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ORIGINAL PAPER

Quantitative Assessment of Autism Symptom-related Traits in Probands and Parents: Broader Phenotype Autism Symptom Scale

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Abstract Autism susceptibility genes likely have effects on continuously distributed autism-related traits, yet few measures of such traits exist. The Broader Phenotype Autism Symptom Scale (BPASS), developed for use with affected children and family members, measures social motivation, social expressiveness, conversational skills, and flexibility. Based on 201 multiplex families, psychometric data on the BPASS are reported. Adequate inter-rater reliability and internal consistency were found. Parents had lower BPASS scores than affected children, after controlling for IQ. Parents and affected children showed overlapping distributions suggesting the BPASS captured variability in traits across groups. BPASS scores were not correlated with ethnicity or parent education; however, some domains were correlated with IQ. The BPASS holds promise as a quantitative phenotypic assessment for genetic studies.

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Introduction

Autism is a syndrome involving impairments in social abilities and communication, and repetitive or stereotyped behaviors and interests. Autism is now recognized as one of the most common developmental disorders, with a prevalence rate of 1/1000 or higher (Arvidsson, Danielsson, Forsberg, Gillberg, & Johansson, 1997; Bryson, 1996; Fombonne, 1999, 2003; Gillberg & Wing, 1999; Yeargin-Allsopp et al., 2003). Twin studies provide strong evidence that there is a heritable component to autism. Folstein and Rutter (1977) found that 4 of 11 monozygotic (MZ) twins were concordant for autism as compared to none of the dizygotic (DZ) twins (n = 10). Furthermore, the non-autistic MZ twins exhibited milder forms of cognitive impairment compared to their affected co-twins. The presence of language delay, reading disability, articulation disorder, and/or mental retardation was found in 82% of the MZ twins and 10% of the DZ twins. Later studies supported the differential concordance rates for MZ and DZ twins (Bailey et al., 1995; Ritvo et al., 1989; Steffenburg et al., 1989). The presence of discordant MZ twins suggests that environmental factors also play a role in the etiology of autism (Bailey, Phillips, & Rutter, 1996).

Sibling risk rates for autism range from 2.8 to 7.0% (Smalley, Asarnow, & Spence, 1988), which is much larger than the risk in the general population. Risk for autism in second-degree relatives is substantially lower

than for siblings (Delong & Dwyer, 1988; Jorde et al., 1990, 1991). The rapid decrease in risk rates from MZ twins to siblings to distant relatives as well as the differential risk rates for male versus female siblings, suggest epistatic effects involving interactions among several genes (estimated to be between 5 and 10 or more; Pickles et al., 1995; Risch et al., 1999) and/or the existence of interactions with shared environmental factors. Susceptibility genes might also have effects on continuously distributed autism-related traits. In theory, multiple genetically related traits might accumulate to cross a threshold into autism. If so, it will be critical to define these traits or endophenotypes and determine their association with specific genes.

Several studies have reported elevated rates of traits related to autism symptoms in both parents and siblings (Bailey et al., 1995, 1996; Baker, Piven, Schwartz, & Patil, 1994; Landa, Folstein, & Isaacs, 1991; Landa et al., 1992; Murphy et al., 2000; Narayan, Moyes, & Wolff, 1990; Wolff, Narayan, & Moyes, 1988). For example, Piven and colleagues (Piven, Palmer, Jacobi, Childress, & Arndt, 1997a; Piven et al., 1997b) reported elevated rates of social and communication impairments and stereotyped behaviors in parents of two or more children with autism. In another study, Piven (2001) found that, compared to parents of children with Down syndrome, parents of children with autism demonstrated higher rates of aloof, rigid and anxious personality traits, fewer close friendships, communication deficits, and impairments in performance IQ and executive function. Other studies have identified elevated rates of specific cognitive and language impairments in family members, including impairments in executive function (Hughes, Plumet, & Leboyer, 1999), reading ability (Piven & Palmer, 1997), and pragmatic language (Landa et al., 1992). Bolton et al. (1994) found that approximately 10–20% of siblings exhibit aspects of the autism syndrome, including language, learning, communication, and social impairments.

Several candidate traits for the broader autism phenotype have been proposed, including mild social and communication impairments, biological characteristics (e.g., serotonin levels, head circumference), and specific neurocognitive profiles (e.g., impairments in face processing, central coherence, executive function) (Dawson et al., 2005, 2002; Folstein, Dowd, Mankoski, & Tadevosyan, 2003; Happe, Briskman, & Frith, 2001; Hughes, Leboyer, & Bouvard, 1997; LeBoyer et al., 1999). Others have argued that genetic liability for autism represents a single, unified social reciprocity trait that is manifest broadly in social deficits, communication impairments, and restricted and repetitive behaviors (Constantino et al., 2004).

The assessment of broader phenotype introduced in this paper, namely, the Broader Phenotype Autism Symptoms Scale (BPASS), separately measures autism-related traits in four domains (two pertaining to social behaviors, one to communicative behavior, and one to flexibility/range of interests). The traits are related to specific autism symptoms, as defined in the DMS-IV (American Psychiatric Association, 1994). A similar approach has been used by others. The Family History Interview, developed by Michael Rutter and Susan Folstein (Bolton et al., 1994; Piven, 2001; Piven et al., 1997a) was designed to measure autism-related traits in family members via interview with a family member (usually the mother of an affected child) about the social and communication skills and range of interests of immediate and extended family members. An algorithm has been developed to determine whether a family member reaches threshold criteria for presence versus absence of the broader phenotype in three separate domains encompassing social, communication, and repetitive behaviors. There are substantial differences in the way in which domains are defined by the FHI versus BPASS. Unlike the FHI, which yields presence versus absence of broader phenotype characteristics, the BPASS scores autism-related traits along a continuum. Also, whereas the communication domain for the BPASS pertains to conversational skills, in the FHI, this domain refers to having a history of language or reading delay, or articulation disorder. Of the three domains, the FHI domain of repetitive behaviors corresponds fairly well to the BPASS domain of flexibility/restricted range of interests.

The BPASS was developed for use in quantitative trait locus (QTL) analyses in the University of Washington genetic study of multiplex autism families. The challenge of developing such a measure of autism-related traits in probands and families was to create one scale that could be used to measure traits among all family members, including children and adults with autism spectrum disorder, parents, and non-affected siblings. Our goal was to create meaningful measures of autism symptom-related traits across this wide range of ages and abilities. To allow for administration to a very wide age range, BPASS questions were worded to be sensitive to potential developmental level and context. For example, in assessing whether a person has an overly restricted range of interests, the interviewer is instructed to consider what kinds of interests would be typical for the developmental level of the interviewee. Thus, a preschooler who has difficulty with changes in routine would be rated as more typical than an adult with the same level of difficulty.

The BPASS assesses autism symptom-related traits in parents, probands, and siblings via parent interview about his or her own functioning, or their child's functioning, as well as through direct observation of the parent and child during individual interactions with a clinical examiner. Non-verbal behaviors, such as eye contact, are assessed via direct observation whereas behaviors related to restricted activities and routines are assessed via interview. Traits in four domains—social motivation, social expressiveness, conversational skills, and repetitive/restricted behaviors—are assessed. Some of the communication items included in the BPASS are based on the work of Piven et al. (1997a). All individuals in the family are rated on the same measure that allows direct comparison of scores. Ratings for most trait domains range from impaired to non-impaired, but also attempt to capture a level above the norm, such that individuals highly unlikely to exhibit the trait are identified. For example, for the sociability with peers item, one end of the scale describes individuals who consistently have a great deal of interest in spending time with others, actively seek out social situations, and enjoy and function well in these situations. This was designed to increase statistical power to detect evidence for genetic effects in QTL-based analyses.

The BPASS was developed through an iterative process of weekly discussions among the BPASS clinical examiners, videotape/DVD review, regular reliability checking, and periodic data analysis. The initial version of the BPASS included several items that are not retained in the current version. For instance, the inter-rater reliability was not achieved on the interview item flexibility in thinking/ideas. It was concluded that this item could not be assessed reliably across raters via the current interview format. The communication items—vague accounts and disorganized accounts—were combined and labeled, sensitivity to listener, which improved inter-rater reliability for this item.

Other quantitative measures of autism symptoms have been published, although most have been developed for the purposes of screening for autism and typically are only applicable to children or adults, but not both. For example, The Childhood Asperger Syndrome Test (Williams et al. 2005) is a parent questionnaire that was developed to screen for Asperger syndrome in children from a general population. The Autism-Spectrum Quotient (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) is a brief, self-administered questionnaire designed to measure the degree to which an adult with normal intelligence has traits associated with autism. Bishop (1998) developed the Children's Communication Checklist that assesses pragmatic language impairment in children. Although valuable, these measures were not originally designed to measure separate domains of autism-related traits, on a single scale, in both children and parents.

The BPASS is more similar to the Social Responsiveness Scale (SRS) developed by Constantino and colleagues (Constantino, Przybeck, Friesen, & Todd, 2000) in its goal of measuring autism-related traits along a continuum for genetic studies. The SRS is a 65-item quantitative measure of social impairment that has been researched in both clinically ascertained and population-based samples of children. It is completed by an adult informant, usually a parent or teacher. Although the SRS primarily focuses a child's ability to engage in emotionally appropriate reciprocal social interaction and communication, some items inquiring about restricted and stereotypic behaviors or interests are included as well. It yields a single score reflecting degree of presence of impairment summed across all symptom domains.

The BPASS differs from the SRS in three key respects: First, whereas the SRS is completed by parents and teachers about a child with whom they are familiar, the BPASS is administered by trained clinicians experienced in assessing psychopathology and clinical interviewing. As such, BPASS interviewers are able to make clinical judgments about the presence and degree of a specific trait, using information about the context, meaning, and developmental-appropriateness of specific responses and observed behaviors. Furthermore, the interviewer is able to follow up with additional questions to clarify the interviewee's response. Second, whereas the SRS is a questionnaire, the BPASS requires direct observation of the adult or child. Judgments based on these observations are based on an established set of rules and criteria, upon which the interviewer has established reliability with other clinical raters. Third, the BPASS provides scores in four separate domains (social motivation, social expressiveness, communication, and flexibility), whereas the SRS yields one score reflecting degree of overall social reciprocity.

This paper describes initial psychometric data on the BPASS, including inter-rater reliability, internal consistency among items within domains, distribution of scores for affected children versus parents, relation between BPASS and specific parent and child characteristics, such as ethnicity, educational level, and IQ, and comparisons between the BPASS and another commonly used measure of autism broader phenotype, the Family History Interview. It is important to keep in

mind that ratings were not conducted blind to diagnosis of the proband, and thus these data were not gathered as a good estimate of the *prevalence* of autism-related traits in family members. Rather, in the present study, the measure was developed to quantify autism-related traits among family members in a multiplex family study and to determine whether this measure adequately captures variability in these traits across probands and family members. Current studies in our laboratory are being conducted using additional comparison groups (e.g., families with one child with autism or a child with other developmental disorder) and utilizing raters blind to child diagnosis. Those studies will address the question of whether these traits are more common in multiplex autism families than other families (singletons, families with a child with another disability or chronic disease).

Methods

Participants

Participants were 690 individuals from 201 families having two or more children with an autism spectrum disorder. Parents' ethnicity was as follows: Caucasian 81.7%, Hispanic or Latino 3.8%, Asian 2.4%, African American 2.1%, Native American/Alaska Native 1.2%, more than one race 2.4%, unknown or not reported 6.5%. Parents' (head of household) occupational status was as follows: Professional 46.2%, Non-manual skilled 13.9%, Manual skilled 14.2%, Partly skilled and unskilled 3.5%, Non-working outside of home 2.1%, Full-time education, 2.1%, not reported, 6.2%. Approximately one-half of the families were from the Puget Sound region. The remainder lived throughout the United States with the exception of 11 families from Canada, and 1 each from Britain and New Zealand. Families were recruited via newspaper articles, parent organizations, NIH announcements, the UW Autism Center website, and a network of community service providers. Approximately 550 families were self-identified as having more than one child with ASD. These families were initially screened through phone interviews and review of medical records to determine whether they met initial inclusion criteria consisting of (a) high probability of affected siblings meeting criteria for idiopathic ASD; (b) ability/willingness to participate in comprehensive diagnostic evaluations; (c) no medical etiology for a neurological disorder among the affected children, such as Fragile-X syndrome, Norrie syndrome, neurofibromatosis, phenylketonuria, or tuberous sclerosis; and (d) English as the primary language. Absence of fragile X was confirmed through genetic testing for all participants. Verbal, performance and full scale IQ were assessed via short forms of the Wechsler Intelligence Scales or the full administration of the Mullen Scales of Early Learning. An estimated full-scale IQ score was calculated using the procedure outlined in Sattler (1992), which takes into account subtest reliability and validity.

Probands

The diagnostic breakdown of the probands in the sample is shown in Table 1. Affected probands were diagnosed as having Autistic Disorder, Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), or Autism Spectrum Disorder using NICHD Collaborative Program of Excellence in Autism (CPEA) diagnostic criteria established by Catherine Lord and other CPEA investigators in May, 2003. The CPEA criteria combines diagnostic information from the Autism Diagnostic Observation Scale – Generic (ADOS; Lord et al., 2000), the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & LeCouteur, 1994), and the clinician's expert rating of DSM-IV diagnostic criteria for Autistic Disorder and PDD-NOS. A diagnosis of Autism Spectrum Disorder was based on following criteria: On the ADI the individual must exceed the cutoff for Autism on the Social score OR Communication score, AND must be within 2 points of the cutoff for Autism on the other scale (Social or Communication). In addition, the individual must meet criteria for Autism or Autism Spectrum Disorder on the ADOS.

Based on the ADOS, 66% of affected children regularly used non-echoed phrases or 2 words or more, while 34% did not. The composite IQ scores for the affected children were distributed as follows: 38% less than 60, 23% between 60 and 79, and 39% 80 or greater.

Table 1 Diagnostic classification of probands from multiplex autism families

Child 1	Child 2	*N* (families)
Autism	Autism	151
	PDD-NOS	13
	Autism Spectrum Disorder	30
PDD-NOS	PDD-NOS	3
	Autism Spectrum Disorder	3
Autism Spectrum Disorder	Autism Spectrum Disorder	1
Total		201

Broader Phenotype Autism Symptom Scale

General Description

There are two sections to the BPASS. The first section consists of a 7-item, semi-structured interview in which traits are assessed by rating parental responses to questions about his or her own functioning or their child's functioning. The second section consists of 6 items that are scored based on direct observation of the parent or child during interactions with the examiner. Several questions and/or probes are made to assess each item. Items are collapsed into four domains with scores from items in each domain summed to yield a composite score. The domains and items that comprise each are listed in Table 2, along with an example of one of the questions or observations that is used to assess each item.

Administration and Training

The BPASS was administered by highly trained clinical examiners (e.g., doctoral-level graduate students, licensed clinical psychologists, etc.) who had previously achieved research reliability on the ADOS and ADI-R. Training and reliability was established in two phases. In the first phase, videotaped BPASS reliability interviews that were administered by senior UW research clinicians were coded by each examiner and checked for scoring reliability. Each examiner was required to obtain ≥80% agreement with the senior clinicians on two videotaped interviews. After achieving 80% or greater agreement, training involved observation of at least two live administrations of the BPASS by senior clinicians. The senior examiner scored the interview independently and if coding differed by two or more points on any item, careful discussion followed to check for understanding. Each examiner was required to obtain 80% or greater inter-rater agreement with the trained examiner on at least two live BPASS interviews. Each examiner was also evaluated for the quality of BPASS administration and interviewing skill.

Examiners were required to maintain a percent exact agreement across items of 80% or higher on at least 15% of the BPASS interviews collected by having a second clinical examiner watch the videotaped interview and independently score it. If agreement dropped below 80%, review of the manual, discussion in the regular clinical examiner group meeting, and follow-up training with additional reliability checks occurred. Regularly scheduled group meetings to discuss questions, challenging cases, and scoring issues were held.

Table 2 BPASS domains and items

Domain	Item	Range	Example of questions/observations
Social motivation	Sociability with peers	1–5	Overall, how much time do you (or your child) prefer to spend with other adults/children?
	Sociability in groups	1–4	How comfortable or uncomfortable are you (or your child) in social situations?
Expressiveness	Eye gaze	1–4	Observe individual's eye contact both when listening and speaking or playing with examiner.
	Social smiling	1–4	Observe individual's response to the examiner's smiles.
	Facial expressions	1–3	Observe range and appropriateness of facial expressions.
	Prosody	1–4	Observe whether individual exhibits atypical rate, rhythm, volume, and/or intonation of speech.
Conversational skills	Detail in conversation	1–4	Observe whether and how frequently individual offers/asks for excessive detail in conversation.
	Sensitivity to listener	1–4	Observe whether the individual uses vague or disorganized accounts when conversing.
Flexibility/range of interests	Flexibility in schedule and routine	1–5	Do you like to have a certain amount of predictability and routine day by day?
	Flexibility in physical environment	1–5	Do you have the kind of house where everything definitely has its place?
	Interests	1–5	Do your (or your child's) interests interfere with (household chores, homework, socializing with friends, caring for children, sleep, work, time with spouse, and so on)?

Except in a minority of cases, the following administration procedure was used: during the same 2-day assessment, parents were interviewed in person. At that time, observations of social and conversational behavior also were made. Mothers and fathers were independently interviewed by different clinicians. Parents were interviewed about themselves first, and then their children. Only one parent (usually the mother) reported on both of the children. For the majority (64%) of the children, the BPASS interview and observation items were completed by the same clinician. For children, the observation items typically were completed following the ADOS administration, which allowed for an observation of social and communicative behaviors.

Scoring

Item scores are ratings based on a 4- or 5-point scale ranging from highly atypical to normal to above average. For one item, there is one 3-point scale (facial expressions) as examiners were unable to achieve reliability on a 4- or 5-point scale. The training manual provides decision rules to assist in scoring responses. The general definition for each score is shown in Table 3. For example, for the item in the social motivation domain that assesses comfort in social groups, a person scoring in the above average range (score = 1) might provide responses such as ''I really like parties.'' ''It's fun to meet new people.'' ''No, I don't feel anxious; as a matter of fact I'd probably be the one breaking the ice for other people who do feel anxious.'' ''I was student body president in junior high school and a cheerleader in high school.'' Individuals in the average range (score = 2) might answer ''I enjoy social activities, especially with people I know well.'' ''I belong to a book club where we have lot of fun.'' Individuals in the low average range (score = 3) might respond with ''I feel nervous in social situation sometimes, but I tend to enjoy myself once I'm there.'' ''It depends on my mood or the person, whether I feel discomfort starting a conversation, but sure, I start conversations with other people.'' A person scoring in the low range (score = 4) might respond with ''I really hate those office parties because I get so nervous. I'm always looking at my watch to see if it's time to go yet''. ''I really prefer for other people to approach me. I will start up a conversation if I'm at a family dinner and I need to find out about how my kids behaved at grandma's house.'' ''I'm not that anxious or anything, I just don't really feel motivated to talk to a bunch of people. I only do it if there is a reason, like to get information from someone.'' Finally, a person who would be scored in the impaired range (score = 5) might state, ''I never go to group things if I can help it.'' ''I could go to a structured support group, but not a party. I even try to avoid family gatherings because I feel overwhelmed. I might just say something so people will think I am interested, but I'd rather just read the newspaper.''

Family History Interview

The FHI was administered to one parent (usually the mother) in a manner similar to methods described in Bolton et al. (1994). Only parents (not probands) were administered the FHI. In the majority of cases (86%) participants were administered the FHI and BPASS by different clinicians on different days. Scores on one instrument were not available during the administration of the second instrument. The algorithm used to define presence or absence of broader phenotype is described in Bolton et al. (1994).

Table 3 BPASS scoring

5-point scale	
1:	Supra-normal, above average, significantly better than most people
2:	Normal, average, typical functioning for a person of that age and life circumstance
3:	On the lower end of the average range or somewhat lower than most people, but not significantly impaired
4:	Outside the normal range, definitely below average, or impaired
5:	Far outside the normal range, well below average, or significantly impaired
4-point scale	
1:	Normal, average, typical functioning for a person of that age and life circumstance
2:	On the lower end of the average range or somewhat lower than most people, but not significantly impaired
3:	Outside the normal range, definitely below average, or impaired
4:	Far outside the normal range, well below average, or significantly impaired

Results

Inter-rater Reliability, Internal Consistency, and Correlations among Domains Scores

Inter-rater Reliability

Inter-rater reliability was assessed on a subset of 15% ($N = 104$) of interviews coded by multiple raters. Inter-rater reliability, based on intraclass correlation coefficients (Shrout & Fleiss, 1979) range from acceptable to high: Social motivation = .95, Expressivity = .84, Conversational skill = .71, Flexibility/Range of interests = .92.

Internal Consistency

The items in the BPASS domains showed very good to adequate internal consistency, Cronbach's alpha: .76 for Social Motivation, .91 for Expressivity, .89 for Conversational Skills, and .60 for Flexibility/Range of Interests.

Correlations Among Domains Scores

The BPASS domain scores show a moderate degree of intercorrelation, both for affected children, mothers, and fathers, as shown in Table 4. Using HLM (Raudenbush & Bryk, 2002) all correlations for affected children were calculated adjusting for the relationship between children within families. The size of the correlations between domain scores suggests that, while not orthogonal, they are not highly correlated.

Distribution of BPASS Scores for Probands and Parents

To be useful as a quantitative measure in genetic analyses, ideally, the BPASS scores should show variability within and overlap between the parent sample and the affected child sample. To explore this, the first set of analyses described the distributions of BPASS scores for affected children and their parents, as shown in Fig. 1. Analyses of variance were conducted comparing affected children and parents as a fixed effect, with non-verbal IQ entered as a fixed covariate to control for differences in intellectual functioning between the affected children and parents. As a group, probands had significantly higher scores in all four BPASS domains compared to parents ($P < .001$ for all four domains), even after accounting for differences in non-verbal IQ. Table 5 shows the adjusted means for each domain for parents and probands. Although there is a large mean difference between the groups, substantial variability was evident, with the distributions for children with ASD overlapping those of the parents (see Fig. 1). Fathers showed significantly higher scores on the expressiveness and conversational skills domains than mothers.

We next examined the BPASS domain scores within the affected children group to determine whether scores differed as a function of severity of diagnosis. Diagnosis was treated as a fixed effect: autism, PDD-NOS, and autism spectrum disorder, while we again used non-verbal IQ as a fixed covariate. Table 6 displays the adjusted means for each domain by diagnostic group. Each BPASS domain differed significantly as a function of diagnosis, with the exception of the conversational skills domain. Children having a diagnosis of autism showed higher BPASS scores than those with ASD, even after controlling for differences in non-verbal IQ.

Relation between BPASS Scores and Parent and Child Characteristics

BPASS and Demographic Variables

Mean BPASS domain scores as a function of sex, ethnicity, and parent education level are provided in

Table 4 Pearson correlations of BPASS scores

	Expressiveness	Conversational skills	Flexibility/range of interests
Children (N = 352)			
Social motivation	.46***	.32***	.24***
Expressiveness	–	.55***	.11*
Conversational skills	–	–	.15**
Mothers (N = 182)			
Social motivation	.31***	.20**	.46***
Expressiveness	–	.29***	.24**
Conversational skills	–	–	.14
Fathers (N = 156)			
Social motivation	.50***	.19*	.56***
Expressiveness	–	.27**	.32***
Conversational skills	–	–	.18*

* $P < .05$, ** $P < .01$, *** $P < .001$

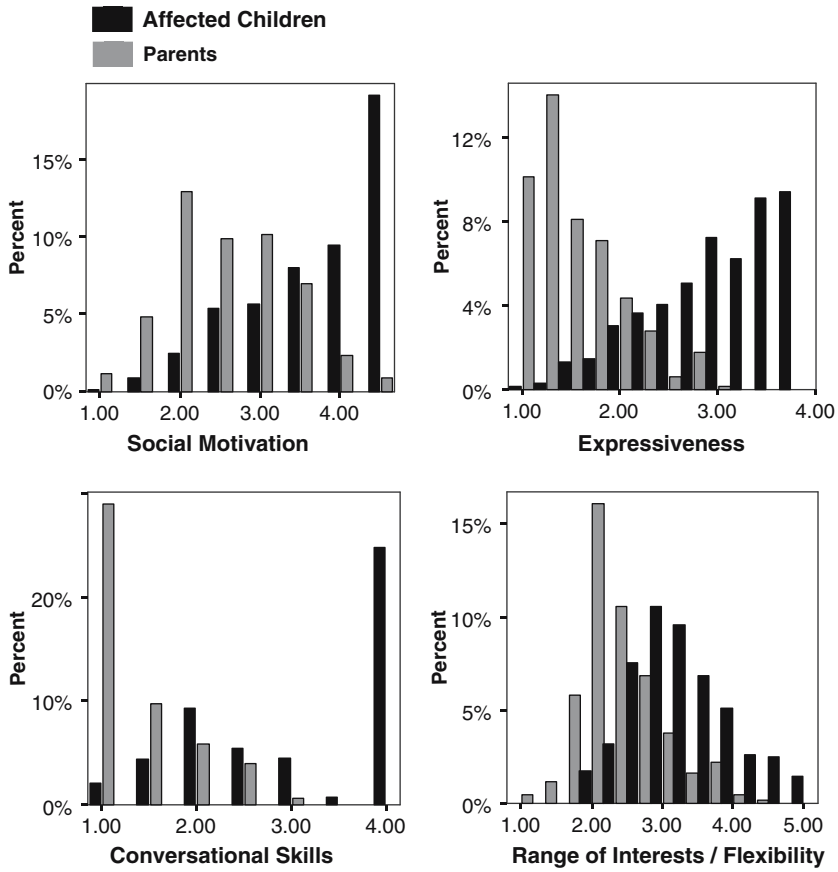

Fig. 1 Distributions of BPASS scores in affected children versus parents

Table 5 Estimated BPASS scores adjusted for non-verbal IQ for affected children and their parents, *F* values, MSE, and Bonferroni adjusted post-hoc comparisons tests

	Affected Children (N = 303)		Mothers (N = 172)		Fathers (N = 151)		F (2,622)	
	M	SD	*M*	SD	*M*	SD	MSE	Post-hoc[a]
Social motivation	3.59	.87	2.58	.84	2.7	.84	82.9* 54.3	AC > *M, F*
Expressiveness	2.86	.57	1.49	.55	1.69	.55	341.6* 97.2	AC > *F* > *M*
Conversational skills	2.96	.78	1.26	.76	1.46	.76	169.4* 90.2	AC > *F* > *M*[b]
Flexibility/Range of interests	3.33	.68	2.28	.66	2.35	.65	157.1* 61.4	AC > *M, F*

* $P < .0001$

[a] Pairwise comparisons with Bonferroni adjustment (P's < .05)

[b] Fathers greater than mothers, $P = .051$

Table 7. There were no significant differences on any of the BPASS scores between affected males versus females, nor significant differences based on ethnicity or parent education level. Fathers had significantly higher ratings than mothers in the social expressiveness domain ($F(1,336) = 18.48$, $P < .001$, MSE = 3.64) and the conversational skills domain ($F(1,336) = 11.38$, $P < .001$, MSE = 2.93). As shown in Table 8, whereas only 6% of mothers scored above 2 (indicating some degree of impairment) in the social expressive domain, 16% of fathers did so. Similarly, whereas only 5.5% of mothers scored above 2 in the conversational skills domain, 13.5% of fathers did so.

Table 6 Estimated BPASS scores adjusted for non-verbal IQ as a function of diagnostic group, *F* values, MSE, and Bonferroni adjusted post-hoc comparisons tests

	Autism (N = 257)		PDD-NOS (N = 15)		ASD (N = 31)		F (2,299)	
	M	SD	M	SD	M	SD	MSE	Post-hoc[a]
Social motivation	3.70	.83	3.43	.84	3.22	.85	5.0** 3.5	Aut > ASD
Expressiveness	3.03	.56	2.59	.57	2.33	.57	23.5*** 7.5	Aut > PDD, ASD
Conversational skills	2.99	.88	3.01	.88	2.66	.89	1.9 1.5	n.s.
Flexibility/Range of interests	3.37	.67	3.10	.67	3.05	.68	4.0* 1.8	Aut > ASD

* $P < .05$, ** $P < .01$, *** $P < .001$

[a] Pairwise comparisons with Bonferroni adjustment (P's < .05)

Table 7 BPASS scores as a function of sex, ethnicity, and parent education

	Social motivation		Expressiveness		Conversational skills		Flexibility/interests	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Sex								
Parents								
Male	2.66	.78	1.62	.49	1.46	.57	2.35	.56
Female	2.52	.74	1.41	.4	1.27	.44	2.29	.58
F (1,336)	2.66		18.48*		11.38*		1.10	
MSE	1.54		3.64		2.93		.36	
Children								
Male	3.69	.83	2.99	.63	3.03	1.02	3.36	.67
Female	3.71	.91	3.01	.69	3.13	1.04	3.22	.81
F (1,350)	.04		.08		.51		2.11	
MSE	.03		.03		.54		1.03	
Ethnicity								
Parents								
Caucasian	2.59	.76	1.53	.45	1.37	.53	2.34	.57
Other	2.55	.72	1.44	.42	1.33	.46	2.25	.53
F (1,315)	.11		1.58		.29		1.04	
MSE	.06		.32		.08		.33	
Children								
Caucasian	3.64	.85	2.99	.64	2.99	1.03	3.32	.69
Other	3.75	.8	2.96	.71	3.27	.98	3.29	.68
F (1,329)	.80		.05		3.56		.07	
MSE	.57		.02		3.73		.03	
Parents' education								
High school	2.55	.83	1.41	.43	1.47	.51	2.21	.49
Some college	2.64	.76	1.60	.45	1.37	.51	2.41	.55
College degree	2.62	.75	1.49	.46	1.38	.52	2.27	.60
Graduate degree	2.61	.71	1.51	.41	1.4	.55	2.37	.65
F (3,226)	.08		1.35		.23		1.14	
MSE	.05		.27		.06		.39	

* $P < .001$

BPASS and IQ

Pearson correlations between full-scale IQ, verbal IQ, and non-verbal IQ and BPASS scores for mothers, fathers, and probands are presented in Table 9. Again, all correlations for affected children were calculated adjusting for the relationship between children within families using HLM (Raudenbush & Bryk, 2002). For parents, overall, IQ was not consistently related to BPASS scores (Table 9). No relationship between IQ and BPASS scores were found in the domains of social motivation, expressiveness, and flexibility/range of interests domains. A modest correlation (r = .17, $P < .05$) between non-verbal IQ and social motivation

for fathers was found. For mothers only, modest correlations were also found between full scale and verbal IQ and conversational skills (r's = –.20, –.22, P's < .01).

For children, BPASS scores were correlated with IQ, especially in the domain of conversational skills. This is not surprising given the scoring framework employed in the BPASS. The conversational domain explicitly assesses language ability. Affected children who are non-verbal are given the highest scores reflecting their greater degree of impairment, which then strongly correlates with scores on IQ measures. Smaller, but nevertheless significant correlations between IQ and BPASS social motivation and expressiveness scores were found, children with lower IQ tended to have higher (more impaired) social motivation scores. This correlation (r = –.26) represents about 5% of the variance in the social motivation score as being shared with IQ for probands. Interestingly, there was no significant correlation between IQ and the flexibility/range of interests score for probands.

Table 8 BPASS Scores in expressiveness and conversational skills for mothers versus fathers

	Percent of sample		
	Scores < 2	Score = 2	Score > 2
Expressiveness			
Mothers	86.8	7.1	6.0
Fathers	73.1	10.9	16.0
Conversational skills			
Mothers	84.1	10.4	5.5
Fathers	73.1	13.5	13.5

Relationship between BPASS and Family History Interview

FHI Results

The presence/absence of symptoms in the three broader phenotype areas yields eight possible combinations for characterizing the broader phenotype in autism. The distribution of broader phenotype features identified by the FHI is presented in Table 10. Each of the eight possible combinations of features was present in this sample of parents.

Overall one-half (50.3%) of the parents were found to have at least one feature identified on the FHI. The most common pattern of broader phenotype was having a single deficit in the communication area (20.9% of the sample). This pattern represents 41.5% of all parents who displayed at least one broader phenotype feature. Of this same group (those with at least one feature) an additional 29.0% of parents exhibited a communication feature together with other features. Thus, overall, 70.5% of parents who showed at least one broader phenotype feature exhibited a communication feature, whereas 45.5% exhibited a social feature, and 35.2% exhibited a repetitive feature. Assessment of the broader phenotype using the FHI in this sample of multiplex parents resulted in a variety in the expression of features of the broader phenotype.

Relation between FHI and BPASS

Given that the FHI is a commonly used measure of the broader autism phenotype based on autism symptom-related traits, it was of interest to compare the BPASS and FHI on the same sample. Note that the BPASS is conducted with each parent independently so information is obtained directly from the individual, as

Table 9 Pearson correlations between BPASS Scores and IQ

	N	Mean	Social Motivation	Expressiveness	Conversational Skills	Flexibility/Range of Interests
Mothers						
Full scale IQ	172	113.3 (13.8)	–.04	–.13	–.20**	–.06
Verbal IQ	168	112.7 (13.3)	–.08	–.15	–.22**	–.07
Non-verbal IQ	172	111.0 (14.9)	–.02	–.10	–.14	–.06
Fathers						
Full scale IQ	151	113.9 (13.6)	.10	.02	.08	.05
Verbal IQ	147	113.8 (14.2)	–.01	–.02	.05	.02
Non-verbal IQ	151	111.0 (15.5)	.17*	.03	.08	.08
Children						
Full scale IQ	304	75.2 (26.4)	–.26***	–.49***	–.62***	–.08
Verbal IQ	300	70.1 (25.5)	–.23***	–.44***	–.60***	–.08
Non-verbal IQ	303	86.1 (27.3)	–.22***	–.41***	–.51***	.07

* P < .05, ** P < .01, *** P < .001

Table 10 Distribution of FHI broader phenotype features in parents

FHI pattern	%
Total with zero feature	49.7
Total with one feature	31.7
Social only	6.9
Communication only	20.9
Repetitive only	4.0
Total with two features	11.4
Social & Communication	4.9
Social & Repetitive	4.0
Communication & Repetitive	2.5
Total with all three features	7.1
Total with at least one Social feature	22.9
Total with at least one Communication feature	35.4
Total with at least one Repetitive feature	17.6

opposed to the FHI which was conducted with one reporter only. Table 11 describes the different constructs measured by the BPASS and FHI. As can be seen in the table, the constructs measured by the different instruments also vary considerably. For example, the FHI social deficit domain includes both language based (e.g., conversational skill) and purely social items, and the social scores pertain primarily to social impairment. In contrast, the BPASS social motivation domain taps solely social preferences and comfort. The BPASS expressiveness domain taps social skills primarily in non-verbal social behavior (eye gaze, facial expression) and, in contrast to the FHI, relies on observation rather than interview. Non-verbal social behavior might be expected to be mildly to moderately correlated with an individual's social relationships (especially on the extremes of the scale), but the method and content differ significantly between the FHI social deficit and BPASS expressiveness domains. The BPASS conversation domain is based on clinician observation of pragmatic language skills, whereas the FHI communication domain is based on a summary of language based learning disabilities, and share virtually no context with any other BPASS items. The only domains that have very similar constructs are the BPASS and FHI restricted range of interest/repetitive behaviors domains. The method and content of these are quite similar.

As can be seen in Table 12, despite the fact that the BPASS and FHI measure somewhat different constructs, there nevertheless were several statistically significant correlations among the BPASS and FHI domains, although the majority are modest in size. The strongest correlation, as predicted, was between the BPASS and FHI repetitive behavior domains. Interestingly, there was a fairly high degree of correlation between the social domains and restricted range of behavior domains across the two instruments. As expected, the FHI communication deficit domain was not significantly correlated with the BPASS

Table 11 Constructs measured by BPASS and FHI

Domain	Method	Content
BPASS		
Social motivation	Interview	Preference for spending time with people, comfort in social situations
Expressiveness	Observation	Eye gaze, smiling, facial expression, prosody
Conversation	Observation	Level of detail, vague/disorganized conversational skills
Range of interests	Interview	Types and intensity of interests Flexibility in routine & environment
FHI		
Social	Interview	Social dysfunction; lack of affection, impaired social play and friendships
Communication	Interview	Language, reading, articulation or spelling delay
Repetitive/stereotyped behavior	Interview	Circumscribed interest, rigidity, repetitive behavior, obsessions/compulsions

Table 12 Pearson correlations between BPASS and FHI domains ($N = 299$)

	FHI Social	FHI Communication	FHI Repetitive
BPASS Social	.35***	.17**	.38***
BPASS Expressiveness	.32***	.15**	.20***
BPASS Conversation	.23***	.05	.15*
BPASS Restricted	.36***	.10	.39***

* $P < .05$, ** $P < .01$, *** $P < .001$

conversation skills domain. Thus, while not completely unrelated, the BPASS and FHI appear to offer somewhat different measures of broader phenotype in parents.

Discussion

This study was designed to introduce and examine some of the psychometric properties of a quantitative measure of autism symptom-related traits, the Broader Phenotype Autism Symptom Scale (BPASS). Four autism symptom-related domains were assessed by the BPASS: social motivation, social expressiveness, conversational skills, and flexibility/range of interests. Based on data collected from a sample of 690 individuals from 201 families with at least two children with an autism spectrum disorder, inter-rater reliability, internal consistency, the distributional properties were examined. Inter-rater reliability of the BPASS domains ranged from excellent to adequate. Internal consistency among items comprising each of the four domains was good.

Children with strict autism showed significantly higher BPASS scores than children with the milder expression of the disorder (PDD-NOS or Autism Spectrum Disorder), even after controlling for non-verbal IQ. To be useful as a quantitative measure in genetic analyses, the BPASS scores should show variability within and overlap between the parent sample and the affected child sample. It was found that the BPASS domain scores adequately captured variability in autism symptom-related traits across affected and non-affected individuals. Despite the presence of clear mean differences on all BPASS domain scores between parents and affected children, even after controlling for non-verbal IQ, substantial individual differences existed, with distributions for probands and parents overlapping for all four domains.

The BPASS scores were not correlated with parent education level or ethnicity, and were not consistently correlated with IQ. For affected children, there were no significant differences on any of the BPASS scores between affected males versus females. However, fathers had significantly higher ratings than mothers in the social expressiveness and conversational skills domains. Whereas only 6% of mothers scored above 2 (indicating some degree of impairment) in the social expressive domain, 16% of fathers did so. Similarly, whereas only 5.5% of mothers scored above 2 in the conversational skills domain, 13.5% of fathers did so. Other studies have found fathers to be more likely than mothers to exhibit impairments in these domains (Piven et al., 1997b; Wolff et al., 1988). Fathers of children with autism have also been found to outperform fathers of children with dyslexia and those with typical development on visual illusions tasks (Happé et al. 2001).

It was found that one-half of the parents were identified as exhibiting at least one broader phenotype feature on the Family History Interview. The most common pattern of broader phenotype was having a single deficit in the communication area (about one-fifth of parents). Of this same group (those with at least one feature) an additional one-third of parents exhibited a communication feature together with other features. The communication domain on the FHI pertains to presence or history of a language-related impairment, such as language, articulation and reading delay. Despite the fact that the BPASS and FHI measure somewhat different constructs, there were, nevertheless, several significant correlations among the BPASS and FHI domains, although most were modest in size. The strongest correlation, as predicted, was between the BPASS flexibility/restricted range of interests and FHI repetitive behavior domains. As expected, the FHI communication deficit domain was not found to be correlated with the BPASS conversation skills domain. Thus, while not orthogonal, the BPASS and FHI appear to offer somewhat different measures of broader phenotype in parents.

Interestingly, the social domains and restricted range of behavior domains were found to correlate with each other. Constantino and colleagues (2004) have argued, based on factor analysis of the Social Reciprocity Scale, that the domains of social impairment and repetitive behaviors do not represent separate factors. Sung et al. (2005) recently conducted a genetic analysis of the BPASS, using the same sample of 201 multiplex autism families described in the present paper. Multivariate polygenic models with ascertainment adjustment to estimate heritabilities and genetic and environmental correlations between the traits were used. It was found that, of the four BPASS trait domains, social motivation and flexibility/range of interests showed the highest heritability, suggesting that these traits are most promising for gene mapping. Moreover, these two traits also showed strong genetic correlation (.92), suggesting a shared genetic basis for the two traits.

Results of this initial study suggests that the BPASS shows promise as an effective quantitative measure of autism symptom-related traits that bridges the continuum between affected and non-affected status as well as characterizing the severity of impairment of those who are affected. Almasy and Blangero (2001) have described three criteria for quantitative risk factors for

psychiatric disease. They argue that, ideally, a risk factor, or endophenotype, should be (a) correlated with a disease and/or disease severity, (b) unaffected relatives of an affected individual should show similar, but milder risk factor profiles, and (c) it must be established that variation in the risk factor is heritable. The results of the present analyses, combined with the recently published genetic analysis of the BPASS (Sung et al., 2005) showing significant heritability for some BPASS domains, suggest that the BPASS meets these criteria. Efforts currently are underway to ascertain the genetic basis of the traits measured by the BPASS, using phenotypic and genotype data from all family members.

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References

Almasy, L., & Blangero, J. (2001). Endophenotypes as quantitative risk factors for psychiatric disease: Rationale and study design. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 105*, 42–44.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: APA.

Arvidsson, T., Danielsson, B., Forsberg, P., Gillberg, C., & Johansson, K. (1997). Autism in 3–6 year old children in a suburb of Goteborg, Sweden. *Autism, 1*, 163–173.

Bailey, A., LeCouteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., et al. (1995). Autism as a strongly genetic disorder: Evidence from a British twin study. *Psychological Medicine, 25*, 63–77.

Bailey, A., Phillips, W., & Rutter, M. (1996). Autism: Towards an integration of clinical, genetic, neuropsychological, and neurobiological perspectives. *Journal of Child Psychology and Psychiatry, 37*(1), 89–126.

Baker, P., Piven, J., Schwartz, S., & Patil, S. (1994). Brief report: Duplication of chromosome 15q11–13 in two individuals with autistic disorder. *Journal of Autism and Developmental Disorders, 24*(4), 529–535.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders, 31*(1), 5–17.

Bishop, D. (1998). Development of the children's communication checklist (CCC): A method for assessing qualitative aspects of communicative, impairment in children. *Journal of Child Psychology and Psychiatry,* 39(6), 879–891.

Bolton, P., Macdonald, H., Pickles, A., Rios, P., Goode, S., Crowson, et al. (1994). A case–control family history study of autism. *Journal of Child Psychology and Psychiatry, 35*(5), 877–900.

Bryson, E. (1996). Brief report: Epidemiology of autism. *Journal of Autism and Developmental Disorders, 26*(2), 165–167.

Constantino, J., Gruber, C. P., Davis, S., Hayes, S., Passanante, N., Przybeck, T., et al. (2004). The factor structure of autistic traits. *Journal of Child Psychology and Psychiatry, 45*, 719–726.

Constantino, J., Przybeck, T., Friesen, D., & Todd, R. D. (2000). Reciprocal social behavior in children with and without pervasive developmental disorders. *Journal of Developmental and Behavioral Pediatrics, 21*, 2–11.

Dawson, G., Webb, S., Schellenberg, G., Dager, S., Friedman, S., Aylward, E., et al. (2002). Defining the broader phenotype of autism: Genetic, brain, and behavioral perspectives. *Development and Psychopathology, 14*, 581–611.

Dawson, G., Webb, S. J., Wijsman, E., Schellenberg, G., Estes, A., Munson, J., et al. (2005). Neurocognitive and electrophysiological evidence of altered face processing in parents of children with autism: Implications for a model of abnormal development of social brain circuitry in autism. *Development and Psychopathology (Special Issue: ''Cognitive and affective neuroscience and developmental psychopathology'' Cicchetti, D. and Posner, M. (Editors)),* 17(3), 679–697.

DeLong, G., & Dwyer, J. (1988). Correlation of family history with specific autistic subgroups: Asperger's syndrome and bipolar affective disease. *Journal of Autism and Developmental Disorders, 18*(4), 593–600.

Folstein, S., Dowd, M., Mankoski, R., & Tadevosyan, O. (2003). How might genetic mechanisms operate in autism? *Novartis Foundation Symposium, 251*, 70–80.

Folstein, S., & Rutter, M. (1977). Infantile autism: A genetic study of 21 twin pairs. *Journal of Child Psychology and Psychiatry, 18*(4), 297–321.

Fombonne, E. (1999). Epidemiological surveys of autism: A review. *Psychological Medicine, 29*, 769–786.

Fombonne, E. (2003). The prevalence of autism. *Journal of the American Medical Association, 289*(1), 87–89.

Gillberg, C., & Wing, L. (1999). Autism: Not an extremely rare disorder. *Acta Psychiatrica Scandinavica, 99*, 399–406.

Happé, F., Briskman, J., & Frith, U. (2001). Exploring the cognitive phenotype of autism: Weak central conference in parents and siblings of children with autism: I. Experimental test. *Journal of child psychology and psychiatry, 42*, 299–307.

Hughes, C., Leboyer, M., & Bouvard, M. (1997). Executive function in parents of children with autism. *Psychological Medicine*, *27*, 209–220.

Hughes, C., Plumet, M., & Leboyer, M. (1999). Towards a cognitive phenotype for autism: Increased prevalence of executive dysfunction and superior spatial span amongst siblings of children with autism. *Journal of Child Psychology and Psychiatry, 40*(5), 705–718.

Jorde, L., Hasstedt, S., Ritvo, E., Mason-Brothers, A., Freeman, B., Pingree, C., et al. (1991). Complex segregation analysis of autism. *American Journal of Human Genetics, 49*(5), 932–938.

Jorde, L., Mason-Brothers, A., Waldmann, R., Ritvo, E., Freeman, B., Pingree, C., et al. (1990). The UCLA-University of Utah epidemiologic survey of autism: Genealogical analysis of familial aggregation. *American Journal of Medical Genetics, 36*(1), 85–88.

Landa, R., Folstein, S., & Isaacs, C. (1991). Spontaneous narrative-discourse performance of parents of autistic individuals. *Journal of Speech and Hearing Research, 34*(6), 1339–1345.

Landa, R., Piven, J., Wzorek, M., Gayle, J., Chase, G., & Folstein, S. (1992). Social language use in parents of autistic individuals. *Psychological Medicine, 22*(1), 245–254.

Leboyer, M., Philippe, A., Bouvard, M., Guilloud-Bataille, M., Bondoux, D., Tabuteau, F., et al. (1999). Whole blood serotonin and plasma beta-endorphin in autistic probands and their first-degree relatives. *Biological Psychiatry, 45*(2), 158–163.

Lord, C., Risi, S., Lambrecht, L., Cook, E., Leventhal, B., DiLavore, et al. (2000). The autism diagnostic observation schedule-generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30*, 205–223.

Lord, C., Rutter, M., & LeCouteur, A. (1994). Autism Diagnostic Interview – Revised: A revised versions of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*, 659–685.

Murphy, M., Bolton, P., Pickles, A., Fombonne, E., Piven, J., & Rutter, M. (2000). Personality traits of the relatives of autistic probands. *Psychological Medicine, 30*(6), 1411–1424.

Narayan, S., Moyes, B., & Wolff, S. (1990). Family characteristics of autistic children: A further report. *Journal of Autism and Developmental Disorders, 20*(4), 523–535.

Pickles, A., Bolton, P., Macdonald, H., Bailey, A., Le Couteur, A., Sim, C., et al. (1995). Latent-class analysis of recurrence risks for complex phenotypes with selection and measurement error: A twin and family history study of autism. *American Journal of Human Genetics, 57*(3), 717–726.

Piven, J. (2001). The broad autism phenotype: A complementary strategy for molecular genetic studies of autism. *American Journal of Medical Genetics, 105*, 34–35.

Piven, J., & Palmer, P. (1997). Cognitive deficits in parents from multiple-incidence autism families. *Journal of Child Psychology and Psychiatry, 38*(8), 1011–1021.

Piven, J., Palmer, P., Jacobi, D., Childress, D., & Arndt, S. (1997a). Broader autism phenotype: Evidence from a family history study of multiple-incidence autism families. *American Journal of Psychiatry, 154*(2), 185–190.

Piven, J., Palmer, P., Landa, R., Santangelo, S., Jacobi, D., & Chilress, D. (1997b) Personality and language characteristics in parents for multiple-incidence autism family. *American Journal of Medical Genetics, 74*, 398–411.

Raudenbush, S. W., & Bryk, A. S. (2002). *Hierarchical linear models: Applications and data analysis methods*. Thousand Oaks: Sage Publications.

Risch, N., Spiker, D., Lotspeich, L., Nouri, N., Hinds, D., Hallmayer, et al. (1999). A genomic screen of autism: Evidence for a multilocus etiology. *American Journal of Human Genetics, 65*(2), 493–507.

Ritvo, E., Jorde, L., Mason-Brothers, A., Freeman, B., Pingree, C., Jones, M., et al. (1989). The UCLA-University of Utah epidemiologic survey of autism: recurrence risk estimates and genetic counseling. *American Journal of Psychiatry, 146*(8), 1032–1036.

Sattler, J. (1992). *Assessment of children: Cognitive applications*. La Mesa, CA: Jerome Sattler Publisher Inc.

Shrout, P., & Fleiss, J. (1979). Intraclass correlation: Uses in assessing rater reliability. *Psychological Bulletin, 86*, 420–428.

Smalley, S., Asarnow, R., & Spence, M. (1988). Autism and genetics: A decade of research. *Archives of General Psychiatry, 45*, 953–961.

Steffenburg, S., Gillberg, C., Hellgren, L., Andersson, L., Gillberg, I., Jakobsson, G., et al. (1989). A twin study of autism in Denmark, Finland, Iceland, Norway, and Sweden. *Journal of Child Psychology and Psychiatry, 30*, 405–416.

Sung, J. U., Dawson, G., Munson, J., Estes, A., Schellenberg, J., & Wijsman, E. M. (2005). Genetic investigation of quantitative traits related to autism: use of multivariate polygenic models with ascertainment adjustment. *American Journal of Human Genetics, 76*, 68–81.

Williams, J., Scott F., Stott C., Allison C., Bolton, P., Baron-Cohen, S., et al. (2005). The CAST (Childhood Asperger Syndrome Test): Test accuracy. *Autism, 9*(1), 45–68.

Wolff, S., Narayan, S., & Moyes, B. (1988). Personality characteristics of parents of autistic children: A controlled study. *Journal of Child Psychology and Psychiatry, 29*(2), 143–153.

Yeargin-Allsopp, M., Rice, C., Karapurkar, T., Doernberg, N., Boyle, C., & Murphy, C. (2003). Prevalence of autism in a metropolitan area. *Journal of the American Medical Association, 289*(1), 49–55.