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ORIGINAL PAPER

Social Responsiveness and Competence in Prader-Willi Syndrome: Direct Comparison to Autism Spectrum Disorder

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Abstract Prader-Willi syndrome (PWS), a neurodevelopmental disorder primarily characterized by hyperphagia and food preoccupations, is caused by the absence of expression of the paternally active genes in the proximal arm of chromosome 15. Although maladaptive behavior and the cognitive profile in PWS have been well characterized, social functioning has only more recently been systematically examined. Findings to date indicate the social impairment exhibited may reflect specific difficulty interpreting and using social information effectively. In addition, evidence suggests that there is an increased risk of social deficits in people with the maternally-derived uniparental disomy (mUPD) subtype of PWS in comparison to those with 15q11–13 paternal deletion (DEL). Using the Social Responsiveness Scale (SRS) and the Social Competence Inventory, our goal was to compare social functioning in PWS to individuals with autism spectrum disorder (ASD). Participants with mUPD scored similarly to the ASD group across most SRS domains. All groups had difficulty with social competence, although the DEL group scored highest on prosocial behavior. Findings suggest further characterization of social behavior in PWS is necessary to aid in advancing the understanding of the contributions of genes in the 15q11–13 critical region to ASD susceptibility, particularly with respect to the overexpression of maternally expressed genes in this region, as well as aiding in awareness and development/implementation of interventions.

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Introduction

Prader-Willi syndrome (PWS) is a genetic neurodevelopmental disorder, primarily characterized by hyperphagia and food preoccupations, which is caused by the absence of expression of the paternally active genes in the proximal arm of chromosome 15. First described in 1956, approximately 70 % of the cases are due to the deletion (DEL) of the paternally inherited chromosome 15 (q11–q13 region), 25 % are due to maternal uniparental disomy (mUPD) of chromosome 15, and the rest are due to either a methylation imprinting defect or a translocation microdeletion (Ledbetter et al. 1981; Nicholls et al. 1989). Individuals with PWS typically exhibit mild to moderate intellectual disability and various internalizing and externalizing symptoms along with repetitive/ritualistic behavior (Clarke et al. 1996; Dimitropoulos et al. 2006; Dykens et al. 1996; Reddy and Pfeiffer 2007; Stein et al. 1994; van Lieshout et al. 1998). Some of the clinical characteristics of individuals with PWS differ according to the specific genetic abnormality. Individuals with the DEL subtype are more severely affected than those with mUPD across a number of domains, which include: the characteristic facial appearance and hypopigmentation (Cassidy 1984), intelligence (Roof et al. 2000), maladaptive behavior (Dykens et al. 1999), and self-injurious behavior (Symons et al. 1999). However, individuals with mUPD are at increased risk for developing atypical psychosis after adolescence (Verhoeven and Tuinier 2006) and autistic-like symptoms (Descheemaeker et al. 2006; Dimitropoulos and Schultz

2007; Greaves et al. 2006; Milner et al. 2005), but are at similar risk to people with DEL for compulsive behavior (Dykens and Roof 2008).

While the behavioral phenotype in PWS has been well characterized with regard to maladaptive behavior and cognitive profile (see recent review by Ho and Dimitropoulos 2010), social functioning has only more recently been examined systematically. This is not surprising given that the immediate needs of individuals with PWS must first focus on dietary control and management of externalizing behavior problems. However, further characterization of the phenotype allows for more targeted behavioral interventions in addition to informing phenotype/genotype expression. As such, there is increasing acknowledgement of social difficulties among individuals with PWS above and beyond what is thought to be experienced by a person with similar level of intellectual impairment. Furthermore, evidence indicating a genetic risk for autism associated with the PWS 15q11–13 region indicates additional characterization of the PWS phenotype may inform the 15q11–13 genotype/phenotype and ASD genetic susceptibility. Of children diagnosed with idiopathic autism, 1–3 % have been shown to have maternally inherited duplications of the 15q11–13 region; one of the more frequent structural variants found in autism (Bolton et al. 2001; Cook et al. 1997; Vorstman et al. 2006). In addition, individuals with isodecentric 15 syndrome are at increased risk for a comorbid autism spectrum disorder (Battaglia 2005). People with mUPD are thought to be at greater risk of autistic symptoms than individuals with DEL because of the maternally inherited duplication and thus overexpression of genes in the 15q11–13 region (Schanen 2006). The exact function of the genes in the PWS critical region has yet to be determined although there are strong candidates for psychosocial behavior in the maternally expressed gene, ubiquitin protein ligase E3A (UBE3A)—the gene that causes Angelman syndrome, and genes altering serotonin functioning such as the small nucleolar RNA (snoRNA) SNORD115 (Schanen 2006; Kishore et al. 2006). Behavioral studies to date, using either symptom checklists or standardized autism evaluations, have shown increased risk of autism symptomatology for people with mUPD (Descheemaeker et al. 2006; Dimitropoulos and Schultz 2007; Greaves et al. 2006; Milner et al. 2005). It is not as clear how much of this risk is due to social functioning however, as much of the past research has used ASD symptom checklists that are overly reliant on repetitive and ritualistic behaviors, which include only a few items pertaining to social functioning or measures that do not yield a separate subscale score for social functioning. That said, even with use of these global symptom checklists, those with mUPD have been reported to have increased risk of social isolation compared to those with DEL (Descheemaeker et al. 2006). In addition, in the one published study that used both the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview, Revised (ADI-R) with individuals with PWS, greater deficits in reciprocal social interaction were shown for individuals with mUPD compared to the DEL subtype (Milner et al. 2005). As such, identifying common behaviors between individuals with mUPD and ASD may further indicate the importance of overexpression of the 15q11–13 region in increasing the risk of ASD and in ASD-related social impairment specifically.

In the past, clinical reports have suggested that the social characteristics of those with PWS change after early childhood. In general, infants and toddlers with PWS initially appear to be happy, affectionate, and friendly, but later develop significant behavior problems that include temper tantrums, stubbornness, and maladaptive behaviors (Cassidy et al. 2000). Both clinical and research reports also suggest that older children and adults with PWS exhibit poor peer relationships, a lack of friends, immaturity, weakness in coping skills, and a preference for solitary activities (Cassidy 1984; Clarke et al. 1996; Dykens and Cassidy 1995; van Lieshout et al. 1998). Negative self-image and isolation have been shown to increase with age and general social inadequacies have been commonly reported in PWS (Dykens and Cassidy 1995). In addition, although social competence has been shown to increase with age in individuals with Williams and Down syndromes, this does not appear to be true for those with PWS (Rosner et al. 2004). While most individuals with PWS do not appear to exhibit the severity of deficits in social reciprocity found in classic autism, many of their social behaviors appear to be on the same continuum of social deficits found in autism spectrum disorder (ASD; e.g., social withdrawal, poor peer relationships, lack of empathy). In fact, Koenig et al. (2004) found strikingly similar social deficits between IQ and age-matched participants with PWS and individuals with ASD using a social attribution task (Klin 2000) that measures the ability to automatically infer social information while viewing an ambiguous video; both groups made fewer attributions of feeling states and shared-feeling states that result from social situations (i.e., jealousy), which were critical to understanding the social story in the task. Other research directly comparing PWS to autism indicates key social relating deficits hallmark to the classic autism diagnosis (i.e., avoiding eye contact, aloofness) were evident in greater than 50 % of the PWS sample (Dimitropoulos et al. 2009). These findings suggest that the social impairment exhibited by individuals with PWS represents a deficit that is not merely a consequence of associated maladaptive behavior, but may reflect a specific difficulty interpreting and using social information effectively.

This growing body of evidence suggests more attention to the PWS social phenotype is warranted. The purpose of this study is to further examine the social phenotype of PWS by directly comparing social competence and responsiveness in individuals with one of the two primary PWS genetic subtypes to participants with an ASD. By directly comparing individuals with PWS to idiopathic autism, common social characteristics among the disorders can be identified. With respect to those with the mUPD subtype, overexpression of genes in the maternal 15q11–13 region and the relatively frequently occurring maternally inherited duplications of 15q11–13 in idiopathic autism make identifying the common characteristics between mUPD and idiopathic autism relevant for ASD susceptibility genes. It is hypothesized that individuals with mUPD will show more significant social responsiveness and competence deficits than those with DEL, thereby displaying behavior more similar to that seen among individuals on the autism spectrum. Using measures designed with specific focus on social functioning we aim to provide a more descriptive characterization of social deficits in this population that will extend the past findings that relied on both ritualistic behavior and social functioning in the assessment of ASD functioning.

Methods

Participants

Participants were 58 individuals aged 7–30 years diagnosed with either PWS (genetic subtype: DEL n = 20, mUPD n = 19) or an autism spectrum disorder (ASD; n = 19). Sample characteristics are provided in Table 1. As Table 1 shows, participants with DEL were, on average, 4 years older than the other two groups. Participants with ASD had significantly higher scores in Performance IQ (PIQ) than those with mUPD; both age and PIQ were used as covariates in all between-group analyses. Participants with PWS were recruited through multiple sources, including: the PWS genetics interdisciplinary clinic at University Hospitals, advertisements through the national PWS Association (PWSA-USA) and Foundation for PWS Research websites, and PWSA state chapter events (Ohio and Pennsylvania). Participants with ASD were recruited through local autism organization newsgroups and events including Autism Speaks, the Autism Society for America, and the University Hospitals Seminars on Autism seminar series. PWS genetic subtype confirmation was provided by parents for 29 participants. For the remaining 10 participants, parents reported genetic testing was completed and provided subtype information for their child (parent report: 7 DEL, 3 mUPD); however, documentation of genetic subtype was not obtained if the participants were seen at their group home residence or camp, and parents were not present for data collection. Mean scores on social measures did not differ between those with parent report of diagnoses and those with documentation for either PWS subtype, thus participants with parent-report diagnosis were included in the final analyses (p value range = .25–.77 for SRS-Total score, SCI-Prosocial, and SCI-Initiative). All individuals included in the ASD sample provided documentation of a primary diagnosis of autism, pervasive developmental disorder-not otherwise specified (PDD-NOS), or Asperger disorder from a pediatrician, clinical psychologist, psychiatrist, or pediatric neurologist prior to enrollment. Diagnosis was confirmed by ADOS (Lord et al. 1999) and ADI-R (Rutter et al. 2003) administered as part of a larger study.

Participant data was collected as part of an ongoing research program examining autistic symptomatology in

Table 1 Participant characteristics

	PWS-DEL (n = 20)	PWS-mUPD (n = 19)	ASD (n = 19)	Post hoc comparison
Age*	18.9 (6.8)	14.4 (5.8)	14.2 (4.2)	DEL > mUPD & ASD
# Male**	6	8	16	
IQ				
Full scale	65.61 (10.9)	62.27 (16.2)	74.47 (23.3)	
Verbal	69.47 (10.8)	70.88 (19.1)	78.05 (20.9)	
Performance*	72.82 (10.7)	64.81 (11.6)	79.47 (23.8)	ASD > mUPD
Adaptive behavior				
Composite	66.0 (16.2)	64.25 (12.0)	66.0 (8.9)	
Daily living	68.0 (19.2)	66.94 (16.8)	68.89 (12.3)	
Communication	66.21 (24.1)	68.0 (10.7)	69.32 (10.9)	
Social	69.00 (12.5)	62.69 (13.7)	64.11 (9.8)	

For age, IQ, and Adaptive Behavior, values are presented as mean (SD). * $p < .01$, ** $p < .001$

PWS and as such, some participants were not administered all measures. For this study, only participants who had complete data on social competence and responsiveness were included. Intellectual abilities were assessed in 52 participants (18 PWS-DEL, 15 PWS-UPD, 19 ASD) using the *Wechsler Intelligence Scale for Children (*WISC-IV; (Wechsler 2003), *Wechsler Adult Intelligence Scale (WAIS-III*; Wechsler 1997), or the *Wechsler Abbreviated Scale of Intelligence* (WASI; Wechsler 1999). Parents of 49 participants completed an interview regarding adaptive behavior (14 PWS-DEL, 16 PWS-UPD, 19 ASD). All participants and/or their caregivers gave informed written consent and were financially compensated for their participation. This research was approved by the University Hospitals Case Medical Center Institutional Review Board for Human Investigation.

Measures

Vineland Adaptive Behavior Scale, Second Edition—Vineland-II (VABS; Sparrow et al. 2005)

The VABS assesses social and personal adaptive abilities of a participant (from birth to adulthood). It consists of 297 items presented in a semi-structured interview to the primary caretaker of the individual. Domains include: communication, daily living skills, and socialization. The instrument is well normed and standardized on a representative national sample selected to match U.S. census data.

Social Responsiveness Scale (SRS; Constantino and Gruber 2005)

The SRS is a 65-item parent/caregiver-report rating questionnaire that examines the social, communication, and repetitive/stereotypic behavior characteristic of autistic spectrum disorders. Informants complete each question using a 0 (*not true*) to 3 (*almost always true*) Likert scale, which makes it useful across a wide range of symptom severity. The SRS has been standardized based on a large sample of children 4–18 years of age. However, the developers have also used it with adults (Constantino and Todd 2005; Reiersen et al. 2008). The survey yields an overall score reflecting severity of social deficits in ASD, as well as five symptom domain scores: Social Awareness (SRS-AWARE), Social Cognition (SRS-COG), Social Communication (SRS-COMM), Social Motivation (SRS-MOTV), and Autistic Mannerisms (SRS-MANN). Reliability estimates are above .90 for males and females and for both clinical and normative samples. Higher scores on the SRS indicate a greater degree of social disability. In validation studies, the SRS has been found to be strongly correlated with the ADI-R algorithm score on reciprocal social interaction (Constantino et al. 2003).

Social Competence Inventory (SCI; Rydell et al. 1997)

The SCI is a 25-item parent/caregiver report questionnaire scored on a five-point Likert scale. It contains two subscales derived through factor analysis: the Prosocial orientation subscale (SCI-PRO) assesses generosity, empathy, understanding of others, conflict handling, and helpfulness which promote smooth social interactions with peers; and, the social initiative subscale (SCI-SI), which identifies both active initiation of social interaction and withdrawal behaviors in social situations. Higher scores indicate better social functioning. Both scales have been validated and have excellent reliability, a = .88 and .75 for SCI-PRO and SCI-SI respectively. Data from the validation sample includes mean scores by peer status group. The popular group [SCI-PRO = 4.11 (.39); SCI-SI = 4.49 (.38)] and the average group [SCI-PRO = 3.65 (.80); SCI-SI = 3.84 (.85)] indicate greater social functioning than the rejected group [SCI-PRO = 2.93 (.94); SCI-SI = 3.32 (1.13)]. The SCI has been used with ASD samples in past research (Meyer et al. 2006; White and Roberson-Nay 2009) and is suggested to be more relevant to the symptoms of autism than other social assessment measures designed to identify disruptive behaviors (White et al. 2007).

Results

The Social Responsiveness Scale

Analysis of covariance (ANCOVA) was used to compare the SRS total and domain scores between groups while controlling for age and PIQ. Neither covariate significantly affected the model for the total or domain scores. Mean SRS T-scores for each group are reported in Table 2. A significant effect of group was found for the SRS Overall score, SRS-COG, SRS-COMM, SRS-MOTV, and SRS-MANN scores with the DEL participant group reporting significantly lower ratings than both the ASD and mUPD groups. SRS-AWARE did not differ significantly by group. Based on the standardization sample for the SRS, T-scores above 60 indicate clinically significant deficits in reciprocal social behavior. Scores between 60 and 75 suggest mild to moderate interference with everyday social interaction. Scores 76 or higher are reported by the authors of the SRS to be strongly associated with a clinical diagnosis of autistic disorder, Asperger's disorder, or more severe cases of pervasive developmental disorder-not otherwise specified and suggest a severe interference with everyday social interaction. Figure 1 shows the percentage of participants

Table 2 Social responsiveness and competence scores by participant group

	PWS-DEL (n = 20)	PWS-mUPD (n = 19)	ASD (n = 19)	F value, pairwise comparison
SRS overall score	70.60 (14.2)	82.32 (10.8)	79.79 (8.9)	7.28**, DEL < ASD & mUPD
Social awareness	63.85 (12.2)	69.53 (13.8)	67.89 (10.9)	2.34
Social cognition	69.9 (15.2)	80.42 (11.45)	77.79 (9.8)	4.19*, DEL < ASD & mUPD
Social communication	67.70 (13.9)	79.84 (11.1)	77.47 (8.9)	6.40**, DEL < ASD & mUPD
Social motivation	60.10 (11.9)	71.63 (12.2)	70.26 (10.9)	5.82**, DEL < ASD & mUPD
Autistic mannerisms	76.75 (13.8)	85.47 (11.4)	82.05 (8.3)	4.56* DEL < ASD & mUPD
SCI prosocial	3.43 (.61)	2.89 (.59)	2.54 (.55)	7.20**, ASD < DEL
SCI social initiative	3.05 (.82)	2.64 (.72)	2.51 (.73)	2.03

Values are presented as mean (SD). * $p < .05$, ** $p < .01$

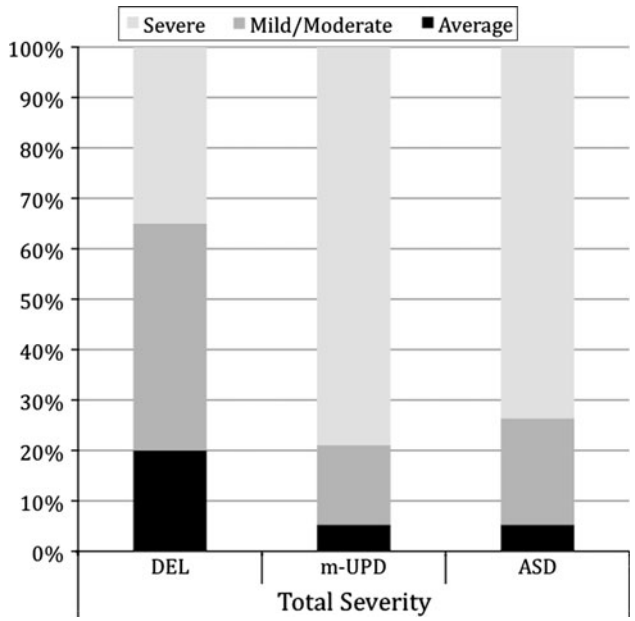

Fig. 1 The percent of participants within each group scoring in the average, mild/moderate, and severe range of social functioning according to the SRS Overall T-score clinical cutoffs

within each group who report average, mild/moderate, and severe social functioning according to the SRS Overall T-score clinical cutoffs.

Within-group correlation analyses were conducted to examine the relation between SRS scores and intellectual functioning (PIQ) as well as with age. There were no significant correlations between SRS scores and age for any participant group. In addition, for the ASD and mUPD groups, no significant correlations were found between SRS scores and PIQ, with the exception of SRS-MANN for the mUPD group ($r = .60$, $p < .01$). Results for the DEL group indicated significant negative correlations between PIQ and SRS Overall score ($r = -.57$, $p < .05$), SRS-AWARE ($r = -.47$, $p = .05$), SRS-COG ($r = -.58$, $p < .05$), SRS-COMM ($r = -.58$, $p < .05$), SRS-MOTV ($r = -.51$, $p < .05$), and approaching significance, SRS-MANN ($r = -.45$, $p = .07$).

Examination of individual items was conducted to determine the types of behaviors most commonly endorsed, as well as those with infrequent endorsement among the PWS subgroups. For item analyses, SRS items were dichotomized into endorsed (response types: often true or almost always true) and not endorsed (response types: not true or sometimes true) and reverse coded items were transformed for reporting consistency. For the mUPD group, 22 items were endorsed by at least 60 % of the sample as compared to 5 items for the DEL group (Table 3). The most frequently endorsed items for the mUPD group consisted primarily of items from the SRS-MANN and SRS-COMM domains. Items that were endorsed frequently for both PWS groups include: having more difficulty than other children with routine changes, perseverative thoughts, playing appropriately with children their own age, understanding or recognizing personal space, and not minding being out of step or 'not on the same wavelength' as others. Items that were never or rarely endorsed for both PWS groups included: touching others in unusual ways, facial expressions not matching what individual says, and reacting to people as if they are objects (Table 3).

The Social Competence Inventory (SCI)

Analysis of covariance (ANCOVA) was used to compare the SCI-PRO and SCI-SI scores between groups while controlling for age and PIQ. Neither covariate significantly affected the model for social competence scores. SCI-PRO differed significantly between groups (Table 2). Pairwise comparisons indicated participants with DEL had significantly higher scores on SCI-PRO (greater prosocial orientation) than both ASD and mUPD groups. There was also a trend toward significant difference between mUPD and ASD ($p = .095$). SCI-SI scores did not differ by group.

Table 3 SRS item endorsement by group

Item description	mUPD	DEL	ASD
SRS items endorsed by at least 60 % of mUPD or DEL groups			
Has more difficulty than other children with changes in his/her routine	89.5	70	68.4
Can't get his/her mind off something once he/she starts thinking about it	89.5	70	73.7
Plays appropriately with children his/her age (REVERSED)	89.5	65	94.7
Thinks or talks about the same thing over and over	84.2	**30**	68.4
Knows when he/she is too close to someone or is invading someone's space(REVERSED)	84.2	60	89.5
Knows when he/she is talking too loud or making too much noise (REVERSED)	78.9	**55**	84.2
When under stress, he/she shows rigid or inflexible patterns of behavior that seem odd	78.9	**45**	78.9
Is not well coordinated	78.9	**55**	**26.3**
Is inflexible, has a hard time changing his/her mind	73.7	**55**	**42.1**
Doesn't seem to mind being out of step with or "not on the same wavelength" as others	68.4	70	68.4
Is able to imitate others' actions (REVERSED)	68.4	**55**	**36.8**
Has difficulty relating to peers	68.4	**30**	73.7
Responds appropriately to mood changes in others (e.g. when a friend's or playmate's mood changes from happy to sad) (REVERSED)	68.4	**55**	78.9
Doesn't understand how events relate to one another (cause and effect) the way other children his/her age do	68.4	**45**	84.2
Is regarded by other children as odd or weird	68.4	**35**	73.7
When under stress, he/she shows rigid or inflexible patterns of behavior that seem odd	63.2	**45**	78.9
Walks in between people who are talking	63.2	**35**	**47.4**
Has difficulty making friends, even when trying his/her best.	63.2	**25**	**57.9**
Gets frustrated trying to get ideas across in conversations	63.2	**25**	**42.1**
Seems self-confident when interacting with others (REVERSED)	63.2	**55**	63.2
Has good self-confidence (REVERSED)	63.2	**55**	63.2
Does not join group activities unless told to do so	63.2	**25**	**47.4**
SRS items endorsed by less than 5 % of mUPD or DEL groups			
Is emotionally distant, doesn't show his/her feelings	**26.3**	5	**21.1**
Talks to people with an unusual tone of voice (e.g., talks like a robot or like he/she is giving a lecture)	**15.8**	5	**26.3**
Avoids starting social interactions with peers or adults	**26.3**	5	**31.6**
Stares or gazes off into space	**26.3**	5	**15.8**
Is overly suspicious	**21.1**	5	10.5
Wanders aimlessly from one activity to another	**21.1**	0	**21.1**
Has overly serious facial expressions	**31.6**	0	10.5
Touches others in an unusual way (e.g. he/she may touch someone just to make contact and then walk away without saying anything)	5.3	0	**31.6**
Expressions on his/her face don't match what he/she is saying	5.3	0	10.5
Seems to react to people as if they are objects	5.3	0	10.5
Avoids people who want to be emotionally close to him/her	**15.8**	0	**26.3**

REVERSED indicates items that have been reverse coded (i.e., 89.5 % of children with mUPD indicated 'not true' or 'sometimes true' to the SRS item, "plays appropriately with children his/her age". Bold values indicates percentages that fall below 60 % endorsement in top half of the table OR percentages that are above 5 % in the bottom section

Within-group correlation analyses indicated no relation between social competence scores and age or PIQ for any participant group. Within the DEL group, a positive correlation between SCI-PRO and PIQ was approaching significance ($r = .44$, $p = .08$).

SCI item analyses was performed by first dichotomizing responses into 'does not apply' (responses 1 or 2) and 'applies or applies very well' (responses 3–5) with reverse scoring appropriately transformed. Several items were endorsed by the majority of respondents (>60 %) in the mUPD group as being low social competence behaviors (scored as 'does not apply') including: preventing conflicts (68.4 %), being a leader in activities/games (84.2 %), intervening in peer's conflicts (73.7 %), inviting shy

Table 4 Correlations between SRS, SCI, and VABS by participant group

	SRS overall score			SCI prosocial			SCI social initiative		
	DEL	mUPD	ASD	DEL	mUPD	ASD	DEL	mUPD	ASD
SCI prosocial	−.69*	−.21	−.09	_	_	_	_	_	_
SCI social initiative	−.67*	−.46*	−.32	_	_	_	_	_	_
VABS composite	−.65*	−.51*	−.18	.62*	.70*	−.16	.44	.32	.27
VABS social	−.70*	−.69*	−.39	.70*	.52*	−.29	.62*	.29	.28

* $p < .05$

children to participate (78.9 %), and being more of a spectator than participant while others play (reverse scored; 63.2 %). For the DEL group, no items were endorsed as being low social competence behaviors by greater than 60 % of respondents.

Comparisons of SRS, SCI, and Adaptive Behavior Ratings

Within-group correlation analyses were conducted to determine the relation between social responsiveness and competence with adaptive behavior. Table 4 shows correlations within group for SRS Overall score, SCI scores, and VABS Adaptive Behavior Composite and Social domain scores. For participants with PWS DEL, the SRS Overall score was significantly correlated with SCI and VABS scores, indicating better social responsiveness (lower scores) with higher overall adaptive and social behavior, as well as prosocial behavior and social initiative. Similar correlations with the SRS Overall score were seen within the mUPD group, albeit somewhat more modestly, with the exception of SCI prosocial behavior. In both PWS groups, the VABS scores were positively correlated with the SCI prosocial behavior scores, indicating higher competence with increased adaptive behavior. Interestingly, scores between the three measures were not significantly correlated within the ASD group.

Discussion

To date, many of the published studies on autistic symptomatology in PWS have used autism symptom checklists that combine repetitive behavior and stereotypies with social functioning items in determining whether the child meets ASD diagnostic criteria. Therefore, it is difficult to tease apart if meeting ASD criteria is over influenced by the presence of repetitive/ritualistic behaviors that are prevalent in PWS. This study uses measures designed and validated to isolate strengths and weaknesses in social functioning specifically. Regardless of genetic subtype, results indicate that people with PWS have significant difficulties with social behavior that are indicative of autism spectrum symptomatology. These findings further indicate that social functioning within the PWS genetic subtypes is differentiated by people with mUPD subtype showing significantly increased likelihood of impaired social functioning compared to those with DEL and more similar functioning to people with an ASD. These findings are both consistent with previous research on autistic symptomatology in PWS and add new information on the specific types of social behavior that are most likely to be impaired across and within the PWS subtypes. Furthermore, this research contributes to the mounting evidence that the 15q11–13 region is implicated in autism susceptibility and specifies the importance of this region to social functioning regardless of repetitive and ritualistic behavior. Based on our findings, overexpression of the maternally inherited genes in this region is associated with increased risk of impairment in social functioning. However, given our findings of significant social impairment in those with the DEL subtype and other work indicating Angelman syndrome's maternal deletions of 15q11–13 are at increased risk of a comorbid ASD diagnosis (Sahoo et al., 2006), the genetic susceptibility is far from straightforward. As the sample size is small, yet well characterized, the results presented here indicate further examination of the PWS social phenotype is warranted in order to further inform how expression of genes in the 15q critical region contribute to social functioning and autism susceptibility and to direct targeted interventions regardless of age or cognitive ability.

In terms of social responsiveness, the total score and mean group domain scores for both DEL and mUPD fall above the cutoff criterion for affected behavior across all domains of social functioning. As would be expected based on prior characterization of the PWS phenotype, the highest group domain score for all groups (including ASD) was the Autistic Mannerisms subscale. While the high scores on the other domains are somewhat surprising, recent research using the SRS in Williams syndrome (WS) has yielded similar group means with the exception of social motivation (Klein-Tasman et al. 2011). While this indicates that these problems with social functioning may

be associated with having a neurodevelopmental disorder, but are not specific to PWS, there is evidence that individuals with WS show increased likelihood of exhibiting autistic symptoms compared to a mixed-etiology group, scoring similarly to individuals with PDD-NOS (Klein-Tasman et al. 2009; Shapiro and Accardo 2010). In addition, there is genetic evidence linking autism to the 7q11.23 WS critical region (Sanders et al. 2011). We have also shown that adults with PWS, WS, and ASD score similarly on portions of the Developmental Behavior Checklist, particularly with regard to preferring the company of adults or young children and being easily led by others, although social relating did distinguish the WS group from the autism sample (Dimitropoulos et al. 2009). However, regardless of whether these deficits in social functioning are specific to PWS, problematic social behaviors are present and span from being inflexible and avoidant, to having difficulty recognizing social cues, communicating, and understanding another's perspective.

As predicted, genetic subgroups differ in their social functioning. The DEL group is reported to have fewer social responsivity problems than their mUPD peers across all domains except Social Awareness. In fact, for many individual items, endorsement rates are higher for mUPD than the ASD sample. It is important to highlight that the ASD sample in this study includes cognitively high-functioning individuals in addition to those who have received significant intervention throughout childhood and have made significant gains in social and adaptive functioning. If the ASD sample were comprised solely of individuals with autistic disorder, we would predict that item endorsement rates for mUPD would be the same or lower than the autism sample. Based on these findings, we expect that people with PWS are more likely to have subtle deficits across social and communication domains of functioning that would indicate more similarities to the broader spectrum of autistic disorders. This is evidenced in this dataset among both PWS groups in the low frequency items, such as 'talks to people in an unusual tone of voice' and 'is emotionally distant'. While the mUPD group includes some participants who report these behaviors, it is clear that these are not significant issues for the DEL participants in this sample. Items most frequently endorsed for mUPD included: difficulty with routine changes, preservative thoughts, and thinking/talking about the same thing repeatedly; all of which have been previously shown to be associated with PWS (see recent review: Dykens et al. 2011). However, behaviors that may be considered more social, such as 'difficulty playing with children his/her age' and 'not knowing when he/she is too close or invading someone's space' were also endorsed by over 80 % of participants with mUPD and over 60 % of the DEL sample. Given the more pressing issues associated with hyperphagia and compulsivity in this population, it is reasonable to argue that these more subtle behaviors may be overshadowed. It is important to note that IQ negatively correlates with domains of social responsiveness for participants with DEL, indicating that those who have higher IQ are less likely to have difficulties with social responsiveness. This relationship does not exist in this sample for the ASD sample, as we would expect based on the diagnostic criteria for ASD, nor does it for the mUPD group, with the exception of the Autistic Mannerisms domain in the opposite direction (higher IQ—more difficulty with SRS-Mann). This is interesting as it may indicate the difference between deficits in social functioning corresponding with cognitive impairment, and those that are present regardless of intelligence as typically seen in the ASD population.

Findings on social competence differed slightly from the SRS data. Groups did not differ on social initiative; all group mean scores were below the validation sample's rejected group mean score. The DEL group performed significantly better than the ASD group on prosocial behavior, with a group mean within range of the validation sample's average group, but did not differ significantly from the mUPD group. No behaviors were endorsed as problematic for the majority (>60 %) of the DEL group. Behaviors that were most frequently reported for the mUPD group focused primarily on difficulties with social initiative and conflict resolution. Age was not related to social competence for any group, and neither was IQ, with the exception of a trend between IQ and prosocial behavior for the DEL group. These findings are consistent with previous research on social competence in PWS, where age was found to be a positive correlate of social competence for WS and Down syndrome but not for PWS (Rosner et al. 2004).

With regard to overall adaptive behavior and social functioning as measured by the VABS, both PWS groups showed moderately strong correlations between social responsivity and adaptive functioning. The same was true for prosocial orientation and both the VABS Composite and Social domain. Social Initiative did not correlate significantly with overall adaptive functioning for any group and only the DEL group showed a significant correlation with the VABS social domain. VABS Composite and Social scores were not correlated with any social measures for the ASD group. Although somewhat surprising, these findings are supported by previous literature that suggests that there is a weak relationship between autistic symptomatology and adaptive behavior (Kanne et al. 2011; Klin et al. 2007). Some have found that the SRS has been shown to correlate with the VABS domains with low to moderate effect sizes (Bolte et al. 2008). This difference in relation to adaptive functioning between the PWS groups and the

ASD group may further support that there are distinct differences between the core social deficits in ASD and general social functioning.

While results from this study indicate further examination of the social phenotype in PWS is warranted, there are several notable limitations to this work. First, the small sample size may lead to spurious findings and increases the chance of both Type I and II errors. While a larger sample size is needed to support these findings, all participants were evaluated in person as part of a larger project, which made recruiting such a rare population more difficult than using mailing survey methodology. However, this method allowed us to assess cognitive ability and adaptive functioning and discuss participant behavior with the parent/caregiver present for the assessment. Second, supplemental genetic subtype confirmation was not available for ten participants with PWS whose parents reported their genetic status. Ideally, documentation on genetic analyses and results performed would confirm group classification but offsite parents did not provide this documentation. Although it is possible that one or more of these participants reported the incorrect genetic subtype or has PWS due to a methylation abnormality, given the rarity of translocations and imprinting center mutations in PWS (<5 %) and our recruitment criteria (specifically for DEL and mUPD), it is unlikely that we have included any of these individuals, however, these findings should be interpreted with a note of caution. Budget and logistical constraints precluded obtaining blood or saliva samples and performing genetic analyses as an alternative means of obtaining this data. However, the addition of the participants with parent-report of genetic status did not alter the group results for either the DEL or the mUPD groups. For participants with DEL, we should also note that the size of the deletion was unknown and thus differences by type 1 [breakpoint(BP)3-BP1] vs. type 2 [BP3-BP2] deletion subtype could not be examined despite past evidence of phenotypic differences with respect to deletion class (Butler et al. 2004; Hartley et al. 2005). Further characterization of social functioning by deletion class in PWS is warranted given the findings of differential prevalence of ASD symptoms by deletion type in Angelman syndrome (Sahoo et al. 2006). It should also be noted that while all participants in the ASD sample also completed the ADOS and ADI-R as part of a larger project, some participants with PWS did not receive the ADOS and/or ADI-R in our offsite data collection, therefore ADOS and ADI-R findings are not reported here. Although the SRS has been shown to correlate strongly with diagnostic measures in ASD samples, correlations between the SRS and diagnostic measures have not yet been investigated in PWS and warrant further study. Thus, as with all parent report measures, additional respondents (i.e., teachers) and direct clinical observation are needed to further characterize the social phenotype.

We have shown here that individuals with PWS evidence significant difficulties with social functioning. These difficulties may affect functioning above and beyond the eating and compulsivity issues prevalent in this population. Children and adults with mUPD subtype of PWS are at increased risk of social impairment similar to those with autism spectrum disorders. Further characterization of social behavior in PWS, irrespective of autism diagnosis, is necessary to aid in advancing the understanding of the contributions of genes in the 15q11–13 critical region to ASD susceptibility, particularly with respect to the overexpression of maternally expressed genes in this region, as well as aiding in awareness and development/implementation of interventions. Moreover, these findings strongly suggest social intervention is necessary regardless of age or cognitive functioning of the child with PWS.

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