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Behavior and Sleep Problems in Children with a Family History of Autism

A.J. Schwichtenberg¹, Gregory S. Young¹, Ted Hutman², Ana-Maria Iosif¹, Marian Sigman², Sally J. Rogers¹, and Sally Ozonoff¹

¹University of California, Davis

²University of California, Los Angeles

Abstract

The present study explores behavioral and sleep outcomes in preschool age siblings of children with autism spectrum disorders (ASD). This study focuses on behavior problems that are common in children with ASD, such as emotional reactivity, anxiety, inattention, aggression, and sleep problems. Infant siblings were recruited from families with at least one older child with ASD (high-risk group, $n = 104$) or families with no history of ASD (low-risk group, $n = 76$). As part of a longitudinal prospective study, children completed the Mullen Scales of Early Learning and the Autism Diagnostic Observation Schedule, and parents completed the Child Behavior Checklist (CBCL) and the Social Communication Questionnaire at 36 months of age. This study focuses on developmental concerns outside of ASD; therefore, only siblings who did not develop an ASD were included in analyses. Negative binomial regression analyses revealed that children in the high-risk group were more likely to have elevated behavior problems on the CBCL Anxious/Depressed and Aggression subscales. To explore sleep problems as a correlate of these behavior problems, a second series of models was specified. For both groups of children, sleep problems were associated with elevated behavior problems in each of the areas assessed (reactivity, anxiety, somatic complaints, withdrawal, attention, and aggression). These findings support close monitoring of children with a family history of ASD for both behavioral and sleep issues.

Keywords

autism; siblings; behavior problems; sleep

Previous studies of infant siblings of children with autism spectrum disorders (ASD) have documented elevated concerns in communication, social skills, and restricted/repetitive behaviors (Rogers, 2009). Recent studies suggest that behavioral and developmental concerns for these children extend beyond the DSM-IV ASD symptom domains as well. Cross-sectional studies report elevated externalizing and internalizing problems in school-age and adult siblings of children with ASD when compared to siblings of children with no

Correspondence concerning this article should be addressed to A.J. Schwichtenberg, M.I.N.D. Institute, Department of Psychiatry and Behavioral Sciences, University of California, 2825 50th Street, Sacramento, CA 95817. ajschwichtenberg@ucdavis.edu.

A.J. Schwichtenberg, Department of Psychiatry and Behavioral Sciences, University of California, Davis; Gregory S. Young, Department of Psychiatry and Behavioral Sciences, University of California, Davis; Ted Hutman, Department of Psychiatry and Biobehavioral Science, University of California, Los Angeles; Ana-Maria Iosif, Department of Public Health Sciences, University of California, Davis; Marian Sigman, Department of Psychiatry and Biobehavioral Science, University of California, Los Angeles; Sally Rogers, Department of Psychiatry and Behavioral Sciences, University of California, Davis; Sally Ozonoff, Department of Psychiatry and Behavioral Sciences, University of California, Davis.

Conflicts of Interest

The authors have no conflicts of interest to declare.

disability (Orsmond & Mailick Seltzer, 2007). Longitudinal infant sibling studies have also found a wide range of behavioral problems in infant siblings, including difficulties with state regulation, elevated activity, and emotional reactivity (Garon et al., 2009; Brian et al., 2008; Zwaigenbaum et al., 2005). The present report extends this line of research, examining both the rate of behavior problems in young infant siblings as well as potential correlates of such problems. This study focuses on behavior problems that are common in children with ASD, such as emotional reactivity, anxiety, inattention, and aggression (Hollander, Kolevzon, & Coyle, 2011). Previous studies of typically developing children show robust associations between sleep and daytime behavior problems (e.g., Goodnight et al., 2007). Therefore, in addition, the present study examined whether sleep problems might help explain daytime behavior problems in high-risk infant siblings. Given previous reports of elevated subclinical autism features and other developmental concerns in high-risk infant siblings, we also explored the relations between behavior problems and both subclinical autism features and developmental functioning.

Children with a family history of ASD are a growing population. As the prevalence of ASD increases (CDC, 2009), so does the prevalence of siblings of children with ASD. Recent US prevalence reports estimate as many as 1 in 88 children have an autism spectrum disorder (CDC, 2012), resulting in over two and a half million families raising a child with ASD and over a million raising siblings at risk for ASD and other developmental difficulties. Recent reviews estimate that up to 40% of younger siblings of children with autism have adverse developmental outcomes other than ASD (Rogers, 2009). Additional research on these at-risk siblings is needed to elucidate these diverse developmental outcomes. The present study focuses on the large subgroup (> 80%) of infant siblings who do not develop ASD (Ozonoff et al., 2011), focusing in particular on behavioral and sleep problems.

In typically developing children, sleep problems are a common but not trivial problem. Approximately 25% of all children will experience a sleep problem some time in early childhood (Mindell & Owens, 2003). These problems are associated with several negative outcomes, including family stress/discord, learning difficulties, and social interaction problems (Durmer, & Dinges, 2005; Dixon, Salley, & Clements, 2006; Reid, Hong, & Wade, 2009; Scher, 2001). In children with developmental delays, behavior and sleep problems are even more common (Hollander et al., 2011; Konstantareas & Stewart, 2006; Richdale & Schreck, 2009); however, it is less clear how these problems interact and contribute to developmental outcomes.

Several studies of typically developing children show associations between sleep and behavior problems, including both internalizing and externalizing problems (Aronen et al., 2000; Lavigne et al., 1999; Paavonen, Porkka-Heiskanen, & Lahikainen, 2009; Shang, Gau, & Soong, 2006; Yokomaku et al., 2008). In clinical samples, researchers have also reported elevated behavior problems in children with co-morbid sleep disorders (Goodlin-Jones et al., 2009; Rzepecka et al., 2011). For example, in a study of children with intellectual disabilities (ID) and/or ASD, Rzepecka and colleagues (2011) reported elevated behavior problems in children who had co-morbid sleep problems. In prospective infant sibling studies, no study to date has examined the incidence of sleep problems or their association(s) with behavioral challenges.

Research Questions and Hypotheses

The current study focused on two primary research questions in infant siblings who do not develop an ASD. First, do parents of children with a family history of ASD report more behavior and sleep problems than parents of children with no family history of ASD? Second, in children with a family history of ASD, are daytime behavior problems associated

with sleep problems, subclinical autism features, or developmental functioning? Consistent with studies of school-age and adult ASD sibling studies, we anticipated elevated behavior problems in children with a family history of ASD. For our second research question, we predicted that elevated behavior problems would be associated with sleep problems, more subclinical manifestations of autism, and developmental concerns.

Method

Participants

One hundred and eighty families participated in this collaborative study between the University of California, Davis ($n = 95$) and the University of California, Los Angeles ($n = 85$). Infant siblings were recruited from families with at least one older child diagnosed with an ASD (high-risk group, $n = 104$) or families with no history of ASD in first, second, or third degree relatives (low-risk group; $n = 76$). The older siblings (i.e., probands) in the high-risk group were diagnosed with autistic disorder, Asperger syndrome, or pervasive developmental disorder – not otherwise specified. Proband diagnostic status was confirmed with the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2002) and the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). Family demographic information, stratified by risk group, is provided in Table 1.

Participants were enrolled between 6 and 18 months of age ($M = 7.51$ months, $SD = 4.79$ months) and were assessed at 6, 12, 18, 24, and 36 months of age. At 36 months, participant autism outcomes were determined. Infant siblings were diagnosed with ASD ($n = 21$) if they scored over the ASD cutoff on the ADOS and met DSM-IV criteria for Autistic Disorder or Pervasive Developmental Disorder Not Otherwise Specified by an expert clinician. Since the present study focuses on non-ASD behavioral outcomes, the children diagnosed with ASD were excluded, resulting in a final sample of 180 participants.

Measures

Child Behavior Checklist—The preschool form of the Child Behavior Checklist (CBCL 1 ½ – 5; Achenbach & Rescorla, 2000) was used to assess children's behavior and sleep problems at 36 months. The CBCL is a commonly used standardized behavior rating scale that is completed by an adult with whom the child lives (Aronen et al., 2000; Goodlin-Jones et al., 2009; Lavigne et al., 1999; Paavonen et al., 2009). The preschool form lists 99 problem behaviors. Parents rated each problem behavior on a three point scale: *not true* (0), *somewhat or sometimes true* (1), or *very true or often true* (2), in reference to the child's behaviors that occurred during the past two months. Responses were summed to generate seven empirically derived subscales: Emotional Reactivity, Anxious/Depressed, Somatic Complaints, Withdrawn, Attention Problems, Aggressive Behavior, and Sleep Problems. Raw scores were then converted to standardized T scores which ranged from 50 to 94. These subscales comprise the widely used Internalizing (Emotional Reactivity, Anxious/Depressed, Somatic Complaints) and Externalizing (Attention Problems and Aggressive Behavior) Problems scores. The CBCL has high internal consistency, with Cronbach's alphas ranging from .78 to .97, and it has been used with children at risk for developmental concerns (e.g., Yu et al., 2006). Within the present study Cronbach's alpha ranged from .71 to .89 across the subscales. Scores above the 93rd percentile (T scores greater than 65) are within the borderline clinical range on each subscale.

Social Communication Questionnaire—The SCQ (Rutter et al., 2003) was completed by parents for the proband at enrollment and for the infant sibling at 36 months of age. The SCQ is a 40-item questionnaire designed to screen for autism symptoms. The SCQ has an established cutoff for ASD and higher scores are indicative of more autism symptoms.

Within the present study, continuous SCQ scores were used to index subclinical autism symptoms in the infant sibling and scores above the ASD cutoff were used as a part of our diagnostic confirmation for the proband. In the low-risk group SCQ scores ranged from 0 to 12 and in the high-risk group scores ranged from 0 to 23. Within the high-risk group, two children scored above the 'possible ASD' cutoff of 15. Both of these children were carefully evaluated and although parents endorsed several ASD features, expert clinician opinions and their ADOS scores did not support an ASD diagnosis. The broader range of scores within the high-risk group is expected given the elevated prevalence of subclinical autism features in siblings of children with ASD (Constantino et al., 2006; Schwichtenberg et al., 2010).

Autism Diagnostic Observation Schedule—The ADOS (Lord et al., 2002) is a semi-structured standardized interaction and observation that evaluates symptoms of ASD. It has two empirically derived cutoffs, one for ASD and one for autistic disorder. It was administered to the proband (older sibling) at the initial visit to confirm inclusion and to the infant sibling at 36 months of age to quantify subclinical autism features and to aid in determining his/her ASD outcome status. Each examiner completed a research ADOS training and maintained 80% or greater agreement with a reliable trainer across all items.

Mullen Scales of Early Learning—The MSEL (Mullen, 1995) is a standardized developmental test for children ages birth to 68 months. The administered subscales included fine motor, visual reception, and expressive and receptive language. To assess child developmental functioning, the Mullen Early Learning Composite (ELC) was calculated and used in analyses.

Procedure

This study was conducted under the approval of the Institutional Review Boards of both universities. The study was explained to parents orally and in writing, all their questions were answered, and consent was obtained before conducting assessments. The CBCL and SCQ were completed by the mother or father as part of the 36 month visit, in which a larger experimental battery was administered.

Results

Data Analysis

All statistical analyses were conducted using SAS Version 9.2 (SAS Institute, 2008). Five sets of analyses were conducted. Initial analyses explored the continuous T scores of each subscale using models for count data and a second set compared children above and below the borderline clinical cutoff (T scores > 65 or above the 93rd percentile; Achenbach & Rescorla, 2000). Because the CBCL is a report of problematic behaviors and most children do not present with such behaviors, the distribution of scores contains a large spike at 50 (the lowest possible standardized score). The count models of Poisson, negative binomial, and zero-inflated were fit to the continuous T scores by graphing each model's predicted probability against the actual data. The negative binomial models provided the best relative fit and were therefore retained for all continuous T score analyses. Given the relatively small number of children who presented with scores above the borderline clinical cutoff (Table 2), Fisher's exact tests were used to explore these group differences. The third set of analyses addressed our research question regarding sleep problems. For these analyses another set of negative binomial models was specified, adding to the core models terms for sleep problems and the interaction between sleep problems and risk group. Our final series of negative binomial models was conducted on the high-risk group only and assessed the relations among behavior problems, subclinical autism features, and developmental functioning.

Group Differences

Each core negative binomial model contained terms for risk group, gender, income, and recruitment site (UC Davis, UCLA). Because seven children had missing data for family income level, group mean imputation was used to include income in all models. All models were refit on the subsample with complete income data and the results were similar to those obtained using imputed income data. Within these models, parents of children in the high-risk group reported more behavior problems on the Anxious/Depressed and Aggressive Behavior subscales ($p < .05$) when compared to parent reports of children in the low-risk group (Table 2). Parents within the high-risk group also tended to report more emotional reactivity and somatic complaints ($p < .08$). Within each model, the impact of gender, income, and recruitment site were not significant. Table 2 also displays the frequency of scores above the borderline clinical cutoff as a function of risk group. Significantly more children in the high-risk group had scores above this cutoff on the Anxious/Depressed, Somatic Complaints, Aggressive Behavior, and Sleep Problems subscales when compared to the low-risk group (see Figure 1 and Table 2). Collapsing across subscales, there were significantly more children with at least one score above the borderline clinical cutoff in the high-risk group ($n = 23$, 22%) than in the low-risk group ($n = 7$, 9%; Fisher's exact test $p = .03$).

Behavior Problems and Sleep Problems

These analyses revealed a main effect for sleep problems across all subscales. Parents who reported elevated sleep problems were more likely to report behavior problems in all of the domains assessed (all $p < .01$). The sleep problem $\times$ group interaction term, gender, income, and recruitment site were not significant for any of the subscales. In sum, a robust association between sleep problems and other behavior problems was apparent in both groups.

Behavior Problems and Autism Symptoms

To explore the associations between elevated behavior problems and subclinical autism features in the high-risk group, a series of negative binomial models compared child behavior problems (continuous T Scores) and child autism features as indexed by the ADOS and SCQ (Table 3). As in the previous models, gender, income, and recruitment site were retained in each model. Examiner-rated ADOS scores were not significantly associated with parent-reported behavior problems (Table 3). In contrast, parent reports on the SCQ were associated with parent reports of behavior problems on the CBCL (Table 3). Parents who reported more concerns about their child's social and communication skills also reported more behavior problems across each subscale. Gender, income, and recruitment site were again not significant predictors.

Behavior Problems and Developmental Functioning

The final series of negative binomial models assessed the relationships among behavior problems (continuous T Scores) and Mullen ELC scores in the high-risk group (while considering gender, income, and recruitment site). Child ELC scores were not significantly associated with parent-reported behavior problems (Table 3).

Discussion

The present study illustrates that developmental problems in at-risk siblings without ASD may include internalizing, aggression, and sleep problems in children as young as 36 months of age.

In this study, 22% of siblings with a family history of autism had behavior or sleep problems that fell in the borderline clinical range on the CBCL. This estimate is consistent with previous school-age sibling studies that report between 20% and 36% of ASD siblings presented in the clinical range on the CBCL (Orsmond & Mailick Seltzer, 2007). Previous studies using the CBCL with siblings of children with ASD have focused on the Externalizing and Internalizing summary scores (Fisman et al., 1996; Fisman et al., 2000; Rodrigue et al., 1993; Smith & Perry, 2005). The present study extends that work by examining the individual subscales that contribute to the overall Externalizing and Internalizing scores. We found that elevated behavior problems are not present across all behavioral domains in the high-risk group but are specific to the Anxiety/Depression, Somatic Complaints, Aggressive Behavior, and Sleep Problems subscales. This is in contrast to three previous studies of school-age siblings of children with ASD that reported no significant group differences across the subscales (Dempsey et al., 2012; Kaminsky & Dewey, 2002; Verte et al., 2003). Direct comparisons among these studies are challenging, as the subscales derived from the school age and preschool CBCL are not identical (e.g., the school age form does not include an emotional reactivity subscale). Additionally, the study by Kaminsky and Dewey (2002) only enrolled siblings with a family history of ASD who were typically developing and excluded siblings with broader developmental or behavioral problems. Consistent with the diverse developmental outcomes experienced by high-risk infant siblings (Garon et al., 2009; Brian et al., 2008; Rogers, 2009), the present study included children with known developmental concerns which may have led to more parent-reported behavior problems. Even with these sample and scale differences, the present study concurs with previous studies that significantly elevated rates of behavior problems in withdrawal and attention are not present in high-risk infant siblings. Convergence across studies in these areas may reflect relative strengths for future studies and/or interventions to draw upon.

Research on sleep and behavior problems in typically developing children presents a clear picture. Children with daytime behavior problems are more likely to have sleep problems and vice versa (Goodnight et al., 2007; Gregory & O'Connor, 2002; Yokomaku et al., 2008). The present study adds to this line of research by examining the associations between sleep and behavior problems in children with a family history of ASD. Consistent with previous literature on typically developing children, elevated sleep problems were associated with daytime behavior problems (regardless of risk group status) in the present study. However, this finding should be considered exploratory because both the sleep problems and behavior problem subscales were based on parent-report only (without corroborating videosomnography or other detailed characterizations of sleep problems) and were derived from a general behavioral questionnaire (the CBCL).

Sleep and behavior problems in the infant siblings were not consistently associated with subclinical autism features or developmental functioning. While parent reports of social and communication concerns (as indexed by the SCQ) were robustly associated with sleep and behavior problems, those rated by expert examiners (using the ADOS) were not. Previous studies report associations between autism features/symptoms and behavior problems in low-risk samples (Moricke, Swinkels, Beuker, & Buitelaar, 2010) and in children with autism (Gray et al., 2012). However, the present study and previous studies relied on parent-report measures and it is possible that the association between subclinical autism features and behavior problems reflect shared method variance (i.e., the negative halo effect).

The current study contains multiple strengths, including a relatively large sample size, established measures of behavior and sleep problems, and a comparison group. However, it has a significant limitation - all sleep and behavioral problem indices are based on parent report. Future studies should aim to replicate these findings within a longitudinal design and

with additional clinical observations, reports from other care providers, or teacher reports. The parent-report limitation may have affected findings in multiple ways. First, parental stress may influence parent reports of child behavior problems. As previous studies have illustrated (Chilcoat & Breslau, 1997; Tompson et al., 2010), parents who are under more stress and/or depressed report more child behavior problems. However, previous studies have also illustrated that these elevated reports have been substantiated by reports from teachers and research examiners (e.g., Achenbach et al., 2002). Second, as highlighted earlier, the associations among subclinical autism features, sleep, and other behavior problems may reflect shared method variance. For example, a parent who reports more problems in one area may also report more problems in other areas. Additionally, caution should be used when considering the directionality of these findings. All data were collected at one time point (36 months); therefore, directionality cannot be verified. Finally, a few of the children in the high-risk group may develop an ASD after 36 months of age; therefore, the differences noted may reflect behaviors of children with forthcoming diagnoses. For these reasons the present study should be considered exploratory until future longitudinal studies using multiple methods provide replication.

In conclusion, this study demonstrates that developmental outcomes for siblings with a family history of ASD are broader than ASD itself and extend to behavior problems and sleep problems. Future replication, monitoring, and surveillance efforts should be extended to include these domains.

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Figure 1. T score histograms for the CBCL subscales of Anxious/Depressed (a), Somatic Complaints (b), Aggressive Behavior (c), and Sleep Problems (d) stratified by risk group. Dotted line indicates borderline clinical cutoff (T scores above 65).

Table 1

Descriptive statistics for demographic and clinical characteristics by risk group

Variable	Risk Group	
	High (<i>n</i> = 104)	Low (<i>n</i> = 76)
Gender (<i>n</i> , % male)	49 (47%)	46 (61%)
Race (<i>n</i> , % Caucasian)	75 (72%)	62 (82%)
Recruitment Location (<i>n</i> , % UC Davis)	55 (53%)	40 (53%)
Family Income (<i>n</i> , %)		
Under \$50,000	20 (19%)	7 (9%)
\$50,000 to \$125,000	52 (50%)	33 (43%)
Over \$125,000	28 (27%)	33 (43%)
No Income Reported	4 (4%)	3 (4%)
Mullen T Scores ¹		
Visual Reception	61.4 (11.4)	60.7 (12.0)
Fine Motor	52.8 (12.4)	54.5 (14.1)
Receptive Language	50.9 (9.8)	53.4 (9.3)
Expressive Language	54.2 (8.9)	55.5 (7.7)
ADOS ²	2.6 (2.1)	2.1 (2.0)
SCQ ³	3.7 (4.0)	3.9 (2.8)

Note. Categorical variables are summarized as frequencies (percentages) and continuous variables as means (standard deviations).

¹ Missing data: *n* = 3 on all four scales in the low-risk group, and *n* = 5 for fine motor, *n* = 2 for receptive and expressive language in the high-risk group.

² Missing data: *n* = 2 in high- and *n* = 1 in low-risk group.

³ Missing data: *n* = 4 in high-risk group.

Group differences in (a) continuous T scores and (b) the frequency/percentage of borderline clinical behavior problems (T scores above 65) (n = 180)

Table 2

CBCL Subscales	Continuous T scores			T scores above Borderline Clinical Cutoff		
	Risk Group		Negative Binomial ^I Estimate (SE)	Risk Group		Fisher Exact Test p-value
	High M(SD)	Low M(SD)		High n (%)	Low n (%)	
Emotionally Reactive	53.6 (6.4)	51.7 (3.6)	0.61 (0.35)	9 (9%)	2 (3%)	.12
Anxious/Depressed	52.9 (5.5)	50.8 (1.5)	1.12 (0.32)	7 (7%)	0 (0%)	.02
Somatic Complaints	53.5 (5.9)	51.3 (2.9)	0.76 (0.42)	12 (12%)	0 (0%)	.001
Withdrawn	52.8 (4.8)	51.7 (3.3)	0.38 (0.31)	3 (3%)	1 (1%)	.64
Attention Problems	53.3 (6.2)	52.5 (4.8)	0.18 (0.35)	11 (11%)	3 (4%)	.16
Aggressive Behavior	54.4 (8.1)	51.7 (3.0)	0.75 (0.33)	6 (6%)	0 (0%)	.04
Sleep Problems	55.3 (7.6)	53.2 (4.4)	0.35 (0.26)	10 (10%)	1 (1%)	.03

Note. ASD = autism spectrum disorders, CBCL = Child Behavior Checklist.

* p < .05.

^I Negative binomial regression models were fit for all seven subscales, adjusting for gender, income, and recruitment site.

Associations between subclinical autism features (ADOS and SCQ) and developmental functioning (Mullen ELC) with continuous T scores in the high-risk group (n = 104)

Table 3

CBCL Subscales	ADOS ¹		SCQ ²		Mullen ELC ³	
	Estimate (SE)	p	Estimate (SE)	p	Estimate (SE)	p
Emotionally Reactive	0.15 (0.12)	.22	0.26 (0.07)	< .001	-0.01 (0.05)	.86
Anxious/Depressed	0.11 (0.11)	.31	0.27 (0.05)	< .001	-0.04 (0.04)	.37
Somatic Complaints	0.17 (0.12)	.16	0.18 (0.06)	< .01	-0.02 (0.04)	.67
Withdrawn	0.18 (0.11)	.12	0.30 (0.07)	< .001	-0.06 (0.04)	.09
Attention Problems	0.18 (0.10)	.07	0.25 (0.06)	< .001	-0.03 (0.05)	.17
Aggressive Behavior	0.15 (0.11)	.20	0.18 (0.05)	< .001	-0.06 (0.04)	.17
Sleep Problems	0.14 (0.08)	.10	0.19 (0.04)	< .001	-0.04 (0.04)	.30

Note. ADOS = Autism Diagnostic Observation Schedule, SCQ = Social Communication Questionnaire, ELC = Early Learning Composite, Negative binomial regression models were fit for high-risk children for all seven subscales, adjusting for gender, income, and recruitment site.

¹ Missing data: n = 2,

² Missing data: n = 4,

³ Missing data: n = 7. Mullen ELC estimates reported for a 10 unit increase in score.