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ORIGINAL PAPER

Sex Differences in Toddlers with Autism Spectrum Disorders

Alice S. Carter · David O. Black · Sonia Tewani · Christine E. Connolly · Mary Beth Kadlec · Helen Tager-Flusberg

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Abstract Although autism spectrum disorders (ASD) prevalence is higher in males than females, few studies address sex differences in developmental functioning or clinical manifestations. Participants in this study of sex differences in developmental profiles and clinical symptoms were 22 girls and 68 boys with ASD (mean age = 28 months). All children achieved strongest performance in visual reception and fine motor followed by gross motor and language functioning. Sex differences emerged in developmental profiles. Controlling for language, girls achieved higher visual reception scores than boys; boys attained higher language and motor scores and higher social-competence ratings than girls, particularly when controlling for visual reception. Longitudinal, representative studies are needed to elucidate the developmental and etiological significance of the observed sex differences.

Keywords Autism · Autism spectrum disorder · Sex differences · Toddlers · Developmental profiles

Introduction

Sex differences in both the prevalence and cumulative incidence of individuals with autism spectrum disorders (ASD) have been documented in multiple epidemiological and clinical studies, with estimates ranging from 2.5:1 to 4:1 when comparing prevalence and incidence estimates for males and females (Fombonne, 1999; Honda, Shimizu, Imai, & Nitto, 2005; Lingam et al., 2003; Yeargin-Allsopp et al., 2003). In contrast to the very consistent and robust findings regarding the higher rates of ASD in boys versus girls, only a small number of published studies address sex differences in the cognitive or clinical manifestations of ASD (Lord, Schopler, & Revicki, 1982; McLennan, Lord, & Schopler, 1993; Pilowsky, Yirmiya, Shulman, & Dover, 1998; Tsai & Beisler, 1983; Volkmar, Szatmari, & Sparrow, 1993).

The existing research on sex differences in cognitive and clinical manifestations of autism spectrum behaviors is difficult to synthesize due to significant methodological differences across studies. A major concern is that these studies span several decades, and as a result, different diagnostic criteria have been employed in assigning participants to autism or broader ASD groups. As noted by Lord and Schopler (1985), the use of different criteria for diagnosing ASD complicates interpretation of findings and may contribute to the variability in findings across studies. Notably, the criteria for autism have changed significantly since the introduction of autism to the Diagnostic and Statistical Manual of Mental Disorders in 1980 (Volkmar & Klin, 2005), and it is quite likely that early studies included more severely affected individuals who had not had the opportunity to benefit from advances in intervention approaches. In addition, although some studies have included very young children, (e.g., Pilowsky et al., 1998; Tsai & Beisler, 1983), and Lord et al. (1982) focused on a narrow

A. S. Carter (✉)
Department of Psychology, University of Massachusetts, Boston, 100 Morrissey Boulevard, Boston, MA 02125-3393, USA
e-mail: alice.carter@umb.edu

A. S. Carter · D. O. Black · S. Tewani · C. E. Connolly · M. B. Kadlec · H. Tager-Flusberg
Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, USA

range of preschool-aged children, the majority of studies addressing sex differences in cognitive functioning and clinical manifestations used samples that were comprised of both children and adults with autism. In part due to the wide age range and the variability in individuals with ASD, researchers have employed multiple measures of cognitive functioning within the same sample, increasing measurement error. Finally, studies vary in their use of matching strategies, with some matching on, or including mental and chronological age as covariates. Pilowsky et al. (1998) and Volkmar et al. (1993) argued for the importance of matching boys and girls on cognitive functioning so that sex differences can be attributed to severity of autism rather than to severity of cognitive deficits. In several studies reported to date, a statistically significant sex difference in clinical manifestations of ASD such as social functioning disappears once IQ is included as a covariate (e.g., Volkmar et al., 1993).

One of the earliest and most consistent sex differences reported in the literature was that the ratio of males to females was moderated by IQ, such that the preponderance of females with autism were in the lower end of the IQ distribution, with the most extreme sex differences among high functioning individuals with autism, or individuals in the non-mentally retarded range of intellectual functioning (Bryson, Clark, & Smith, 1988; Volkmar et al., 1993; Wing, 1981). The findings from subsequent studies have corroborated that females evidenced lower IQs than males (Lord et al., 1982) and that mental retardation occurs in higher percentages of girls with autism than in boys with autism (Volkmar et al., 1993), although the magnitude of the differences was not as striking as in Wing's initial report. Lord et al. (1982) noted that girls in their preschool sample were more impaired than the boys on every measure related to cognitive functioning that had been administered, including IQ, the Vineland social quotient, receptive vocabulary, eye-hand integration tasks, and perceptual skills. In addition to studies of clinical samples, population studies of ASD have also reported fewer females than males among higher functioning individuals (Honda et al., 2005; Yeargin-Allsopp et al., 2003).

Findings in other realms of functioning have been less consistently observed. Lord et al. (1982) noted that males had more frequent unusual visual interests than females and less appropriate, more routinized, and stereotypic play even after controlling for differences in IQ. McLennan et al. (1993) examined sex differences in Autism Diagnostic Interview (ADI) items, controlling for IQ by recruiting high functioning participants, defined as IQ > 60, and matching participants on chronological age. They reported that males had more deviant development than females in imitative play and in the subdomain of seeking and offering comfort. However, males only differed on the separation anxiety item within the seeking and offering comfort subdomain. In addition, when parents recalled their children's development prior to age 5, males were rated as more impaired in social interaction and communication. In contrast, when asked about current friendships, females were more impaired than males, with all of the females obtaining a score outside the normal range. Sex differences were not observed on any of the restricted, repetitive, or stereotyped behavior items. Volkmar et al. (1993) examined sex differences on the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984), ratings on the Autism Behavior Checklist (Krug, Arich, & Almond, 1980), and ICD-10 symptoms (World Health Organization, 1990). No sex differences were observed in analyses that included IQ as a covariate. Consistent with this, Pilowsky et al. (1998) found no sex differences in an age and mental age matched sample of 18 males and 18 females on ADI-R (Le Couteur et al., 1989) or Childhood Autism Rating Scale (Schopler, Reichler, & Renner, 1986) items.

Although sex differences in studies of individuals with autism appear to be largely confined to IQ (Volkmar et al., 1993), sex differences in autistic features have been noted in community samples of typically functioning individuals. For example, in a total population study of 7–9-year old children who were assessed by both parent and teacher report on the Autism Spectrum Screening Questionnaire, boys were rated as having more autistic features than girls (Posserud, Lundervold, & Gillberg, 2006). Similarly, in a general population twin study, boys were rated by parents as having more autistic traits than girls on the Social Responsiveness Scale (Constantino & Todd, 2003). Further, when compared to men, women self report higher social functioning on two recently developed measures for use with adults with normal intelligence. These measures, the Empathy Quotient (Baron-Cohen & Wheelwright, 2004) and the Friendship Questionnaire (Baron-Cohen & Wheelwright, 2003), distinguish between individuals with high functioning autism or Asperger's syndrome and typically functioning individuals. Higher empathy has also been observed in younger, typically developing girls than boys (e.g., Zahn-Waxler, Robinson, & Emde, 1992). Further, in a representative sample of children born healthy, girls were rated by parents as having more advanced social-emotional competencies than boys (Carter, Briggs-Gowan, Jones, & Little, 2003). With respect to studies of cognition in very young, typically developing children, there have been no consistent findings favoring either boys or girls (cf., Spelke, 2005).

The goal of the present study was to examine sex differences in toddlers with ASD with respect to profiles of developmental functioning, including verbal, nonverbal, and motor abilities and clinical manifestations of ASD, including social functioning, communication, and repetitive and stereotypical behaviors. A unique aspect of this study is that we included very young children and the age range of participants is relatively homogeneous. To our knowledge, this is the first study of sex differences in this age range. We hypothesized that, consistent with previous studies, girls would evidence lower developmental functioning than boys (verbal and nonverbal abilities). We also explored sex differences in clinical manifestations of ASD, including social and communicative functioning and repetitive stereotypical behaviors. We expected that any observed findings in clinical phenomenology would be mediated fully by observed differences in developmental functioning.

Methods

Ninety children (22 girls and 68 boys) between the ages of 18 and 33 months (M = 28.1 ± 3.9, range = 20–33; boys M = 28.4 ± 3.5, range = 20–33; girls M = 27.1 ± 4.8, range = 20–33) diagnosed with an ASD were included in this study. Children with known genetic disorders, physically handicapping conditions, and neurological diseases were excluded. The sample is comprised of the first 90 children recruited to participate in a longitudinal study of developmental trajectories of neurocognitive and clinical phenomenology in children with ASD and parental well-being. The sample was predominantly white and middle- to upper-class, the mean age of mothers was 32.7 ± 4.6 years (range = 23–55) and most mothers had a minimum of some college education. All of the children met research diagnostic criteria for an ASD on the ADI-R (Lord, Rutter, & Le Couteur, 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000), and the diagnosis was confirmed by expert clinical impression. Means, standard deviations and ranges for the entire sample and for boys and girls separately on the ADI-R and ADOS are presented in Table 1.

Measures

Diagnostic Instruments

The ADI-R (Lord et al., 1994) and ADOS (Lord et al., 2000) were used to confirm diagnosis of an ASD. The ADI-R is a parent/informant interview for the diagnosis of ASD in children from age 18 months into adulthood. The ADOS is a semi-structured observation of children in a controlled setting, which is used to evaluate social and communicative functioning in individuals suspected of having an ASD. There are four developmental modules of the ADOS, only one of which is given to each child, dependent on his or her

Table 1 Diagnostic profile as assessed by ADI-R and Autism Diagnostic Observation Schedule (ADOS)

Measure	All participants				Female				Male				F sex	Partial η^2
	N	*M*	*SD*	Range	*N*	*M*	*SD*	Range	*N*	*M*	*SD*	Range		
ADI-R														
Reciprocal Social Interaction	90	16.6	±4.1	8.0–25.0	22	17.5	±3.9	11.0–23.0	68	16.3	±4.1	8.0–25.0	3.15**	.04
Nonverbal Communication	82	10.8	±2.4	5.0–14.0	21	11.0	±2.6	5.0–14.0	61	10.8	±2.4	5.0–14.0	2.11	.03
Restricted, Repetitive, and Stereotyped Behavior	90	4.4	±2.1	.0–9.0	22	4.1	±2.3	1.0–8.0	68	4.5	±2.0	.0–9.0	.75	<.01
ADOS														
Reciprocal Social Interaction	90	10.5	±2.8	4.0–14.0	22	10.8	±2.6	5.0–14.0	68	10.4	±2.8	4.0–14.0	1.51	.02
Communication	90	4.4	±1.5	2.0–8.0	22	4.8	±1.6	2.0–8.0	68	4.3	±1.5	2.0–7.0	4.47*	.06
Stereotyped Behaviors and Restricted Interests	90	3.9	±1.6	.0–6.0	22	3.8	±1.8	.0–6.0	68	4.0	±1.5	1.0–6.0	.13	<.01

Note: *p < .05; **p < .10; All comparisons were conducted with ANCOVA, covarying age and Mullen Visual Reception standardized raw score language abilities. Children in this study were administered either Module 1 (preverbal or single words; $n = 87$) or Module 2 (phrase speech; $n = 3$). For both the ADOS and ADI-R, continuous scores can be generated in the following 3 symptom areas: communication, reciprocal social interaction, and stereotyped behaviors and restricted interests. For both instruments, a standardized diagnostic algorithm can be calculated, consistent with autism criteria in DSM-IV/ICD-10 and they both have demonstrated reliability and validity and discriminates among individuals with ASD and mental-aged matched non-autistic comparison groups (Lord et al., 1994).

Social Functioning

Level of social functioning was assessed with the Vineland Adaptive Behavior Scales, Interview Edition, Expanded Form (VABS; Sparrow et al., 1984) and the Infant-Toddler Social and Emotional Assessment (ITSEA; Carter et al., 2003). The VABS is a measure of social and personal sufficiency that is administered to the parent and consists of four domains, Communication, Daily Living Skills, Socialization, and Motor Skills, each of which contains multiple subdomains. The VABS also yields a summary score, the Adaptive Behavior Composite. The VABS has adequate psychometric properties, with reliability coefficients ranging from .83 to .99 (Sparrow et al., 1984). It is routinely used in autism research to estimate adaptive functioning.

The ITSEA is a parent report measure of social-emotional and behavioral problems and competencies for infants and toddlers. The measure consists of 169 items in four domains (Internalizing, Externalizing, Dysregulation, and Competence), each with several subdomains, a Maladaptive index, as well as two other indices of behaviors relevant to autism and pervasive developmental disorder (PDD) (Atypical and Social Relatedness). The ITSEA domains have demonstrated acceptable internal consistency (Cronbach's $\alpha = .80$–.90) and test–retest reliability (Intraclass correlation = .82–.90), as well as validity relative to observational measures and other parent-report checklists. Items are rated on the following 3-point scale: (0) *Not true/rarely*, (1) *Somewhat true/sometimes*, and (2) *Very true/often*. A "No opportunity" code allows parents to indicate that they have not had the opportunity to observe certain behaviors (e.g., behavior with peers in daycare). The ITSEA has been nationally standardized (Carter & Briggs-Gowan, 2006) and yields *T* scores for the four broad domains and scaled scores for the subscales within 6 month age by sex groupings, thus providing a means of comparing a child's problems and competencies with same age and sex children. The ITSEA has demonstrated validity in distinguishing children with diagnosed psychiatric conditions and autistic spectrum disorders from age and sex matched controls (Carter & Briggs-Gowan, 2006). Because *t*-scores were not available at the time of submission, standardized raw scores were used in all analyses.

Cognitive and Developmental Functioning

Cognitive and developmental functioning was assessed with the Mullen Scales of Early Learning (Mullen, 1995). The Mullen is a measure of developmental functioning and is administered to children from birth to 68 months. It yields five scales (Fine Motor, Gross Motor, Visual Reception, Expressive Language, and Receptive Language) and an Early Learning Composite, a standard score that aggregates all scales but the Gross Motor Scale. Age equivalent scores from each scale were used to profile developmental functioning. In addition, the Mullen Visual Reception Scale score was used as a measure of nonverbal ability. Means, standard deviations and ranges for the full sample and for boys and girls on the Mullen Scales of Early Learning and the Vineland Adaptive Behavior Scales are presented in Table 2.

Procedures

Following an initial phone screening, families were sent a booklet of questionnaires, which included the ITSEA and questions about socio-demographic status, and two visits were scheduled. One visit involved parent interviews, including the ADI-R and the VABS. The second visit involved direct assessment of the child, including the Mullen and the ADOS.

Data Analytic Plan

Data Reduction

Multiple measures of each of the three of primary dependent variables assessed were gathered: social, language, and motor development. To conserve statistical power and simplify results, composite variables were created and used to assess domain specific developmental functioning. Because of considerable variability in our sample and because of the insensitivity of standard scores among our lower functioning study participants, raw scores for each scale were converted to

Table 2 Cognitive and adaptive functioning as assessed by Mullen and Vineland age equivalents (in months)

Measure	All participants				Male				Female				F sex	Partial η^2
	N	*M*	*SD*	Range	*N*	*M*	*SD*	Range	*N*	M	*SD*	Range		
Mullen														
Receptive Language	89	13.8	±7.0	3.0–36.0	22	12.2	±6.4	6.0–30.0	67	14.3	±7.2	3.0–36.0	.90	.01
Expressive Language	89	15.6	±7.9	3.0–36.0	22	13.3	±6.9	4.0–29.0	67	16.4	±8.1	3.0–36.0	1.74	.02
Visual Reception	89	20.6	±6.0	6.0–46.0	22	21.4	±5.8	10.0–24.0	67	20.3	±6.1	6.0–46.0	1.09	.01
Gross Motor	83	18.5	±3.3	13.0–28.0	22	17.1	±2.9	14.0–28.0	61	19.0	±3.3	13.0–28.0	4.42 *	.05
Fine Motor	89	21.0	±4.0	9.0–30.0	22	19.6	±4.6	10.0–28.0	67	21.4	±3.7	9.0–30.0	3.06**	.03
Vineland														
Communication Domain	88	14.9	±4.8	3.0–29.0	21	13.6	±4.8	3.0–26.0	67	15.3	±4.7	5.0–29.0	4.75 *	.05
Daily Living Skills Domain	88	16.8	±2.6	12.0–23.0	21	16.2	±2.2	13.0–20.0	67	17.0	±2.7	12.0–23.0	1.49	.02
Socialization Domain	88	12.6	±2.9	7.0–19.0	21	12.0	±2.9	7.0–18.0	67	12.8	±3.0	7.0–19.0	3.35 #	.04
Motor Skills Domain	88	21.6	±3.8	12.0–30.0	21	20.4	±3.2	14.0–27.0	67	22.0	±3.9	12.0–30.0	4.77 *	.05

Note: *$p < .05$; **$p < .10$; Mullen comparisons were conducted with ANCOVA, covarying age; Vineland comparisons were conducted with ANCOVA covarying age and the Mullen Visual Reception standardized raw score

standardized *z*-scores (mean = 0; *SD* = 1.0) for the combined sample of boys and girls. Intercorrelations and scatterplots of candidate variables for each composite variable were examined. For all composite variables, the intercorrelations were ≥.4 and inspection of the scatterplots suggested the results were not due to outliers in the data.

A composite measure of general social functioning that was independent of the diagnostic assessment was computed from the mean of the standardized raw scores from the Vineland Socialization Domain, the ITSEA Imitation/Play, Pro-social Peer Relations, and Empathy Subscales, and the ITSEA Social Relatedness Item Cluster. Intercorrelations among the five standardized scales ranged from .40 to .56 and did not appear driven by abnormal distribution in the data. Chronbach's α was .82, which indicates excellent scale inter-reliability.

Language ability was assessed with the VABS Communication Domain and the Mullen Expressive and Receptive scales. The mean of the standardized raw scores from the Receptive and Expressive Language subscales of the Mullen and the Expressive and Receptive Language subdomains of the Communication domain of the VABS was computed to create the language composite. Intercorrelations among the four standardized scales ranged from .61 to .85 and did not appear driven by abnormal distribution of the data. Chronbach's α was .91, which indicates excellent scale internal consistency.

Motor ability was assessed with the Mullen Gross and Fine Motor scales and the VABS Gross and Fine Motor Subdomains from the Motor domain to create a composite measure of general motor ability. The mean of the standardized raw scores from the Fine and Gross Motor subscales of the Mullen and the Fine and Gross motor subdomains of the Motor Skills domain of the VABS was computed to create the motor composite. Intercorrelations among the four standardized scales ranged from .40 to .66 and did not appear driven by abnormal distribution in the data. Chronbach's α was .83, which indicates excellent scale inter-reliability.

Data Analysis

Sex differences were first analyzed by domain using the composite variables described above. To account for individual variation in age and because raw and age-equivalent scores rather than age-adjusted standard scores were used to estimate developmental level, age at testing was included in all models as a covariate. Sex differences in the development of verbal and nonverbal cognitive abilities were assessed using repeated measures ANCOVA with sex as the fixed factor and cognitive domain (language composite versus Mullen Visual Reception standardized raw score) as the repeated factor. A second repeated measures ANCOVA using age equivalent scores (in months) from each of the five Mullen scales (Expressive Language, Receptive Language, Fine Motor, Gross Motor, and Visual Reception) was conducted to provide a clinically accessible analysis of the data. To examine domain specific sex differences and the extent to which sex differences within each domain might be a function of nonverbal level, several hierarchical multiple regressions equations were computed. For each equation, sex, age at assessment, and nonverbal level (Mullen Visual Reception standardized raw score) were entered as predictors. The composite variable for each domain (i.e., language, motor skills, and socialization) served as outcome variables. Part correlations were used to determine the influence of predictors on each outcome variable. Effect size estimates are reported as R-squares calculated from the part correlation. There were no sex by nonverbal level interactions and so interaction effects are not reported in the results.

Three multivariate ANCOVA analyses were run to examine sex differences in clinical symptoms in the following areas estimated by the ADOS (Module 1 only [n = 87]) and ADI: social deficits, communication deficits, and repetitive and stereotypical behaviors. Age and nonverbal level were included as covariates in these analyses.

To evaluate whether observed findings varied as a function of assessment method (direction observation vs. parent report) and to provide effect size estimates on individual measures for future research, sex differences were examined for each of the measures employed to generate the composite scores using analysis of covariance. Age at assessment was entered as the covariate to adjust for differences in chronological age affecting performance on outcome measures. Age equivalent scores from the Mullen and VABS were analyzed because standard scores were insensitive among lower functioning children.

Results

Prior to testing primary hypotheses, boys and girls were compared on several sociodemographic and intervention characteristics to determine the need for possible inclusion in models as covariates. There were no statistically significant child sex differences on any demographic or intervention characteristic, including child and parent age, race, parent education, income, age at diagnosis or duration of early intervention services.

Primary Analyses

Cognitive Level

To test for differences in cognitive abilities between boys and girls, a repeated measures ANCOVA with sex as a fixed factor and cognitive level (2: language composite versus Mullen Visual Reception) as a repeated factor was completed. Results yielded a significant child sex by cognitive ability interaction ($F(1, 86) = 6.54$, $p = .012$, $\eta^2 = .07$) indicating that girls have significantly different cognitive profiles than boys. There was no main effect for sex ($F(1, 86) = .00$, p = n.s.). Main effects for cognitive level are not interpreted because the Mullen Visual Reception scale and the language composite are not on equivalent scales and thus not directly comparable. Inspection of Fig. 1 suggests that boys achieved higher scores on measures of language than girls and girls performed better on a measure of visual reception relative to boys. This interpretation was supported by the results of follow-up ANCOVAs testing for sex differences on Visual Reception while covarying composite language level and age ($F = 5.5$, $p < .05$, Partial $\eta^2_{sex} = .06$) as well as testing for sex differences on composite language level while covarying Visual Reception and age ($F = 5.8$, $p < .05$, Partial $\eta^2_{sex} = .06$). Girls achieved higher scores than boys on visual reception (Adjusted Means = .28, SD = .15 for girls and –.12, SD = .08 for boys). Boys achieved higher scores than girls on the language composite (Adjusted Means = .06, SD = .07 for boys and –.29, SD = .13 for girls).

To further explore this interaction and provide clinically interpretable results, a second repeated measures ANCOVA was conducted with sex as a fixed factor and the five age equivalent subscale scores (reported in months) of the Mullen as a repeated factor (See Fig. 2). Consistent with the initial analysis, results yielded a significant sex by Mullen subscale interaction ($F(4, 320) = 2.43$, $p = .047$, $\eta^2_{sex} = .03$) indicating that girls and boys with ASD evidence different developmental profiles. Follow-up paired comparisons covarying age indicated a significant effect for gross motor skills ($F(1, 86) = 4.42$, $p = .04$) and a trend-level difference for fine motor skills ($F(1,86) = 3.06$, $p = .08$) both favoring boys. There were no sex differences on the language or visual reception subscales (all ps > .05). There was a main effect for Mullen subscale ($F(4, 320) = 4.41$, $p = .002$, $\eta^2_{sex} = .05$). Follow-up paired comparisons indicated that both boys and girls achieved their highest scores on visual

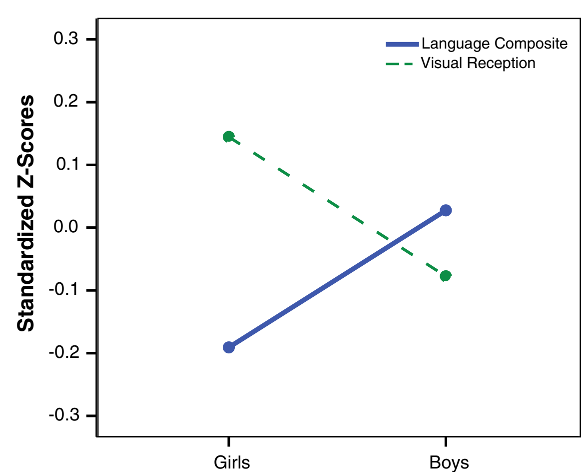

Fig. 1 Differences in language and visual reception by sex

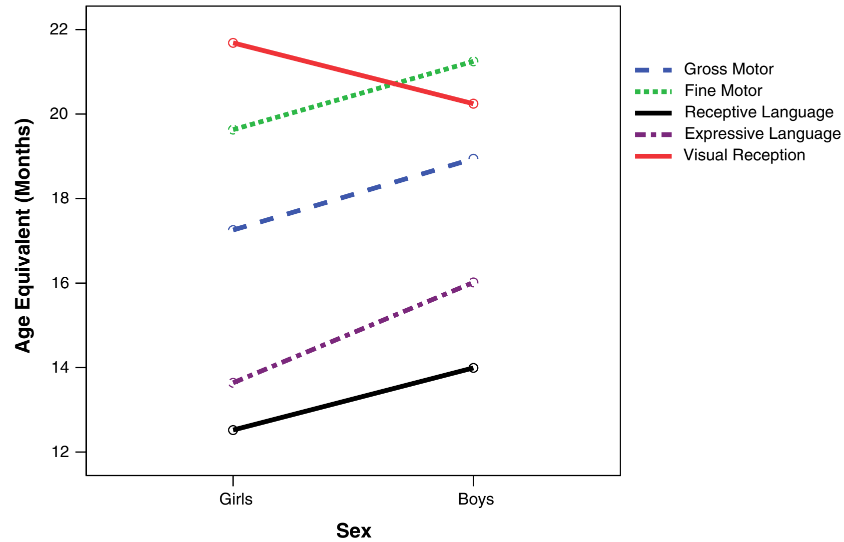

Fig. 2 Differences in age-equivalent Mullen's Scale scores by sex

reception and fine motor skills, (which were not significantly different from one another), followed by gross motor, expressive language, and receptive language. Gross motor, receptive language, and expressive language are significantly different from each other and from visual reception and fine motor skills (all *ps* ≤ .02). There were no main effects for sex ($F(1, 80) = .89$, p = n.s., $\eta^2_{sex} = .01$).

Language

A hierarchical multiple regression model with the language composite as the dependent variable was conducted entering the Mullen visual reception score, age at assessment, and sex as predictors. Results revealed a significant model overall ($F(3, 85) = 34.72$, $p < .001$). After accounting for variance explained by visual reception and chronological age, sex was a significant predictor (see Table 3, Model 1), accounting for nearly 3% of the variance in language level. After controlling for differences in nonverbal abilities, boys demonstrated more developed language skills than girls. Visual reception significantly contributed to this model, accounting for 44% of the variance in the language composite, indicating that better visual reception was associated with better language skills.

Motor Skills

A multiple hierarchical regression model with the motor composite as the dependent variable was conducted entering the Mullen Visual Reception score, age at assessment, and sex as predictors. The overall model was significant ($F(3, 85) = 41.74$, $p < .001$) with sex accounting for 5% of the variance after covarying chronological age and visual reception (Table 3, Model 2). Boys demonstrated significantly better motor skills than girls. Visual reception was also a significant

Table 3 Model summary of sex predicting language levels after accounting for visual reception and mental age

Models	*F*	Exp(B)	*T*	*p*	Part *r*	R^2
Model 1: Language composite						
Mental age		.16	2.12	.037	.15	.02
Visual reception		.68	9.14	<.001	.67	.44
Sex		.18	2.41	.02	.18	.03
Overall model	34.72			<.001		.55
Model 2: Motor composite						
Mental age		.18	2.49	.02	.17	.03
Visual reception		.70	9.84	<.001	.68	.46
Sex		.22	3.09	.003	.32	.10
Overall model	41.74			<.001		.60
Model 3: Social composite						
Mental age		.05	.46	*n.s.*	.01	<.01
Visual reception		.36	3.59	.001	.35	.13
Sex		.22	2.19	.03	.22	.05
Overall model	6.28			.001		.18

predictor, accounting for 46% of the variance in motor skills, indicating that better visual reception predicted better motor skills.

Social Development

The multiple regression model with social development was significant ($F(3, 84) = 6.28$, $p = .001$) with sex accounting for 5% of the variance after accounting for chronological age and visual reception (Table 3, Model 3). Boys were rated by parents as having more advanced social development than girls. Visual reception was a significant predictor, accounting for nearly 13% of the variance.

Clinical Symptoms

Three multivariate ANCOVA analyses were run to examine sex differences in clinical symptoms in the following areas: communication, social reciprocal interaction, stereotyped behaviors and restricted interests. Algorithm scores from both the ADOS (Module 1 only) and ADI were used as dependent variables and age and Mullen Visual Reception standardized raw score were entered as covariates in each model. Results yielded a trend-level sex effect for communication ($F(1,72) = 2.50$, $p = .09$, $\eta^2_{sex} = .07$), suggesting that girls have a somewhat greater communication impairment. As shown in Table 1, ANCOVAs revealed a sex difference on the ADOS but not on the ADI. The multivariate model for sex was not significant either for the socialization or repetitive behavior domains (all Fs < 1.9, all ps > .17). Age was not a significant predictor in any of the models (all Fs < 2.2, all ps > .1). Visual reception was a significant predictor in all three models: communication: $F(1, 73) = 11.27$, $p < .001$, $\eta^2_{sex} = .24$; social: $F(1, 80) = 11.08$, $p < .001$, $\eta^2_{sex} = .22$; and stereotyped behaviors and restricted interests: $F(1, 80) = 3.87$, $p = .03$, $\eta^2_{sex} = .09$.

Vineland Adaptive Behavior Scales (VABS)

ANCOVA analyses were employed to examine sex differences in age equivalent scores on each domain of the VABS. Mullen Visual Reception and child age were covaried. For domains that varied significantly across boys and girls, ANCOVA analyses for subdomains were examined. As shown in Table 2, there were significant sex differences in the Communication and Motor domains and a trend level difference in the Motor Domain. In each case, boys were described as having more advanced skills than girls. Within the Communication domain, boys were described as having significantly stronger expressive language skills ($F_{sex} = 4.2$; $p < .05$; $\eta^2 = .05$; $M = 12.3$, $SD = 4.2$ for girls; $M = 13.8$, $SD = 4.9$ for boys) and there was a trend for boys to have more advanced receptive language skills ($F_{sex} = 2.8$; $p < .10$; $\eta^2 = .03$; $M = 15.5$, $SD = 7.0$ for girls; $M = 18.0$, $SD = 7.8$ for boys). Within the Motor domain, boys were rated as having more advanced gross motor skills than girls ($F_{sex} = 6.0$; $p < .05$; $\eta^2 = .07$; $M = 20.5$, $SD = 3.1$ for girls; $M = 22.5$, $SD = 3.7$ for boys), but there were no differences in fine motor skills.

Infant-Toddler Social and Emotional Assessment (ITSEA)

ANCOVAs with sex as the fixed factor and age and Mullen Visual Reception as covariates were employed to examine sex differences on each domain and the item clusters of the ITSEA (See Table 4). The percentage of girls and boys above the clinical cut-point were compared using cross tabs and phi reported as a measure of effect size. For domains with significant differences, sex effects in scales within domains were also explored with similar statistics.

There were no sex differences in any of the ITSEA problem domains, Internalizing, Externalizing or

Table 4 Infant-Toddler Social and Emotional Assessment (ITSEA) standardized scores

Measure	All participants				Female				Male				F sex	Partial η^2
	N	*M*	*SD*	Range	*N*	M	*SD*	Range	*N*	*M*	*SD*	Range		
Externalizing domain	89	.49	±.31	.03–1.46	21	.48	±.24	.03–.89	68	.50	±.33	.03–1.46	.12	.00
Internalizing domain	89	.58	±.24	.03–1.14	21	.63	±.24	.03–.97	68	.56	±.24	.19–1.14	2.04	.03
Dysregulation domain	89	.67	±.33	.06–1.57	21	.66	±.23	.32–1.07	68	.68	±.35	.06–1.57	.03	.00
Competence domain	89	.73	±.26	.28–1.54	21	.62	±.24	.28–.96	68	.76	±.26	.29–1.54	5.56*	.06
Maladaptive Item cluster	88	.17	±.18	.00–.77	21	.17	±.22	.00–.77	67	.17	±.17	.00–.77	.39	<.01
Social relatedness Item cluster	88	1.19	±.32	.10–1.90	21	1.12	±.29	.60–1.50	67	1.21	±.33	.10–1.90	1.23	.01
Atypical Item cluster	88	.88	±.32	.00–1.63	21	.97	±.24	.50–1.38	67	.85	±.33	.00–1.63	2.90**	.03

Note: *$p < .05$; **$p < .10$; All comparisons were conducted with ANCOVA, covarying age and Mullen Visual Reception standardized raw score

Dysregulation (all $Fs_{sex} < 2.05$; all ps = n.s.). In contrast, girls were rated as having lower Competence than boys. There was also a trend for a sex difference in the number of children with Competence scores below the cut-point (phi = .20, $p < .10$), with 100% of girls and 85% of boys scoring below the cut-point. Within the scales that comprise the Competence domain there were significant differences between girls' and boys' mean scores in Empathy ($F_{sex} = 8.2$; $p < .05$; $\eta^2 = .09$; $M = .08$, $SD = .10$ for girls; $M = .33$, $SD = .37$ for boys) and Mastery Motivation ($F_{sex} = 4.2$; $p < .05$; $\eta^2 = .05$; $M = .96$, $SD = .57$ for girls; $M = 1.14$, $SD = .40$ for boys), both indicating that girls were rated as having lower competence than boys. Further, on Empathy there were more girls than boys below the cut-point (phi = .22, $p < .05$; 100% vs. 82%, respectively). Girls and boys did not differ in the percentage below the cut-point on Mastery Motivation (66% vs. 67%, respectively).

With respect to Item Clusters, there were trends for girls to have higher mean scores on the Atypical Item Cluster ($F_{sex} = 2.90$; $p < .10$; $\eta^2 = .03$; $M = .98$, $SD = .07$ for girls; $M = .85$, $SD = .04$ for boys) and for girls to exceed the cut-point as compared to boys (phi = .21, $p < .10$; 85.7% vs. 63.2%, respectively). For the Social Relatedness Item Cluster, there were no differences in mean scores ($F_{sex} = 1.23$; p = n.s.), but there was a trend-level difference placing more girls than boys below the cut-point (66.2%; phi = .18, $p < .05$; 85.7% vs. 66.2%, respectively). There was also a trend level difference in means for the Depression/Withdrawal scale ($F_{sex} = 3.4$; $p < .10$; $\eta^2 = .04$; $M = .44$, $SD = .23$ for girls; $M = .37$, $SD = .22$ for boys), suggesting that girls evidenced more depression and/or social withdrawal than boys. There were no differences in the percentage of girls and boys above the cut-point on this scale (phi = .15, p = n.s.; 81% vs. 65%, respectively).

Discussion

Consistent with previous work (Joseph, Tager-Flusberg, & Lord, 2002; Lincoln, Allen, & Kilman, 1995), boys and girls evidenced a relative strength in visual reception and fine motor skills as compared with gross motor skills and expressive and receptive language, with language emerging as the weakest domain of developmental functioning. In contrast to these expected patterns, our hypothesis that girls would evidence poorer performance in all aspects of developmental functioning was not supported. The findings revealed a statistically significant interaction between child sex and cognitive domain (verbal versus nonverbal) and child sex and the 5 Mullen Scales of Early Learning (Visual Reception, Fine Motor, Expressive Language, Receptive Language, and Gross Motor), indicating that girls and boys with ASD show different cognitive and developmental profiles. Consistent with the expectation that boys would show more advanced development, boys evidenced stronger verbal and motor skills, particularly once differences in visual reception were covaried. Controlling for language level, girls evidenced significantly stronger skills in visual reception, or the nonverbal problem solving domain. In addition, boys were described as having more advanced social functioning than girls. Although the present sample is one of convenience, recruited from early intervention programs serving children with developmental delay and ASD, the expected 3:1 ratio of males to females was observed.

The findings of differences in developmental profiles between boys and girls are in marked contrast to previous literature in older children and adults with ASD indicating that males consistently exhibit superior performance when compared to females in all domains of cognitive functioning assessed (Lord et al., 1982; Volkmar et al., 1993). Moreover, nonverbal reasoning, as assessed by the Visual Reception scale of the Mullen, appears to play a very important role in early development. While sex and nonverbal reasoning did not interact in predicting performance on composite measures of language, motor, or social abilities, nonverbal reasoning was the most significant predictor in each of these models, accounting for 13–46% of the variance explained. Especially when compared to variance explained by age (0–3%) and sex (3–10%), these findings make it clear that nonverbal reasoning is a critical factor in multiple domains of functioning for young children with ASD.

The finding that girls had more impaired gross motor functioning than boys based on both parental reports and direct assessments may be viewed as consistent with an early report by Tsai and Beisler (1983), who also reported that boys tended to develop better physical skills than girls upon direct assessment. In addition, Tsai, Stewart, and August (1981) reported that abnormal movements such as dystonic posturing of hands and fingers and hand flapping were more common in girls than boys. However, it is important to note that sex differences in repetitive and stereotypical movements were not observed in this sample, which is where many of the abnormal movements noted by Tsai et al. (1981) would now be classified. The difference in study findings may be due in part to the very young age of the current participants, as contrasted with those in the Tsai et al. (1981) study, as some repetitive and stereotypical movements may emerge later in development.

It is important to note that consistent with previous work with older children and adults, very young boys and girls did not differ with respect to clinical manifestations of autism. Thus, the subtle differences in developmental profiles that were observed do not appear to be associated with clinical symptomatology but appear to be restricted to aspects of developmental functioning. Multivariate analyses of autism symptoms (social, communication, and repetitive and stereotyped behaviors) based on Module 1 ADOS and ADI scores were non-significant and only the ADOS Communication algorithm score indicated a significant sex difference (favoring boys who had lower domain scores). This finding on the ADOS Communication score may be best explained by boys' superior performance relative to girls on language functioning and the restriction of analyses to children who were administered Module 1 of the ADOS, which may emphasize limitations in normative communication relative to atypical communication. Communication algorithm items from the Module 1 ADOS that occur in typical language development include the following: directed vocalizations, pointing, and use of gestures; other items reflecting atypical development are use of stereotyped/idiosyncratic words and phrases and use other's body to communicate.

Of interest, in contrast to findings in typically developing children in which parents rate girls as having higher competence than boys (Carter et al., 2003), parents rated girls with ASD as having lower competence than boys with ASD, particularly with respect to empathy. Given that differences in social functioning were not observed on the ADOS, it is possible that mothers have higher expectations of their girls' social-emotional competence relative to boys' and therefore employ a higher threshold that results in comparable behaviors being rated as reflecting greater deficits among girls relative to boys. It is also possible that mothers are attending to subtle aspects of social behavior in the home that is captured on the ITSEA but not observed during the child's responses to the social presses of the ADOS.

A strength of the measurement approach employed in this study was the multi-method assessment of constructs of interest. For the motor domain, a consistent pattern of boys evidencing more advanced skills was observed across both parent report and direct assessment methods. In contrast, for the social and language domains, significant sex differences were only observed in parent reports whereas no significant sex differences emerged on direct assessments. Unfortunately, it was not possible to evaluate non-verbal reasoning using both parent and direct assessment methods.

This study had sufficient power to observe small to medium effect sizes, participants across a very narrow age range were included, and the same developmental assessment instrument was administered to all participants. Nevertheless, a major limitation of this study is the lack of a representative sampling frame. Thus, it is not clear whether the current findings, which are discrepant from previous work, can be attributed to the relatively young age of the sample or something unusual about this particular sample of very young toddlers. Another possible confound is that many of the children included in this report had been exposed to some early intervention, although the majority of children had been diagnosed within the past 3 months and had just begun to receive appropriate intervention services within the past 2 months. Interpretation is somewhat constrained by this methodological limitation, and there is a need for additional studies with representative samples to replicate these findings.

The preponderance of males relative to females among individuals with autism and previous findings suggesting that girls are more impaired than boys has been used to hypothesize about possible modes of familial transmission. Specifically, it has been argued that as compared to boys, girls require a higher threshold or dose of genetic vulnerability to result in an affected phenotype (Tsai et al., 1981). This model predicts that girls would therefore be affected less often, but when affected, would exhibit more severe impairments. This model is not supported by the current findings and has not received support from large epidemiological studies (e.g., Pickles et al., 1995; Szatmari et al., 2000). More recently, Stone et al. (2004) investigated genetic aspects of the sex bias in the prevalence of ASD by examining changes in linkage patterns when families were subdivided on the basis of the sex of the proband. The results indicated that stratifying families based on proband sex produced a highly significant enhancement of the linkage scan data, with one male-specific region of linkage identified on chromosome 17q11. Thus, the sex differences in developmental functioning observed in this study may reflect different underlying genetic mechanisms for boys and girls, or for subsets of boys and girls. It is also possible that hormonal influences or differences in the development of male and female brains moderate shared genetic influences (Baron-Cohen, Knickmeyer, & Belmonte, 2005). Ideally, longitudinal studies with larger representative samples of boys and girls that can subtype children on the basis of both phenotypic and genotypic presentation will lead to a more refined understanding of the development of sex differences in neurocognitive profiles and begin to address the mechanisms that contribute to these differences.

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References

Baron-Cohen, S., Knickmeyer, R. C., & Belmonte, M. K. (2005). Sex differences in the brain: Implications for explaining autism. *Science, 310*(5749), 819–823.

Baron-Cohen, S., & Wheelwright, S. (2003). The friendship questionnaire: An investigation of adults with Asperger Syndrome or High-Functioning Autism, and normal sex differences. *Journal of Autism and Developmental Disorders, 33*(5), 509–517.

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: An investigation of adults with Asperger Syndrome or High-Functioning Autism, and normal sex differences. *Journal of Autism and Developmental Disorders, 34*(2), 163–175.

Bryson, S. E., Clark, B. S., & Smith, I. (1988). First report of a Canadian epidemiological study of autistic syndromes. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 29*, 433–446.

Carter, A. S., & Briggs-Gowan, M. J. (2006). *Manual for the Infant-Toddler Social & Emotional Assessment (ITSEA)—Version 2*. San Antonio, Texas: Psychological Corporation, Harcourt Press.

Carter, A. S., Briggs-Gowan, M. J., Jones, S. M., & Little, T. D. (2003). The Infant-Toddler Social and Emotional Assessment (ITSEA): Factor structure, reliability, and validity. *Journal of Abnormal Child Psychology, 31*(5), 495–514.

Constantino, J. N., & Todd, R. D. (2003). Autistic traits in the general population: A twin study. *Archives of General Psychiatry, 60*, 524–530.

Fombonne, E. (1999). The epidemiology of autism: A review. *Psychological Medicine, 29*(4), 769–786.

Honda, H., Shimizu, Y., Imai, M., & Nitto, Y. (2005). Cumulative incidence of childhood autism: A total population study of better accuracy and precision. *Developmental Medicine and Child Neurology, 47*, 10–18.

Joseph, R. M., Tager-Flusberg, H., & Lord, C. (2002). Cognitive profiles and social-communicative functioning in children with autism spectrum disorder. *Journal of Child Psychology and Psychiatry, 43*(6), 807–821.

Krug, D. A., Arich, J., & Almond, P. (1980). Behavior checklist for identifying severely handicapped individuals with high levels of autistic behavior. *Journal of Child Psychology and Psychiatry, 21*, 221–229.

Le Couteur, A., Rutter, M., Lord, C., Rios, P., Robertson, S., Holdgrafer, M., & McLennan, J. D. (1989) Autism diagnostic interview: A semistructured interview for parents and caregivers of autisitic persons. *Journal of Autism and Developmental Disorders, 19*, 363–387.

Lincoln, A. J., Allen, M., & Kilman, A. (1995). The assessment and interpretation of intellectual abilities in people with autism. In E. Schopler, & G. Mesibov (Eds.), *Learning and cognition in autism* (pp. 89–117). New York: Plenum.

Lingam, R., Simmons, A., Andrews, N., Miller, E., Stowe, J., & Taylor, B. (2003). Prevalence of autism and parentally reported triggers in a north east London population. *Archives of Disease in Childhood, 88*, 666–670.

Lord, C., Risi, S., Lambrecht, L., Cook, E., Leventhal, B., DiLavore, P. 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., & Le Couteur, A. (1994). Autism diagnostic interview—revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*, 659–685.

Lord, C., & Schopler, E. (1985). Differences in sex ratios in autism as a function of measured intelligence. *Journal of Autism and Developmental Disorders, 15*, 185–193.

Lord, C., Schopler, E., & Revicki, D. (1982). Sex differences in autism. *Journal of Autism and Developmental Disorders, 12*(4), 317–330.

McLennan, J. D., Lord, C., & Schopler, E. (1993). Sex differences in higher functioning people with autism. *Journal of Autism and Developmental Disorders, 23*(2), 217–227.

Mullen, E. M. (1995). *Mullen scales of early learning*. Circle Pines, MN: American Guidance Service, Inc.

Pickles, A., Bolton, P., MacDonald, H., Le Couteur, A., Sim, C. H., & Rutter, M. (1995). Latent-class analysis of recurrence risk for complex phenotypes with selection and measurement error: A twin and family history study of autism. *American Journal of Human Genetics, 57*, 717–726.

Pilowsky, T., Yirmiya, N., Shulman, C., & Dover, R. (1998). The autism diagnostic interview-revised and the childhood autism rating Scale: Differences between diagnostic systems and comparison between genders. *Journal of Autism and Developmental Disorders, 28*(2), 143–151.

Posserud, M., Lundervold, A. J., & Gillberg, C. (2006). Autistic features in a total population of 7–9-year-old children assessed by the ASSQ (Autism Spectrum Screening Questionnaire). *Journal of Child Psychology and Psychiatry, 47*(2), 167–175.

Schopler, E., Reichler, R., & Renner, B. R. (1986). *The Childhood Autism Rating Scales (CARS) for diagnostic screening and classification of autism*. New York: Irvington.

Sparrow, S. S., Balla, D. A., & Cicchetti, D. V. (1984). *Vineland Adaptive Behavior Scales*. Circle Pines, MN: American Guidance Service, Inc.

Spelke, E. S. (2005). Sex differences in intrinsic aptitude for mathematics and science? A critical review. *American Psychologist, 60*(9), 950–958.

Stone, J. L., Merriman, B., Cantor, R. M., Yonan, A. L., Gilliam, T. C., Geschwind, D. H. et al. (2004). Evidence for sex-specific risk alleles in autism spectrum disorder. *American Journal of Human Genetics, 75*, 1117–1123.

Szatmari, P., MacLean, J. E., Jones, M. B., Bryson, S. E., Zwaigenbaum, L., Bartolucci, G., Mahoney, W. J., & Tuff, L. (2000). The familial aggregation of the lesser variant in biological and nonbiological relatives of PDD probands: A family history study. *Journal of Child Psychology and Psychiatry, 41*(5), 579–586.

Tsai, L. Y., & Beisler, J. M. (1983). The development of sex differences in infantile autism. *British Journal of Psychiatry, 142*, 373–378.

Tsai, L., Stewart, M. A., & August, G. (1981). Implication of sex differences in the familial transmission of infantile autism. *Journal of Autism and Developmental Disorders, 11*(2) 165–173.

Volkmar, F. R., & Klin, A. (2005). Issues in the classification of autism and related conditions. In F. R. Volkmar, R. Paul, A. Klin, & D. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders, Vol. 1: Diagnosis, development,* *neurobiology, and behavior* (3rd Ed., pp. 5–41). Hoboken, NJ: John Wiley & Sons, Inc.

Volkmar, F. R., Szatmari, P., & Sparrow, S. S. (1993). Sex differences in pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 23*(4), 579–591.

Wing, L. (1981). Sex ratios in early childhood autism and related conditions. *Psychiatric Research, 5*, 129–137.

World Health Organization. (1990). *International classification of diseases (10th rev.); Criteria for research*. Geneva, Switzerland: Author.

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

Zahn-Waxler, C., Robinson, J. L., & Emde, R. N. (1992). The development of empathy in twins. *Developmental Psychology, 28*, 1038–1047.