Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-021-04973-2

ORIGINAL PAPER

Sleep Disturbances and Sensory Sensitivities Co-Vary in a Longitudinal Manner in Pre-School Children with Autism Spectrum Disorders

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Accepted: 10 March 2021

Abstract

Previous research has demonstrated that sleep disturbances are positively correlated with sensory sensitivities in children with ASD. Most of these studies, however, were based on cross-sectional analyses, where the relationship across symptom domains was examined at a single time-point. Here, we examined the development of 103 pre-school children with ASD over a 1–3-year period. The results revealed that spontaneous longitudinal changes in sleep disturbances were specifically correlated with changes in sensory sensitivities and not with changes in other sensory processing domains nor with changes in core ASD symptoms. These finding demonstrate a consistent longitudinal relationship between sleep disturbances and sensory sensitivities, which suggests that these symptoms may be generated by common or interacting underlying physiological mechanisms.

Keywords Autism Spectrum disorder · Sleep disturbances · Sensory processing · Sensory sensitivities

Introduction

ASD symptoms vary dramatically across cases. This heterogeneity is apparent in the core social impairments and repetitive behaviors that define the disorder (APA, 2013), and in a long list of secondary symptoms that are common in ASD including sleep disturbances (Mazurek & Sohl, 2016; Reynolds et al., 2019) and sensory problems (Ayelet Ben-Sasson et al., 2009; Little et al., 2018). One of the foremost challenges of contemporary autism research is to better characterize and quantify the severity of these symptoms, and determine how they co-vary across individuals with ASD. Such associations across symptom domains may prove useful for understanding population responses to treatment (i.e., understanding why some individuals respond well to specific treatments while others do not) and revealing underlying biological mechanisms that may generate specific combinations of symptoms. Particularly interesting are symptoms that are associated not only in cross-sectional analyses, but also in a longitudinal manner such that changes in one symptom domain are correlated with changes in another symptom domain. Such co-variation overtime is expected from symptoms that are generated by common or interacting physiological mechanisms.

Liora Manelis-Baram and Gal Meiri are having equal contribution as first authors.

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Sleep Disturbances in ASD

Sleep disturbances are a common secondary symptom of ASD that negatively impacts the quality of life for children with ASD and their families (Delahaye et al., 2014; Hodge et al., 2013; Meltzer, 2008, 2011). Studies using parent

Published online: 09 April 2021

questionnaires have demonstrated that the most frequently described sleep disturbances are sleep onset delays, shorter sleep time, frequent night awakenings, and lower sleep efficiency (Elrod & Hood, 2015; Krakowiak et al., 2008; Richdale & Schreck, 2009; Souders et al., 2017). The incidence of these sleep disturbances is considerably higher in children with ASD (50–80%) as compared with the general population (20–40%) (Hirata et al., 2016; Little et al., 2018; Owens et al., 2000; Van Litsenburg et al., 2010). Studies using actigraphs at home or polysomnography in sleep labs have mostly validated the reports of parents (Arazi et al., 2020; Veatch et al., 2016; Yavuz-Kodat et al., 2019) and demonstrated that children with ASD sleep, on average, 30–40 min less per night in comparison to typically developing children (Elrod & Hood, 2015; Humphreys et al., 2014; Van der Heijden et al., 2018). These sleep disturbances are associated with the prevalence of irritability, inattention, hyperactivity, and physical aggression in children with ASD (Hollway et al., 2013; May et al., 2015; Mazurek & Sohl, 2016). While some have reported significant negative correlations between sleep disturbances and cognitive abilities or adaptive behaviors (Taylor et al., 2012), others have not (Krakowiak et al., 2008; Richdale & Schreck, 2009; Sikora et al., 2012). Similarly, while some have reported significant positive correlations between sleep disturbances and core ASD symptoms (Schreck et al., 2004; Veatch et al., 2017) others have not (Tzischinsky et al., 2018; Wiggins et al., 2019). These mixed findings suggest that sleep disturbances appear in many cases of ASD regardless of ASD severity, level of adaptive behaviors, or cognitive abilities.

Sensory Problems in ASD

Another common symptom of ASD is sensory problems, which are often quantified in two dimensions. The first is sensitivity (i.e., detection thresholds) to different stimuli and the second is responsivity (i.e., regulating the response) to the stimuli (Dunn, 2014). Note that sensory problems may vary across senses and contexts. The prevalence of sensory problems in children with ASD is estimated at 69–95% in comparison to 3–14% in typically developing children (Ahn et al., 2004; Baranek et al., 2006; Tomchek & Dunn, 2007). This has motivated the addition of sensory problems as one of the four criteria in the restricted and repetitive behaviors (RRB) symptom domain of the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM–5; APA, 2013). While some have reported that ASD children with sensory problems experience more social difficulties (Hilton et al., 2010; Matsushima & Kato, 2013), sensory problems are more strongly associated with the severity of RRB symptoms rather than social symptoms (Ben-Sasson et al., 2008; Boyd et al., 2010; Leekam & Prior, 2011; Schulz & Stevenson, 2018). A variety of techniques have been developed to treat sensory problems in ASD, including sensory integration (i.e., sensory-motor exercises), massage, and music therapy (Case-Smith et al., 2015; Weitlauf et al., 2017).

The Relationship Between Sleep Disturbances and Sensory Problems

Previous cross-sectional studies have repeatedly demonstrated a significant relationship between sleep disturbances and sensory hyper-sensitivity (or over-reactivity) in children with ASD (Liu et al., 2006; Mazurek & Petroski, 2015), particularly in the tactile (Tzischinsky et al., 2018) and auditory domains (Reynolds et al., 2012). Similar relationships have also been reported in typically developing children (Shochat et al., 2009; Spira et al., 2019; Vasak et al., 2015), suggesting a general association between the two symptom domains regardless of ASD. Indeed, sensory hyper-sensitivity may contribute to hyper-arousal, which is one of several mechanisms that are hypothesized to exacerbate sleep problems in children with ASD (Souders et al., 2017) and cause insomnia in the general population (Riemann et al., 2010).

Several longitudinal studies have reported that sleep disturbances persist over time in most children with ASD (Anders et al., 2012; Mannion & Leader, 2016). However, a recent study that followed 437 children over four years reported that 31% of children exhibited improvements in sleep disturbances, while 46% remained static, and 23% deteriorated (Mazurek et al., 2019). Similarly, sensory problems are also thought to be a persistent problem in ASD with little change at the group level over time (McCormick et al., 2016; Perez Repetto et al., 2017). However, some sensory intervention strategies may improve sensory sensitivities in children with ASD, thereby demonstrating that individual change is possible (Case-Smith et al., 2015; Weitlauf et al., 2017).

Longitudinal studies also enable assessment of early predictors for later outcome. One recent study used a path analysis to demonstrate that sensory over-reactivity scores predicted later sleep problems in toddlers but not in preschool age children (Mazurek et al., 2019). While this relationship is not necessarily causal (i.e., other intervening variables that were not measured may be at play), it reveals an association that may be particularly useful for designing interventions that can address causality. For example, one may hypothesize that applying techniques to reduce sensory over-responsivity may reduce sleep disturbances (Souders et al., 2017) and prevent later deterioration.

The goal of our study was to further examine the longitudinal relationship between sleep disturbances and sensory sensitivities. Specifically, we hypothesized that longitudinal changes in the severity of sleep disturbances would be correlated with longitudinal changes in sensory sensitivities. We tested this in 103 pre-school children with ASD who participated in two successive assessments at the National Autism Research Center of Israel (NARCI). We also examined the longitudinal relationship between sleep disturbances and ASD severity in a subset of the children who participated in Autism Diagnostic Observation Scale-2 (ADOS-2) assessments at both time-points.

Methods

Participants and Procedure

A total of 103 children participated in this study, which was performed at the NARCI (Dinstein et al., 2020; Meiri et al., 2017). This sample of convenience included all children who were diagnosed with ASD at NARCI between 2015 and 2020 (before the Covid-19 outbreak), and whose parents completed both the Child Sleep Habit Questionnaire (CSHQ, Owens et al., 2000) and the Sensory Profile (SP, Dunn, 2014) at two separate time-points (Time 1 and Time 2). On average, children were 3 years old at Time 1 and 4.5 years old at Time 2 (Table 1). All children fulfilled DSM-5 criteria for ASD as determined by both a physician (child psychiatrist or pediatric neurologist) and a developmental psychologist (APA, 2013). None of the children had epilepsy or any known genetic syndrome.

Eighty-three of the children completed an ADOS-2 assessment (Lord et al., 2012) within 5 months of Time 1. In the 20 remaining cases, ADOS assessments were not performed due to lack of family or clinician availability. Furthermore, 57 of the children returned for a second ADOS-2 assessment within 5 months of Time 2. All ADOS-2 assessments were performed by the same trained clinician with over 5 years of experience diagnosing ASD and research reliability, thereby ensuring comparability of scores across children and time-points. Finally, 64 of the children completed cognitive assessments using either the Bayley scales of infant and toddler development third edition (Bayley, 2006) or the Wechsler preschool and primary scale of intelligence, third edition (WPPSI, Wechsler, 2002) within 5 months of Time 1. Parents of participating children signed an informed consent form and the study was approved by the Soroka Medical Center Helsinki committee.

Measures

Child Sleep Habit Questionnaire (CSHQ)

Parents completed the validated Hebrew version of the CSHQ (Tzchishinsky et al., 2008), which is a parent-report questionnaire designed to screen for sleep disturbances. The CSHQ yields both a total sleep disturbance score and eight subscale scores (Bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep disordered breathing, daytime sleepiness) that were found to consistently differentiate between children with and without sleep disorders (Owens et al., 2000). The CSHQ was also validated for screening sleep problems in toddlers and preschool aged children (Goodlin-Jones, Sitnick, et al., 2008; Goodlin-Jones, Tang, et al., 2008). While for school

Table 1 Descriptive Statistics of the age, gender, sleep measures, sensory profile scores, ADOS-2 scores, and cognitive scores of participating children

	Time 1 Mean (SD)	Time 2 Mean (SD)
Age (years)	3.04 (1.12)	4.47 (1.19)
Gender (girls, %)	25 (24%)	
Sleep measures		
CSHQ Total sleep disturbance score	49.04 (9.4)	49.7 (9.04)
Night sleep duration (Hours:Minutes)	8:55 (1:20)	9:06 (1:12)
Total sleep duration (including naps) (Hours:Minutes)	10:26 (1:36)	9:58 (1:24)
Sensory Profile scores		
Sensation seeking	0.11 (0.9)	0.4 (0.8)
Sensation avoiding	0.47 (1)	0.67 (0.8)
Sensory sensitivity	0.46 (1)	0.71 (0.9)
Low registration	0.5 (1)	0.45 (0.9)
ADOS-2 scores		
Total Calibrated Severity Score (CSS)	7.5 (2.21)	6.8 (1.97)
Social Affect (SA) CSS	7.29 (1.79)	7.61 (1.49)
Restricted Repetitive Behaviors (RRB) CSS	7.56 (1.83)	6.96 (1.84)
Cognitive scores	79.32 (17.34)	–

Mean and standard deviation (in parenthesis). Sleep measures and SP scores were available for all children at both time-points. ADOS-2 scores were available for 83 of the children at Time 1 and 57 of the children at Time 2. Cognitive scores were available for 64 of the children at Time 1 age children, a total score of 41 is often used as a cutoff for sleep disturbances (Owens et al., 2000), in the current study we used a more conservative cutoff of 48 that was previously reported as more appropriate for younger children aged 2–5 years old (Reynolds et al., 2019).

In addition, parents provided quantitative data regarding their child's sleep schedule during the last week by answering the following questions; "What time did your child go to bed in the evening?" "How long did it take your child to fall asleep?" "What time did your child wake up in the morning?" "How many times did your child wake up during the night?" "How long was the child awake during the night?" "How much time did your child sleep during the day?".

Night sleep duration was calculated as the difference between the time children went to bed and their wake-up times minus sleep latency and time awake during the night. Total sleep duration, was calculated as the sum of night sleep duration and nap duration. The sleep duration of participating children was compared to the average sleep duration of typically developing children as reported in large international studies of toddlers (younger than 3 years old, M = 10, SD = 1:34, Mindell et al., 2010) and preschool children (3–6-years-old, M = 10:32, SD = 1:01, Mindell et al., 2013).

Infant/Child Sensory Profile (SP)

The SP is a caregiver questionnaire that quantifies behaviors associated with sensory processing dysfunction (Dunn, 2014), which has been validated in Israel (Millo, 2017). For example, caregivers rate how often the child covers their ears in response to aversive sounds or how often they are distressed by bright lights. The questionnaire yields four quadrant scores that sum ratings across multiple senses: sensation seeking (high sensory threshold and active self-regulation strategy), sensation avoiding (low sensory threshold and active self-regulation strategy), sensory sensitivity (low sensory threshold and passive self-regulation strategy) and low registration (high sensory threshold and passive self-regulation strategy). We used the Infant SP questionnaire (48 items) for children aged 35 months and younger and the Child SP questionnaire (89 items) for children older than 36 months. The SP scoring system enables transformation of raw scores into standardized scores (M = 0, SD = 1), which allow comparison of each individual to the distribution of scores in the general population, while accounting for the child's age.

ADOS-2

The ADOS-2 is a semi-structured evaluation that enables clinicians to assess the existence and severity of core ASD symptoms (Lord et al., 2012) and has been validated in Israel (Millo, 2016). Participants in our sample completed either the toddler module, module 1, module 2, or module 3 of the ADOS-2, according to their age and language abilities. The ADOS-2 scoring system enables transformation of raw scores into calibrated severity scores (CSS), which allow comparison of ASD severity across children of different ages and language capabilities (Esler et al., 2015; Gotham et al., 2009). ADOS-2 CSS were computed separately for each of the two core ASD symptom domains; social affect (SA), and restricted and repetitive behaviors (RRB) (Esler et al., 2015; Hus et al., 2014).

Cognitive Assessments

Younger children completed the Bayley (Bayley, 2006), suitable for children ages 1–42 months old. Older children completed the WPPSI (Wechsler, 2002), suitable for children ages 2.6–7.3 years old. Bayley cognitive scores exhibit strong correlations with general intelligence WPPSI scores (Bayley, 2006; Bode et al., 2014) and both tests yield equivalent standardized scores with a mean of 100 and a standard deviation of 15. Hence we combined scores from the two assessments in all analyses.

Quantifying Changes in Symptom Severity

We quantified changes in sleep disturbance and Sensory Profile scores by subtracting Time 2 scores from Time 1 scores (i.e., Time 1–Time 2 = change). Hence, negative values indicated a deterioration in symptoms (i.e., Time 1 scores lower than Time 2 scores) while positive values indicated an improvement in symptoms (i.e., Time 1 scores higher than Time 2 scores). To estimate individual changes in a more categorical manner we classified children into the following three groups based on the magnitude of change: "no change" (between −0.5 and 0.5 SD), "improved" (change greater than 0.5 SD) or "deteriorated" (change smaller than −0.5 standard deviation). While 0.5 standard deviation is an arbitrary threshold, previous research has suggested that it is a credible and reliable measure of change (Norman et al., 2003). SP scores are inherently based on units of standard deviation (Dunn, 2014), making it easy to compute changes in standard deviation across time-points. To translate CSHQ scores into units of standard deviation we utilized data from a previous study with similarly aged toddlers where the standard deviation across sleep disturbance scores was 6.7 (Reynolds et al., 2019).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics (Version 23). Paired t-tests were used to assess the significance of change in sleep disturbances scores and SP scores across Time 1 and Time 2. Pearson correlations were used to assess the relationships between sleep scores, SP scores, and ADOS-2 total CSS, ADOS-2 SA CSS, or ADOS-2 RRB CSS. We also performed partial correlation analyses to determine the unique relationship between sleep disturbances and each of the four SP quadrant scores. Finally, we performed several step-wise hierarchical regression analyses to examine the ability of specific measures from Time 1 to predict the severity of sleep disturbances scores at Time 2 or their change over time. The initial step always included two measures: the age of the children at Time 1 and the time between assessments. Additional measures (e.g., sleep disturbances at Time 1) were then added as predictors to the regression model in separate steps to assess their additive explanatory power after accounting for the children's age and the time across assessments. Kolmogorov–Smirnov tests indicated that the distributions of all variables included in the correlation and regression analyses were not significantly different from a normal distribution (all $p > 0.05$). We did not perform any corrections for multiple comparisons throughout the study in order to increase sensitivity.

Results

A large percentage of ASD children exhibited CSHQ sleep disturbance scores that were larger than our cutoff of 48 (Fig. 1). This was similarly apparent in the first (50 children, 48.5%) and second (56 children, 54.3%) time-points of the study (Fig. 1). In contrast, previous studies have reported that only 23–32% of typically developing children at similar ages exhibit sleep disturbances that exceed this cutoff (Krakowiak et al., 2008; Owens et al., 2000; Reynolds et al., 2019).

Sleep problems were also evident when comparing the sleep duration at night reported by parents in our study with those reported by parents of typically developing children in two large international studies (Mindell et al., 2010, 2013). At Time 1 children in our study were, on average, 3-years-old, and slept 8:54 (SD = 1:18) hours during the night and 10:28 (SD = 1:36) hours in total (when including naps). In contrast, typically developing 2–3-year-old children sleep, on average, 10 (SD = 1:34) hours during the night and 13:01 (SD = 2:01) hours in total (Mindell et al., 2010). Similarly, at Time 2 children in our study were, on average, 4.5-years-old and slept 9:07 (SD = 1:12) hours during the night and 9:58 (SD = 1:24) hours in total. In contrast, typically developing 3–6-year-old children sleep, on average, 10:32 (SD = 1:01) hours during the night and 11 (SD = 1:01) hours in total (Mindell et al., 2013). This suggests that children with ASD in our sample were sleeping 1–2:35 hours less than their typically developing peers.

A large percentage of children with ASD also exhibited sensory problems (Fig. 1). Forty two children at Time 1 (40.8%) and 41 children at Time 2 (39.8%) exhibited SP

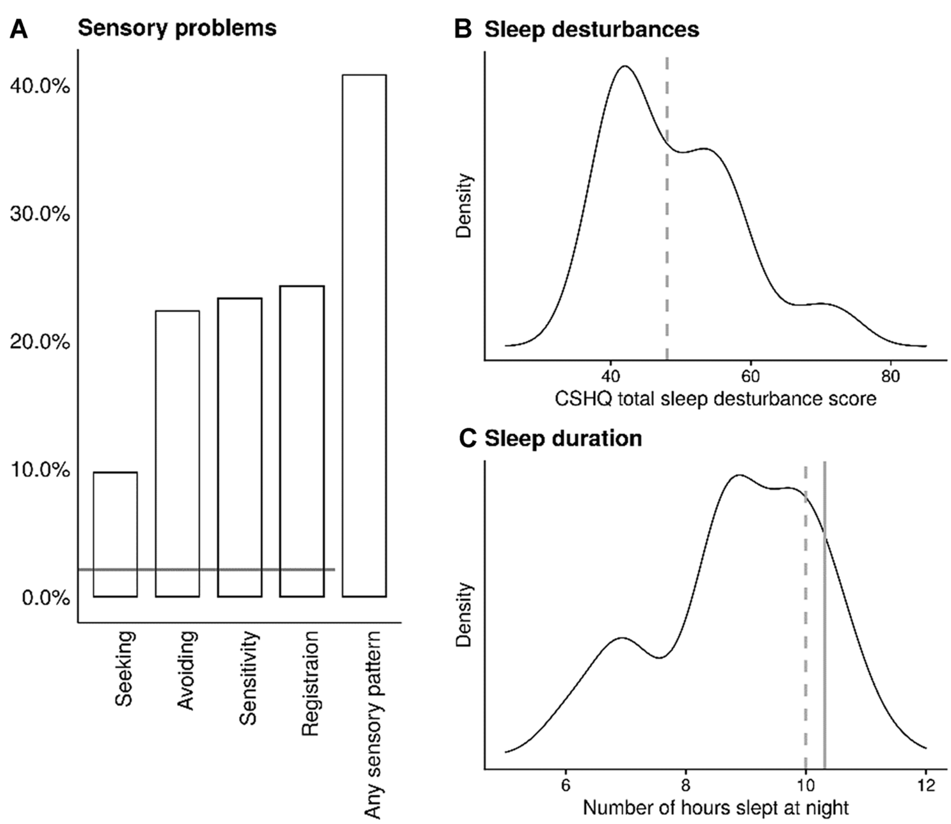

Fig. 1 Sensory and sleep problems at Time 1. **a** Percentage of children with Sensory Profile scores that were greater than 2 standard deviations from the general population mean. *Horizontal line*: expected percentage in typically developing children. **b** Density plot of CSHQ sleep disturbance scores. Vertical dashed line: cutoff score of 48 for sleep disturbances in preschool age children. **c** Density plot for night sleep duration in hours. *Vertical lines*: average sleep duration at night for toddlers (dashed line = 10 h) and preschool age children (solid line = 10:32 h) as reported by two large international studies (see methods)

scores that were greater than 2 standard deviations in at least one sensory quadrant. The percentage of ASD children who exhibited SP scores greater than 2 standard deviations in the seeking, avoiding, sensitivity, and registration quadrants were 9%, 22%, 23%, and 24% at Time 1, and 15%, 21%, 26%, and 18% at Time 2, respectively. Note that only 2.14% of children in the general population are expected to exhibit such high Sensory Profile scores in each quadrant (Dunn, 2014).

Sleep Disturbances are Correlated with Sensory Problems, But Not with ADOS-2 or Cognitive Scores

We performed a cross-sectional analysis examining the relationship between sleep, sensory, ADOS-2, and cognitive measures that were available for Time 1 (Table 2). Significant Pearson correlations were found between total sleep disturbance scores and sensory sensitivity ($r = 0.57$, $p < 0.001$), sensation avoiding ($r = 0.49$, $p < 0.001$), low registration ($r = 0.37$, $p < 0.001$), and sensation seeking ($r = 0.24$, $p = 0.014$) scores. Given the strong correlations across Sensory Profile quadrants (see below), we also performed a partial correlation analysis that quantified the unique relationship between each SP quadrant and sleep disturbances. This analysis revealed that sensory sensitivity scores were the only measure that was reliably correlated with sleep disturbances scores when controlling for the other sensory quadrants ($r = 0.35$, $p < 0.001$). In contrast, sensory seeking ($r = -0.13$, $p = 0.17$), sensation avoiding ($r = 0.1$, $p = 0.28$), and low registration ($r = 0.01$, $p = 0.9$) scores were not.

Equivalent results were apparent when correlating the four sensory quadrant scores with measures of sleep duration as reported by the parents. Night-time sleep duration was significantly, negatively correlated with sensory sensitivity ($r = -0.28$, $p = 0.006$) and sensation avoiding ($r = -0.24$, $p = 0.018$), but not with sensation seeking ($r = -0.12$, $p = 0.2$) and low registration ($r = -0.11$, $p = 0.2$). These relationships were stronger when examining total sleep duration (i.e., including naps). Significant negative correlations were evident with sensory sensitivity ($r = -0.4$, $p < 0.001$), sensation avoiding ($r = -0.3$, $p = 0.003$), and sensation seeking ($r = -0.36$, $p < 0.001$), but not with low registration ($r = -0.18$, $p = 0.08$). Here too, sensory sensitivity scores exhibited the strongest correlations with both measures of sleep duration.

Cognitive scores and ADOS-2 CSS were available for 64 (62%) and 83 (80%) of the children, respectively. All of the examined sleep measures were not significantly correlated with either cognitive scores or ADOS-2 CSS (Table 2). SP scores in all four quadrants were also not significantly correlated with either cognitive scores or ADOS-2 CSS (Table 2).

Table 2 Relationship between measures of sleep, sensory profile scores, cognitive scores, and ADOS-2 CSS at Time 1

	Sensation seeking ($n = 103$)	Sensation avoiding	Sensory sensitivity	Low registration	Cognitive score ($n = 64$)	ADOS-2 Total CSS ($n = 83$)	ADOS-2 SA CSS	ADOS-2 RRB CSS
Sleep measures								
CSHQ total sleep disturbance score	**0.24***	**0.49*****	**0.57*****	**0.37*****	0.06	−0.13	−0.04	−0.02
Night-time sleep duration	−0.12	**−0.24***	**−0.28****	−0.11	0.04	0.07	0.02	0.04
Total sleep duration	**−0.36*****	**−0.3****	**−0.4*****	−0.18	−0.01	−0.21	0.17	−0.26
Sensory Profile scores								
Sensation seeking		**0.5*****	**0.57*****	**0.53*****	0.21	−0.09	−0.13	0.12
Sensation avoiding			**0.78*****	**0.69*****	0.11	−0.09	0.03	−0.03
Sensory sensitivity				**0.64*****	0.06	−0.07	−0.02	0.01
Low registration					0.15	0.09	0.02	0.1

Top rows: Pearson correlation coefficients between sleep measures and each of the sensory quadrant scores, cognitive scores, and ADOS-2 CSS (Total, SA, and RRB). *Bottom rows:* Same as top row for each of the sensory quadrant scores. Asterisks indicate statistical significance of correlation coefficients: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$, not corrected for multiple comparisons

This Indicates that sleep disturbances and sensory problems were similarly evident in children with autism who had different autism severities and cognitive abilities. To ensure the representativeness of the 64 children with cognitive scores and the 83 children with ADOS scores at Time 1, we compared their sleep and sensory scores to those of the entire sample ($n = 103$). No significant differences were found in any of the sleep or sensory measures across groups (all $p > 0.2$).

Interestingly, strong and significant correlations were apparent across the different SP quadrants ($r = 0.5$–0.78, $p < 0.001$, Table 2). These correlations demonstrate a paradoxical and un-intuitive overlap in the sensory problems exhibited by ASD children. For example, ASD children can exhibit both low sensory thresholds (i.e., high sensitivity scores) along with low responsivity to sensory stimuli (i.e., high registration scores) as indicated by the strong correlation between sensory sensitivity and low registration scores ($r = 0.64$, $p < 0.001$). We speculate that this overlap in opposing symptoms is due to the remarkable variability of behaviors apparent in ASD children under different circumstances and contexts.

Longitudinal Changes in Sleep Disturbances and Sensory Problems

We examined longitudinal changes in symptom severity by subtracting the scores at Time 1 from the scores at Time 2. Note that positive values indicate improvement in symptoms while negative values indicate deterioration in symptoms. Sleep disturbance scores did not change significantly across Time 1 and Time 2 ($t(102) = -0.71, p = 0.47$, Table 1). However, significant deterioration between Time 1 and Time 2 was apparent in sensation seeking ($t(102) = -3.3, p = 0.001$) and sensory sensitivity ($t(102) = -2.7, p = 0.008$) scores. There was also a trend in the same direction in sensation avoiding scores ($t(102) = -1.8, p = 0.07$), and no significant change in low registration scores ($t(102) = -0.5, p = 0.61$). Note that these mean changes in SP scores were relatively small in magnitude and did not exceed 0.2 standard deviations (Table 1).

While group differences across the two time-points were relatively small, individual children exhibited considerably larger changes over time (Fig. 2). We classified individual children into groups exhibiting deterioration, stability, or improvement over time (see methods). When examining sleep disturbance scores, 35% ($n = 36$) of the children deteriorated, 34% ($n = 35$) remained stable, and 31% ($n = 32$) improved. In the sensory sensitivity quadrant, 28% ($n = 29$) deteriorated, 55% ($n = 57$) remained stable, and 17% ($n = 17$) improved. In the sensation-avoiding quadrant, 34% ($n = 35$) deteriorated, 43% ($n = 44$) remained stable, and 23% ($n = 24$) improved. In the sensation seeking quadrant, 34% ($n = 35$) deteriorated, 49% ($n = 51$) remained stable, and 17% ($n = 17$) improved. Finally, in the sensory registration quadrant, 23% ($n = 24$) deteriorated, 52% ($n = 53$) remained stable, and 25%

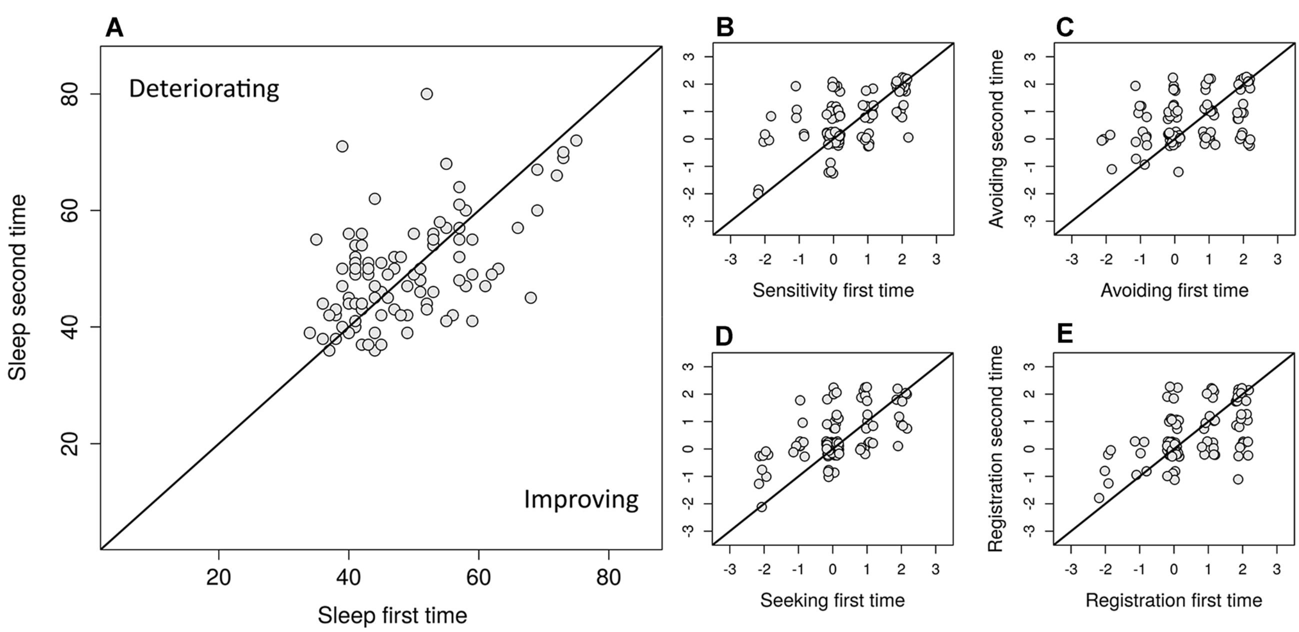

Fig. 2 Changes in symptom severity of individual children between Time 1 and Time 2. Scatter plots demonstrate the magnitude of change in scores of: **a** Total sleep disturbance **b** Sensory sensitivity **c** Sensation avoiding **d** Sensation seeking **e** Sensory registration. Each point represents an individual child with ASD. *Solid line*: unity line. Children below the unity line exhibited improvement over time (i.e., lower scores at Time 2 relative to Time 1) while children above the line exhibited deterioration

($n = 26$) improved. These results demonstrate that more than 50% of children with ASD exhibit substantial positive or negative changes in the severity of sleep and/or sensory symptoms over time.

Changes in Sleep Disturbances are Correlated with Changes in Sensory Sensitivity

We examined whether individual changes in sleep disturbances were correlated with individual changes in each of the four sensory quadrants (Fig. 3). We found significant positive correlations between the changes in sleep disturbance scores and the changes in sensory sensitivity ($r = 0.42$, $p < 0.001$), sensation avoiding ($r = 0.3$, $p = 0.002$), and sensory registration ($r = 0.24$, $p = 0.01$) scores, but not with changes in sensation seeking scores ($r = 0.12$, $p = 0.2$).

Given the strong correlation across SP quadrant scores (Table 2), we performed a partial correlation analysis that examined the independent relationship between changes in sleep disturbance scores and changes in each of the SP quadrants (i.e., while controlling for the three other sensory quadrants). This analysis revealed that changes in sleep disturbances were specifically associated only with changes in sensory sensitivities ($r = 0.31$, $p = 0.002$) and not with changes in sensation avoiding ($r = 0.05$, $p = 0.61$), sensory registration ($r = 0.13$, $p = 0.19$) or sensation seeking ($r = -0.06$, $p = 0.54$). Adding the child's age at time 1 and the time-gap between assessments to this partial correlation analysis as control variables did not alter the results – only the relationship with sensory sensitivity remained significant ($r = 0.3$, $p = 0.002$).

Longitudinal changes in sleep disturbances or sensory problems were not significantly correlated with changes in ADOS-2 CSS. This was apparent in a sub-group of 57 children who participated in two ADOS-2 assessments that were administered in proximity to Time 1 and Time 2. No significant correlations were found between changes in ADOS-2 CSS and changes in sleep disturbance ($r(57) = -0.04$, $p = 0.75$) or sensory problems (all $r < 0.18$ and $p > 0.16$).

Predicting Sleep Disturbances and Change in Sleep Disturbances

We performed two hierarchical step-wise regression analyses to determine whether it was possible to predict the severity of sleep disturbance scores at Time 2. In the first analysis (Model 1), the predictors included the age of the child at Time 1, time between assessments, sleep disturbance scores at Time 1, and SP scores (from each of the four quadrants) at Time 1. In the second analysis (Model 2), performed with a subset of 58 children, we also added the ADOS-2 CSS and cognitive scores as predictors. Both analyses demonstrated that the sleep disturbance score at Time 1 was the only measure with significant predictive value regarding the severity of the sleep disturbance score at Time 2 (Table 3). Adding Sensory Profile scores from Time 1 to either model did not significantly increase their predictive ability.

We then performed two additional hierarchical step-wise regression analyses in an attempt to predict the change in sleep disturbance scores over time (i.e., Time 1–Time 2). Here too, the only variable from Time 1 with significant predictive value was the sleep disturbance score at Time 1 (Table 4). This indicated that children with more severe sleep disturbances at Time 1 were more likely to improve while children with less severe sleep disturbances at Time 1 were more likely to deteriorate. This is also evident when examining Fig. 2a. Adding Sensory Profile, ADOS, or cognitive scores from Time 1 to either model did not significantly increase their predictive ability.

In a final hierarchical regression analysis (Table 5), we substituted the SP scores from Time 1 with their change over time (i.e., Time 1–Time 2). This analysis revealed that the change in sensory sensitivity scores added significant predictive ability to the regression model, above and beyond the predictive ability of sleep disturbance scores at Time 1. Changes in sensory sensitivity were the *only* SP measure that improved prediction of changes in sleep disturbances score. These results further demonstrate that changes in sensory

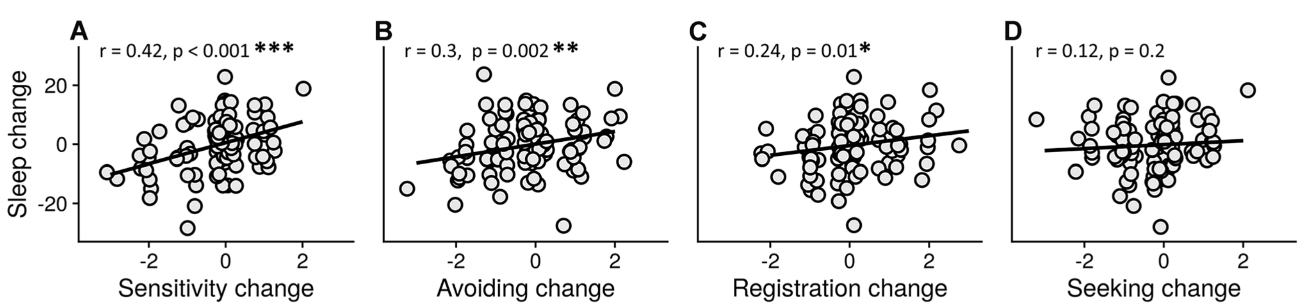

Fig. 3 Scatter plots demonstrating the relationship between change in sleep disturbance and change in each of the SP quadrants. **a** Sensory sensitivity **b** Sensation avoiding **c** Low registration **d** Sensation seeking. Each circle represents a single ASD child. Pearson's correlation coefficients are noted in each panel. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$, not corrected for multiple comparisons

Table 3 Hierarchical regression analyses to predict Time 2 sleep disturbance scores using variables from Time 1

		Predicting Time 2 sleep disturbance scores				
		β (beta)	P	*R^2 change*	*F change*	P
Model 1[a]	***Step 1***			0.005	0.27	0.7
	Age at time 1 (months)	−0.07	0.5			
	Time between assessments (months)	−0.05	0.6			
	Step 2			**0.27**	**36.4**	**< 0.001********
	Time 1 sleep disturbance score	**0.55**	**< 0.001*****			
	Step 3			0.02	0.6	0.6
	Time 1 sensation seeking	0.1	0.4			
	Time 1 sensation avoiding	−0.03	0.8			
	Time 1 sensory sensitivity	−0.14	0.3			
	Time 1 low registration	0.12	0.3			
Model 2[b]	***Step 1***			0.01	0.4	0.6
	Age at time 1	−0.01	0.9			
	Time between assessments	−0.03	0.8			
	Step 2			0.02	0.6	0.5
	Cognitive score	−0.01	0.9			
	ADOS-2 comparison score	0.17	0.2			
	Step 3			**0.19**	**13**	**0.001*****
	Time 1 sleep disturbance score	**0.48**	**0.002****			
	Step 4			0.05	0.8	0.5
	Time 1 sensation seeking	0.14	0.3			
	Time 1 sensation avoiding	0.01	0.9			
	Time 1 sensory sensitivity	−0.23	0.3			
	Time 1 low registration	0.18	0.2			

Variables were added to the models in consecutive steps. Beta values and their *p*-values are presented for each predictor. Change in R^2 and related F- and *p*-values are presented for each step. *Asterisks:* significant β values or R^2 change ($^{**}p < 0.01$; $^{***}p < 0.001$)

[a]Model 1 included data from all children ($n = 103$)

[b]Model 2 included children with cognitive and ADOS-2 scores at time 1 ($n = 58$)

sensitivity over time (rather than their initial values) are tightly coupled with changes in sleep disturbances.

Discussion

Our results revealed a significant longitudinal relationship between changes in the severity of sleep disturbances and changes in the severity of sensory sensitivities (Fig. 3). ASD children who improved in one symptom domain tended to improve in the other symptom domain such that changes in the severity of sensory problems explained ~ 17% of changes in sleep disturbance (Fig. 3a). This relationship remained significant even after controlling for a variety of other measures including the children's age, the time between assessments, and the initial severity of sleep disturbances (Table 5). These findings demonstrate that the severity of the two symptoms is coupled, to some degree, over relatively long periods of time (1–3 years), potentially indicating that these symptoms are generated by common or interacting underlying physiological mechanisms.

Initial sensory profile scores at Time 1 were not predictive of sleep disturbances scores at Time 2 or their change over time (Tables 3 and 4). This demonstrated that changes in sleep disturbances scores were tied to changes in sensory sensitivity scores rather than their initial severity at Time 1 (Table 5). Hence, children who improve in their sensory sensitivity scores are likely to improve in their sleep disturbance scores regardless of their initial sensory sensitivities. Furthermore, children were more likely to improve in their sleep disturbance scores if their initial sleep disturbance scores at Time 1 were higher (Table 5).

Taken together, these findings suggest that reducing sensory sensitivities in children with higher sleep disturbances scores at Time 1 is likely to yield the largest clinical impact for improving sleep disturbances. Further studies that will assess the severity of the two symptom domains before and after interventions that target one of them (e.g., use

Table 4 Hierarchical Regression Analyses to Predict change in Sleep Disturbance Scores over time using variables from Time 1

		Predicting change in sleep disturbance scores over time				
		β (beta)	P	*R^2 change*	*F change*	p
Model 3[a]	***Step 1***			0.02	1.2	0.3
	Age at time 1 (months)	0.07	0.5			
	Time between assessments (months)	0.05	0.6			
	Step 2			**0.26**	**35.6**	**< 0.001*****
	Time 1 sleep disturbance score	**0.49**	**< 0.001*****			
	Step 3			0.02	0.6	0.64
	Time 1 sensation seeking	−0.1	0.4			
	Time 1 sensation avoiding	0.03	0.8			
	Time 1 sensory sensitivity	0.13	0.4			
	Time 1 low registration	−0.12	0.3			
Model 4[b]	***Step 1***			0.02	0.6	0.5
	Age at time 1	0.08	0.9			
	Time between assessments	0.02	0.8			
	Step 2			0.04	1.2	0.3
	Cognitive score	0.01	0.9			
	ADOS CSS	−0.16	0.2			
	Step 3			**0.2**	**14.9**	**< 0.001*****
	Time 1 sleep disturbance score	**0.43**	**0.004****			
	Step 4			0.05	0.8	0.5
	Time 1 sensation seeking	−0.14	0.3			
	Time 1 sensation avoiding	−0.01	0.9			
	Time 1 sensory sensitivity	0.23	0.3			
	Time 1 low registration	−0.18	0.3			

Variables were added to the models in consecutive steps. Beta values and their *p*-values are presented for each predictor. Change in R^2 and related F- and *p*-values are presented for each step. *Asterisks*: significant β values or R^2 change ($^{**}p < 0.01$; $^{***}p < 0.001$) indicating significant predictive ability

[a]Model 3 included data from all children ($n = 103$)

[b]Model 4 included children with cognitive scores and ADOS-2 CSS at time 1 ($n = 58$)

Table 5 Hierarchical Regression Analysis to Predict change in Sleep Disturbance Scores over time using SP score changes over time

		Predicting change in sleep disturbance scores over time				
		β (beta)	P	*R^2 change*	*F change*	p
Model 5	***Step 1***			0.02	1.2	0.3
	Age at time 1 (months)	0.008	0.9			
	Time between assessments (months)	0.05	0.5			
	Step 2			**0.56**	**35.6**	**< 0.001*****
	Time 1 sleep disturbance score	**0.46**	**<0.001*****			
	Step 3			**0.11**	**4.5**	**0.002****
	Sensation seeking change (Time1–Time2)	0.03	0.7			
	Sensation avoiding change (Time1–Time2)	0.09	0.3			
	Sensory sensitivity change (Time1–Time2)	**0.23**	**0.02***			
	Low registration change(Time1–Time2)	0.08	0.3			

Variables were added to the models in consecutive steps. Beta values and their *p*-values are presented for each predictor. Change in R2 and related F- and *p*-values are presented for each step. Asterisks: significant β values or R2 change ($^{**}p < 0.01$; $^{***}p < 0.001$) indicating significant predictive ability. This analysis included all children ($n = 103$)

of Melatonin; Rossignol & Frye, 2011, or techniques that reduce sensory sensitivities; Souders et al., 2017, Weitlauf et al., 2017) are highly warranted for elucidating the causal relationship between the two symptom domains.

The Relationship Between Sleep Disturbances and Sensory Problems

Sleep disturbances and sensory problems are clearly more prevalent in children with ASD (Ben-Sasson et al., 2009; Little et al., 2018; Mazurek & Sohl, 2016; Reynolds et al., 2019; Table1 and Fig. 1). Several recent cross-sectional studies have reported that the severity of sleep disturbances in ASD children are correlated with the severity of their sensory problems and particularly with the severity of sensory sensitivities (Liu et al., 2006; Malow et al., 2014; Mazurek & Petroski, 2015; Tzischinsky et al., 2018). This was also clearly apparent in our study, where the severity of sensory sensitivities explained ~ 32% of the variance in sleep disturbance scores at Time 1 (Table 2). Importantly, sensory sensitivity scores were the only sensory measure that was uniquely associated with sleep disturbances when performing a partial correlation analysis as also reported in several other studies (Liu et al., 2006; Mazurek & Petroski, 2015; Tzischinsky et al., 2018). Note that a similar association between sensory sensitivities and sleep disturbances was also apparent in studies with typically developing toddlers (Vasak et al., 2015) and children (Shochat et al., 2009), where sensory sensitivity scores explained ~ 30% of the variance in sleep disturbances scores (Spira et al., 2019). This suggests that there is a general association between the two symptom domains, which may be particularly important to address in children with ASD where the severity of symptoms in both domains is considerably higher.

Previous longitudinal studies have reported that sleep disturbances (Anders et al., 2012; Mannion & Leader, 2016) and sensory problems (McCormick et al., 2016; Perez Repetto et al., 2017) are persistent symptoms that appear in cross-sectional comparisons of children, adolescents, and adults with ASD versus controls. While differences between ASD and control groups may be apparent at multiple ages, longitudinal studies have demonstrated that individual children with ASD can improve, remain static, or deteriorate in symptom severity over time. For example, one recent study reported that 31% of 2–10-year-old children with ASD improved, 46% remained static, and 23% deteriorated in sleep disturbances scores over a 4 year period (Mazurek et al., 2019). Here, we report similar findings in 1–6-year-old children where 34% of the children improved, 31% remained static, and 35% deteriorated in their sleep disturbance symptoms. In addition, the same children in our study also exhibited clear longitudinal changes in sensory sensitivities with 17% of the children improving, 55% remaining static, and 28% deteriorating (Fig. 2). These findings demonstrate that sensory and sleep symptom severity can change dramatically in individual children, thereby highlighting the opportunity for developing and implementing effective targeted interventions.

The main contribution of this study is in demonstrating that longitudinal changes in sensory sensitivity scores can explain ~ 17% of the variability in changes of sleep disturbances scores. We suggest that this longitudinal coupling is indicative of shared or interacting physiological mechanism that may generate both symptoms. Indeed, previous research has suggested that sensory sensitivities may be a causal component in generating severe sleep disturbances such as insomnia, which are present in 60–80% of children with ASD (Goodlin-Jones, Sitnick, et al., 2008; Goodlin-Jones, Tang, et al., 2008; Robinson-Shelton & Malow, 2016).

Insomnia is thought to be generated by a variety of intrinsic and extrinsic factors (Souders et al., 2017). Intrinsic factors include the genetic, biological, and psychiatric characteristics of the child while extrinsic factors include the child's sensory environment, exposure to stressors, availability of caffeine, and the presence of overly accommodating parents. Sensory hyper-sensitivity is one of several intrinsic factors that are thought to create hyper-arousal, which delays sleep onset and induces night waking (Bonnet & Arand, 2010). According to this model, sensory hyper-sensitivities may exacerbate sleep disturbances in children with ASD in a causal manner. While our study does not provide direct evidence for a causal relationship, it does demonstrate that changes in the severity of the two symptom domains are correlated, as expected from a causal relationship.

The Relationship Between Sleep Disturbances, Core ASD Symptoms, and Cognitive Function

While sleep disturbances were correlated with sensory sensitivities, they were not associated with the severity of core ASD symptoms as assessed by the ADOS-2 (Table 2). Furthermore, changes in the severity of sleep disturbances were not correlated with changes in ADOS-2 scores, suggesting that there was no significant longitudinal relationship within the examined 1–3-year period. While some previous studies have reported that the severity of sleep problems is related to the severity of ASD symptoms, most of these studies used parent reports (e.g., the Gilliam Autism Rating Scale; Hoffman et al., 2005; Schreck et al., 2004). Studies that used direct clinical assessments with the ADOS-2 did not report significant associations (Sannar et al., 2018; Wiggins et al., 2019). The difference in findings may be due to a systematic bias in parent reports, which is a known limitation of parental questionnaires (Podsakoff et al., 2003), or to a potential lack of sensitivity in the ADOS-2 assessments

(Green et al., 2010). Regardless, sleep disturbances are prevalent in many ASD children with varying degrees of core symptom severity.

Given the immense importance of sleep for human development, emotional regulation, and cognitive functioning (Walker, 2017), it is likely that sleep disturbances do have some impact on the development of social communication abilities. For example, ASD children with larger sleep disturbances exhibit increased irritability and social withdrawal (Johnson et al., 2018). While we did not find a longitudinal relationship between changes in sleep disturbance and ADOS-2 scores, we believe that studies assessing changes in core ASD symptoms before and after sleep interventions are highly warranted and currently lacking (Lord, 2019). In line with multiple previous studies (Johnson et al., 2018; Krakowiak et al., 2008; Mayes & Calhoun, 2009; Sikora et al., 2012), our results also demonstrated no significant relationship between the severity of sleep disturbances and individual cognitive abilities (Table 2).

Limitations

The current study had several limitations that should be acknowledged. First, while the CSHQ and the sensory profile are widely validated questionnaires, they are based on parent report and may include subjective bias (Rónnlund et al., 2016). Further research examining the longitudinal relation between sleep and sensory processing using more objective measures of sleep (e.g., actigraphy or polysomnography) and sensory processing (e.g., direct estimation of sensory thresholds) is highly warranted. Second, in the current study we did not examine the relationship between sleep disturbances or sensory processing and other important symptom domains such as adaptive behaviors (Krakowiak et al., 2008; Sikora et al., 2012), aberrant behaviors, and anxiety (Mazurek & Petroski, 2015; Wigham et al., 2015). Given the multitude of internal factors that may drive sleep disturbances (Souders et al., 2017), longitudinal studies examining multiple factors at multiple time-points are likely to be highly informative in determining their relative impact in children with ASD. Finally, we also do not know whether participating children were receiving specific medications, therapies, or special diets that may have affected their sleep or sensory sensitivities across assessments.

Conclusions

The current study reveals that sleep disturbances and sensory sensitivities co-vary in a longitudinal manner. We speculate that these two symptom domains are co-dependent with sensory sensitivities likely exacerbating sleep disturbances in children with ASD. Additional studies examining the effects of sensory processing interventions (Case-Smith et al., 2015; Weitlauf et al., 2017) on sleep disturbances are highly warranted for determining a potential causal relationship.

Acknowledgments No acknowledgments

Author contribution LMB contributed to the study design, performed all analyses, created all figures, and wrote the manuscript. GM contributed to the study design, recruitment of families, data collection, and interpretation of results. MI, MF, AM, HF, and IM contributed to recruitment of families, data collection, and interpretation of results. ID conceived the study, designed the study, guided data analyses, and wrote the manuscript with LMB.

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