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Evidence for broader autism phenotype characteristics in parents from multiple incidence autism families

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Abstract

The broader autism phenotype was assessed in parents who have two or more children with ASD (multiplex autism), parents who have no more than one child with ASD (simplex autism), parents who have a child with developmental delay without ASD, and parents who have typically developing children. Clinicians, naive to parent group membership status, rated broader autism phenotype characteristics from videotaped administration of the Broader Autism Phenotype Symptom Scale (BPASS). Differences among groups in BPASS scores in the four assessed domains (social motivation, conversational skills, expressiveness, and restricted interests) were examined using multivariate ANOVA and post-hoc comparisons. Further, ratings of videotapes by observers naive to family status were compared to live, non-naïve ratings by observers who were aware of family status (non-naïve). Findings demonstrate that the BPASS is an instrument resistant to rater bias. Parents from multiplex autism families showed significantly more autism phenotype characteristics than the parents in the other groups. Moreover, the parents from simplex autism families did not differ from the parents of children with developmental delay or typical development. Finally, no differences between live, non-naïve ratings and videotaped, naïve ratings were observed. These findings suggest that characteristics of the broader autism phenotype, specifically in the social and communication domains, are present in multiplex autism parents to a greater degree than simplex autism and control parents. Further, the results provide support for the notion that genetic transmission mechanisms may differ between families with more than one child with autism and families with only one child with autism.

Keywords

broader autism phenotype; autism spectrum disorders; genetics; autism assessment

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder with a genetic etiology. Twin studies indicate strong heritability of ASD (Bailey et al., 1995; Folstein & Rutter, 1977) and although the specific etiology is unknown for most cases of ASD, in approximately 10–20% of cases, the cause has been identified. Causes include syndrome

related etiologies (e.g., Fragile X) and structural variations in genomic architecture with each rare variant accounting for no more than a small percent of cases (Abrahams & Geschwind, 2008).

ASD is characterized by impairments in social communication and the presence of restricted and repetitive interests and behaviors with great variability in the symptom profiles among individuals with ASD. Thus, while one child with ASD may be non-verbal and have repetitive motor mannerisms, a second child with ASD may speak fluently and have interests of unusual intensity, but no repetitive motor movements. Thus, the use of overarching diagnostic categories in multifaceted psychiatric disorders such as ASD has the potential to obscure genetic findings by increasing heterogeneity of the disorder. As a result, an area of focus for such studies has been to investigate component traits that are theoretically more closely tied to genetic vulnerability than a qualitative diagnosis (Berrettini, 2005; Gottesman & Gould, 2003; Gould & Gottesman, 2006). Additionally, these traits are often present to a lesser degree in *unaffected* relatives of individuals with the disorder, yielding insight into inheritance patterns. In the field of ASD, this highly replicated phenomenon is called the *broader autism phenotype (BAP)*.

Studies indicate that parents of children with ASD are more likely to show measurable impairments in traits related to the diagnostic criteria of ASD as compared to parents of children without ASD including language and conversational skills (Landa, Piven, Wzorek, & Gayle, 1992; Piven, Palmer, Landa et al., 1997; Ruser et al., 2007), face processing and memory (Baron-Cohen & Hammer, 1997; Dawson et al., 2005), theory of mind (Baron-Cohen & Hammer, 1997; Di Michele, Mazza, Cerbo, Roncone, & Casacchia, 2007), and social relations (Landa et al., 1992; Losh & Piven, 2007; Piven, Palmer, Jacobi, Childress, & Arndt, 1997). Most studies find that at least half of the relatives studied do *not* have quantifiable impairments, which suggests that BAP traits are present in only a subset of family members (Bolton, Macdonald, Pickles, & Rios, 1994; Pickles et al., 2000; Piven, Palmer, Jacobi et al., 1997).

Most individuals with ASD do not have a significant family history for the disorder. These simplex families (SPX) have been the focus of recent genetic and phenotypic research. Some studies suggest that de novo copy number variants (CNVs) are more common in autism SPX families as compared to both autism multiplex families (MPX) and families without any history of ASD (Marshall et al., 2008; Sebat et al., 2007; Weiss et al., 2008). Elevated rates of de novo genetic mutations in SPX families suggest an increased likelihood of sporadic versus familial pattern of inheritance for ASD. Thus, genetic transmission mechanisms in ASD may differ between single-incidence and multiple-incidence families.

Examination of the BAP in SPX and MPX families may provide insight into the differing genetic transmission patterns in ASD. If individuals with ASD from SPX families are more likely than individuals with ASD from MPX families to develop ASD as a result of a de novo genetic event, then relatives in SPX families should show less pronounced features of the BAP as compared to relatives in MPX families, who may be at risk for ASD symptoms given shared genetic vulnerability.

Several studies have examined the BAP in SPX and MPX families. Szatmari and colleagues (2000) found increased social impairments but not communication impairments or restricted/repetitive behaviors in immediate and extended family members of MPX families compared to SPX relatives. Using a computerized facial affect detection program, Bölte and Poustka (2003) found that parents of SPX families demonstrated better emotion recognition skills compared to parents of MPX families. Fathers in MPX families show elevated scores on the Social Responsiveness Scale (SRS; Constantino, Przybeck, Friesen, & Todd, 2000)

compared to fathers of SPX families, but no such difference is noted in mothers from MPX and SPX families (Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009). Losh and colleagues (2008) compared parents of MPX and SPX families and parents of children with Down Syndrome on cognitive ability, personality traits associated with ASD, friendships, and pragmatic language. In a sample of 25 MPX families, 40 SPX families, and 30 Down syndrome families, the authors found a consistent linear trend across measures with parents in MPX families showing more BAP traits than SPX families and the fewest traits in parents of Down syndrome families. Further, it was more common in MPX families for both parents to show features of the BAP compared to SPX families (Losh, et al., 2008). These findings in the existing literature using non-naïve coders suggest that MPX families may carry a higher loading for ASD-related traits since such traits occur more often in MPX families compared to SPX.

To examine the BAP in MPX and SPX families without bias, a measure that is scored by clinicians naïve to family group, that captures traits showing heritability, and that is applicable for relatives across families with ASD, families with non-ASD developmental disabilities, and typical families, is necessary. The Broader Phenotype Autism Symptom Scale (BPASS) is a quantitative measure of four ASD related traits (social motivation, social expressiveness, conversation skills, and flexibility/range of interests) that incorporates interview and direct observation along a continuum to capture the wide range of skills shown by individuals with ASD and undiagnosed individuals. Described in Dawson et al., (2007), the instrument was originally developed for use in ASD Quantitative Trait Locus analyses and has shown evidence of heritability for two trait domains: social motivation and range of interest/flexibility (Sung et al., 2005). The BPASS has adequate psychometric properties, provides information regarding four ASD related symptom areas, uses direct observation, shows evidence of heritability, and provides a scale to assess all members in a family, including children and adults with ASD and siblings, parents, and other relatives without a diagnosis. In addition, the BPASS is conducted by examiners, rather than by self-report, and thus has the potential to produce scores that are not affected by knowledge of family status (e.g., MPX, SPX, TYP). As such, it provides useful information beyond that provided by questionnaire or interview alone and is an effective quantitative trait measure of the BAP.

The current study aimed to compare the BAP in parents in MPX families as defined by having two or more children diagnosed with ASD; SPX families, defined as having no more than one child diagnosed with ASD, families with non-ASD developmental disabilities (DD), and families with typical development (TYP) using BPASS ratings made by coders naïve to family diagnostic status. We included parents of children with DD to control for potential influences of parenting a child with a disability, such as increased parent stress. We included the TYP group to evaluate scores in the typical population. By comparing ratings made by clinicians naïve to family diagnostic status to those ratings made by clinicians not naïve to family status, the resilience of the BPASS to rater bias was examined. In addition, these ratings also allowed the evaluation of potential impact of coding from videotape versus live interviewing. Given the potential differences in genetic mechanisms of transmission of ASD suggested by previous research in this area, we hypothesized that (1) parents from MPX families would demonstrate increased BAP traits compared to parents from SPX, DD, and TYP families, and (2) parents from SPX families would show greater BAP traits compared to DD and TYP families. We further hypothesized that (3) the BPASS would be robust against rater bias due to prior knowledge of the disability status of children in the family such that no differences would be found between non-naïve ratings based on live administrations and naïve ratings based on video recordings.

Method

Participants

Participants included 39 parents from families with two children with ASD (MPX), 22 parents from single-incidence ASD families (SPX), 20 parents from families with a developmentally delayed child without ASD (DD), and 20 parents from families with a typically developing child (TYP). Participants were screened regarding family history of ASD out to three degrees from the child. Participants in the DD and TYP groups had no family history of ASD. MPX families were ascertained through a study on the genetics of autism conducted at the University of Washington Autism Center (Collaborative Programs of Excellence in Autism, CPEA; see Schellenberg et al., 2006 for details), which focused on families with two or more individuals with ASD. SPX families and DD families were recruited for a longitudinal study on the neurobiology and developmental course of ASD also conducted at the University of Washington Autism Center (CPEA; see Dawson et al., 2004 for details). While the presence of a second child with a disability was not exclusionary for participation in the longitudinal study, only single incidence families were included in the current study. The TYP group was recruited through local parent advocacy groups, community agencies, clinics, hospital, and public schools.

The children of the parents in the MPX, SPX, and DD groups were directly assessed by trained clinicians and classified as having an ASD or developmental delay without ASD. Children in the ASD groups (MPX, SPX) met diagnostic criteria for ASD on the Autism Diagnostic Interview-Revised (ADI-R; Risi et al, 2006) and the Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000) and according to expert clinical judgment using DSM-IV (American Psychiatric Association, 1994) criteria. Children in the DD group did not meet criteria for ASD on the ADI-R, ADOS-G, or DSM-IV, but did exhibit delays on the Mullen Scales of Early Learning (Mullen, 1995) when assessed between 3 to 4 years of age. Children in the TYP group demonstrated no cognitive delays, had no known psychiatric history, and had no family history of ASD. Families in all groups were excluded if a child had a history of serious traumatic brain injury, significant sensory or motor impairment, major physical abnormalities, or neurological disease. Families in the ASD group were excluded for the presence of a neurological disorder of known etiology.

The characteristics of parents and children from the four family groups are described in Table 1.

Measures

The Broader Phenotype Autism Symptom Scale (BPASS; Dawson, Estes, Munson, Abbott, Bernier, 2005) is a quantitative measure of autism-related traits that is appropriate for use with all family members, including children and adults with ASD, parents and siblings. The BPASS assesses autism-related traits in four domains (described below) via both direct observation and interview through 13 coded items. Interviews are individually conducted with adult participants regarding their own functioning. Parents are interviewed to obtain ratings on children. Scores for each of the items range from impaired to non-impaired, with some items providing scores indicating supra normal traits (e.g., very outgoing individuals). Inter-rater reliability based on intraclass correlation coefficients range from acceptable to high and items in the BPASS domains show very good to adequate internal consistency (Dawson et al., 2007). QTL analyses revealed that two of the phenotypic domains (social motivation and range of interests/flexibility) showed the highest heritability and genetic correlation and yield strong potential for future gene mapping (Sung et al., 2005). Training procedures for establishing reliability on the BPASS include reliable administration and

coding (over 80% agreement) during three live administrations supervised by a previously trained, reliable BPASS clinician.

Four domains are measured by the BPASS.

Social Motivation (Social)—The Social domain of the BPASS is derived from interview questions assessing child- and adulthood social interest in peers and groups and assesses social motivation. Specific items include self-perception of social comfort in groups and preference for alone time versus time spent with others across settings.

Social Expressivity (Expressiveness)—The Expressiveness domain is based on parent nonverbal social communication observed during the BPASS interview and assesses social expressivity. Clinicians rate the use of appropriate and integrated eye gaze, social smiling, facial expressions, and prosody during the course of the interview.

Conversational Skills (Conversation)—The Conversation domain is scored from clinical observations of conversation skills during the BPASS interview and assesses conversational skills. Particular attention is paid to instances of excessive detail that impede conversation and decreased sensitivity to the listener by, for example, making comments out of context and/or without adequate background information.

Flexibility/Range of Interests (Restricted Interests)—The Flexibility/Restricted Interests domain pertains to parent self-report of flexibility and interests in both child- and adulthood. The breadth and type of interests are assessed as well as the intensity of these interests. Parents are also asked to describe how they prefer to arrange their daily schedule and physical environment, with scores ranging from extremely flexible in routine and physical space to marked rigidity in these areas causing impairment in relationships or emotional distress if disrupted.

Procedures

The children in the ASD and DD groups were evaluated by experienced clinicians to determine diagnostic status and eligibility for study participation. For children in the MPX group, cognitive ability was assessed using the age-appropriate abbreviated Wechsler battery, either Wechsler Intelligence Scale for Children or Wechsler Preschool and Primary Scale of Intelligence (Wechsler, 1997). The Differential Ability Scales (Elliot, 1990) was utilized for children in the SPX, DD, and TYP groups. The BPASS was obtained as part of parental participation in the genetics of autism study for the MPX group, the longitudinal study in the case of the SPX and DD groups, and for the purposes of the current study for the TYP group.

Because of the nature of the studies in which the BPASS was administered (e.g., longitudinal studies which included direct assessment of the children), it was not possible for the initial interviews to be completed by raters naïve to family status. As a result, the initial interviews were conducted by trained clinicians who were aware of the children's diagnostic status. All BPASS administrations were coded by the non-naïve clinician administering the measure and videotaped for later offline coding by a naïve rater. The videotapes were coded by trained, research-reliable BPASS clinicians who were naïve to family status (i.e., whether the family was in the MPX, SPX, DD, or TYP group). Videotapes were screened for mention of children's diagnostic status or related topic. Any topic raised during the assessment that might indicate the diagnostic status of the children in the family or the number of children in the family was edited and removed. All videotapes were edited and small segments removed such that these edits equally distributed across all

tapes to ensure naïveté. As a final precaution, the BPASS coder completed a rating of their level of naïveté, ranging from 0 (completely unaware of child's diagnostic status), to 1 (possibly aware with description of why) and 2 (aware of child's diagnostic status). In one interview, the naïve clinician was aware of the child's diagnostic status. This case was excluded from analysis. Of the total sample of 101 parents from the 101 families interviewed as part of the current study, a subgroup of 38 was randomly selected from the MPX group to compare videotaped, naïve ratings to the live, non-naïve ratings.

Analyses

Potential differences related to demographic variables were addressed using analysis of variance and Tukey post hoc comparisons (child age, child IQ, parent age, number of children in family) or using Chi-square analyses (child gender, child race, parent gender, parent race, and parent education).

Group differences on BPASS ratings were examined using multivariate analysis of variance with group status as the independent variable and ratings from each of the four BPASS domains as dependent variables (Social, Expressiveness, Conversation, and Restricted Interests).

Correlations between live, non-naïve scores and videotaped, naïve scores were examined. Differences between the two rating types were assessed using paired samples *t*-tests and comparing live, non-naïve scores to videotaped, naïve scores on each of the four BPASS domains.

Results

As shown in Table 1, assessment of group differences on demographic variables indicated that groups did not differ on child or parent age or parent education level. Overall family size also differed by group, $F(3, 97) = 4.15, p < .01$, with the MPX group having larger families than the TYP group, but no differences in number of children between the MPX and SPX families. Child Full Scale IQ differed across groups, $F(3, 126) = 20.09, p < .05$. Tukey post hoc comparisons of the four groups indicate that children in the TYP group had significantly higher Full Scale IQ scores than the other three groups, as expected. The MPX, SPX, and DD groups did not differ on Full Scale IQ. The groups differed on child and parent race ($X^2(18) = 36.84, p < .05$) with the SPX and DD group consisting of fewer Caucasian participants than the MPX and TYP groups. Child gender also differed ($X^2(3) = 9.11, p < .05$) with the DD group containing a larger percentage of female children than the MPX, SPX or TYP groups. Parent gender also differed by group ($X^2(3) = 25.5, p < .001$). This was due to the TYP group consisting only of mothers.

Given the identified differences in parent gender by group, Multivariate analysis of variance was conducted with gender entered as a covariate to examine family group differences on BPASS scores. After controlling for gender, the MANOVA yielded a significant main effect for family group for three of the four BPASS domains (Social: $F(3, 96) = 3.19, p < .05$, partial $\eta^2 = .09$; Expressiveness: $F(3, 96) = 4.34, p < .01$, partial $\eta^2 = .12$; Conversation: $F(3, 96) = 2.13, p = \text{n.s.}$, partial $\eta^2 = .06$; Restricted Interests: $F(3, 96) = 4.34, p < .01$, partial $\eta^2 = .12$). Tukey post-hoc comparisons of the four groups were calculated to identify differences across the three identified domains. Means for each domain score shown are presented in Figure 1. In the Social domain, post hoc comparisons indicate that the MPX parents received significantly higher (i.e., more impaired) scores than the SPX, DD, and TYP groups (mean difference = 0.58, 0.65, 0.52, $p < .05$, Cohen's $d = .75$; $p < .01$, $d = .84$; $p < .05$, $d = .77$; respectively). There were no differences among the other three groups in the Social domain. In the Expressiveness domain, MPX parents scored significantly higher

(more impaired) than the TYP parents (mean difference = .439, $p < .001$, $d=1.28$) as did the DD parents (mean difference = .383, $p < .01$, $d=1.20$). No other differences were observed among groups on Expressiveness. In the Restricted Interests domain, the MPX group received significantly higher scores (i.e., less flexible in interest, schedule or space) than the TYP group (mean difference = .435, $p < .05$, $d=.93$). No other group differences were identified in this domain.

Given the differences in parent gender by group, an additional MANOVA was computed using only the mothers in each group. The MANOVA yielded a significant main effect for family group for all four BPASS domains (Social: $F(3,65) = 2.67$, $p < .05$, partial $\eta^2=.11$; Expressiveness: $F(3,65) = 6.79$, $p < .001$, partial $\eta^2=.24$; Conversation: $F(3,65) = 3.31$, $p < .05$, partial $\eta^2=.13$; Restricted Interests: $F(3,96) = 4.86$, $p < .01$, partial $\eta^2=.18$). Post hoc comparisons in the Social domain indicate that the MPX parents received significantly higher (i.e., more impaired) scores than the SPX group (mean difference = 0.62, $p < .05$, $d=.79$). There were no other differences among the groups in the Social domain. In the Expressiveness domain, MPX parents scored significantly higher (more impaired) than the TYP parents (mean difference = .35, $p < .01$, $d=1.25$), as did the DD parents (mean difference = .40, $p < .01$, $d=1.25$). The DD group also scored higher than the SPX group (mean difference = .31, $p < .05$, $d=.87$), but there were no differences between the SPX and TYP groups or the DD and MPX groups. In the Conversation domain, the MPX parents received significantly higher scores than the SPX group (mean difference = .47, $p < .05$, $d=1.20$), but no other differences were observed. In the Restricted Interests domain, the MPX group received significantly higher scores (i.e., less flexible in interest, schedule or space) than both the SPX group (mean difference = .56, $p < .05$, $d=.92$) and the TYP group (mean difference = .61, $p < .01$, $d=1.12$). No other group differences were identified in this domain.

Live, non-naïve and videotaped, naïve BPASS ratings were significantly correlated across all four domains (Social: $r(38) = .81$, $p < .001$; Expressiveness: $r(38) = .52$, $p < .001$; Conversational Skills: $r(38) = .32$, $p < .05$; Restricted Interests: $r(38) = .62$, $p < .001$). Paired samples t -tests yielded no significant differences across any of the four BPASS domains.

Discussion

The primary goal of this study was to examine similarities and differences in the broader autism phenotype (BAP) among parents in MPX families, SPX families, families with non-ASD developmental disabilities (DD), and families with typical development (TYP) using Broader Phenotype Autism Symptom Scale (BPASS) ratings made by examiners naïve to family status. A second goal was to determine how robust the BPASS scores were against rater bias and rating medium by comparing scores made during live interviews by non-naïve examiners to ratings made by naïve examiners viewing videotaped interviews.

The analysis revealed partial support for our hypothesis that MPX families would show a greater number and degree of BAP characteristics compared to the other family groups. Across three of the four BPASS domains, parents from the MPX group scored higher than parents from at least one other family group. In the Social domain, the MPX group scored significantly higher than the three other family groups, and no differences were found among the SPX, DD, and TYP parent groups. The same general pattern of results emerged in the Conversation domain, with parents from the MPX group demonstrating greater impairment than parents from the SPX group. The SPX group did not differ from DD or TYP group. In the Restricted Interests domains, however, the MPX group showed significantly greater impairment than the TYP group, but no significant differences were found between the SPX, DD, and TYP groups in these domains. On the whole, these results

suggest that a different mode of genetic transmission is present in MPX families compared with SPX families. The social and repetitive behavior domains, based on the BPASS, have previously demonstrated heritability indicating that these two domains have strong potential for leading gene mapping in family studies of ASD (Sung et al., 2005). Furthermore, similarity in BPASS ratings between the SPX, DD, and TYP groups suggests that parents in the SPX group do not possess a greater number or intensity of BAP traits than the population at large. A lack of evidence for the BAP in these areas in the SPX group is consistent with recent genetic findings that the development of ASD in SPX ASD families is more often the result of de novo, non-inherited genetic events than in MPX families (e.g., Sebat et al., 2007). Thus, if parents in SPX families are less likely to carry ASD risk genes, they would also be less likely to display ASD-related traits in comparison with parents from the MPX group.

It is important to consider alternative explanations for these findings. Specifically the pattern of findings in the current study--increased social and conversation challenges and restricted interests in the MPX group, could be due to non-genetic factors. For example, living with one or more children with significant disabilities, particularly ASD, is known to increase parental stress (e.g., Estes, et al., 2009). Increased stress could plausibly result in observable changes in social functioning or in less flexibility and thus higher scores in the social and repetitive domains. This effect could be amplified in parents with two or more children with ASD compared with one child with ASD or DD. However, it should be noted that BPASS ratings are not solely based on current functioning, but also on report of functioning and ability during childhood and adulthood prior to having a child (or children). Given this consideration of pre-parenthood functioning in BPASS scores, it is unlikely that observed group differences reflect only the psychosocial impacts of having multiple children with disabilities.

The MPX group showed greater impairment compared to the TYP group in the Restricted Interests domain. However, no differences were observed between parents in the MPX compared with SPX and DD groups. If this BPASS domain reflected a BAP construct it would be expected that the MPX group would demonstrate more intense BAP characteristics than the DD control group. It is possible that having one or more children with a disability could contribute to the observed differences. For example, a parent of a child with ASD may be reluctant to change schedules and routine due to distress in the child. It is equally plausible that the scheduling needs of two children with disabilities could, over time, impact a parent's need for sameness or routine and limit that parent's range of activities. Although BPASS examiners attempt to disentangle these features by inquiring about pre-parenthood preferences, it is possible that parent report was influenced by their current lifestyle. Losh et al., (2008) found that although parents in the MPX and SPX groups showed significantly more BAP traits than the comparison group (parents of a child with Down's Syndrome), they found rigidity was the personality trait most often observed in the comparison group and highlighted that this trait may reflect the needs of caring for a child with a disability rather than an inherent personality trait.

The findings of higher BPASS ratings in the parents in the MPX group across three of the four domains provides partial support for the findings of Losh et al., (2008) of a linear trend in BAP characteristics across MPX, SPX, and DD groups. The MPX group scored significantly higher on BAP characteristics than the control groups, but the SPX group did not. An often-discussed inherent limitation of simplex studies is that the diagnostic status of future children, of course, cannot be determined. Therefore, it is impossible to say for certain that SPX families reported a sporadic case of ASD. Given the 5–10% sibling recurrence risk rate and a 4:1 ratio of affected males to females, families with a single affected child might become multiplex if more (particularly male) children were

subsequently born into the family. Some families decide to stop having children after receiving an ASD diagnosis for their youngest child, which further complicates the validity of family status. Despite the foregoing limitations, SPX families are likely to have increased rates of sporadic ASD. Thus, the presence of the BAP in these families should be similar to control groups. The use of additional inclusion criteria, such as the presence of at least one other undiagnosed child in the family, or the use of assessments of BAP in other family members may help to clarify simplex status in future work.

The ratings utilized in the analyses were based on raters scoring from videotaped interviews who were naïve to family status. Importantly, the ratings made by clinicians who were aware of family status during the live administration correlated strongly with naïve ratings. Further, no statistically significant differences were found between scores as a function of naiveté or medium of scoring (i.e., live versus videotaped). This suggests that the BPASS may yield ratings robust enough to counter any bias that may be introduced by the clinician's awareness of family status and that ratings from videotaped interviews yield similar scores to live coding. However, this finding of no differences could reflect a lack of power rather than a true finding of equivalence in ratings across scoring medium.

There are several limitations of this study. First is the difference in gender composition of the groups. None of the parents assessed in the TYP group were male but over half of the MPX parents who were assessed were male. Although both mothers and fathers in all family groups were approached to participate, fewer fathers chose to participate overall and no fathers of typically developing children chose to participate. This gender disparity was addressed statistically by using gender as a covariate in the analysis. Even when gender was controlled, the pattern of BAP elevation in MPX parents relative to the other groups was found. Subsequent analyses conducted only with the mothers in all four groups also yielded similar patterns of elevation among BPASS domain scores in the MPX group relative to the other three groups. Additionally, as discussed, it is possible that the findings of increased BAP traits in MPX families could be the result of increased parent stress due to the demands of raising multiple children with ASD. Future studies should include measure of parenting-related stress and parental psychological distress to investigate and control for these factors. An ideal comparison group would consist of families with multiple children with non-ASD developmental disabilities. Finally, the small sample sizes utilized in the present study are a limitation of this study; replication of these findings with larger samples is needed.

Overall, these findings provide further support that parents from MPX families show a greater number and intensity of specific BAP traits—traits falling in the social and communication domains, relative to parents from SPX, DD, or TYP families and that the BPASS, especially the Social domain, is an effective tool for detecting these BAP differences. Further, the results of the present study are consistent with the notion that the development of ASD in SPX families may more likely be due to a de novo event because BAP traits in SPX parents did not differ from families with children who were developmentally delayed or had typical development.

The use of quantitative measures of autism characteristics may allow more sensitive genetic analyses in future studies. In addition, estimates of the rates of observed milder autism traits in families may be useful in recommending monitoring for mild impairments in siblings who may be helped by intervention for milder difficulties in the domains of social interaction and language.

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Figure 1.
Parent mean BPASS domain scores as a function of family group membership.

Table 1**Child and Parent Characteristics by Group Membership**

Variable (N = # of families)	MPX N=39	SPX N=22	DD N=20	TYP N=20	F or χ^2 (df)	p
Mean # of total children in family (SD)	2.85 (.99)	2.18 (.79)	2.85 (1.6)	2.00** (.79)	4.15	<.01
Ascertained Child (# of children in family with ASD or DD)	N=89	N=22	N=21	N=0		
Age (in months)	126.56 (49.96)	114.64 (9.23)	112.19 (8.95)	119.30 (4.54)	1.15 (3,148)	n.s.
Gender (% female)	19%	9%	38%	5%	9.11 (3)	<.05
Race (% Caucasian)	80%	55%	62%	80%	36.84 (18)	<.05
Full Scale IQ	77.96 (26.34)	78.55 (24.38)	65.71 (21.97)	118.55* (11.19)	20.09 (3,126)	<.05
Parent (# of participants)	N=39	N=22	N=20	N=20		
Age (in months)	498.26 (78.02)	508.09 (61.07)	508.55 (58.67)	514.80 (50.56)	.27 (3,92)	n.s.
Gender (% female)	41%	73%	85%	100%	25.5 (3)	<.001
Race	80%	55%	62%	80%	36.84 (18)	<.05
Parent's Education Level:						
Up to some college	55%	30%	51%	33%	11.2 (11)	n.s.
College degree	39%	50%	44%	66%		
Graduate degree	6%	20%	5%	0%		

MPX = multiplex ASD family; SPX = simplex ASD family; DD = developmental disability, not ASD family; TYP = neurotypical family

* TYP significantly differs from other three groups.

** TYP significantly differs only from MPX group.