual impairment	Over-reliance on case studies and small sample sizes; confounding factor of intellectual functioning; lack of studies with young children; use of non-standardized measures/ screening tools
Fragile X syndrome	25 – 50%	Atypical language development; poor eye contact; social avoidance & anxiety; hand & finger mannerisms; lack of pretend/imaginative play	Behavioral difficulties; intellectual impairment; sensory sensitivity; perseverative behaviors; difficulty with changes in routine; self-injurious behavior	Few studies of developmental trajectory; role of intellectual functioning; behaviors differentiating FXS+ASD from FXS alone; use of non-standardized measures/screening tools
Rett syndrome	80 – 100%	Lack of language; difficulties with social interactions; repetitive hand movements; atypical use of eye contact	Developmental regression	Nature of typical development before regression suggests possible non-ASD classification; developmental trajectory; differentiation of motor stereotypies from those found in ASD; use of non-standardized measures/screening tools

Genetic Disorder	Reported rates of comorbid ASD	Behavioral Overlap with Autism Spectrum	Features Associated with Autism Spectrum	Notable limitations to interpretation/ areas for future research
Angelman syndrome	1%	Severe expressive language deficits; stereotyped & repetitive behaviors; atypical use of gestures & eye contact; deficits in play skills	Intellectual impairment	Association of comorbid ASD with intellectual disability and epilepsy; further characterization of the phenotype; use of non-standardized measures/screening tools
Smith-Magenis syndrome	<1%	Repetitive behaviors; language difficulties	Behavioral difficulties; sleep difficulties; self-injurious behaviors; intellectual impairment	Lack of evidence for deficits in core areas of impairment in ASD; role of intellectual functioning; use of non-standardized measures/ screening tools
15q11-q13 Duplication Disorders	???	Language delays; atypical use of language; decreased eye contact; lack of social reciprocity; repetitive & stereotyped behaviors	Emotion regulation difficulties, tantrums; behavioral difficulties; developmental delay; regression; sensory sensitivity	Small sample sizes; use of case studies; difference between duplications and triplications; use of non-standardized measures/ screening tools
22q11.2 Deletion syndrome	14 – 30%	Preference for aloneness; poor social skills; atypical approach behaviors	Behavioral difficulties	Small sample sizes; use of case studies; use of non-standardized measures/screening tools
Williams syndrome	???	Language delays; atypical use of language; delays in use of gestures; atypical eye contact; social isolation;	Behavioral difficulties; social cognitive deficits; sensory sensitivity	Further characterization to differentiate WS from WS+ASD; potential overlap with active-but-odd subtype

Table 2
ADOS Module 2 Items in Children with Williams Syndrome Classified Spectrum vs. Non-spectrum

ADOS Item	ASD Mean Rank	NS Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	22.31	16.02	65.50	-1.92	.120	
Amt Soc Overtures/Maintenance of Attn	25.25	15.12	42.00	-3.19	.010	*
Speech Abnormalities Assoc with Autism	24.94	15.21	44.50	-2.76	.013	*
Immediate Echolalia	23.31	15.71	57.50	-2.17	.058	
Stereotyped/Idiosyncratic Words/Phrases	25.50	15.04	40.00	-3.27	.008	*
Conversation	26.88	14.62	29.00	-3.35	.001	*
Pointing	20.50	16.58	80.00	-1.20	.347	
Gestures	17.00	17.65	100.00	-0.18	.889	
Unusual Eye Contact	22.50	15.96	64.00	-2.32	.110	
Facial Expressions Directed to Others	24.38	15.38	49.00	-2.58	.025	+
Shared Enjoyment in Interaction	23.00	15.81	60.00	-2.70	.077	
Response to Name	19.13	17.00	91.00	-1.80	.618	
Showing	20.88	16.46	77.00	-1.22	.288	
Spontaneous Initiation of Joint Attention	23.25	15.73	58.00	-3.04	.064	
Response to Joint Attention	18.63	17.15	95.00	-0.90	.735	
Quality of Social Overtures	27.13	14.54	27.00	-3.83	.001	*
Quality of Social Response	27.00	14.58	28.00	-3.68	.001	*
Amount of Reciprocal Social Comm	23.00	15.81	60.00	-2.19	.077	
Overall Quality of Rapport	26.13	14.85	35.00	-3.64	.004	*
Functional Play with Objects	24.63	15.31	47.00	-2.77	.020	+
Imagination/Creativity	19.50	16.88	88.00	-0.74	.537	
Unusual Sensory Int in Play Mat/Person	22.44	15.98	64.50	-1.73	.110	
Hand, Finger, and Other Mannerisms	23.50	15.65	56.00	-2.09	.053	
Self-Injurious Behavior	19.13	17.00	91.00	-1.80	.618	
Unusually Rep Interests/Stereotyped Beh	23.44	15.67	56.50	-2.12	.053	
Overactivity	19.00	17.04	92.00	-0.74	.647	
Tantrums, Aggr, Negative/Disruptive Beh	20.69	16.52	78.50	-1.26	.307	
Anxiety	14.63	18.38	81.00	-1.09	.368	

+ $p < .05$, * $p < .01$

Table 3
ADOS Module 3 Items in Children with Williams Syndrome Classified Spectrum vs. Non-spectrum

ADOS Item	ASD Mean Rank	NS Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-echoed Language	30.85	22.74	189.50	-2.17	.030	+
Speech Abnormalities Assoc with Autism	33.03	21.62	152.50	-3.14	.002	*
Immediate Echolalia	26.47	25.00	264.00	-1.39	.164	
Stereotyped/Idiosyncratic Words/Phrases	28.12	24.15	236.00	-1.12	.265	
Offers Information	32.24	22.03	166.00	-3.09	.002	*
Asks for Information	25.15	25.68	247.50	-0.17	.869	
Reporting of Events	31.71	22.30	175.00	-2.63	.008	*
Conversation	34.68	20.77	124.50	-4.107	<.001	*
Gestures	27.03	24.71	254.50	-0.80	.425	
Unusual Eye Contact	33.24	21.52	149.00	-3.75	<.001	*
Facial Expressions Directed to Others	32.56	21.86	160.50	-2.90	.004	*
Lang Prod & Linked Nonverbal Comm	26.79	24.83	258.50	-0.54	.588	
Shared Enjoyment in Interactions	33.74	21.26	140.50	-4.14	<.001	*
Empathy/Comments on Others' Emotions	30.12	23.12	202.00	-1.73	.084	
Insight	35.41	20.39	112.00	-3.78	<.001	*
Quality of Social Overtures	35.32	20.44	113.50	-3.95	<.001	*
Quality of Social Response	37.12	19.52	83.00	-5.10	<.001	*
Amt of Reciprocal Social Comm	30.82	22.76	190.00	-3.08	.002	*
Overall Quality of Rapport	37.68	19.23	73.50	-5.41	<.001	*
Imagination/Creativity	27.24	24.61	251.00	-0.70	.483	
Unusual Sensory Int in Play Mat/Person	27.53	24.45	246.00	-0.98	.326	
Hand, Finger, and Other Mannerisms	29.38	23.50	214.50	-2.24	.025	+
Self-Injurious Behavior	26.47	25.00	264.00	-1.39	.164	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	25.59	25.45	279.00	-0.05	.963	
Compulsions or Rituals	27.85	24.29	240.50	-1.18	.237	
Overactivity/Agitation	29.00	23.70	221.00	-1.56	.119	
Tantrums, Aggr, Negative/Disruptive Beh	30.35	23.00	198.00	-3.25	.001	*
Anxiety	23.94	26.30	254.00	-0.96	.336	

+ $p < .05$, * $p < .01$

Table 4
ADOS Module 2 Items in Children with Williams Syndrome and Children with PDD-NOS

ADOS Item	WS Mean Rank	PDD-NOS Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	36.60	32.40	506.50	-1.16	.246	
Amt Soc Overtures/Maintenance of Attn	29.71	39.29	415.00	-2.31	.021	+
Speech Abnormalities Assoc with Autism	26.81	42.19	316.50	-3.44	.001	*
Immediate Echolalia	29.38	39.62	404.00	-2.32	.020	+
Stereotyped/Idiosyncratic Words/Phrases	23.90	45.10	217.50	-4.75	<.001	*
Conversation	24.88	44.12	251.00	-4.29	<.001	*
Pointing	27.35	41.65	335.00	-3.35	.001	*
Gestures	30.18	38.82	431.00	-1.99	.047	+
Unusual Eye Contact	26.03	42.97	290.00	-3.90	<.001	*
Facial Expressions Directed to Others	32.03	36.97	494.00	-1.17	.241	
Shared Enjoyment in Interaction	31.82	37.18	487.00	-1.48	.138	
Response to Name	27.62	41.38	344.00	-3.87	<.001	*
Showing	30.68	38.32	448.00	-1.72	.085	
Spontaneous Initiation of Joint Attention	25.25	43.75	263.50	-4.39	<.001	*
Response to Joint Attention	34.00	35.00	561.00	-0.46	.645	
Quality of Social Overtures	26.90	42.10	319.50	-3.57	<.001	*
Quality of Social Response	27.21	41.79	330.00	-3.35	.001	*
Amount of Reciprocal Social Comm	26.90	42.10	319.50	-3.51	<.001	*
Overall Quality of Rapport	26.51	42.49	306.50	-3.67	<.001	*
Functional Play with Objects	34.18	34.82	567.00	-0.16	.872	
Imagination/Creativity	31.01	37.99	459.50	-1.62	.106	
Unusual Sensory Int in Play Mat/Person	33.03	35.97	528.00	-0.65	.515	
Hand, Finger, and Other Mannerisms	35.74	33.26	536.00	-0.55	.580	
Self-Injurious Behavior	33.54	35.46	545.50	-0.98	.328	
Unusually Rep Interests/Stereotyped Beh	32.59	36.41	513.00	-0.86	.390	
Overactivity	28.99	40.01	390.50	-2.77	.006	*
Tantrums, Aggr, Negative/Disruptive Beh.	33.87	35.13	556.50	-0.32	.751	
Anxiety	34.09	34.91	564.00	-0.20	.843	

+ $p < .05$, * $p < .01$

Table 5
ADOS Module 3 Items in Children with Williams Syndrome and Children with PDD-NOS

ADOS Item	WS Mean Rank	PDD-NOS Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	44.59	46.64	954.50	-0.43	.669	
Speech Abnormalities Assoc with Autism	40.46	51.80	748.00	-2.38	.017	*
Immediate Echolalia	43.40	48.13	895.00	-1.97	.048	+
Stereotyped/Idiosyncratic Words/Phrases	36.37	56.91	543.50	-4.11	<.001	*
Offers Information	45.18	45.90	984.00	-.017	.864	
Asks for Information	32.38	61.90	344.00	-5.79	<.001	*
Reporting of Events	40.44	51.83	747.00	-2.34	.019	*
Conversation	39.54	52.95	702.00	-2.82	.005	*
Gestures	39.92	52.48	721.00	-2.83	.005	*
Unusual Eye Contact	38.10	54.75	630.00	-3.36	.001	*
Facial Expressions Directed to Others	43.90	47.50	920.00	-0.76	.447	
Lang Prod & Linked Nonverbal Comm	45.20	45.88	985.00	-0.15	.884	
Shared Enjoyment in Interaction	41.10	51.00	780.00	-2.26	.024	+
Empathy/Comments on Others' Emotions	39.82	52.60	716.00	-2.43	.015	*
Insight	41.31	50.74	790.50	-1.82	.069	
Quality of Social Overtures	41.12	50.98	781.00	-2.02	.043	+
Quality of Social Response	35.70	57.75	510.00	-4.55	<.001	*
Amt of Reciprocal Social Comm	41.09	51.01	779.50	-2.43	.015	*
Overall Quality of Rapport	36.34	56.95	542.00	-4.16	<.001	*
Imagination/Creativity	40.78	51.40	764.00	-2.13	.033	+
Unusual Sensory Int in Play Mat/ Person	40.91	51.24	770.50	-2.29	.022	+
Hand, Finger, and Other Mannerisms	42.36	49.43	843.00	-1.79	.073	
Self-Injurious Behavior	44.43	46.84	946.50	-1.22	.224	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Beh	39.23	53.34	686.50	-3.09	.002	*
Compulsions or Rituals	41.10	51.00	780.00	-2.26	.024	+
Overactivity/Agitation	37.45	55.56	597.50	-3.69	<.001	*
Tantrums, Aggr, Negative/Disruptive Beh	45.00	46.13	975.00	-0.37	.710	
Anxiety	43.98	47.40	924.00	-0.98	.326	

+ $p < .05$, * $p < .01$

Table 6
ADOS Algorithm and Severity Scores in Williams Syndrome Subgroups and Contrast Groups

Comparison	WS Group Mean (SD)	Contrast Group Mean (SD)	t-value	Sig.	
Module 2, WSNS/PDD					
SA Algorithm	2.58 (1.33)	7.88 (3.52)	-7.28	<.001	*
Total Algorithm	4.58 (2.00)	12.09 (4.56)	-7.83	<.001	*
Severity Score	2.12 (.91)	6.15 (1.64)	-11.29	<.001	*
Module 2, WSASD/PDD					
SA Algorithm	7.50 (2.56)	7.88 (3.52)	-0.29	.775	
Total Algorithm	12.63 (3.54)	12.09 (4.56)	0.31	.758	
Severity Score	6.13 (1.13)	6.15 (1.64)	-0.04	.971	
Module 3, WSNS/PDD					
SA Algorithm	1.42 (1.12)	6.95 (3.94)	-7.80	<.001	*
Total Algorithm	2.24 (1.48)	9.57 (4.74)	-8.54	<.001	*
Severity Score	1.39 (.61)	5.58 (2.57)	-9.12	<.001	*
Module 3, WSASD/PDD					
SA Algorithm	6.94 (1.35)	6.95 (3.94)	-0.01	.993	
Total Algorithm	8.59 (1.50)	9.57 (4.74)	-0.84	.406	
Severity Score	5.35 (1.06)	5.58 (2.57)	-0.34	.733	
Module 2, WSNS/ME					
SA Algorithm	2.58 (1.33)	3.55 (2.26)	-1.97	.053	+
Total Algorithm	4.58 (2.00)	5.50 (2.74)	-1.47	.147	
Severity Score	2.12 (.91)	2.89 (1.62)	-2.12	.030	+
Module 2, WSASD/ME					
SA Algorithm	7.50 (2.56)	3.55 (2.26)	4.39	<.001	*
Total Algorithm	12.63 (3.54)	5.50 (2.74)	6.36	<.001	*
Severity Score	6.13 (1.13)	2.89 (1.62)	5.34	<.001	*
Module 3, WSNS/ME					
SA Algorithm	1.42 (1.12)	3.72 (2.55)	-4.95	<.001	*
Total Algorithm	2.24 (1.48)	4.58 (2.90)	-4.38	<.001	*
Severity Score	1.39 (.61)	2.64 (1.71)	-4.05	<.001	*
Module 3, WSASD/ME					
SA Algorithm	6.94 (1.35)	3.72 (2.55)	5.05	<.001	*
Total Algorithm	8.59 (1.50)	4.58 (2.90)	5.52	<.001	*
Severity Score	5.35 (1.06)	2.64 (1.71)	6.27	<.001	*

WSNS = Williams syndrome, non-spectrum group; PDD = Pervasive Developmental Disorder-Not Otherwise Specified group; WSASD = Williams syndrome, autism spectrum group; ME = developmental conditions of mixed etiology group; SA Algorithm = ADOS Social Affect algorithm
+ $p < .05$, * $p < .01$

Table 7
ADOS Module 2 Items in Williams syndrome Non-spectrum (WS NS) vs. PDD-NOS

ADOS Item	WS NS (n = 26) Mean Rank	PDD-NOS (n = 34) Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	31.19	29.97	424.00	-0.39	.700	
Amt Soc Overtures/Maintenance of Attn	23.46	35.88	259.00	-3.21	.001	*
Speech Abnormalities Assoc with Autism	21.13	37.66	198.50	-3.89	<.001	*
Immediate Echolalia	23.98	35.49	272.50	-2.76	.006	*
Stereotyped/Idiosyncratic Words/Phrases	18.31	39.82	125.00	-5.12	<.001	*
Conversation	18.38	39.82	127.00	-5.00	<.001	*
Pointing	22.54	36.59	235.00	-3.46	.001	*
Gestures	26.38	33.65	335.00	-1.75	.080	
Unusual Eye Contact	20.04	38.50	170.00	-4.47	<.001	*
Facial Expressions Directed to Others	26.04	33.91	326.00	-1.97	.049	+
Shared Enjoyment in Interaction	26.23	33.76	331.00	-2.31	.021	+
Response to Name	23.00	36.24	247.00	-3.84	<.001	*
Showing	25.63	34.22	315.50	-2.04	.041	+
Spontaneous Initiation of Joint Attention	19.94	38.57	167.50	-4.68	<.001	*
Response to Joint Attention	29.65	31.15	420.00	-0.76	.448	
Quality of Social Overtures	19.88	38.62	166.00	-4.65	<.001	*
Quality of Social Response	20.19	38.38	174.00	-4.43	<.001	*
Amt of Reciprocal Social Comm	21.23	37.59	201.00	-3.99	<.001	*
Overall Quality of Rapport	19.94	38.57	167.50	-4.57	<.001	*
Functional Play with Objects	28.08	32.35	379.00	-1.17	.241	
Imagination/Creativity	26.46	33.59	337.00	-1.73	.083	
Unusual Sensory Int in Play Mat/Person	27.81	32.56	372.00	-1.11	.265	
Hand, Finger, and Other Mannerisms	29.81	32.56	424.00	-0.29	.770	
Self-Injurious Behavior	29.00	31.65	403.00	-1.54	.123	
Unusually Rep Interests/Stereotyped Beh	26.87	33.28	347.50	-1.52	.130	
Overactivity	24.38	35.18	283.00	-2.84	.005	*
Tantrums, Aggr, Negative/Disruptive Beh	28.90	31.72	400.50	-0.76	.448	
Anxiety	30.92	30.18	431.00	-0.19	.852	

+ $p < .05$, * $p < .01$

Table 8
ADOS Module 3 Items in Williams syndrome Non-spectrum (WS NS) vs. PDD-NOS

ADOS Item	WS NS (n = 33) Mean Rank	PDD-NOS (n = 40) Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	33.85	39.60	556.00	-1.35	.176	
Speech Abnormalities Assoc with Autism	29.24	43.40	404.00	-3.20	.001	*
Immediate Echolalia	34.50	39.06	577.50	-2.09	.037	+
Stereotyped/Idiosyncratic Words/ Phrases	26.61	45.58	317.00	-4.21	<.001	*
Offers Information	34.18	39.33	567.00	-1.51	.132	
Asks for Information	24.15	47.60	236.00	-5.00	<.001	*
Reporting of Events	29.89	42.86	425.50	-3.01	.003	*
Conversation	27.64	44.73	351.00	-4.12	<.001	*
Gestures	30.73	42.18	453.00	-2.82	.005	*
Unusual Eye Contact	24.82	47.05	258.00	-5.07	<.001	*
Facial Expressions Directed to Others	32.64	40.60	516.00	-1.83	.068	
Lang Prod & Linked Nonverbal Comm	36.17	37.69	632.50	-0.37	.713	
Shared Enjoyment in Interaction	29.55	43.15	414.00	-3.70	<.001	*
Empathy/Comments on Others' Emotions	29.94	42.83	427.00	-2.71	.007	*
Insight	28.79	43.78	389.00	-3.24	.001	*
Quality of Social Overtures	28.61	43.93	383.00	-3.51	<.001	*
Quality of Social Response	22.65	48.84	186.50	-6.02	<.001	*
Amt of Reciprocal Social Comm	30.56	42.31	447.50	-3.35	.001	*
Overall Quality of Rapport	23.02	48.54	198.50	-5.87	<.001	*
Imagination/Creativity	31.64	41.43	483.00	-2.16	.030	+
Unusual Sensory Int in Play Mat/Person	31.59	41.46	481.50	-2.43	.015	+
Hand, Finger, and Other Mannerisms	32.21	40.95	502.00	-2.55	.011	*
Self-Injurious Behavior	35.50	38.24	610.50	-1.60	.111	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	30.58	42.30	448.00	-2.77	.006	*
Compulsions or Rituals	31.73	41.35	486.00	-2.44	.015	+
Overactivity/Agitation	27.68	44.69	352.50	-3.83	<.001	*
Tantrums, Aggr, Negative/Disruptive Beh	34.50	39.06	577.50	-2.09	.037	+
Anxiety	36.15	37.70	632.00	-0.47	.640	

+ $p < .05$, * $p < .01$

Table 9
ADOS Module 2 Items in Williams syndrome Autism Spectrum (WS ASD) vs. PDD-NOS

ADOS Item	WS ASD (n = 8) Mean Rank	PDD-NOS (n = 34) Mean Rank	Mann-Whitney U	Z	Sig.
Overall Level of Non-Echoed Language	28.19	19.93	82.50	-2.23	.087
Amt Soc Overtures/Maintenance of Attn	24.00	20.91	116.00	-0.73	.539
Speech Abnormalities Assoc with Autism	19.25	22.03	118.00	-0.62	.582
Immediate Echolalia	20.94	21.63	131.50	-0.15	.888
Stereotyped/Idiosyncratic Words/Phrases	16.06	22.78	92.50	-1.50	.167
Conversation	20.00	21.85	124.00	-0.43	.718
Pointing	17.00	22.56	100.00	-1.31	.261
Gestures	16.50	22.68	96.00	-1.42	.210
Unusual Eye Contact	19.50	21.97	120.00	-0.55	.626
Facial Expressions Directed to Others	25.50	20.56	104.00	-1.19	.320
Shared Enjoyment in Interaction	24.00	20.91	116.00	-0.76	.539
Response to Name	16.63	22.65	97.00	-1.44	.222
Showing	21.06	21.60	132.50	-0.12	.912
Spontaneous Initiation of Joint Attention	16.50	22.68	96.00	-1.39	.210
Response to Joint Attention	22.13	21.35	131.00	-0.32	.888
Quality of Social Overtures	23.69	20.99	118.50	-0.69	.582
Quality of Social Response	24.00	20.91	116.00	-0.73	.539
Amt of Reciprocal Social Comm	19.31	22.01	118.50	-0.62	.582
Overall Quality of Rapport	21.88	21.41	113.00	-0.10	.937
Functional Play with Objects	28.00	19.97	84.00	-1.89	.100
Imagination/Creativity	19.81	21.90	122.50	-0.48	.671
Unusual Sensory Int in Play Mat/Person	24.00	20.91	116.00	-0.69	.539
Hand, Finger, and Other Mannerisms	29.00	19.74	76.00	-2.04	.056
Self-Injurious Behavior	22.31	21.31	129.50	-0.41	.838
Unusually Rep Interests/Stereotyped Beh	25.19	20.63	106.50	-1.02	.352
Overactivity	17.94	22.34	107.50	-1.03	.368
Tantrums, Aggr, Negative/Disruptive Beh	24.00	20.91	116.00	-0.75	.539
Anxiety	18.38	22.24	111.00	-0.94	.440

+ $p < .05$

Table 10
ADOS Module 3 Items in Williams Syndrome Autism Spectrum (WS ASD) vs. PDD-NOS

ADOS Item	WS ASD (n = 17) Mean Rank	PDD-NOS (n = 40) Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	32.44	27.54	281.50	-1.18	.238	
Speech Abnormalities Assoc with Autism	29.24	28.90	336.00	-0.09	.932	
Immediate Echolalia	27.68	29.56	317.50	-0.74	.460	
Stereotyped Use of Words or Phrases	22.32	31.84	226.50	-2.19	.028	+
Offers Information	33.53	27.08	263.00	-1.62	.105	
Asks for Information	15.35	34.80	108.00	-4.23	<.001	*
Reporting of Events	27.91	29.46	321.50	-0.35	.724	
Conversation	29.65	28.73	329.00	-0.22	.829	
Gestures	24.76	30.80	268.00	-1.46	.145	
Unusual Eye Contact	30.88	28.20	308.00	-0.59	.553	
Facial Expressions Directed to Others	32.76	27.40	276.00	-1.38	.169	
Lang Prod & Linked Nonverbal Comm	29.74	28.69	327.50	-0.26	.796	
Shared Enjoyment in Interaction	30.53	28.35	314.00	-0.52	.606	
Empathy/Comments on Others' Emotions	26.00	30.28	289.00	-0.94	.349	
Insight	32.62	27.46	278.50	-1.14	.256	
Quality of Social Overtures	32.41	27.55	282.00	-1.21	.227	
Quality of Social Response	28.03	29.41	323.50	-0.38	.707	
Amt of Reciprocal Social Comm	28.53	29.20	332.00	-0.17	.868	
Overall Quality of Rapport	29.21	28.91	336.50	-0.07	.945	
Imagination/Creativity	25.53	30.48	281.00	-1.21	.262	
Unusual Sensory Int in Play Mat/Person	26.00	30.28	289.00	-1.03	.304	
Hand, Finger, and Other Mannerisms	29.06	28.98	339.00	-0.02	.983	
Self-Injurious Behavior	28.76	29.10	336.00	-0.16	.875	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	23.03	31.54	238.50	-2.02	.044	+
Compulsions or Rituals	26.29	30.15	294.00	-0.95	.345	
Overactivity/Agitation	23.41	31.38	245.00	-1.79	.074	
Tantrums, Aggr, Negative/Disruptive Beh	32.38	27.56	282.50	-1.52	.129	
Anxiety	26.18	30.20	292.00	-1.33	.185	

+ $p < .05$, * $p < .01$

Table 11
ADOS Module 2 Items in Children with Williams Syndrome and Mixed Etiology Group

ADOS Item	WS Mean Rank	ME Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	36.00	36.95	629.00	-0.23	.816	
Amt Soc Overtures/Maintenance of Attn	37.44	35.66	614.00	-0.47	.637	
Speech Abnormalities Assoc with Autism	33.34	39.33	538.50	-1.34	.182	
Immediate Echolalia	35.79	37.13	622.00	-0.31	.759	
Stereotyped/Idiosyncratic Words/Phrases	33.38	39.29	540.00	-1.41	.160	
Conversation	29.68	42.61	414.00	-2.85	.004	*
Pointing	33.16	39.49	532.50	-1.49	.137	
Gestures	37.72	35.41	604.50	-0.53	.597	
Unusual Eye Contact	36.53	36.47	645.00	-0.02	.988	
Facial Expressions Directed to Others	40.44	32.97	512.00	-1.82	.069	
Shared Enjoyment in Interaction	39.35	33.95	549.00	-2.13	.033	+
Response to Name	35.12	37.74	599.00	-1.20	.229	
Showing	39.44	33.87	546.00	-1.31	.192	
Spontaneous Initiation of Joint Attention	36.87	36.17	633.50	-0.24	.814	
Response to Joint Attention	37.62	35.50	608.00	-1.51	.132	
Quality of Social Overtures	35.69	37.22	618.50	-0.37	.709	
Quality of Social Response	32.21	40.34	500.00	-1.87	.062	
Amt of Reciprocal Social Comm	35.85	37.08	624.00	-0.30	.764	
Overall Quality of Rapport	32.40	40.17	506.50	-1.84	.066	
Functional Play with Objects	38.03	35.13	594.00	-0.73	.466	
Imagination/Creativity	36.51	36.49	645.50	-0.01	.995	
Unusual Sensory Int in Play Mat/Person	42.41	31.21	445.00	-2.50	.012	*
Hand, Finger, and Other Mannerisms	42.94	30.74	427.00	-2.77	.006	*
Self-Injurious Behavior	36.56	36.45	644.00	-0.08	.937	
Unusually Rep Interests/Stereotyped Beh	40.97	32.50	494.00	-1.89	.059	
Overactivity	33.94	38.79	559.00	-1.30	.193	
Tantrums, Aggr, Negative/Disruptive Beh	37.94	35.21	597.00	-0.70	.485	
Anxiety	39.26	34.03	552.00	-1.29	.197	

+ $p < .05$, * $p < .01$

Table 12
ADOS Module 3 Items in Children with Williams Syndrome and Mixed Etiology Group

ADOS Item	WS Mean Rank	ME Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	61.24	63.35	1787.00	-0.37	.712	
Speech Abnormalities Assoc with Autism	69.13	58.02	1518.50	-1.89	.059	
Immediate Echolalia	61.73	63.02	1811.50	-0.64	.522	
Stereotyped/Idiosyncratic Words/Phrases	63.21	62.02	1814.50	-0.22	.823	
Offers Information	68.49	58.45	1550.50	-2.93	.017	+
Asks for Information	45.90	73.72	1020.00	-4.64	<.001	*
Reporting of Events	59.90	64.26	1720.00	-0.79	.433	
Conversation	63.22	62.01	1814.00	-0.24	.811	
Gestures	58.59	65.14	1654.50	-1.34	.181	
Unusual Eye Contact	57.84	65.65	1617.00	-1.43	.153	
Facial Expressions Directed to Others	76.20	53.24	1165.00	-4.15	<.001	*
Lang Prod & Linked Nonverbal Comm	67.82	58.91	1584.00	-1.75	.080	
Shared Enjoyment in Interaction	65.40	60.54	1705.00	-1.18	.236	
Empathy/Comments on Others' Emotions	58.42	65.26	1646.00	-1.10	.271	
Insight	64.46	61.18	1752.00	-0.54	.593	
Quality of Social Overtures	63.69	61.70	1790.50	-0.35	.725	
Quality of Social Response	55.30	67.36	1490.00	-2.14	.032	+
Amt of Reciprocal Social Comm	63.04	62.14	1823.00	-0.24	.813	
Overall Quality of Rapport	51.31	70.06	1290.50	-3.22	.001	*
Imagination/Creativity	67.82	58.91	1584.00	-1.54	.124	
Unusual Sensory Int in Play Mat/Person	67.59	59.06	1595.50	-2.17	.030	+
Hand, Finger, and Other Mannerisms	62.34	62.21	1842.00	-0.07	.947	
Self-Injurious Behavior	63.24	62.00	1813.00	-1.22	.224	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	62.08	62.78	1829.00	-0.16	.876	
Compulsions or Rituals	65.80	60.27	1685.00	-1.38	.169	
Overactivity/Agitation	55.29	67.37	1489.50	-2.14	.032	+
Tantrums, Aggr, Negative/Disruptive Beh	61.25	63.34	1787.50	-0.56	.573	
Anxiety	61.98	63.85	1824.00	-0.23	.820	

+ $p < .05$, * $p < .01$

Table 13
ADOS Module 2 Items in Williams Syndrome Non-spectrum (WS NS) and Mixed Etiology Group

ADOS Item	WS NS (n = 26) Mean Rank	ME (n = 38) Mean Rank	Mann-Whitney U	Z	Sig	
Overall Level of Non-Echoed Language	30.38	33.95	439.00	-0.94	.346	
Amt Soc Overtures/Maintenance of Attn	30.85	33.63	451.00	-0.84	.400	
Speech Abnormalities Assoc with Autism	27.19	36.13	356.00	-2.10	.036	+
Immediate Echolalia	30.04	34.18	430.00	-1.01	.311	
Stereotyped/Idiosyncratic Words/Phrases	26.69	36.47	343.00	-2.51	.012	*
Conversation	22.46	39.37	233.00	-3.89	<.001	*
Pointing	28.21	35.43	382.50	-1.78	.075	
Gestures	33.87	31.57	458.50	-0.55	.584	
Unusual Eye Contact	30.54	33.84	443.00	-1.03	.305	
Facial Expressions Directed to Others	34.08	31.42	453.00	-0.71	.479	
Shared Enjoyment in Interaction	33.46	31.84	469.00	-0.93	.351	
Response to Name	30.50	33.87	442.00	-1.70	.090	
Showing	34.37	31.22	445.00	-0.78	.433	
Spontaneous Initiation of Joint Attention	30.83	33.64	450.50	-1.18	.239	
Response to Joint Attention	33.23	32.00	475.00	-1.21	.227	
Quality of Social Overtures	28.35	35.34	386.00	-1.89	.059	
Quality of Social Response	24.56	37.93	287.50	-3.27	.001	*
Amt of Reciprocal Social Comm	29.88	34.29	426.00	-1.16	.247	
Overall Quality of Rapport	25.40	37.36	309.50	-3.06	.002	*
Functional Play with Objects	31.65	33.08	472.00	-0.40	.690	
Imagination/Creativity	31.85	32.95	477.00	-0.26	.795	
Unusual Sensory Int in Play Mat/Person	36.94	29.46	378.50	-1.79	.074	
Hand, Finger, and Other Mannerisms	36.54	29.74	389.00	-1.69	.092	
Self-Injurious Behavior	32.00	32.84	481.00	-0.83	.408	
Unusually Rep Interests/Stereotyped Beh	34.98	30.80	429.50	-0.97	.330	
Overactivity	29.35	34.66	412.00	-1.49	.136	
Tantrums, Aggr, Negative/Disruptive Beh	32.81	32.39	486.00	-0.14	.887	
Anxiety	36.23	29.95	397.00	-1.60	.110	

+ $p < .05$, * $p < .01$

Table 14
ADOS Module 3 Items in Williams Syndrome Non-spectrum (WS NS) and Mixed Etiology Group

ADOS Item	WS NS (n = 33) Mean Rank	ME (n = 74) Mean Rank	Mann-Whitney U	Z	Sig	
Overall Level of Non-Echoed Language	48.76	56.34	1048.00	-1.36	.174	
Speech Abnormalities Assoc with Autism	55.50	53.33	1171.50	-0.38	.705	
Immediate Echolalia	52.50	54.67	1171.50	-1.17	.243	
Stereotyped/Idiosyncratic Words/Phrases	52.67	54.59	1177.00	-0.37	.710	
Offers Information	54.92	53.59	1190.50	-0.39	.696	
Asks for Information	37.94	61.16	691.00	-3.87	<.001	*
Reporting of Events	46.92	57.16	987.50	-1.91	.056	
Conversation	47.82	56.76	1017.00	-1.96	.050	+
Gestures	48.88	56.28	1052.00	-1.53	.126	
Unusual Eye Contact	41.85	59.42	820.00	-3.36	.001	*
Facial Expressions Directed to Others	62.32	50.29	946.50	-2.34	.020	+
Lang Prod & Linked Nonverbal Comm	58.33	52.07	1078.00	-1.28	.200	
Shared Enjoyment in Interaction	50.62	55.51	1109.50	-1.49	.136	
Empathy/Comments on Others' Emotions	46.85	57.19	985.00	-1.69	.092	
Insight	48.82	56.31	1050.00	-1.25	.213	
Quality of Social Overtures	47.98	56.68	1022.50	-1.61	.107	
Quality of Social Response	38.18	61.05	699.00	-4.23	<.001	*
Amt of Reciprocal Social Comm	50.59	55.52	1108.50	-1.50	.133	
Overall Quality of Rapport	33.52	63.14	545.00	-5.25	<.001	*
Imagination/Creativity	58.15	52.15	1084.00	-1.05	.293	
Unusual Sensory Int in Play Mat/Person	57.64	52.38	1101.00	-1.48	.139	
Hand, Finger, and Other Mannerisms	50.79	55.43	1115.00	-1.26	.207	
Self-Injurious Behavior	54.00	54.00	1221.00	-1.26	.207	
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	53.50	54.22	1204.50	-0.16	.872	
Compulsions or Rituals	55.53	53.32	1170.50	-0.60	.547	
Overactivity/Agitation	44.29	58.33	900.50	-2.53	.011	*
Tantrums, Aggr, Negative/Disruptive Beh	49.00	56.23	1056.00	-2.21	.027	+
Anxiety	54.68	53.70	1198.50	-0.25	.801	

+ $p < .05$, * $p < .01$

Table 15
ADOS Module 2 Items in Williams Syndrome Spectrum (WS ASD) and Mixed Etiology Group

ADOS Item	WS ASD (n = 8) Mean Rank	ME (n = 38) Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	28.25	22.50	114.00	-1.29	.283	
Amt Soc Overtures/Maintenance of Attn	32.88	21.53	77.00	-2.66	.029	+
Speech Abnormalities Assoc with Autism	27.31	22.70	121.50	-0.95	.384	
Immediate Echolalia	28.50	22.45	112.00	-1.28	.258	
Stereotyped/Idiosyncratic Words/Phrases	29.13	22.32	107.00	-1.45	.201	
Conversation	27.13	22.74	123.00	-0.95	.416	
Pointing	23.25	23.55	150.00	-0.07	.966	
Gestures	24.25	23.34	146.00	-0.20	.876	
Unusual Eye Contact	30.00	22.13	100.00	-1.91	.138	
Facial Expressions Directed to Others	35.13	21.05	59.00	-3.22	.006	*
Shared Enjoyment in Interaction	32.50	21.61	80.00	-3.87	.036	*
Response to Name	24.13	23.37	147.00	-0.27	.898	
Showing	29.94	22.14	100.50	-1.75	.138	
Spontaneous Initiation of Joint Attention	30.50	22.03	96.00	-2.36	.109	
Response to Joint Attention	25.88	23.00	133.00	-2.18	.599	
Quality of Social Overtures	33.56	21.38	71.50	-2.66	.018	+
Quality of Social Response	31.06	21.91	91.50	-2.02	.079	
Amt of Reciprocal Social Comm	29.25	22.29	106.00	-1.55	.191	
Overall Quality of Rapport	29.13	22.32	107.00	-1.43	.201	
Functional Play with Objects	32.75	21.55	78.00	-2.56	.031	+
Imagination/Creativity	25.69	23.04	134.50	-0.57	.618	
Unusual Sensory Int in Play Mat/Person	34.19	21.25	66.50	-2.81	.011	*
Hand, Finger, and Other Mannerisms	37.75	20.50	38.00	-3.74	<.001	*
Self-Injurious Behavior	25.38	23.11	137.00	-1.23	.680	
Unusually Rep Interests/Stereotyped Beh	34.44	21.20	64.50	-2.79	.009	*
Overactivity	22.88	23.63	147.00	-0.18	.898	
Tantrums, Aggr, Negative/Disruptive Beh	28.63	22.42	111.00	-1.48	.246	
Anxiety	23.13	23.58	149.00	-0.11	.943	

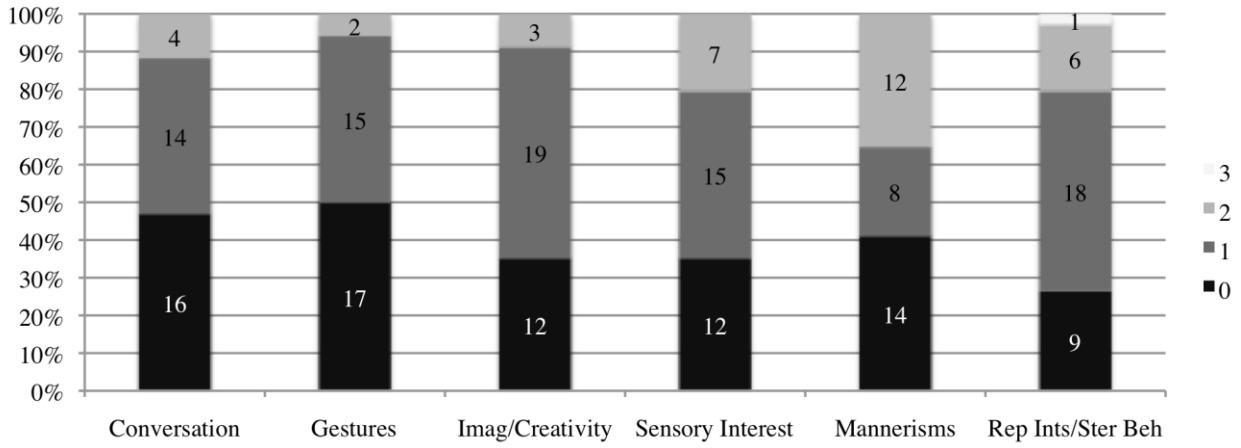
+ $p < .05$, * $p < .01$

Table 16
ADOS Module 3 Items in Williams Syndrome Spectrum (WS ASD) and Mixed Etiology Group

ADOS Item	WS ASD (n = 17) Mean Rank	ME (n = 74) Mean Rank	Mann-Whitney U	Z	Sig.	
Overall Level of Non-Echoed Language	52.47	44.51	519.00	-1.28	.202	
Speech Abnormalities Assoc with Autism	62.59	42.19	347.00	-3.18	.001	*
Immediate Echolalia	46.65	45.85	618.00	-0.32	.752	
Stereotyped/Idiosyncratic Words/Phrases	50.68	44.93	549.50	-0.99	.325	
Offers Information	61.82	42.36	360.00	-4.15	<.001	*
Asks for Information	28.35	50.05	329.00	-3.28	.001	*
Reporting of Events	52.09	44.60	525.50	-1.21	.226	
Conversation	60.12	42.76	389.00	-2.99	.003	*
Gestures	44.44	46.36	602.50	-0.35	.729	
Unusual Eye Contact	55.88	43.73	461.00	-1.92	.055	
Facial Expressions Directed to Others	70.15	40.45	218.50	-5.05	<.001	*
Lang Prod & Linked Nonverbal Comm	53.24	44.34	506.00	-1.66	.096	
Shared Enjoyment in Interaction	61.09	42.53	372.50	-3.79	<.001	*
Empathy/Comments on Others' Emotions	47.88	45.57	597.00	-0.34	.731	
Insight	61.82	42.36	360.00	-2.89	.004	*
Quality of Social Overtures	61.18	42.51	371.00	-2.97	.003	*
Quality of Social Response	55.53	43.81	467.00	-1.89	.059	
Amt of Reciprocal Social Comm	54.21	44.11	489.50	-2.21	.027	+
Overall Quality of Rapport	52.85	44.43	512.50	-1.32	.186	
Imagination/Creativity	53.59	44.26	500.00	-1.49	.137	
Unusual Sensory Int in Play Mat/Person	53.91	44.18	494.50	-2.42	.015	+
Hand, Finger, and Other Mannerisms	51.76	44.68	531.00	-1.51	.132	
Self-Injurious Behavior	48.18	45.50	592.00	-2.09	.037	+
Excess Int in/Ref to Unusual/Highly Spec Topics/Objects or Repetitive Behavior	45.74	46.06	624.50	-0.07	.947	
Compulsions or Rituals	52.74	44.45	514.50	-1.92	.055	
Overactivity/Agitation	43.65	46.54	589.00	-0.46	.647	
Tantrums, Aggr, Negative/Disruptive Beh	52.03	44.61	526.50	-1.62	.105	
Anxiety	43.15	46.66	580.50	-0.87	.382	

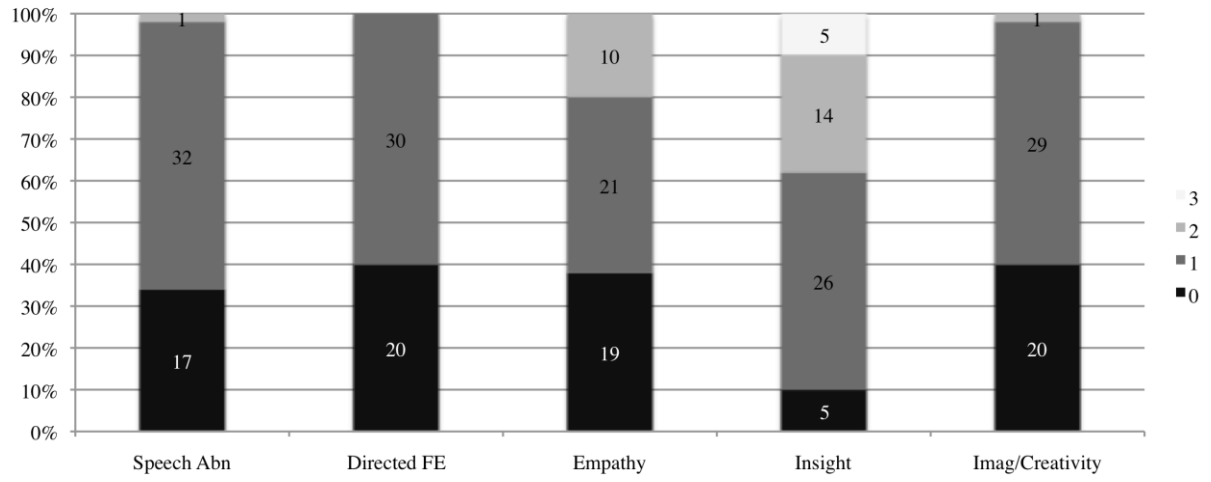
+ $p < .05$, * $p < .01$

Figure 1
Frequently Endorsed Module 2 Items



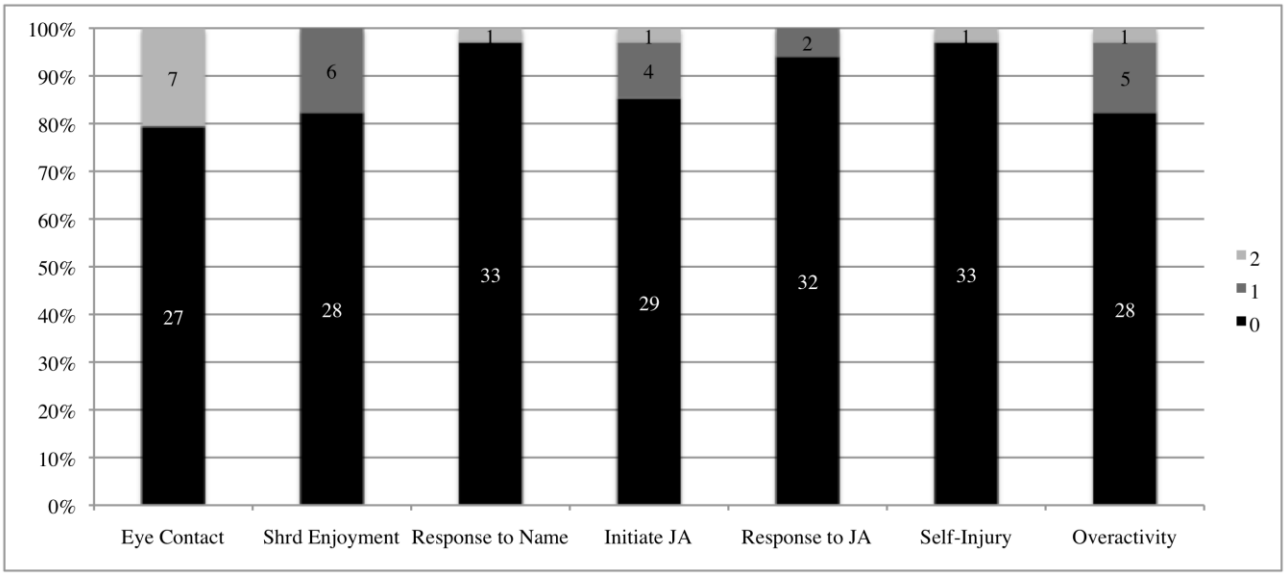
Note: Imag/Creativity = Imagination/Creativity; Sensory Interest = Unusual Sensory Interest in Play Material/Person; Mannerisms = Hand and Finger and Other Complex Mannerisms; Rep Ints/Ster Beh = Unusually Repetitive Interests or Stereotyped Behaviors

Figure 2
Frequently Endorsed Module 3 Items



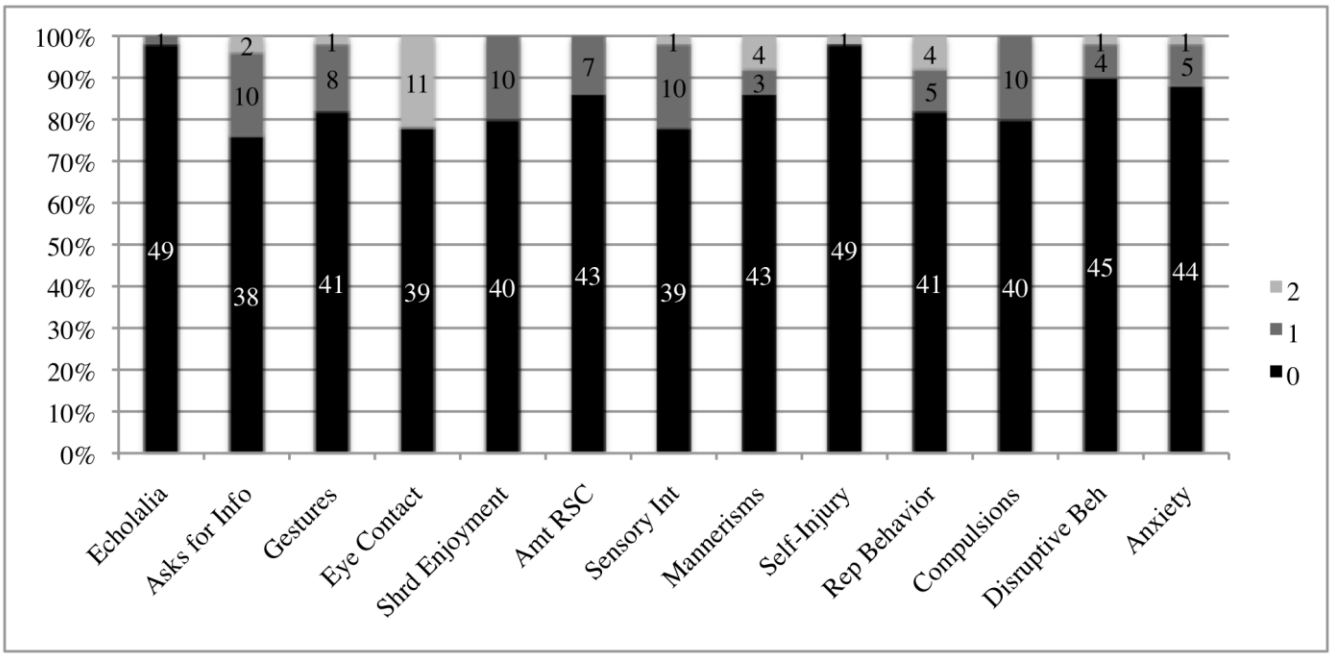
Note: Speech Abn = Speech Abnormalities Associated with Autism; Directed FE = Facial Expressions Directed to Others; Imag/Creativity = Imagination/Creativity

Figure 3
Rarely Endorsed Module 2 Items



Note: Shrd Enjoyment = Shared Enjoyment in Interaction; Initiate JA = Spontaneous Initiation of Joint Attention

Figure 4
Rarely Endorsed Module 3 Items



Note: Shrd Enjoyment = Shared Enjoyment in Interaction; Amt RSC = Amount of Reciprocal Social Communication; Sensory Int = Unusual Sensory Interest in Play Material/Person; Rep Behavior = Excessive Interest in or References to Unusual or Highly Specific Topics or Objects or Repetitive Behavior

CIRRICULUM VITAE

EDUCATION

August 2008 – May 2014 *University of Wisconsin, Milwaukee; Milwaukee, WI*
Doctor of Philosophy in Clinical Psychology
Advisor: Bonita P. Klein-Tasman
Masters of Science in Psychology Awarded May 2011

September 2001 – June 2005 *University of California, San Diego; La Jolla, CA*
Bachelors of Arts in Human Development
Awarded: June 2005

PRE-DOCTORAL INTERNSHIP

August 2013 – present *Child Development & Rehabilitation Center*
Oregon Health & Science University
Major rotations in Pediatric Psychology, Psychology Assessment Clinic, and LEND Clinic; minor rotations in Inpatient Consultation/Liaison Service, Neuropsychology, NICU Follow-up Clinic, and Behavioral Pediatrics
Director of Clinical Training: Kurt Freeman, Ph.D.

EMPLOYMENT

July 2006 – July 2008 *Pediatric & Developmental Neuropsychiatry Branch*
National Institutes of Health; Bethesda, MD
Intramural Research Training Apprenticeship Fellow
Duties: develop manual of operations for protocols; maintain subject databases; serve as main point of contact for interested participants; assist in assessments; administration of selected measures
Branch Chief: Susan Swedo, M.D.

June 2005 – June 2006 *Infant Vision Laboratory*
University of California, San Diego; La Jolla, CA
Research Assistant I, Lab Coordinator
Duties: maintain subject database; serve as main point of contact for interested participants; schedule and consent procedures for participants; daily organization of laboratory; administer developmental assessments to 6-month old infants
Lab Director: Karen Dobkins, Ph.D.

AWARDS AND HONORS

2014 David Zeaman Travel Award, Gatlinburg Conference
2012 Williams Syndrome Association Professional Conference Award
2010 University of Wisconsin, Milwaukee Graduate School Travel Award
2004 National Society of Collegiate Scholars

2001-2005 Revelle College Dean's List, awarded each quarter

CLINICAL EXPERIENCE

September 2011 – July 2013 *Medical College of Wisconsin*
Neuropsychology Department
Administer standardized measures as part of comprehensive neuropsychological evaluations with toddlers and children through age 18; assist licensed psychologists in case conceptualization and report writing process
Supervisor: Jennifer Koop, Ph.D.

September 2010 – May 2011 *University of Wisconsin, Milwaukee*
Tic Disorders Specialty Clinic
As a student therapist, provided behavioral interventions for the treatment of skin picking and stereotypic movement disorder
Supervisor: Douglas Woods, Ph.D.

September 2010 – May 2011 *Children's Hospital of Wisconsin*
Constipation and Fecal Incontinence Clinic
As a student therapist, provided behavioral interventions for the treatment of fecal soiling in individual and group therapy sessions.
Supervisors: W. Hobart Davies, Ph.D., Alan Silverman, Ph.D., & Andrea Begotka, Ph.D.

August 2009 – July 2013 *University of Wisconsin, Milwaukee*
Child Neuropsychology Clinic (CNC)
As part of the CNC, assessments were conducted with children and adolescents with autism spectrum disorders, learning disabilities, and other developmental concerns. Full reports of results were written.
Supervisor: Bonita P. Klein-Tasman

September 2009 – May 2010 *University of Wisconsin, Milwaukee*
Practicum in Assessment
Conducted 5 full assessments, including structured background interviews, administration of standardized assessment tools, scoring and interpretation of testing results, report writing, and feedback sessions
Supervisors: Bonita P. Klein-Tasman, Ph.D. and David Osmon, Ph.D.

September 2008 – May 2009 *University of Wisconsin, Milwaukee*
1st Year Practicum
Conducted assessments with volunteers and 1 client, including structured background interviews, administration of standardized assessment tools, and scoring of testing results.
Supervisor: David Osmon, Ph.D.

August 2008 – July 2013 *University of Wisconsin, Milwaukee*
Child Neurodevelopmental Research Lab (CNRL)

As part of ongoing research projects, assessments were conducted with young children with Neurofibromatosis-1, Williams, syndrome, and autism spectrum disorders, as well as typically developing children. Full reports of results were written.
Supervisor: Bonita P. Klein-Tasman, Ph.D.

July 2006 – July 2008 *National Institutes of Health*
Pediatric & Developmental Neuropsychiatry Branch (NIMH)
Aided in the administration of standardized measures as part of assessments with children with autism spectrum disorders, speech and language disorders, and general developmental delays, as well as typically developing children.
Branch Chief: Susan Swedo, M.D.
Clinical Supervisor: Audrey Thurm, Ph.D.

June 2005 – June 2006 *Infant Vision Laboratory*
University of California, San Diego; La Jolla, CA
Administered developmental assessments to 6-month old infants as part of a longitudinal study of infant siblings of children with autism spectrum disorders.
Lab Director: Karen Dobkins, Ph.D.

September 2003 – June 2004 *Autism Research Laboratory*
University of California, San Diego; La Jolla, CA
Undergraduate Research Assistant
Trained in Pivotal Response Training (PRT) and Picture Exchange Communication System (PECS) for in-home therapy provision to young children with autism as part of research projects
Supervisor: Laura Schreibman, Ph.D.

January – June 2005 *Children's Hospital Preschool, San Diego, CA*
Volunteer
Served as a teacher's assistant in a preschool for children with autism spectrum disorders
Supervisor: Aubyn Stahmer, Ph.D.

RESEARCH EXPERIENCE

August 2008 – present *University of Wisconsin, Milwaukee*
Ongoing research projects in the Child Neurodevelopment Research Lab (CNRL) include investigations of young children with Neurofibromatosis-1, Williams syndrome, and autism spectrum disorders
Supervisor: Bonita P. Klein-Tasman

July 2006 – July 2008 *Pediatric & Developmental Neuropsychiatry Branch*
National Institutes of Health; Bethesda, MD
Intramural Research Training Apprenticeship Fellow
Created and maintained databases, developed protocols for the running of research projects, conducted literature reviews

Branch Chief: Susan Swedo, M.D.

June 2005 – June 2006 *Infant Vision Laboratory*
University of California, San Diego; La Jolla, CA
Research Assistant I, Lab Coordinator
Maintained subject information and results databases
Lab Director: Karen Dobkins, Ph.D.

January 2005 – June 2005 *UCSD Autism Center of Excellence*
University of California, San Diego; La Jolla, CA
Undergraduate Research Assistant
Assisted graduate students in various research projects, which included duties such as creating stimuli for fMRI studies, aiding in subject participation, and medical record review and data extraction
Lab Director: Eric Courchesne, Ph.D.

September 2004 – June 2005 *Developmental Neuroscience Laboratory*
University of California, San Diego; La Jolla, CA
Undergraduate Research Assistant
Assisted graduate students in various research projects, which included duties such as running electroencephalograms on young children, coding of behavioral protocols, and data entry
Lab Director: Leslie Carver, Ph.D.

TEACHING EXPERIENCE

May –June 2013 *Course Instructor, University of Wisconsin, Milwaukee*
Course: Online Child Psychology

September – December 2012 *Course Instructor, University of Wisconsin, Milwaukee*
Course: Online Child Psychology

January – May 2012 *Course Instructor, University of Wisconsin, Milwaukee*
Course: Online Child Psychology

June – July 2011 *Course Instructor, University of Wisconsin, Milwaukee*
Course: Online Child Psychology

August 2010 – May 2011 *Teaching Assistant, University of Wisconsin, Milwaukee*
Course: 1st Year Clinical Practicum
Duties: Supervise graduate students conducting interviews and administering standardized measures; providing feedback to students
Supervisor/Course Instructor: David Osmon, Ph.D.

August 2010 – May 2013 *Teaching Assistant, University of Wisconsin, Milwaukee*

Course: 2nd Year Clinical Practicum
Duties: Supervise graduate students conducting interviews and administering standardized measures; providing feedback to students
Supervisor/Course Instructors: Hanjoo Lee, Ph.D. & Bonita P. Klein-Tasman, Ph.D.

January 2010 – May 2010 Teaching Assistant, University of Wisconsin, Milwaukee
Course: Child Psychology
Duties: monitor student question board and provide assistance; manage technical aspects of online course; grade student discussions; develop test questions
Supervisor/Course Instructor: Bonita P. Klein-Tasman, Ph.D.

August 2009 – January 2010 Teaching Assistant, University of Wisconsin, Milwaukee
Course: Introduction to Psychology
Duties: facilitate in-class discussions of 6 sections of 20 undergraduate students; proctor exams; maintain grade records
Supervisor/Course Instructor: John Moore, Ph.D.

August 2008 – May 2009 Teaching Assistant, University of Wisconsin, Milwaukee
Course: Child Psychology
Duties: facilitate in-class discussion of 5 sections of 30 undergraduate students; develop test questions; proctor exams; maintain grade records
Supervisor/Course Instructor: Richard Passman, Ph.D.

PUBLICATIONS AND PAPERS

Klein-Tasman, B.P., Colon, A.M., Brei, N., **van der Fluit, F.,** Casnar, C.L., Janke, K.M., Basal, D., Siegel. D.H., & Walker, J.A. (2013). Adaptive Behavior in Young Children with Neurofibromatosis Type 1. *International Journal of Pediatrics, 2013.*

Klein-Tasman, B.P., Janke, K.M., Luo, W., Casnar, C.L., Hunter, S.J., Tonsgard, J., Trapane, P., **van der Fluit, F.,** & Kais, L.A. (2013). Cognitive and Psychosocial Phenotype of Young Children with Neurofibromatosis-1. *Journal of the International Neuropsychological Society, 20,* 1-11.

Ricketts, E.J., Bauer, C.C., **van der Fluit, F.,** Capriotti, M.R., Espil, F.M., Snorrason, I., Ely, L.J., Walther, M.R., & Woods, D.W. (2013). Behavior Therapy for Stereotypic Movement Disorder in Typically Developing Children: A Clinical Case Series. *Cognitive and Behavioral Practice, 20(4),* 544-555.

van der Fluit, F., Gaffrey, M., & Klein-Tasman, B.P. (2012). Social Cognition in Williams Syndrome: Relations Between Performance on the Social Attribution Task and Cognitive and Behavioral Characteristics. *Frontiers in Developmental Psychology, 3.*

van der Fluit, F. & Klein-Tasman, B.P. (in press). *Williams Syndrome.* In Encyclopedia of Autism Spectrum Disorders.

Klein-Tasman, B.P. & **van der Fluit, F.** (in press). *Williams Syndrome.* In Encyclopedia of Clinical Neuropsychology. Kreutzer, J.S., DeLuca, J., & Caplan, B. (Eds).

CONFERENCE PRESENTATIONS

van der Fluit, F., Mervis, C.B., Lord, C., & Klein-Tasman, B.P. (2014, March). *Socio-Communicative Functioning of Verbal Children with Williams Syndrome: Performance on the Autism Diagnostic Observation Schedule Modules 2 and 3.* Symposium discussion presented at the Gatlinburg Conference on Research and Theory in Intellectual and Developmental Disabilities, Chicago, IL.

van der Fluit, F., Hefflefinger, A.K., & Koop, J.I. (2013, February). *Examination of the Effects of Perinatal Neurological Insult on Visual Attention.* Poster presented at the 41st Annual Meeting of the International Neuropsychological Society: Waikoloa, Hawaii.

Janke, K.M., Casnar, C., **van der Fluit, F.,** Haberman, D.A., Brei, N.G., Hunter, S.J., & Klein-Tasman, B.P. (2013, February). *Concurrent relations between early neuropsychological and academic skills in young children with NF1 and typically developing peers.* Poster accepted for presention at the 41st Annual Meeting of the International Neuropsychological Society: Waikoloa, Hawaii.

van der Fluit, F.,Klein-Tasman, B.P., & Bennaton, E.C. (2012, May). *Parent-Reported Autism Spectrum Symptomatology in Children with Williams Syndrome.* Poster presented at the International Meeting for Autism Research, Toronto, Ontario, Canada.

van der Fluit, F. & Klein-Tasman, B.P. (2012, March). *A Case Study of Co-occurring 15q13.3 deletion and Williams syndrome.* Poster presented at the Gatlinburg Conference on Research and Theory in Intellectual and Developmental Disabilities, Annapolis, MD.

Casnar, C.L., Kais, L. A., **van der Fluit, F.**, Klein-Tasman. (2012, February). *Fine Motor Abilities in Young Children with Neurofibromatosis-1.* Poster presented at the 40th Annual Meeting of the International Neuropsychological Society: Montreal, Quebec.

van der Fluit, F., Erdmann, E.K., Bennaton, E.C., Schram, S.L., Gaffrey, M., & Klein-Tasman, B.P. (2011, May). *Social Cognition in Williams Syndrome: Relations Between the Social Attribution Task and Parent-Reported Socio-Communicative Functioning.* Poster presented at the annual meeting of the International Meeting for Autism Research, San Diego, CA.

van der Fluit, F., Janke, K.M., Erdmann, E.K., & Klein-Tasman, B.P. (2010, May). *The Use of New ADOS Diagnostic Algorithms in Young Children with Williams Syndrome.* Poster presented at the annual meeting of the International Society for Autism Research, Philadelphia, PA.

Bennaton, E.C., **van der Fluit, F.,** Klein-Tasman, B.P. (2010, April). *Autism Spectrum Disorder Screening Measures in Children with Williams Syndrome.* Poster presented at the Midwest Psychological Association, Chicago, IL.

van der Fluit, F., Bennaton, E.C., & Klein-Tasman, B.P. (2010, February). *Socio-Communicative Behaviors and Autism Spectrum Classification in Young Children with Williams Syndrome*. Poster presented at the annual meeting of the International Neuropsychological Society, Acapulco, Mexico.

Shumway, S., Thurm, A., **van der Fluit, F.,** & Swedo, S. (2008, May). *Regression Histories and Current Cognitive and Adaptive Status in Young Children in the Autism Phenome Project.* Poster presented at the annual meeting of the International Society for Autism Research, London, England.

PROFESSIONAL AFFILIATIONS

Student Member, International Society for Autism Research (INSAR)
Association of Graduate Students in Psychology, University of Wisconsin, Milwaukee
Student Member, International Neuropsychological Society (INS)

REFERENCES

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