J Autism Dev Disord (2012) 42:409–418
DOI 10.1007/s10803-011-1263-4

ORGINAL PAPER

# Neurocognitive and Behavioral Outcomes of Younger Siblings of Children with Autism Spectrum Disorder at Age Five

**Zachary E. Warren · Jennifer H. Foss-Feig · Elizabeth E. Malesa · Evon Batey Lee · Julie Lounds Taylor · Cassandra R. Newsom · Julie Crittendon · Wendy L. Stone**

Published online: 26 April 2011


**Abstract** Later-born siblings of children with Autism Spectrum Disorders (ASD) are at increased risk for ASD as well as qualitatively similar traits not meeting clinical cutoffs for the disorder. This study examined age five neurocognitive and behavioral outcomes of 39 younger siblings of children with ASD (Sibs-ASD) and 22 younger siblings of typically developing children (Sibs-TD) previously assessed in a longitudinal investigation starting in the second year of life. There were few group differences between Sibs-TD and Sibs-ASD on global measures of IQ, language, or behavior problems. Sibs-ASD did show vulnerabilities on measures of executive functioning, social cognition, and repetitive behaviors. These results highlight the importance of following sibling risk groups over an extended time period and employing measures targeting broader aspects of development.

**Keywords** Autism · Siblings · Cognition · Language · Behavior · Broad autism phenotype

Z. E. Warren (✉) · E. B. Lee · J. L. Taylor · C. R. Newsom · J. Crittendon
Department of Pediatrics, Vanderbilt Kennedy Center/TRIAD, Vanderbilt University, PMB 74, 230 Appleton Pl, Nashville, TN 37203, USA
e-mail: zachary.warren@vanderbilt.edu

Z. E. Warren · E. B. Lee · C. R. Newsom · J. Crittendon
Department of Psychiatry, Vanderbilt Kennedy Center/TRIAD, Vanderbilt University, PMB 74, 230 Appleton Pl, Nashville, TN 37203, USA

J. H. Foss-Feig · E. E. Malesa · E. B. Lee
Department of Psychology and Human Development, Vanderbilt Kennedy Center/TRIAD, Vanderbilt University, PMB 74, 230 Appleton Pl, Nashville, TN 37203, USA

J. L. Taylor
Department of Special Education, Vanderbilt Kennedy Center/TRIAD, Vanderbilt University, PMB 74, 230 Appleton Pl, Nashville, TN 37203, USA

W. L. Stone
Department of Psychology, University of Washington, Seattle, WA, USA

## Introduction

Autism Spectrum Disorders (ASD) are considered among the most heritable of neurodevelopmental disorders. While the prevalence of ASD in the general population is close to 1% (Centers for Disease Control and Prevention 2009), the recurrence risk for later-born siblings of children with ASD (Sibs-ASD) is close to 20% (Rogers 2009; Yirmiya and Charman 2010; Zwaigenbaum et al. 2009). This elevated genetic liability has led to increased interest in the prospective study of Sibs-ASD as an efficient approach for identifying early markers for the disorder. A wide range of developmental differences has been documented between Sibs-ASD and later-born siblings of children without a family history of ASD (Sibs-TD) in the first years of life. Identified vulnerabilities have been found in cognitive skills, motor development, sensory functioning, attention, perception, social communication, and play (Rogers 2009; Stone et al. 2007). Despite the frequency with which early group differences are identified, the predictive utility of these differences as they might relate to ultimate ASD diagnosis has yet to be adequately demonstrated and replicated within and across samples (Rogers 2009; Yirmiya and Charman 2010; Zwaigenbaum et al. 2009).

Neurodevelopmental theories of ASD risk and early brain plasticity posit that early differences in core cognitive, socioemotional (e.g., joint attention, affect sharing),

and behavioral skills may lead to either atypical trajectories associated with a range of maladaptive outcomes, or trajectories wherein early differences are overcome with maturation and experience (Dawson et al. 2000; Dawson 2008; Mundy and Crowson 1997; Mundy and Neal 2001). In this regard, despite a literature suggesting the impact of early differences, there is emerging evidence that some early behavioral differences between sibling groups may not necessarily predict diagnostic outcomes in Sibs-ASD. For example, increased focus on mouth during facial viewing tasks differentiated Sibs-ASD from Sibs-TD in infancy, yet higher levels of this behavior were not associated with a later diagnosis of autism (Merin et al. 2007; Young et al. 2009). Most sibling research to date has highlighted early differences without reference to later outcomes (see Yirmiya and Charman 2010). Only one group to date has reported on the developmental outcome of Sibs-ASD beyond four years of age. Gamliel et al. (2007, 2009) reported that by approximately 54 months of age, early differences in cognitive abilities were no longer present for Sibs-ASD (Gamliel et al. 2007). However, at seven years of age, differences were noted between sibling groups with increased numbers of Sibs-ASD exhibiting cognitive, language, or academic difficulties relative to Sibs-TD (Gamliel et al. 2009). In contrast to the Sibs-ASD group, which was characterized by fluctuation in skills across development, children from the Sibs-TD group showed more consistency in their development, in that those who exhibited early differences in language continued to exhibit language difficulties at both follow-up assessments. This discrepant course of development between the sibling groups—as made evident when followed to older ages—suggests that limiting our observations to the first years of life is a suboptimal approach to adequately characterizing Sibs-ASD. In particular, one possibility may be that Sibs-ASD manifest subtle early vulnerabilities that may be less apparent in the preschool years, but become more prominent at the start of school age or later due to increased psychosocial and academic demands.

Beyond targeting Sibs-ASD to better understand the development of ASD itself, increasingly researchers are examining 'subclinical' concerns related to ASD, as well as other potential neurocognitive and behavioral vulnerabilities in this genetically at-risk population. In part, such researchers are attempting to better understand and define concerns related to a conceptualized broader autism phenotype (BAP), which may represent the manifestation of traits qualitatively similar to those seen in autism but not meeting clinical threshold for the disorder. Although this term is controversial and still without a widely agreed upon definition within child populations, preliminary work in this area suggests that Sibs-ASD show patterns of vulnerability related to language, cognition, and social interaction relative to Sibs-TD (Gamliel et al. 2007, 2009; Sullivan et al. 2007; Toth et al. 2007), consistent with findings in adolescent and adult family members of individuals with ASD (Constantino et al. 2006; Piven and Palmer 1999). Assessment of broader neurocognitive and behavioral outcomes in sibling groups is likely to shed light on the variable expression of autism specific concerns, as well as other potential related vulnerabilities, in those Sibs-ASD not meeting full clinical criteria for an ASD diagnosis themselves.

Thus, there is much still to be learned about the significance of early differences between Sibs-ASD and Sibs-TD in terms of both their stability over time and their import for diagnostic outcomes. As yet, there is no index or combination of indices that reliably predicts individual diagnostic outcomes or clinically significant areas of concern over time. Further, the meaning of early group differences that do not carry risk for later developmental or behavioral concern is not yet fully understood (Rogers 2009). High-risk sibling studies afford researchers a unique opportunity to address these issues when expanded in several ways. First, additional prospective research over a more prolonged time frame (i.e., to the start of school age through adolescence/young adulthood) is necessary for clarifying the stability of early-observed differences. Second, the inclusion of standardized measures of broader neurodevelopmental and behavioral outcomes is indicated to capture more subtle vulnerabilities that might manifest in Sibs-ASD. Adding these components to longitudinal sibling studies may lead to better understanding of whether early differences or broader variants of ASD expression in younger siblings of children with ASD translate into clinically meaningful differences for this population over time.

The present study poses a unique contribution to the existing literature in several ways. First, we extended our follow-up of a high-risk ASD sibling sample to the start of school age (i.e., age 5). Specifically, our study assessed school-age outcome in a group of Sibs-ASD and chronological age-matched Sibs-TD whose early social and communication development was previously followed longitudinally over a period of 18 months starting in the second year of life (see Yoder et al. 2009). Ongoing work with this sample utilizing a longitudinal approach (i.e., relating early differences in social communication skills to later cognitive and behavioral vulnerabilities) has suggested that initial early joint attention skills may be equally predictive of language and social skills at age five in both Sibs-ASD and Sibs-TD groups (Malesa et al. under review). Further, despite often obtaining lower scores on joint attention measures at younger ages, the Sibs-ASD sample performed similarly to the Sibs-TD sample on gross measures of language and social skills assessed at age five.

Such work demonstrating equivalent abilities despite early differences in related skills (Stone et al. 2007) leaves remaining questions as to the nature and import of neurodevelopmental differences in Sibs-ASD samples over time. To this end, we incorporated broad assessments at follow-up selected to capture an array of potential neurocognitive and behavioral concerns that may reflect areas of vulnerability for siblings of children with ASD and could be examined in relation to early differences in further investigations. In addition to assessing autism-specific symptom profiles and employing global measures of cognition and language, we included neuropsychological measures of executive functioning, continuous measures of social communication development, and measures of additional behavioral and psychiatric comorbidities in order to obtain a rich assessment of subtle, broader difficulties potentially related to ASD. We hypothesized that Sibs-ASD would show a range of deficits relative to Sibs-TD across measures, given that these same children showed differences between groups in infancy (Presmanes et al. 2007; Stone et al. 2007), and that family members of individuals with ASD often show a broad range of differences across social, language, executive functioning, and psychiatric domains.

## Method

### Participants

Later-born siblings of children with ASD (Sibs-ASD; $n = 54$) and typically developing children (Sibs-TD; $n = 31$) who participated in a longitudinal investigation of early joint attention and social orienting were invited to return for a follow-up visit at approximately five years of age (see Yoder et al. 2009 for original recruitment and eligibility criteria). Although participants had provided consent for potential contact in the future, this follow-up visit had not formally been incorporated into the original study's longitudinal methodology and design. As such, no research contact for this study took place in the 18–30 months between the end of the original study and the follow-up (i.e., contact information was not updated and systems for retention were not employed in this interval). Of the 85 families eligible for participation, 61 (71.8%) completed the follow-up visit: 39 Sibs-ASD (22 [56.4%] male) and 22 Sibs-TD (14 [63.6%] male). Gender composition did not differ between groups, $\chi^2(1, N = 61) = .30$, $p = .39$. Further, despite some variability in age at entry, mean age did not differ between groups (Sibs-ASD: M = 63.38 months, SD = 8.28, Range = 50–88 months; Sibs-TD: M = 64.32 months, SD = 4.05, Range = 60–76 months; $t(59) = -.50$, $p = .56$).

Of the remaining 24 children (15 Sibs-ASD, 9 Sibs-TD) lost to attrition, 4 families could not be located due to changed address and phone number, 8 moved out of state and were unable to return for an in-person visit, 2 were scheduled but failed to show up for their visit and could not be contacted subsequently, and 10 declined to participate. Analyses conducted to assess for differential attrition (i.e., returners vs. non-returners) found no differences related to child gender, race, IQ at any time point measured, or final diagnosis at original study outcome. Only two group differences between returners and non-returners were significant: greater number of original study visits completed for returners ($\chi^2 = 14.76$, $p = .01$) and higher levels of maternal education for the returning group ($\chi^2 = 10.99$, $p = .03$). Differences between returners and non-returners were also examined separately for both Sibs-ASD and Sibs-TD. Only number of visits completed differed between returning and non-returning Sibs-ASD. Among Sibs-TD, no differences were found between returners and non-returners.

### Procedure

Families who participated in the original study were contacted via mail and phone, in proximity to the target child's fifth birthday. Informed consent was obtained from parents before initiating any research procedures. Parents completed questionnaires and children participated in a single three to four hour clinical assessment session, which included diagnostic assessment of ASD symptoms as well as administration of outcome measures described below. For children attending school, packets of teacher questionnaires were mailed directly to their teachers.

### Measures

A variety of cognitive, neuropsychological, language, social, and behavioral assessments were completed at follow-up in addition to autism diagnostic measures:

#### Cognitive and Executive Functioning

*Differential Ability Scales—Second Edition* (DAS-II; Elliott, 2007). The DAS-II is a widely used, individually administered measure of cognitive ability that takes 30-45 min to complete. The DAS-II provides standard scores for overall ability (Global Conceptual Ability [GCA]), in addition to standard scores for the Verbal, Nonverbal, and Spatial domains. All standard scores have a mean of 100 and a standard deviation of 15.

*NEPSY-II (Korkman* et al. 2007*).* The Executive Functioning subtests from the neuropsychological assessment system for children were used to assess this area of

cognitive ability. The Design Fluency, Auditory Attention, Inhibition (Naming and Inhibition conditions), and Statue subtests were administered to all children above age five years. Children under five did not receive the Inhibition or Auditory Attention tasks per NEPSY-II age specifications. The NEPSY-II does not provide an executive functioning composite; thus, aggregate (i.e., average) scores were created, contingent upon significant correlations among component subtests. Based on this criterion, an Executive Functioning (EF) Composite was derived from the Auditory Attention, Statue, Inhibition-Naming, and Inhibition-Inhibition subtests, since all were significantly correlated, $rs > .39$, $ps < .01$. The Design Fluency subtest score was not correlated with scores from the other four subtests in this sample and thus was not included in the EF composite for analysis. The EF composite and individual subtests yield scaled scores with a mean of 10 and a standard deviation of 3.

### Language Functioning

*Clinical Evaluation of Language Fundamentals- Preschool* (CELF-P; Wiig et al. 2004); *CELF—Fourth Edition* (CELF-4; Semel et al. 2003). The CELF is an individually administered test intended to assess performance in aspects of language that are fundamental to the development of effective communication skills (e.g., semantics, morphology, syntax, and auditory memory). The CELF-P was administered to children who were between four and six years old ($n = 57$), and the CELF-4 was administered to those children who were seven or older ($n = 2$). The CELF provides a Core Language Score (CLS), a Receptive Language Index (RLI), and an Expressive Language Index (ELI) score, all with a mean of 100 and a standard deviation of 15.

*Children's Communication Checklist-2 for Parents* (CCC-2; US Edition, Bishop 2006). The CCC-2 is a 70-item, norm-referenced, parent-completed questionnaire assessing language competence in a variety of domains. The version used in this study is standardized for children four to seven years of age. The CCC-2 provides a General Communication Composite (GCC) score (mean = 100; SD = 15), as well as individual scores for nine subscales.

### ASD-related Symptoms

*Autism Diagnostic Observation Schedule* (ADOS; Lord et al. 2000). The ADOS is a semi-structured, standardized assessment of communication, social interaction, and play or imaginative use of materials. It was designed for use with individuals for whom there are concerns about possible autism spectrum disorders. The ADOS consists of four modules, with the specific module administered dependent upon the expressive language level and chronological age of the person to whom it is given. All children included in this sample were administered Module 3, which is designed for individuals with fluent speech. The revised ADOS algorithms (Gotham et al. 2007) yield Social Affect, Restricted and Repetitive Behavior, and an overall total score across domains.

*Social Responsiveness Scale* (SRS; Constantino and Gruber 2005). The SRS is a questionnaire aimed at indexing symptoms and social deficits associated with the autism spectrum. Parents and teachers were both asked to complete this questionnaire about participating children. In addition to a total score (mean = 50; SD = 10) reflecting severity of social deficits associated with the autism spectrum, the SRS generates scores for five subscales: social awareness, social cognition, social communication, social motivation, and autistic traits.

### Social and Behavioral Functioning

*Achenbach Child Behavior Checklist (CBCL) and Teacher Report Form (TRF)* (Achenbach and Rescorla 2001). Parents and teachers were asked to complete the CBCL and TRF, respectively, for participating children to index a range of behavioral difficulties. The most recent versions of the CBCL and TRF provide internalizing, externalizing, and total problem domain scores (mean = 50; SD = 10) in addition to subdomain scores and DSM-IV diagnostic risk profiles.

*Social Skills Rating System* (SSRS; Gresham and Elliott 1990). The SSRS is a norm-referenced scale for parent and teacher ratings of a child's overall social skills. The preschool form of the SSRS was completed for children under five and the elementary level form was completed for children five and older. The SSRS has empirically derived subscales for social skills, which together comprise a Total Social Skills Scale standard score, which has a mean of 100 and a standard deviation of 15.

### Clinical Diagnosis

Clinical diagnoses for participants were determined by experienced clinical psychologists on the basis of clinical judgment as well as research-reliable administration of the ADOS. Many parents also completed the Autism Diagnostic Interview—Revised (ADI-R [Lord et al. 1994]) during the current study visit. The ADI-R is an extended, semi-structured interview designed to obtain the developmental history and behavioral information needed to make diagnoses of autism spectrum diagnoses for individuals with a mental age of two years and above. Research reliable ADI-R data were not available for all participants in the current study due to mid-study protocol changes, but

when available, data were incorporated into diagnostic judgment.

### Data Analysis

Between group comparisons (Sibs-ASD vs. Sibs-TD) were conducted using independent sample *t* tests. Although we examined all subtests, for the sake of clarity, we only present subtest analyses when the *t* test for the highest-order composite score was statistically significant ($p < .05$) or when Cohen's d indicated at least a medium effect size for the composite group differences (Cohen's d = .50 or greater). When multiple subtests or subscales were assessed within a single measure, Bonferroni corrections were conducted to control for multiple comparisons and maintain family-wise Type I error rates below .05 within a given measure.

Two children in the Sibs-ASD group (and none in the Sibs-TD group) received a final outcome diagnosis of ASD at age five, confirming their initial diagnosis from the original longitudinal study. These children were not included in data analyses presented below to ensure that group differences were not driven by the effect of this small number of children manifesting the clinical syndrome itself. Data from the maximum number of participants possible were included for each measure in order to optimize statistical power; however, missing data existed in both groups, particularly for teacher report measures. The number of participants for whom data were included is reported for each measure; no differences in age or gender were observed between Sibs-ASD and Sibs-TD subgroups represented in the data for any measure.

## Results

### Cognitive and Executive Functioning

Table 1 presents group means, test statistics, and effect sizes for the cognitive and executive functioning variables. DAS-II scores were available for 35 children in the Sibs-ASD group and all 22 children in the Sibs-TD group. Group comparisons for the DAS-II GCA did not reach the threshold for statistical significance; however, group differences approached significance and the effect size fell just short of moderate, with Sibs-ASD scoring lower than Sibs-TD, $t\ (56) = -1.74$, $p = .09$.

Analyses of NEPSY-II scores were conducted in a subset of 22 Sibs-ASD and 19 Sibs-TD because the Auditory Attention and Inhibition subtests are only administered to children ages five and older, per test protocol. An independent samples *t* test for the EF composite yielded significant group differences, with Sibs-ASD scoring lower than Sibs-TD (see Table 1). Follow-up comparisons of the four component NEPSY-II subtests using Bonferroni corrections revealed differences for the Auditory Attention scaled score, with Sibs-ASD having lower scores than Sibs-TD. Though the Inhibition-Naming scaled score and the Statue scaled score did not meet the corrected threshold for statistical significance, medium effect sizes were observed for both subtests. Group differences were not observed for the Inhibition–Inhibition subtest score.

### Language functioning

Independent samples *t* tests to explore differences in language functioning between Sibs-ASD and Sibs-TD were conducted with composite scores from the CELF and CCC-2, which were available for all children in both groups (see Table 2). No significant group differences were found for either the CELF CLS composite or the CCC-2 GCC composite, and effect sizes for both composites were small.

#### *ASD-related Symptoms*

Independent samples *t* tests to explore potential differences between Sibs-ASD and Sibs-TD in ASD-related symptoms were conducted with the Social Affect and Restricted and Repetitive Behavior domain scores from the ADOS (Gotham et al. 2007) as well as the Total score from both the Parent and Teacher versions of the SRS (see Table 3). ADOS scores were available for all children in both groups, SRS Parent scores were available for 35 children in the Sibs-ASD group and 21 children in the Sibs-TD group, and SRS Teacher scores were available for 27 children in the Sibs-ASD group and 18 children in the Sibs-TD group. Significant group differences with a medium effect size were found for the ADOS Restricted and Repetitive Behavior domain score, with Sibs-ASD having higher scores (i.e., greater symptomatology) than Sibs-TD. Item level analyses indicated that this difference may be driven by increased levels of restricted interests and repetitive reference to unusual or highly specific topics in Sibs-ASD. Specifically, seven children in the Sibs-ASD group (18.9%) received non-zero scores on this item, whereas no children in the Sibs-TD group were coded on this item. In contrast, no significant group differences were observed for the ADOS Social Affect domain score and the effect size for this comparison was small.

Though between-group comparisons for SRS total scores did not yield statistically significant differences in parent-reported skills, a medium effect size was observed. No group differences were observed in teacher-reported skills on the SRS. Therefore, follow-up analyses were conducted with subscales from the parent, but not teacher version of the SRS.

**Table 1** Cognitive and neuropsychological outcomes

| Measure | Sibs-ASD | | | Sibs-TD | | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | SD | N | Mean | SD | *t*-value | *p*-value | Cohen's *d* |
| DAS-II scores: | | | | | | | | | |
| GCA | 36 | 107.36 | 14.5 | 22 | 113.36 | 9.3 | −1.74 | .088 | .49 |
| NEPSY-II scores: | | | | | | | | | |
| EF composite*+ | 22 | 8.91 | 2.6 | 19 | 11.26 | 2.8 | −2.82 | .007 | .87 |
| Auditory attention*+ | 22 | 8.68 | 3.3 | 19 | 11.68 | 3.5 | −2.81 | .008 | .88 |
| Inhibition–naming+ | 22 | 9.00 | 4.2 | 19 | 12.00 | 3.9 | −2.34 | .025 | .74 |
| Inhibition–inhibition | 22 | 8.55 | 3.2 | 19 | 10.26 | 4.4 | −1.44 | .158 | .44 |
| Statue+ | 22 | 9.41 | 3.0 | 19 | 11.11 | 2.7 | −1.89 | .067 | .60 |
| Design fluency | 26 | 9.38 | 2.8 | 20 | 10.25 | 2.7 | −1.06 | .294 | .32 |

* Statistically significant *p*-value. + Moderate effect size, indicated by Cohen's d ≥ .50. For EF Composite subscales, only Auditory Attention survived Bonferroni-correction with a significant adjusted *p*-value of <.0125. *DAS-II* Differential Ability Scale—Second Edition; *GCA* Global Conceptual Ability; *EF* Executive Functioning

**Table 2** Language outcomes

| Measure | Sibs-ASD | | | Sibs-TD | | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | SD | N | Mean | SD | *t*-value | *p*-value | Cohen's *d* |
| CELF CLS | 37 | 103.65 | 14.0 | 22 | 108.59 | 12.4 | −1.37 | .177 | .37 |
| CCC-2 GCC | 37 | 110.68 | 13.8 | 22 | 114.36 | 14.5 | −.98 | .334 | .26 |

*CELF* Clinical Evaluation of Language Fundamentals; *CLS* Core Language Scale; *CCC-2* Children's Communication Checklist—Second Edition; *GCC* General Communication Composite

Using Bonferroni corrections with the five subscales, group differences did not reach statistical significance for any SRS subscale. However, the effect size for observed differences in the Social Cognition domain was medium, indicating that the magnitude of differences in social cognitive abilities between Sibs-ASD and Sibs-TD, as reported by parents, was considerable, despite their not reaching the corrected threshold for statistical significance.

### Behavior and social problems

Individual samples *t* tests to explore potential differences in parent and teacher reported behavior problems between Sibs-ASD and Sibs-TD were conducted with Total Problems composite scores from the Achenbach CBCL and TRF, respectively. Results are presented in Table 4. CBCL scores were available for all children in the Sibs-ASD group and 21 children in the Sibs-TD group, while TRF scores were available for 26 children in the Sibs-ASD group and 17 children in the Sibs-TD group. No significant group differences were found for either the CBCL Total Problem score or the TRF Total Problem score, and effect sizes for both composites were small.

Individual samples *t* tests to explore potential differences in parent and teacher reported social problems were conducted with composite scores from the parent and teacher versions of the SSRS. SSRS—Parent scores were available for 36 children in the Sibs-ASD group and 19 children in the Sibs-TD group, while SSRS—Teacher scores were available for 26 children in the Sibs-ASD group and 15 children in the Sibs-TD group. No significant group differences were found for either the SSRS—Parent social skills composite score or the SSRS—Teacher social skills composite score (Table 4), and effect sizes for both composites were small.

## Discussion

Over the past decade, many research groups have initiated prospective investigations of younger siblings of children with ASD to explore early markers of ASD diagnosis and risk status, as well as to examine more subtle differences in this genetically vulnerable population. As a whole, this research has identified a range of early differences in groups of Sibs-ASD when contrasted with Sibs-TD, and has confirmed heightened risk for the disorder in Sibs-ASD. At the same time, findings have been somewhat heterogeneous, both within and across studies, and the clinical predictive value of early differences as they relate

**Table 3** ASD-related outcomes

| Measure | Sibs-ASD | | | Sibs-TD | | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | *N* | Mean | SD | *N* | Mean | SD | *t*-value | *p*-value | Cohen's *d* |
| ADOS scores: | | | | | | | | | |
| Social affect | 37 | 1.97 | 2.5 | 22 | 1.27 | 1.6 | 1.18 | .243 | .33 |
| RRB*+ | 37 | .49 | .9 | 22 | .14 | .4 | 2.17 | .035 | .50 |
| SRS parent scores | | | | | | | | | |
| Total+ | 36 | 46.86 | 7.6 | 21 | 43.38 | 5.5 | 1.82 | .075 | .53 |
| Social awareness | 36 | 48.33 | 9.6 | 21 | 45.48 | 8.4 | 1.13 | .262 | .32 |
| Social cognition+ | 36 | 47.36 | 6.5 | 21 | 43.81 | 5.0 | 2.15 | .036 | .61 |
| Social communication | 36 | 46.64 | 8.0 | 21 | 43.62 | 5.9 | 1.51 | .136 | .43 |
| Social motivation | 36 | 47.81 | 8.5 | 21 | 45.10 | 5.1 | 1.32 | .140 | .39 |
| Autistic mannerisms | 36 | 46.86 | 6.6 | 21 | 44.76 | 6.5 | 1.17 | .248 | .32 |
| SRS teacher scores | | | | | | | | | |
| Total | 27 | 45.07 | 6.3 | 18 | 42.89 | 6.9 | 1.10 | .276 | .33 |

* Statistically significant *p*-value. +Moderate effect size, indicated by Cohen's d $\geq$ .50. For the total scores (Social Affect, RRB, SRS Parent Total, SRS Teacher Total), *p*-values <.05 were considered statistically significant. For the SRS Parent subscales, Bonferroni-corrected *p*-values <.01 were considered statistically significant. *ADOS* Autism Diagnostic Observation Schedule; *RRB* Restricted and Repetitive Behavior Domain; *SRS* Social Responsiveness Scale

**Table 4** Behavioral and social outcomes

| Measure | Sibs-ASD | | | Sibs-TD | | | Statistics | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | SD | N | Mean | SD | *t*-value | *p*-value | Cohen's *d* |
| CBCL scores | | | | | | | | | |
| Total problems | 37 | 44.59 | 9.2 | 21 | 42.10 | 9.4 | .99 | .327 | .27 |
| TRF scores | | | | | | | | | |
| Total problems | 26 | 47.50 | 10.2 | 17 | 46.00 | 10.5 | .47 | .644 | .15 |
| SSRS parent scores | | | | | | | | | |
| Total social skills | 36 | 103.58 | 14.3 | 19 | 100.89 | 13.5 | .67 | .503 | .19 |
| SSRS teacher scores | | | | | | | | | |
| Total social skills | 26 | 108.15 | 12.8 | 15 | 111.60 | 13.6 | -.81 | .423 | .26 |

*CBCL* Childhood Behavior Checklist; *TRF* Teacher Report Form; *SSRS* Social Skills Rating Scale

to ASD-specific outcomes is often lacking (Rogers 2009; Yirmiya and Charman 2010; Young et al. 2009). Beyond its import for identifying early clinically meaningful diagnostic markers, sibling research affords the additional opportunity to explore whether clinical patterns of vulnerability in language, cognitive, and social abilities exist among Sibs-ASD who do not themselves have ASD diagnoses (Constantino et al. 2006). Evidence of such vulnerabilities would suggest potential markers of a broader autism phenotype or other neurobehavioral concerns, preferentially expressed in the at-risk sibling group. However, given the substantial family—and systems-related stressors associated with increased ASD-related concerns (see Bailey 2008), there is a pressing need to understand which early hypothesized and detected differences *are not* associated with clinically significant outcomes.

To these ends, the present study compared the age five cognitive, language, executive functioning, social, and behavioral profiles of a group of Sibs-ASD and Sibs-TD who were originally recruited in the second year of life as part of a longitudinal study of social communicative development. Of note, the sample of Sibs-ASD described here did not include siblings who themselves received ASD diagnoses, but nonetheless represented a sample of at-risk siblings who during the course of the original longitudinal investigation expressed early group differences from Sibs-TD in their cognitive, language, joint attention, social-communication skills, and ASD symptom expression at a mean age of 16 months (Stone et al. 2007).

Results of the present study only partially confirmed our initial hypothesis, which predicted that the Sibs-ASD sample would show a range of differences and deficits

relative to Sibs-TD across neurocognitive, language, social, and behavioral measures. The Sibs-ASD group did demonstrate several subtle patterns of difference within their neuropsychological and social behavioral profiles, when compared to a gender-, age-, and SES-matched group of Sibs-TD. Specifically, the Sibs-ASD group demonstrated vulnerabilities related to high-level executive functioning processes (e.g., auditory attention, rapid naming, and inhibition), parents of Sibs-ASD more often reported broad social cognitive difficulties for their children, and the Sibs-ASD sample showed elevated levels of restricted interests and repetitive behaviors relative to the Sibs-TD group. Yet, as a group, Sibs-ASD demonstrated global cognitive abilities, language skills, and behavior regulation capacities that did not vary significantly from those of children in the Sibs-TD group, who, on average, scored at the top of the average range on cognitive and language measures. In the social realm, which is thought to be the hallmark area of deficits for individuals with ASD, we saw limited evidence of impairments, with no group differences noted in direct assessment of social interaction (i.e., ADOS scores). Further, cognitive, language, and behavior regulation abilities among Sibs-ASD generally fell well within normal limits across standardized measures.

So do the available data constitute evidence of a broader autism phenotype in siblings of children with ASD? The current study employed the necessary design for answering this question (i.e., a comparison of well-characterized group of high-risk children who do not themselves develop ASD to a low-risk group) (see Toth et al. 2007; Rogers 2009). Yet, within this study, global differences in abilities between groups across measures of cognitive functioning, language ability, or social and behavioral development were not revealed. Rather, we observed more subtle patterns of difference across areas thought to be either directly or indirectly impacted in ASD itself (i.e., executive functioning, social cognition, atypical behaviors). However, we must be cautious in interpreting these group *differences* as meaningful group *deficits* within this sample. While differences between Sibs-ASD and Sibs-TD were statistically significant and reflective of moderate effect sizes, the Sibs-ASD group still ultimately was performing well within developmentally appropriate expectations (i.e., average performance among Sibs-ASD within one standard deviation of the normative mean across all areas). Further, our comparison sample often displayed abilities nearing the top end of the average range in certain key areas and significant findings (i.e., SRS) were often tied to parent report of difficulty, not clinical observation during the assessment or by teacher report, suggesting a role for potential reporting bias related to varied experience bases within this group of parents with another child with ASD. As such, the clinical importance of observed differences as potential markers of a broader autism phenotype within a high-risk sample is in question without further replication. This finding is further complicated by the fact that our lack of robust broad differences, specifically in language and in cognitive domains potentially tied to academic functioning, does not replicate the findings of the only other published work following a Sibs-ASD sample to school age (Gamliel et al. 2009). However, the operationalization of BAP-related impairment used by Gamliel and colleagues (i.e. presence of one or more score at least 1.5 standard deviation below the mean) differed from the standard-score based group comparison methodology employed in this study. Further, given their relevance to higher-order skills, moderate executive functioning and social cognitive differences observed in the present study have the potential for clinically-relevant impact later in childhood and adolescence, a possibility that should be explored in high-risk samples followed toward these later points in development. In isolation the import and meaning of these subtle vulnerabilities is hard to interpret, but future examination of such domains in relation to both early deficits as well as potential impairments at even later points of development would clarify our understanding of these differences.

Ultimately, clinically meaningful evidence for a broader familial autism phenotype in siblings requires not only difference in direct group comparisons, but also deviance from population norms over time. While the current work did find subtle patterns of the former, findings did not meet the latter criterion. However, these results must be interpreted cautiously given our relatively small sample size, the significant attrition experienced between the initial longitudinal study and the present outcome study, as well as overarching methodological concerns regarding interpreting null findings. A better understanding of the existence and nature of a potential broader familial phenotype of ASD in later-born siblings awaits additional data from larger studies. Future research aimed at clarifying such questions would also benefit from assessing and examining a number of different processes that might significantly impact children's abilities and vulnerabilities over time. While one hypothesis surrounding the development of ASD related vulnerabilities in at-risk sibling groups is clearly related to the heritability of the disorder itself, it is also possible that various psychosocial factors, such as different parenting attitudes and behaviors as well as family stress, may affect siblings of children with ASD in a different manner than siblings of typically developing children. Incorporating methodological controls related to these complex and important factors will help tease apart the nature of vulnerabilities, or the lack thereof, within this population.

The question about whether broader expression of ASD symptomatology exists in sibling groups, as well as

whether potential early markers associated with clinically-significant difficulties can be identified, is neither abstract nor simply semantic. In fact, this question is tied to important ethical and clinical issues with regard to the growing trend toward identifying ASD at increasingly early ages (Warren and Stone, in press; Zwaigenbaum et al. 2009). Given the high recurrence rate for Sibs-ASD, families who already have a child diagnosed with ASD are routinely faced with the challenge of attempting to make sense of early differences, and what they may or may not mean in terms of immediate and future clinical implications for their youngest children. The process of noticing, developing, discussing, and acting on ASD concerns in very young children is an extremely challenging and taxing one for families as well as community systems of care (Bailey 2008; Warren and Stone, in press). As such, differentiating true markers of concern from developmental variations that are not cause for alarm is an extremely important area of clarification likely to have great importance for families who already have experienced the challenges and stressors of an ASD diagnosis and associated sequelae.

This work represents a unique contribution to the existing literature in terms of extending the age and scope of measurement of a previously evaluated, high-risk sample. However, group level comparisons do not adequately describe risk trajectories in terms of the implications of early differences for later development, or for possible early predictors of differences not observed until the start of early school age. Ongoing work with this sample examining early differences in social communication skills in relation to later cognitive and behavioral vulnerabilities, has suggested that (1) initial early joint attention skills are predictive of important language and social skills at age five in both Sibs-ASD and Sibs-TD groups (Malesa et al. under review) and (2) that early deficits within the Sibs-ASD sample in these core domains are not robust predictors of later deficits. As such, the combination of present findings with such prospective data reinforces the notion that ASD-risk trajectories are not simple. Patterns of risk and resilience are both substantial within this group of Sibs-ASD, who show relatively few differences at age five, despite many varied developmental differences and vulnerabilities early on. Future work examining specific trajectories and patterns of change from infancy to later ages is needed to clarify the ultimate import and clinical significance of early differences, as well as potential predictors of differences in higher-level skills (e.g., executive functioning, social cognition, academics, personality structure, relational systems) that may emerge later in development (i.e., adolescence or adulthood). Ultimately, this line of research will yield significant contributions to the identification of early neurodevelopmental differences associated with ASD itself, those associated with broader clinically-meaningful deficits, and mechanisms by which resilience occurs despite early differences.

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