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## Autism Spectrum Symptomatology in Children with Williams Syndrome who have Phrase Speech or Fluent Language

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### Abstract

To characterize autism spectrum-related symptomatology in children with Williams syndrome (WS) with phrase speech or fluent language, the Autism Diagnostic Observation Schedule (Lord et al., 1999) Module 2 or 3 was administered. The cutoff for autism spectrum was met by 35% (14/40) who completed Module 2 and 30% (18/60) who completed Module 3. Similarities and differences in socio-communicative strengths and weaknesses as a function of language ability were identified. Symptom severity was negatively associated with IQ for participants with phrase speech but not for those with fluent language. The findings suggest an elevated risk of ASD for individuals with WS relative to the general population and contribute to a more nuanced sense of the socio-communicative functioning of children with WS.

### Keywords

Williams syndrome; intellectual disability; autism spectrum disorders; social communication

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Williams syndrome (WS), a rare neurodevelopmental disorder caused by hemideletion of 26 – 28 genes on chromosome 7q11.23 (Hillier et al., 2003), is associated with a characteristic cognitive and behavioral phenotype. Intellectual ability typically is at the mild intellectual disability level, but the range is from severe intellectual disability to average intellectual

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ability (Martens, Wilson, & Reuters, 2008; Mervis & John, 2010). The cognitive profile, which includes relative strengths in (concrete) language, verbal short-term memory, and nonverbal reasoning contrasted with considerable weakness in visuospatial construction, is present across the lifespan and across intellectual ability levels (Mervis et al., 2000; Mervis & John, 2010). Similarly, the personality profile of high levels of social approach, empathy, and anxiety (Klein-Tasman & Mervis, 2003; Tomc, Williamson, & Pauli, 1990) and a strong interest in strangers (Fisher, 2014; Mervis et al., 2003) is present from a very early age. These characteristics have sometimes led to conceptualizations of WS that are in direct contrast to autism (Bloom, 2017; Rapin & Tuchman, 2008). However, a sharp contrast with autism spectrum disorder (ASD) does not provide an accurate characterization of the behavioral profile of WS, as researchers have identified a consistent pattern of difficulties in socio-communicative functioning and repetitive and restrictive behaviors in both children and adults with this syndrome (reviewed below).

### **Socio-communicative Difficulties, Repetitive Behaviors, and Preoccupations**

Although the social drive of individuals with WS has been well-documented (Klein-Tasman & Mervis, 2003; Ng, Järvinen, & Bellugi, 2014; Zitzer-Comfort, Doyle, Masataka, Korenberg, & Bellugi, 2007), difficulties with a variety of aspects of social communication have nevertheless been described. Comprehension and production of communicative gestures such as pointing or showing are delayed (Becerra, 2016; Laing et al., 2002; Mervis & Becerra, 2007; Mervis & Bertrand, 1993, 1997), with onset of referential pointing even more delayed than onset of expressive language. Difficulties with triadic joint attention and social referencing are common (John, Dobson, Thompson, & Mervis, 2012; John & Mervis, 2010a; John, Rowe, & Mervis, 2009; Laing et al., 2002; Mervis & Becerra, 2007; Thurman & Mervis, 2013) as are atypical patterns of eye gaze in communicative settings (Jones et al., 2000; Mervis et al., 2003). While young children with WS are responsive to verbal and nonverbal displays of emotionality in others, they often do not use this information to support high-quality social interactions (Fidler, Hepburn, Most, Philofsky, & Rogers, 2007). Difficulties with language pragmatics and associated nonverbal aspects of communication are common both in school-aged children and adults with WS (Gosch, Ståding, & Pankau, 1994; Laws & Bishop, 2004; Philofsky, Fidler, & Hepburn, 2007), leading, for example, to inappropriate initiation of conversation and use of stereotyped conversation.

Repetitive behavior and preoccupations or obsessions also are common (Davies, Udwin, & Yule, 1998; Janes, Riby, & Rodgers, 2014; Royston et al., 2018). Obsessive questioning related to anxiety-provoking topics such as natural disasters or to anticipation of upcoming events such as birthdays or holidays occurs frequently among both children and adults. Compulsive greetings, watching spinning objects, and an obsessive need to locate the sources of sounds also have been reported (Semel & Rosner, 2003) and are related to sensory processing abnormalities, problem behaviors, and limitations in adaptive behavior (John & Mervis, 2010b; Riby, Janes, & Rodgers, 2013; Semel & Rosner, 2003). The obsessive interests of children with WS have often been discussed in the context of a potential anxiety disorder diagnosis for Obsessive-Compulsive Disorder (OCD); however,

these obsessive interests rarely meet criteria for OCD (Royston, Howlin, Waite, & Oliver, 2017).

Klein-Tasman, Li-Barber, and Magargee (2011) found that although the social motivation of 4 – 16-year-olds with WS was within the expected range for the general population, significant abnormalities in social reciprocity (including social awareness, social communication, and social cognition) and in restricted and repetitive behaviors as measured by the Social Responsiveness Scale (SRS; Constantinople & Gruber, 2005) were consistently identified by both parents and teachers. These findings provide further confirmation that difficulties that overlap with those seen for children with ASD are present among many children and adolescents with WS.

## **Studies using Gold-Standard ASD Diagnostic Instruments in Williams Syndrome**

Previous researchers have found that the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) successfully differentiates individuals with ASDs from those with other developmental difficulties, particularly language delays (Bishop & Norbury, 2002; Noterdaeme, Mildenberger, Sitter, & Amorosa, 2002; Noterdaeme, Sitter, Mildenberger, & Amorosa, 2000). While there is a paucity of research using gold-standard ASD diagnostic tools with children with WS, the ADOS Module 1 (designed for children with either no spoken language or very limited spoken language) has been used in three studies of individuals with WS.

Lincoln et al. (2007), studying a group of 20 young children with WS and a contrast group of children with autism, found differing behavioral profiles in terms of both severity and type. Although 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, they did not show impairments in other areas related to social functioning. In particular, they demonstrated generally typical behavior in terms of shared enjoyment, vocalizations and facial expressions directed to others, response to joint attention, and quality of social interactions and did not produce unusual eye contact. Only two children (10%) evidenced difficulties significant enough to exceed the ADOS cutoff for a classification of Autism Spectrum (one for PDD-NOS, one for autistic disorder). Two children met the DSM-IV criteria for autistic disorder (including the child who met the ADOS criterion) and two additional children met the DSM-IV criteria for PDD-NOS (including the child who met the ADOS criterion), for a total of 20% of the sample.

Klein-Tasman, Mervis, Lord, and Phillips (2007) studied a group of 29 children with WS with no or very limited expressive language and found a considerably higher proportion of children (14 of 29; 48%) met the ADOS criterion for autism spectrum (11 for PDD-NOS, 3 for autistic disorder). Atypical eye contact and difficulties with both initiation and response to joint attention, integrating gaze with communicative behaviors, reciprocal social smiling, and use of pointing to communicate were common, as were abnormalities in play behavior and repetitive and restricted interests. Clinical evaluations were not conducted so it is

unknown what proportion of children would have met DSM-IV diagnostic criteria for autistic disorder or PDD-NOS.

Further comparison of these children to three groups of sex, chronological age, and intellectual ability-matched controls (PDD-NOS, autism, or non-spectrum developmental disability of mixed etiology) was conducted by Klein-Tasman, Phillips, Lord, Mervis, and Gallo (2009). The WS group evidenced more social interaction difficulties than the non-spectrum mixed etiology group, indicating greater socio-communicative impairment than expected based on developmental delay alone. Consistent with Lincoln et al.'s (2007) findings, the WS group clearly showed less impairment than the autism group. The behavioral profile of the WS group was most similar to that of the PDD-NOS group. However, the children with WS who were classified as ASD by the ADOS (almost half of the sample) showed somewhat *greater* difficulties, on average, than matched control participants with PDD-NOS. These findings are consistent with increased risk for substantial ASD symptomatology in young children with WS with very limited language abilities.

Tordjman et al. (2012) administered the ADOS Module 1 to nine individuals with WS ranging in age from 4 – 37 years who were identified in autism care centers. Seven individuals were nonverbal; the remaining two had very limited language. Caregivers also completed the Autism Diagnostic Interview-Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003). Consistent with their placement at autism care centers, these individuals all demonstrated significant impairments in communication, social interaction, and restricted and repetitive behavior, meeting criteria for autistic disorder on both the ADOS and the ADI-R.

## Summary and Rationale for the Present Study

Studies of children with WS who have no or very limited expressive language on the ADOS Module 1 indicate that a large proportion has socio-communicative difficulties that overlap significantly with those of children with ASD. Based on findings from both experiments and informant questionnaire studies of socio-communicative abilities of children with WS who have more advanced language, it appears that the overlap in symptomatology with the autism spectrum persists even once language has improved. However, studies using the ADOS with children with WS who have either phrase speech or fluent expressive language (as operationally defined by the ADOS) have not been reported. In the present study we administered the ADOS Module 2 or 3 to 100 children with WS who either used phrase speech or had fluent language, in order to comprehensively examine social communication and repetitive behavior overlaps with the autism spectrum in children with WS who had relatively strong language abilities.

## Method

### Participants

The study included 100 children with classic WS deletions. Forty children (17 girls, 23 boys) were assessed with the ADOS Module 2 and 60 children (32 girls, 28 boys) with Module 3. Descriptive information regarding age and IQ is provided in Table 1. IQ scores

were consistent with those typically reported for individuals with WS on this measure of intellectual ability.

Based on previous research demonstrating differences in behavioral presentation in children with WS based on ADOS classification (Klein-Tasman et al., 2007), participants were further divided into two groups for each module based on ADOS classification. (See below for a more thorough description of the ADOS classification process.) This yielded a group of children with total scores below the cutoff for ASD, referred to as the WS non-spectrum group (WS-NS), and a group of children with ADOS scores at or exceeding the cutoff, referred to as the WS spectrum group (WS-ASD), for each module.

## Materials

**Autism Diagnostic Observation Schedule (ADOS), Module 2 or 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; per ADOS standardization, phrase speech is defined as “spontaneous, non-echoed, meaningful three-word utterances that sometimes include a verb.” Module 3 is administered to individuals with fluent speech; per ADOS standardization, fluent speech is defined as using a range of sentence types and grammatical forms, including the use of conjunctions such as “but” or “though,” roughly approximate to the language level of a typical 4-year-old. Individuals who produce multi-word utterances that are not as complex as those required to meet the ADOS definition of fluent speech are administered Module 2.

Communicative overtures, reciprocal social interactions, and restricted and repetitive behaviors are coded according to descriptions provided in the ADOS manual, with higher ratings indicating more impaired functioning. Behaviors that are consistent with those of typically developing individuals are given a code of 0, while behaviors that are considered mildly abnormal are scored 1 and behaviors indicating more severe impairments receive codes of 2 or 3. The subset of items that was previously determined to be most likely to distinguish between individuals with ASDs and those without is included in the total scoring algorithm. The revised algorithms (Gotham, Risi, Pickles, & Lord, 2007; Gotham et al., 2008), which generate cutoff scores for a social affect domain (SA) and a social affect plus restricted interests and repetitive behaviors domain (SA + RRB), were used. In addition, severity ratings (Gotham, Pickles, & Lord, 2009) were used to quantify the degree to which individuals are impaired by autism spectrum symptomatology.

**Kaufman Brief Intelligence Test (KBIT; Kaufman & Kaufman, 1990)**—The KBIT is a short measure of intellectual functioning for individuals aged 4 through 90 years. It yields an IQ Composite, a Vocabulary standard score (SS) providing an estimate of verbal functioning, and a Matrices SS providing an estimate of nonverbal reasoning ability. For the general population,  $M = 100$  and  $SD = 15$  for the IQ Composite and the Verbal and Matrices SSs.

## Procedure

The KBIT was administered according to the standardized procedures as part of a larger battery of cognitive and language assessments. The appropriate module of the ADOS was administered by an examiner trained to research reliability. Item ratings were made according to the operational definitions provided in the ADOS manual (Lord et al., 1999).

## Analytic Approach

Analyses were conducted in SPSS Version 24 (IBM Corp., 2016). Parametric statistics were used when the dependent variable was KBIT IQ composite, Verbal SS, or Matrices SS. When the dependent variable was ADOS Comparison score, ADOS item score, or ADOS classification, nonparametric statistics were used.

## Results

### ADOS Classification

Of the 40 children who were administered Module 2 of the ADOS, 27 (68%) were classified “non-spectrum” on the SA domain. The remaining 13 children (32%) were classified on the autism spectrum (8 “ASD” and 5 “autism”). When the RRB domain was combined with the SA domain, 26 children (65%) were classified “non-spectrum,” while the remaining 14 children (35%) were classified on the autism spectrum (3 “ASD” and 11 “autism”).

Of the 60 children who were administered Module 3 of the ADOS, 44 (73%) were classified “non-spectrum” on the SA domain. The remaining 16 children (27%) were classified on the autism spectrum (10 “ASD” and 6 “autism”). When the RRB domain was combined with the SA domain, 42 children (70%) were classified “non-spectrum”, while the remaining 18 children (30%) were classified on the autism spectrum (10 “ASD” and 8 “autism”).

### Comparison Scores

ADOS Comparison scores (Gotham et al., 2009) reflect the severity of symptoms as measured by the ADOS. These scores were derived based on age and language level and provide a measure of an individual’s ASD symptomatology relative to individuals with known ASD diagnoses. The mean Comparison score was 3.65 ( $SD = 2.03$ ) for children administered Module 2 and 2.55 ( $SD = 2.08$ ) for children administered Module 3. The distributions of Comparison scores are shown in Figure 1 separately for Module 2 and Module 3.

### Item Level Findings

There were a number of items on which most children with WS did not evidence impairment. Figures 2 (Module 2) and 3 (Module 3) provide the frequencies of endorsement for items on which at least 75% of the children received a code of “0”, suggesting behaviors that are less commonly seen as problematic in WS. On Module 2 ( $n = 40$ ), the unusual eye contact ( $n = 30$ ; 75%), shared enjoyment in interaction ( $n = 32$ ; 80%), response to name ( $n = 36$ ; 90%), spontaneous initiation of joint attention ( $n = 34$ ; 85%), response to joint attention ( $n = 36$ ; 90%), self-injurious behavior ( $n = 39$ ; 98%), and overactivity ( $n = 32$ ; 80%) items were rated typical (i.e., code = 0) for at least 75% of the participants. On Module 3 ( $n = 60$ ),



the immediate echolalia ( $n = 59$ ; 98%), unusual eye contact ( $n = 50$ ; 83%), offers information ( $n = 45$ ; 75%), shared enjoyment in interaction ( $n = 47$ ; 78%), amount of reciprocal social communication ( $n = 52$ ; 87%), overall rapport ( $n = 45$ ; 75%), unusual sensory interests ( $n = 48$ ; 80%), hand, finger, and other complex mannerisms ( $n = 54$ ; 90%), self-injurious behavior ( $n = 58$ ; 97%), excessive interest in or references to unusual or highly specific topics or objects of repetitive behaviors ( $n = 49$ ; 81%), compulsions or rituals ( $n = 48$ ; 80%), tantrums, aggression, negative or disruptive behavior ( $n = 52$ ; 87%), and anxiety ( $n = 53$ ; 88%) items were rated typical (i.e., code = 0) for at least 75% of the participants.

There also were a number of items for which a large proportion of children evidenced difficulties. The items for which at least 50% of the participants demonstrated some degree of difficulty (score of 1, 2, or 3) are indicated in Figure 4 (Module 2) and Figure 5 (Module 3). On Module 2, at least half of the children received a score of 1, 2, or 3 on the following items: speech abnormalities associated with autism ( $n = 21$ ; 52%), immediate echolalia ( $n = 20$ ; 50%), conversation ( $n = 28$ ; 70%), gestures ( $n = 22$ ; 65%), directed facial expression ( $n = 21$ ; 52%), showing ( $n = 21$ ; 52%), imagination/creativity ( $n = 28$ ; 70%), unusual sensory interest in play material/person ( $n = 26$ ; 65%), hand and finger and other complex mannerisms ( $n = 25$ ; 62%), and unusually repetitive interests or stereotyped behaviors ( $n = 30$ ; 75%). On Module 3, at least half of the sample demonstrated some degree of difficulty on the following items: speech abnormalities associated with autism ( $n = 35$ ; 58%), directed facial expressions ( $n = 31$ ; 52%), empathy/comments on others' emotions ( $n = 36$ ; 60%), insight ( $n = 52$ ; 87%), and imagination/creativity ( $n = 36$ ; 60%).

### Relations to Demographic Variables

For the Module 2 sample, children who met the cutoff for ASD had significantly lower overall intellectual functioning as measured by KBIT IQ composite,  $t(35) = 2.54, p = .016$ ; Vocabulary SS,  $t(35) = 2.34, p = .024$ ; and Matrices SS,  $t(35) = 2.57, p = .014$ , than children who did not. There also was a significant negative correlation between severity of symptoms and KBIT IQ composite,  $\rho(37) = -.52, p < .001$ ; Vocabulary SS,  $\rho(43) = -.51, p < .001$ ; and Matrices SS,  $\rho(43) = -.49, p = .002$ .

In contrast, for the Module 3 sample, there was no significant difference in KBIT IQ composite,  $t(49) = 1.56, p = .125$ ; Vocabulary SS,  $t(49) = 1.77, p = .083$ ; or Matrices SS,  $t(49) = 1.05, p = .299$ , between those children who met the cutoff for ASD and those who did not. Correlations between severity of symptoms and KBIT IQ composite were nonsignificant and very small,  $\rho(51) = -.17, p = .240$ ; Vocabulary SS,  $\rho(51) = -.12, p = .420$ ; and Matrices SS,  $\rho(51) = -.20, p = .159$ .

For the Module 2 sample, there were no significant sex differences in likelihood of autism spectrum classification,  $\chi^2(1, N = 40) = 1.71, p = .190$ , or in severity of symptoms,  $z = -0.06, p = .955$ . There also were no significant sex differences in likelihood of autism spectrum classification,  $\chi^2(1, N = 60) = 0.82, p = .366$ , or in severity of symptoms,  $z = -1.18, p = .145$ , for the Module 3 sample.

## Effects of Module

The rate of ASD classification across modules was examined in two ways. First, the effect of module on Comparison score was considered. The distribution of Comparison scores for Module 2 differed significantly from that for Module 3 ( $z = -3.72, p = .001$ ), with higher Comparison scores observed for Module 2. Second, the rate of ASD classification by module was examined. There was no significant effect of module on ASD classification [Yates-corrected  $\chi^2 = 0.09$ , exact  $p = .664$ ,  $\Phi = -.053$ ].

## Comparison of WS-NS and WS-ASD Groups

By definition, the WS-ASD group had a significantly higher overall score on the ADOS algorithm than did the WS-NS group. To determine if a consistent pattern of specific difficulties at the item level also separated the WS-ASD group from the WS-NS group, Mann-Whitney U tests were used to compare item scores for each of the ADOS items, separately for each module. As indicated in Table 2, for children who completed Module 2, the WS-ASD group had significantly higher scores (indicating greater abnormality) on 17 of the 28 items (61%). Similarly, as shown in Table 3, for children who completed Module 3, the WS-ASD group showed significantly greater abnormality than the WS-NS group on 18 of 29 items (62%).

## Discussion

In the present study of the ADOS performance of children with WS who have phrase speech or fluent language, about one-third were classified on the autism spectrum, indicating that socio-communicative difficulties and repetitive behaviors were common among children with WS. This proportion is clearly elevated relative to the general population. At the same time, it is important to note that most children with WS who have phrase speech or fluent language do not show ASD symptomatology sufficient for consideration of an ASD diagnosis. Furthermore, some socio-communicative and repetitive behavior difficulties that were common among children with WS did not relate to ASD classification. For children with phrase speech, these included difficulties with gestures and showing, imagination/creativity, and various repetitive behaviors. For children with fluent speech, these included empathy, insight, and imagination/creativity. In the case of a child with WS, these types of difficulties may be better characterized as part of the behavioral phenotype of WS rather than as indicative of an additional diagnosis of ASD.

In contrast, children with ASD classifications on the ADOS had significantly worse ratings on overall quality of social overtures and response, eye contact, and conversation, and more pronounced speech abnormalities associated with autism than did children who were classified non-spectrum. These behaviors should be given additional weight when there is a question of a possible comorbid ASD diagnosis for a child with WS. Care should be taken to avoid diagnostic overshadowing (attributing all difficulties observed only to WS without considering the possibility that they may be due to comorbid ASD), as children with WS who also have ASD are likely to benefit from interventions designed for children with ASD.



## Developmental Patterns of Performance on Specific ADOS Items

It is notable that for many of the items for which Klein-Tasman et al. (2007) found significant differences between the WS-NS and WS-ASD groups on Module 1, this same pattern also was found for the older more verbal participants in the present study. Across modules, the WS-ASD group consistently evidenced significant reductions relative to the WS-NS group in efforts to maintain the attention of others (e.g., frequency of vocalizations directed toward others in Module 1; reduced social overtures to maintain others' attention in Module 2, reduced offering of information in Module 3). Unusual eye contact and poor overall quality of social overtures differentiated children meeting ASD classification from those who did not across all three modules, suggesting that these behaviors continue to be problematic even as children gain additional communication skills. ASD status differences in difficulties consistently directing facial expressions toward others to communicate also persist with development, as these were observed both for Module 1 and Module 3.

For most items that are present in all three modules and were not related to ASD classification for children with WS, rates of difficulty were lower in children with more developed language. This pattern is consistent with prior observations regarding developmental trajectories in WS. For example, unlike typically developing children, almost all children with WS begin to comprehend and produce pointing gestures *after* they begin to talk, so do not use pointing to communicate during the prelinguistic period. Thus, the higher rates of difficulties on certain items (e.g., pointing) for children with WS who have very limited or no expressive language may be related to differences in the sequence of acquisition of particular socio-communicative abilities relative to typically developing children rather than reflecting lifelong differences. As expressive language increases, typically developing children are more likely to communicate with language rather than gesture (Capirci, Iverson, Pizzuto, & Volterra, 1996) and children with WS begin to comprehend and produce pointing gestures, making the differences in this aspect of socio-communication less striking.

While differences in aspects of socio-communication that are expected to be acquired early are reduced with increasing age and language abilities, difficulties in more advanced aspects of socio-communication (e.g., insight) become clearer. This is perhaps not unexpected; the reason that some of the ADOS tasks, codes, and algorithm items vary across modules is because the core behavioral manifestations of ASD change with age and language abilities. Thus, although the nature of the difficulties evidenced by children with WS may change over time, individuals with WS, whether or not they are classified as autism spectrum on the ADOS, continue to evidence a number of behavioral similarities that overlap with the autism spectrum.

Consistent abnormalities in play also were observed across modules, with at least 60% of children with WS showing difficulties with imagination/creativity on Module 1 (Klein-Tasman et al., 2007), Module 2, and Module 3. Among children with very limited or no expressive language (Module 1) or with phrase speech (Module 2), the level of difficulty with imagination/creativity was significantly higher for children in the WS-ASD group than children in the WS-NS group. For children with fluent language (Module 3), however, level of difficulty with imagination/creativity was independent of ADOS classification.

Abnormalities in play appear to be a common component of the behavioral phenotype of children with WS.

A somewhat different pattern was shown for restricted and repetitive patterns of behavior. Unusual sensory interests and repetitive finger and body movements were very common among children who completed Module 1 (Klein-Tasman et al., 2007) and Module 2. However, these types of behaviors were considerably less common among children with fluent language (Module 3). This pattern suggests that for children with WS, these types of repetitive behaviors may decrease in their prominence as age and/or language abilities increase. At the same time, other types of restricted or repetitive behaviors (e.g., restricted interests) clearly are present in individuals with WS who have fluent language (Davies et al. 1998; Janes et al., 2014, Royston et al., 2018), although they may not be fully captured by the brief interaction setting of the ADOS.

### **Developmental Effects of Sex and Intellectual Ability on ADOS ASD Classification**

Studies of children with WS with very limited expressive language skills using ADOS Module 1 (Klein-Tasman et al., 2007, 2009; Lincoln et al., 2007) reported no significant effects of sex on social communication challenges. Findings from the present study confirmed this same pattern for children with either phrase speech (Module 2) or fluent language (Module 3). While rates of ASD are higher in males than females in the general population, there does not appear to be a sex effect on ASD symptomatology among children with WS.

In contrast, we have identified a developmental pattern to relations between intellectual abilities and ASD symptomatology for children with WS. Klein-Tasman et al. (2007) found that children classified as autism spectrum on the ADOS had significantly weaker intellectual abilities than children classified non-spectrum. In the current study, this same pattern was found for children who used phrase speech. In contrast, there was no significant relation between autism spectrum classification and intellectual functioning for children with fluent language. While socio-communicative difficulties are significantly related to intellectual functioning in younger children with poorer language skills, this relation appears to dissipate with age and language development. This same developmental pattern was found for children with 7q11.23 duplication syndrome (Klein-Tasman & Mervis, 2018). Children with this syndrome have an extra copy of the same genes as are deleted in WS (Mervis et al., 2015). The prevalence of ASD in 7q11.23 duplication syndrome, based on gold-standard diagnostic assessments, is 19%, with 25.4% meeting or exceeding the autism spectrum cutoff on the ADOS (Klein-Tasman & Mervis, 2018).

### **Conceptualization of Socio-communicative Difficulties in Williams Syndrome**

Wing and Gould (1979) suggested three social subtypes in ASDs: aloof, passive, and active-but-odd. Individuals within the active-but-odd subtype seek out interactions with others and appear to be socially motivated and interested. However, they lack the skills necessary to have meaningful reciprocal social interactions. Conversation is 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, leading to social approach behaviors that often are inappropriate.

Descriptions of this active-but-odd subtype are similar in many ways to descriptions of the behavioral phenotype of WS. For example, individuals with WS are socially motivated (Klein-Tasman et al., 2011) and frequently seek out interactions with others; in fact, they have been described as considerably less reserved toward strangers and more willing to approach people they do not know than either typically developing children or children with other developmental disabilities (Fisher, 2014; Gosch & Pankau, 1997; Klein-Tasman & Mervis, 2003; Lough & Fisher, 2016; Zitzer-Comfort et al., 2007). At the same time, deficits in social interaction skills (Klein-Tasman et al., 2011; Mervis, Klein-Tasman, & Mastin, 2001; Mervis & Pitts, 2015) including significant difficulty with pragmatic aspects of conversation such as perseverative focus on topics not of interest to the conversational partner, difficulty staying on topic when the topic was chosen by the conversational partner, and use of stereotyped language (Laws & Bishop, 2004; Philofsky et al., 2007; Udwin & Yule, 1990) and limited comprehension of more nuanced aspects of social interactions such as subtle humor (Sullivan, Winner, & Tager-Flusberg, 2003) are very common. Individuals with WS also have difficulty establishing and maintaining friendships (Einfeld, Tonge, & Florio, 1997; Elison, Stinton, & Howlin, 2010; Udwin & Yule, 1991).

In the present study, difficulties consistent with what would be expected for individuals with the active-but-odd subtype of ASD were common among children with WS whether they were classified WS-NS or WS-ASD. However, not surprisingly, the children in the WS-ASD group evidenced even more difficulty with these items, as described earlier in the Discussion. Taken together, these difficulties point to the presence of social overtures and interactions for most children with WS but at the same time indicate that these overtures often are odd in some manner (e.g., intonation, difficulties with conversation, overall quality of overtures), consistent with the active-but-odd subtype of ASD. Given the role of ADOS ratings in the diagnostic process, these findings are suggestive of elevated rates of ASD diagnosis among children with WS. One may question whether this ASD symptomatology represents a second diagnosis for children with WS or whether these difficulties should be attributed to WS. In this context, it is critical to note that there are many children with WS who do not show the socio-communicative impairments and restricted and repetitive behaviors that are indicative of ASD. For example, more than 50% of the children who completed Module 3 earned ADOS Comparison scores of 1 (the lowest possible Comparison score). Thus, ASD is not best characterized as simply part of WS.

It also is important to note that 7q11.23 copy number variation (CNV) has been found to be a risk factor for ASD (Crespi & Procyshyn, 2017; Klein-Tasman & Mervis, 2018) and that both 7q11.23 duplication syndrome and WS are associated with atypical gene methylation patterns, with the set of differently methylated genes enriched for those associated with ASD (Strong et al., 2015). Studies of very rare children with smaller deletions are needed to identify which gene(s) in the WS region is associated with ASD symptomatology. Crespi and Procyshyn (2017) have argued that *GTF2I* is the most likely candidate, but more research is needed. Furthermore, having WS may increase an individual's liability for ASD in the presence of other genetic (or environmental) liabilities for the development of ASD.

Our perspective is that a diagnosis of ASD should be strongly considered for children with WS who show ASD symptomatology that in the absence of WS would meet criteria for ASD diagnosis. These children are likely to need additional intervention beyond what is currently provided to children with WS to address their ASD symptomatology. The overlap observed in the current study sheds light on the presence of social communication challenges in WS and underscores the importance of considering socio-communicative challenges as targets for intervention.

### Limitations and Future Directions

The present study is the first systematic observational study of the socio-communicative behavior of children with WS who have phrase speech or fluent language using a gold-standard autism diagnostic instrument, the ADOS. The results are important in understanding the nature of the WS socio-communicative profile, including areas in which developmental differences are found. However, as formal ASD diagnostic evaluations were not conducted, the proportion of children with WS who would be expected to meet gold-standard criteria for a clinical diagnosis of ASD could not be determined. Future investigations that include formal evaluations for ASD would be valuable. In addition, future studies that include comparison groups of IQ-matched children with ASD who do not have a known syndrome and children with developmental disabilities who do not have ASD are needed to determine the specificity of the patterns observed to WS. Finally, the intervention literature related to ASD is growing and has identified interventions with good empirical support. Anecdotal reports indicate that children with WS may benefit from the interventions that have a strong evidence base in the ASD literature, including Applied Behavior Analysis approaches. Formal research about the effectiveness of evidence-based ASD interventions for use with children with WS would be valuable.

### Summary and Conclusions

Past reports of the socio-communicative behavior of young, minimally verbal children with WS described significant difficulties in about half of the participants. Using similar methodology with older children with WS who had phrase speech or fluent language, about one-third of the current sample demonstrated significantly impaired socio-communicative abilities. These findings are suggestive of an elevated risk of ASD for individuals with WS in comparison to the general population and contribute to a more nuanced sense of the socio-communicative functioning of children with WS. Although prior literature regarding the behavioral phenotype of children with WS often emphasized their gregariousness and strong interest in interaction with others, this description by itself belies the significant socio-communicative challenges that typically are present. The present findings also highlight the importance of careful consideration of typical phenotypic presentation in all genetic conditions to accurately identify individual children's needs. Children with WS who show ASD-related symptomatology are likely to benefit from evidence-based interventions designed for children with ASD.

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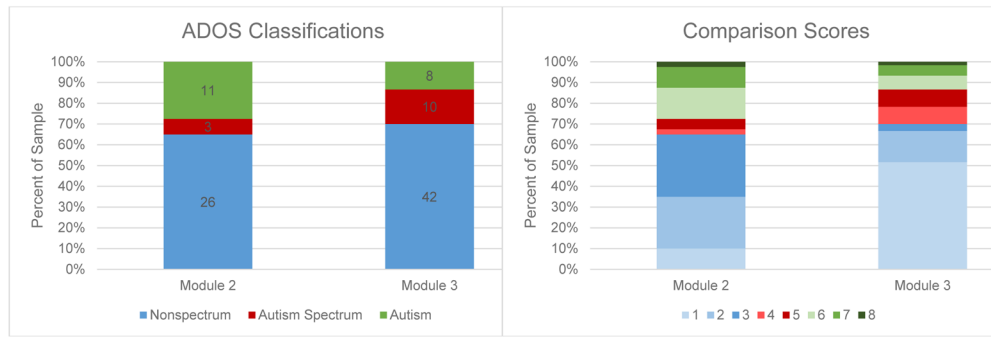
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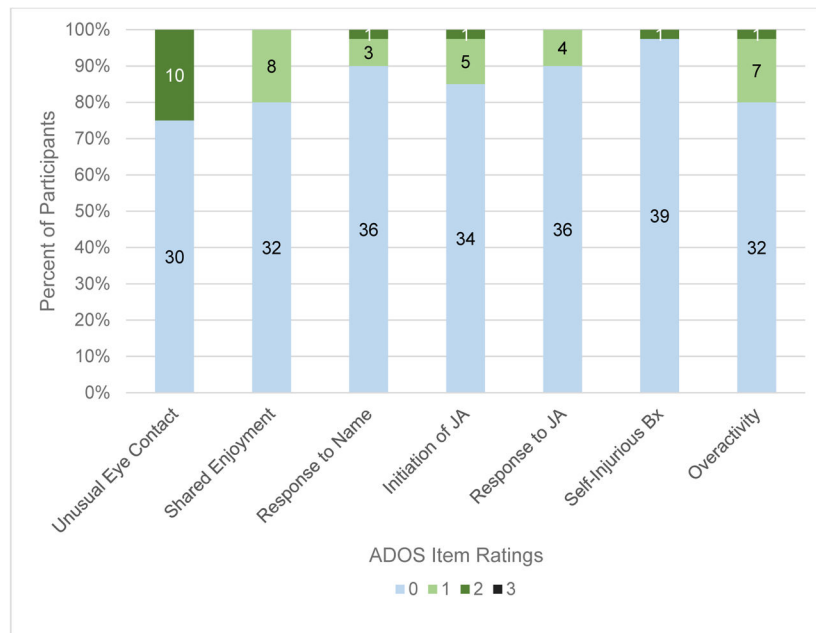
**Figure 1.** Distribution of ADOS Classifications and Comparison Scores by Module

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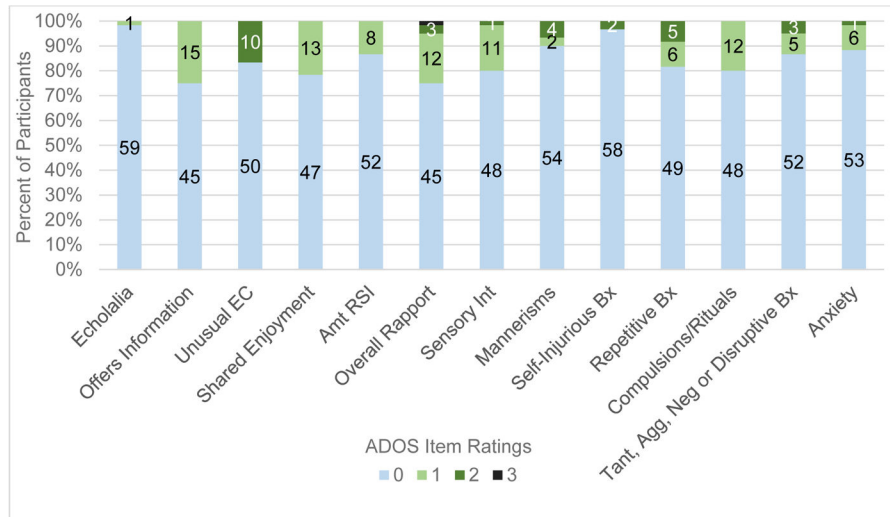
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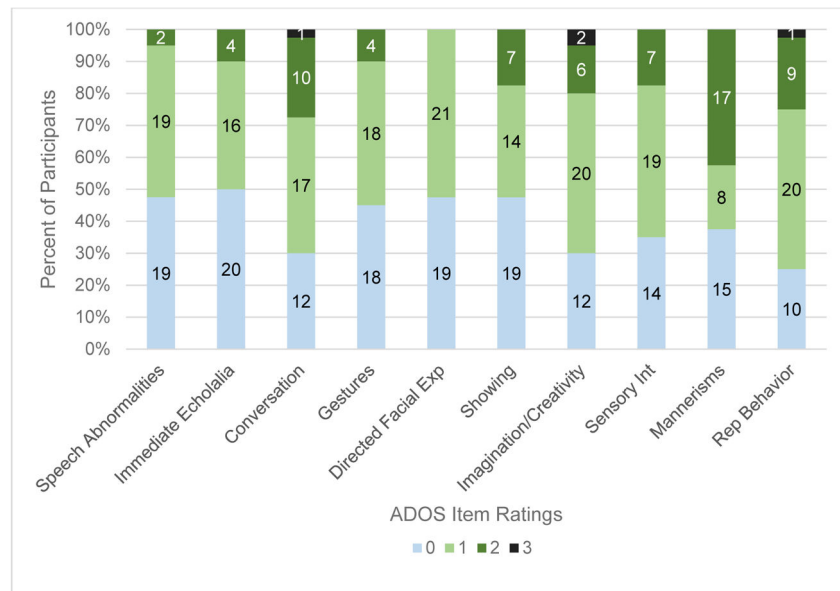
**Figure 2. Module 2 Items with Infrequent Abnormality: Item Ratings**

Note: Shared Enjoyment = Shared Enjoyment in Interaction; Initiation of JA = Spontaneous Initiation of Joint Attention; Response to JA = Response to Joint Attention; Self-Injurious Bx = Self-Injurious Behavior. The numbers on each bar indicate how many children (out of 40) received that score for that item.



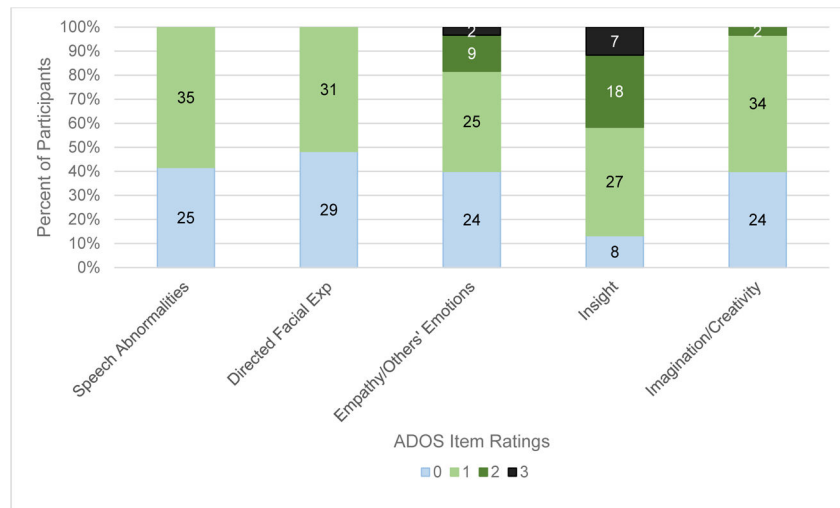
**Figure 3. Module 3 Items with Infrequent Abnormality: Item Ratings**

Note: Unusual EC = Unusual Eye Contact; Shared Enjoyment = Shared Enjoyment in Interaction; Amt RSI = Amount of Reciprocal Social Interaction; Sensory Int = Unusual Sensory Interests in Play Material/Person; Mannerisms = Hand, Finger, and Other Complex Mannerisms; Rep Bx = Excessive Interest in or References to Unusual or Highly Specific Topics or Objects or Repetitive Behavior; Tant, Agg, Neg or Disruptive Bx = Tantrums, Aggression, Negative or Disruptive Behavior. The numbers on each bar indicate how many children (out of 60) received that score for that item.



**Figure 4. Module 2 Items with Frequent Abnormality: Item Ratings**  
 Note: Speech Abnormalities = Speech Abnormalities Associated with Autism; Directed Facial Exp = Directed Facial Expressions. The numbers on each bar indicate how many children (out of 40) received that score for that item.





**Figure 5. Module 3 Items with Frequent Abnormality: Item Ratings**

Note: Speech Abnormalities = Speech Abnormalities associated with Autism; Directed Facial Exp: Facial Expressions Directed toward Others; Empathy/Others' Emotions = Empathy/Comments on Others' Emotions. The numbers on each bar indicate how many children (out of 60) received that score for that item.

**Table 1**

Participant CA and IQ as a Function of ADOS Module Administered.

Demographics	Module 2 (N = 40)			Module 3 (N = 60)		
	Mean	SD	Range	Mean	SD	Range
CA (in years)	5.63	2.13	3.13 – 15.02	10.19	2.74	5.09 – 15.25
KBIT IQ Composite <sup>a</sup>	73.65	19.57	40 <sup>b</sup> – 112	78.84	13.62	40 <sup>b</sup> – 104

Note: CA = chronological age; KBIT = Kaufman Brief Intelligence Test.

<sup>a</sup>KBIT IQ data were available for 37 of 40 participants who completed Module 2 and 51 of 60 who completed Module 3.

<sup>b</sup>Lowest possible KBIT IQ.

Comparison of Performance on ADOS Module 2 Items for Children with Williams Syndrome Classified Non-spectrum (WS – NS) vs. Spectrum (WS-ASD)

Table 2

ADOS Item	WS-NS		WS-ASD		z	p
	M	SD	M	SD		
Overall Level of Non-Echoed Language	.27	.45	.86	.54	-3.18	.001
Ant Soc Overtures/Maintenance of Attn	.15	.37	.64	.50	-3.11	.002
Speech Abnormalities Assoc with Autism	.38	.57	.93	.48	-2.93	.003
Immediate Echolalia	.42	.58	.93	.73	-2.20	.027
<i>Stereotyped/Idiosyncratic Words/Phrases</i>	.23	.51	.71	.61	-2.71	.007
Conversation	.65	.69	1.64	.63	-3.64	<.001
<i>Pointing</i>	.35	.49	.36	.50	-.07	.945
<i>Gestures</i>	.58	.64	.79	.70	-.94	.347
<i>Unusual Eye Contact</i>	.08	.39	1.21	.98	-4.12	<.001
<i>Facial Expressions Directed to Others</i>	.42	.50	.71	.47	-1.74	.082
<i>Shared Enjoyment in Interaction</i>	.08	.27	.43	.51	-2.62	.009
Response to Name	.04	.20	.29	.61	-1.77	.077
<i>Showing</i>	.58	.70	.93	.83	-1.34	.180
<i>Spontaneous Initiation of Joint Attention</i>	.08	.39	.36	.50	-2.54	.011
Response to Joint Attention	.04	.20	.21	.43	-1.75	.081
<i>Quality of Social Overtures</i>	.19	.40	.93	.62	-3.72	<.001
Quality of Social Response	.31	.47	1.00	.68	-3.16	.002
<i>Amount of Reciprocal Social Comm</i>	.27	.45	.86	.77	-2.57	.010
<i>Overall Quality of Rapport</i>	.19	.40	.79	.70	-2.95	.003
Functional Play with Objects	.27	.45	1.21	.89	-3.74	<.001
Imagination/Creativity	.69	.62	1.43	.94	-2.53	.011
<i>Unusual Sensory Int in Play Mat/Person</i>	.62	.64	1.21	.70	-2.50	.012
<i>Hand, Finger, and Other Mannerisms</i>	.77	.91	1.57	.65	-2.66	.008
Self-Injurious Behavior	.00	.00	.14	.54	-1.36	.173
<i>Unusually Rep Interests/Stereotyped Beh</i>	.73	.67	1.57	.65	-3.28	.001
Overactivity	.15	.37	.36	.63	-1.06	.289

ADOS Item	WS-NS		WS-ASD		z	p
	M	SD	M	SD		
Tantrums, Aggr, Negative/Disruptive Beh	.23	.43	.57	.60	-1.49	.137
Anxiety	.42	.58	.43	.51	-.17	.868

\*  $p < .05$ ,

\*\*  $p < .01$

Note: Italicized items are ADOS-2 algorithm items. Amt Soc Overtures/Maintenance of Attn = Amount of Social Overtures/Maintenance of Attention; Speech Abnormalities Assoc with Autism = Speech Abnormalities Associated with Autism (Intonation/Volume/Rhythm/Rate); Stereotyped/Idiosyncratic Words/Phrases = Stereotyped/Idiosyncratic Use of Words or Phrases; Gestures = Descriptive, Conventional, Instrumental, or Informational Gestures; Amount of Reciprocal Social Comm = Amount of Reciprocal Social Communication; Unusual Sensory Int in Play Mat/Person = Unusual Sensory Interest in Play Material/Person; Hand, Finger, and Other Mannerisms = Hand, Finger, and Other Complex Mannerisms; Unusually Rep Interests/Stereotyped Beh = Unusually Repetitive Interests or Stereotyped Behaviors; Tantrums, Aggr, Negative/Disruptive Beh = Tantrums, Aggression, Negative or Disruptive Behavior; Note: WS-NS = WS non-spectrum group; WS-ASD = WS ASD group

Table 3  
 Comparison of Performance on ADOS Module 3 Items for Children with Williams Syndrome Classified Non-spectrum (WS-NS) vs. Spectrum (WS-ASD)

ADOS Item	WS-NS		WS-ASD		z	p
	M	SD	M	SD		
Overall Level of Non-echoed Language	.31	.52	.56	.51	-1.87	.062
Speech Abnormalities Assoc with Autism	.43	.50	.94	.24	-3.68	<.001
Immediate Echolalia	.00	.00	.06	.24	-1.53	.127
<i>Stereotyped/Idiosyncratic Words/Phrases</i>	.24	.48	.61	.70	-2.27	.023
Offers Information	.12	.33	.56	.51	-3.55	<.001
Asks for Information	.31	.56	.33	.59	-.14	.892
<i>Reporting of Events</i>	.24	.48	.72	.58	-3.28	.001
<i>Conversation</i>	.10	.30	.78	.55	-4.92	<.001
<i>Gestures</i>	.26	.45	.33	.59	-.24	.809
<i>Unusual Eye Contact</i>	.10	.43	.89	1.02	-3.75	<.001
<i>Facial Expressions Directed to Others</i>	.40	.50	.78	.43	-2.63	.009
Lang Prod & Linked Nonverbal Comm	.29	.46	.44	.51	-1.18	.236
<i>Shared Enjoyment in Interaction</i>	.07	.26	.56	.51	-4.14	<.001
Empathy/Comments on Others' Emotions	.64	.73	1.22	.88	-2.43	.015
Insight	1.07	.68	2.17	.79	-4.30	<.001
<i>Quality of Social Overtures</i>	.17	.38	.83	.51	-4.56	<.001
<i>Quality of Social Response</i>	.07	.26	.78	.43	-5.52	<.001
<i>Ant of Reciprocal Social Comm</i>	.02	.15	.39	.50	-3.78	<.001
<i>Overall Quality of Rapport</i>	.02	.15	1.00	.77	-6.12	<.001
Imagination/Creativity	.57	.50	.78	.65	-1.11	.265
<i>Unusual Sensory Int in Play/Mat/Person</i>	.17	.38	.33	.59	-1.06	.290
<i>Hand, Finger, and Other Mannerisms</i>	.07	.34	.39	.78	-2.08	.038
Self-Injurious Behavior	.00	.00	.22	.65	-2.18	.029
<i>Excess Interest/Repetitive Behavior</i>	.21	.52	.39	.78	-.66	.510
Compulsions or Rituals	.17	.38	.28	.46	-.98	.328
Overactivity/Agitation	.26	.54	.61	.70	-2.17	.030

ADOS Item	WS-NS		WS-ASD		z	p
	M	SD	M	SD		
Tantrums, Aggr, Negative/Disruptive Beh	.05	.31	.50	.71	-3.70	<.001 **
Anxiety	.17	.44	.06	.24	-.971	.332

\*  $p < .05$ ,

\*\*  $p < .01$

Note: Italicized items are ADOS-2 algorithm items. Amt Soc Overtures/Maintenance of Attn = Amount of Social Overtures/Maintenance of Attention; Speech Abnormalities Assoc with Autism = Speech Abnormalities Associated with Autism (Intonation/Volume/Rhythm/Rate); Stereotyped/Idiosyncratic Words/Phrases = Stereotyped/Idiosyncratic Use of Words or Phrases; Gestures = Descriptive, Conventional, Instrumental, or Informational Gestures; Lang Prod & Linked Nonverbal Comm = Language Production and Linked Nonverbal Communication; Amount of Reciprocal Social Comm = Amount of Reciprocal Social Communication; Unusual Sensory Int in Play Mat/Person = Unusual Sensory Interest in Play Material/Person; Hand, Finger, and Other Mannerisms = Hand and Finger and Other Complex Mannerisms; Excess Interest/Repetitive Behavior = Excessive Interest in or References to Unusual or Highly Specific Topics or Objects or Repetitive Behaviors; Tantrums, Aggr, Negative/Disruptive Beh = Tantrums, Aggression, Negative or Disruptive Behavior; Note: WS-NS = WS non-spectrum group; WS-ASD = WS ASD group