The Interplay Between Sleep and Executive Functioning in Children with Autism

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Abstract

Study Objectives: Up to 80% of children with autism spectrum disorder (ASD) experience sleep disturbance. Poor sleep impairs executive functioning (EF), a lifelong difficulty in ASD. Evidence suggests EF impairments in ASD is exacerbated by poor sleep. We examine whether early childhood sleep disturbances are associated with worsening EF trajectories in school-aged children with ASD.

Methods: A subsample ($n = 217$) from the *Pathways in ASD* longitudinal study was analyzed. The *Children's Sleep Habits Questionnaire* captured sleep duration, onset, and night awakenings before age 5 (Mean=3.5 years). Metacognition (MI) and Behavioral Regulation (BRI) indices on the *Teacher Behavior Rating Inventory of Executive Functioning* measured EF difficulties at four time-points (7-11 years). We applied latent growth curve models to examine associations between sleep and EF, accounting for relevant covariates, including school-age sleep (Mean=6.7 years).

Results: Longer sleep onset at 3.5 years predicted a worsening BRI difficulties slope ($b = 2.07, p < 0.04$), but conversely predicted lower BRI difficulties at age 7.7 ($b = -4.14, p = 0.04$). A longer sleep onset at age 6.7 predicted higher BRI difficulties at age 7.7 ($b = 7.78, p < 0.01$). Longer sleep duration at age 6.7 predicted higher BRI difficulties at age 7.7 ($b = 3.15, p = 0.01$), but subscale analyses revealed shorter sleep duration at age 6.7 predicted a worsening inhibition slope ($b = -0.597, p = 0.01$).

Conclusions: Different sleep phenotypes have different age-related impacts on selective behavioral regulation components, but not metacognition. Delayed sleep onset is a robust early predictor, whereas shorter sleep duration is a later predictor of worsening behavior regulation in school-aged children with ASD.

Introduction

In typically developing (TD) children, the first 5 years are marked by rapid attainment of EF, while more complex EFs develop. Sleep is disturbed in up to 80% of children with ASD Spectrum Disorder (ASD)¹. Shorter sleep duration and traits related to insomnia, including difficulty falling asleep and frequent night awakenings, are most commonly reported². Problematic sleep in ASD is found early in infancy and contrary to observations in typical development, sleep problems have been found to persist in ASD³.

Poor sleep in children impairs executive functioning (EF)⁴, a well-documented lifelong difficulty in individuals with ASD⁵. EF is an umbrella term that describes higher order cognitive processes that enable individuals to engage in deliberate, goal-directed thoughts and actions and is known to play a pivotal role in early social-cognitive development⁶. These processes are commonly condensed into three core components: working memory, inhibitory control and cognitive flexibility⁶. Behavioral regulation (BR) and metacognition (MC) are evaluated on frequently used EF questionnaires⁷, to capture “hot” and “cold” EF respectively. Cold EF is suggested to encompass purely cognitive processes (e.g., planning and organizing), whereas hot EF refers to cognitive processes underlying the management of affective behavior (e.g., emotional control)⁸.

In typically developing (TD) children, the first 5 years are marked by rapid attainment of EF, while more complex EFs develop during middle childhood and adolescence⁹. Such complex EFs are needed for higher level problem solving and negotiating with evolving environmental intricacies⁹. The development of complex EF is predicted by early attainment of foundational EF⁶.

Despite consistent documentation of everyday EF impairments in ASD across a wide age range⁵, to our knowledge, only one longitudinal study has been conducted. Parent-reported BR and MC abilities in children with ASD aged 7-14 years did not significantly change when reported 2 years later, but at both time-points, children with ASD had poorer BR and MC abilities compared to TD controls¹⁰. This study provides evidence that EF dysfunction appears to be stable in middle

childhood and adolescence in ASD, periods when complex EF skills are emerging. However, due to the wide age range of the sample, the study does not allow for any conclusions to be made about the developmental trajectory of EF in childhood and adolescence. Reviews of cross-sectional studies of EF in ASD suggest that, whilst EF is consistently impaired compared to normative samples, there is linear development in EF throughout childhood and adolescence, with discrepancies of EF performance becoming less pronounced in adulthood^{5,11}. Currently, there are no investigations of EF trajectories and factors that may contribute to successful EF development across childhood in ASD. This is problematic because executive dysfunction in ASD is known to contribute to a poorer quality of life, increased psychiatric comorbidities, and adaptive functioning difficulties^{12–14}. One possible mechanism underlying executive dysfunction in ASD is poor sleep. Numerous observational and experimental studies with TD children as well as other highly co-morbid neurodevelopmental disorders in ASD, like attention-deficit/hyperactivity disorder (ADHD), have associated poor sleep with deficits in hot and cold EF performance¹⁵.

Developmental changes in typical EF occur in parallel to significant structural and functional changes in the prefrontal cortex, a core region subserving EF⁸ and characterized by abnormalities in ASD¹⁶. Sleep deprivation negatively disrupts prefrontal cortex connectivity and it has long been hypothesized that the prefrontal cortex benefits from the regenerative role of sleep^{17,18}. It is well established that poor sleep and executive functioning performance are both related to atypical prefrontal cortex activity^{19,20}. Arguably, developmental accounts on the interplay between sleep and EF from youth with traumatic brain injury (TBI) provides the most insightful evidence to draw from in the context of the frontal cortex. Incurring a TBI commonly affects frontal brain regions impairing prefrontal cortical functioning²¹. Both EF impairments and sleep disturbance are commonly reported in youth following mild or moderate/severe forms of TBI and seen to persist during long-term follow-ups²². Recent accounts suggest early brain damage to such frontal regions, compounded by sleep disturbances, results in poorer EF²³. Moreover, similar disruptions to neurotransmitters that modulate cortical synchrony and activation in the prefrontal cortex are linked

to impaired EF, ASD and disturbed sleep-wake cycles (for reviews see: Ballester et al²⁴, Logue and Gould²⁵, Veatch et al²⁶). Therefore, EF deficits in ASD may be caused by neurochemical and connectivity disruptions associated with the prefrontal cortex, which are in turn exacerbated by elevated sleep disturbance affecting the same neural pathways. If sleep disturbances occur at time points associated with rapid age-related changes in neural circuitry responsible for the development of EF, this can be even more problematic.

Preliminary evidence in TD children demonstrates that insufficient sleep duration early in childhood predicts worse EF in later childhood, including BR and MC impairments²⁷. To date, only two cross-sectional studies have examined the relationship between sleep and EF in children with ASD. Reynolds et al²⁸, found that elevated total sleep problems were correlated with worse BR and MC reported by parents in 6-11-year-old children with comorbid ASD and ADHD. However, a subsequent multivariate analysis including IQ, ADHD and ASD severity, and other confounders, found no association between sleep and EF. A second study examining 477 children with ASD aged 1-15 years, found parent-reported total sleep problems were not associated with working memory on an experimental task²⁹. However, cross-sectional studies with wide age ranges do not allow us to ascertain whether certain developmental periods when sleep problems manifest have a greater impact on various aspects of EF development. Further, much of these investigations have been limited to “total sleep problem” scores from parent-reported questionnaires, collapsing multiple sleep phenotypes. Investigations into specific sleep phenotypes are needed, as they have been shown to have variations in genetic underpinnings^{30,31}, as well as differential impacts on cognitive outcomes³².

The aim of the current study was to examine whether early-reported sleep problems in toddlers and preschoolers with ASD are associated with later EF trajectories. Specifically, we hypothesized that shorter sleep duration, frequent night awakenings, and longer sleep onset at 2-4 years of age would be associated with worsening BR and MC trajectories in 7- to 11-year-olds with ASD, as reported by teachers at four time-points.

Methods

Design and Participants

Participants were enrolled in *Pathways in ASD*, a Canadian multisite longitudinal study examining the developmental trajectories in an inception cohort of children with ASD recruited across five provinces. The study was approved by the Research Ethics Boards at participating sites. Children in the study met the following inclusion criteria: a) were 2-4 years of age at the time of diagnosis; (b) met diagnostic criteria for ASD on the *Autism Diagnostic Observation Schedule* (ADOS)³³ and in the social and one other domain of the *Autism Diagnostic Interview-Revised*³⁴; and (c) met criteria for ASD at each phase of assessment on the DSM-IV-TR³⁵ according to clinicians with diagnostic expertise. Exclusion criteria included known genetic or chromosomal abnormalities, neuromotor disorders, and/or severe hearing and/or vision impairment.

From a total of 421 Pathways participants, 348 had complete sleep data at their time one (T1) visit. Three participants were excluded due to data input errors. EF data from at least one out of four time points were available for 217 children, and thus comprise the sample reported in this study (mean age at T1 = 3.5 years; SD = 0.77) at T1. We compared the 217 included in the analysis to the 204 who did not have follow-up teacher data, presented in the Table S1. The 217 participants were significantly more likely to belong to the high income category (50.1% versus 37.3%, $p=.009$), had significantly higher cognitive standard scores (mean=56.06, SD=.17.95 versus mean 50.56 SD=17.58; $p=.031$), and were more likely to be from the Montreal site ($p=.003$) and less likely to be from Edmonton ($p=.009$) or Vancouver ($p=.026$) (Hamilton site used as reference category). However, there were no significant differences on any of the T1 sleep variables, age of T1 assessment, or ADOS symptom severity between included and excluded participants. Descriptive data for the included sample can be found in Table 1.

Measures

Sleep. Parent-reported sleep concerns were obtained using the *Children Sleep Habits Questionnaire (CSHQ)*³⁶, that comprised 33 items and eight subscales. The frequency of each sleep behavior corresponds to responses of: 1 = *never/rarely (0-1 nights per week)*, 2 = *sometimes (2-4 nights per week)*, 3 = *usually (5-7 nights per week)*. The CSHQ was used to assess sleep at T1 and at T4 when children were on average 6.7 years old (SD = 0.31). We selected items corresponding to commonly identified sleep problems in ASD from both parent and objective reports in the literature, such as insomnia traits (i.e., night awakenings, sleep onset) and sleep duration². **Sleep onset** was assessed based on the one-item subscale of the CSHQ; '*child falls asleep within 20 minutes*,' and was scored from 1 to 3 (reverse-coded). **Night awakenings** was assessed based on two items, '*awake once*' and '*awakes more than once*.' Both items were scored from 1-3; hence, our overall night awakening score ranged from 2 to 6. The third item of the original CSHQ night awakenings subscale, '*moving to other's beds during the night*', was not included. Items were selected to investigate the frequency of awakenings, rather than reasons for their occurrence. Insomnia traits are generally required to be present for three or more nights a week³⁷, which spans the 'sometimes' and 'always' response categories. In this sample, the 'always' response was endorsed relative infrequently, which could lead to problems with empty cells in the growth curve models. We therefore transformed night awakenings and sleep onset into binary variables for the growth curve analysis, responses of '*never/rarely*' were coded as 0 and '*sometimes*' to '*always*' were coded as 1. **Sleep duration** was reported within an hour range, then averaged.

Executive Functions. The Behavior Rating Inventory of Executive Function⁷, was used to measure EF reported by teachers at four time points (T5-T8) with an approximate one-year interval from 7.7 to 11.8 years. The BRIEF consists of 86 items assessing EF in real world settings over the past 6 months. It is composed of eight subscales collapsed into two indices. MC difficulties are measured on the Metacognition Index (MI), which comprises five subscales (Initiate, Organize/Plan, Organization of Materials, Working Memory, and Monitor). BR difficulties are measured with

the Behavioral Regulation Index (BRI), which comprises three subscales (Inhibit, Emotional Control and Shifting).

Cognition. The Merrill-Palmer-Revised Developmental Index Standard Score³⁸ is a standardized measure of intellectual ability for children 2 to 78 months of age. Higher cognitive raw scores correspond to stronger early cognitive skills. The Cognitive Index raw score was used to measure early cognitive ability as a proxy for IQ at T1.

ASD Severity. The ADOS calibrated severity score³⁹ (CSS), a 10-point scale derived from raw ADOS scores, was used to measure ASD symptom severity at T1. The ADOS CSS captures core ASD symptom severity of independent of age and language level. Higher scores indicate greater symptom severity.

Income. Family income was reported by parents on the Family Background Information Questionnaire developed for the Pathways study. Caregivers reported their family incomes on a scale ranging from 1 (< CAD\$5,000) to 11 (> CAD\$80,000). Similar to Bennett et al.⁴⁰, a binary variable for income was created based on the median of \$70,000.

Data Analysis

To analyze the association between sleep at 3.5 years (T1) and the BRI and MI assessed four times between 7.7-11.8 years, two separate growth curve models were estimated in Mplus v8.4. The use of latent growth curves allows testing of the contribution of poor sleep to the initial starting point of the trajectory (intercept) and to change in EF over time (slope). EF time-points for the slope growth factor were fixed at 0, 1, 2, and 3 to define a growth model with equidistant time-points, and we tested for both linear and quadratic growth. The zero-time score for the slope growth factor at T1 defined the intercept factor. To handle missing data, Full Information Maximum Likelihood estimation was used.

We fit unconditional growth curve models for both the MI and BRI, first with a linear growth factor and then with both a linear and quadratic growth factor. In the first conditional model,

covariates from T1 (age, family income, and testing site) and T1 sleep variables were entered as predictors of the intercept and slope. In the second model, early cognition and ASD severity were added to Model 1 as confounding variables to test the specificity of results to EF. In the third model, T1 and T4 sleep were added to test whether sleep at 3.5 years of age was still associated with later EF after accounting for more proximal sleep problems. Covariates from Model 1 were also included. Finally, in Model 4, early cognition and ASD severity were added to Model 3, to test the specificity of results to EF. Few participants were taking medications known to disrupt or augment sleep, including melatonin. Hence, medication was not controlled for (*see supplementary materials*). Post hoc analyses applying Bonferroni corrections for multiple comparisons were conducted to further investigate subscales of significant BR or MI models.

All continuous predictors were centered to aid interpretation. A Root Mean Square Error (RMSEA) below 0.60 and Comparative Fit Index (CFI) $\geq .90$ was considered an adequate model fit⁴¹. Descriptive analyses were conducted using SPSS 25. Linear and logistic regressions were used to test for differences in characteristics between participants who provided T1 data and BRIEF data from at least one-time point from T1-T5 and participants who had missing data. Bivariate, point-biserial and tetrachoric correlations were estimated for associations between binary and continuous variables. A log transformation of MI raw scores at T8 was applied to generate an approximately normal distribution for bivariate analysis.

Results

See Table 1 for participant characteristics. Participants had a mean sleep duration of 11.0 hours (SD = 1.35) at T1, consistent with National Sleep Foundation (NSF) recommendations⁴² for toddlers (11–14 hours) and preschoolers (10-13 hours). However, 32.4% of toddlers and 21.4% of preschoolers at T1 slept for a shorter duration than recommended for their age group. Less than 3% of toddlers and 4.7% of preschoolers slept longer than their recommended duration. The average sleep duration reported at T4 when participants were school-aged was 10.2 hours (SD = 0.92), also

Table.1 *Pathways participant characteristics*

		Time-points	N (%)	Mean	SD
Age (years)		T1		3.46	0.77
		T4		6.66	0.31
		T5		7.74	0.22
		T6		8.73	0.21
		T7		9.71	0.22
		T8		10.77	0.25
Sex		T1			
	Male		183 (84.3)	-	-
	Female		34 (15.7)	-	-
Site		T1			
	Halifax		28 (12.9)	-	-
	Montreal		83 (38.2)	-	-
	Hamilton		23 (10.6)	-	-
	Vancouver		57 (26.3)	-	-
	Edmonton		26 (12.0)	-	-
Income		T1			
	Less than \$5000		2 (0.9)	-	-
	Less than \$10,000		4 (1.8)	-	-
	Less than \$15,000		4 (1.8)	-	-
	Less than \$20,000		7(3.2)	-	-
	Less than \$30,000		13(6.0)	-	-
	Less than \$40,000		10(4.6)	-	-
	Less than \$50,000		12(5.5)	-	-
	Less than \$60,000		34(15.7)	-	-
	Less than \$70,000		21(9.7)	-	-
	Less than \$80,000		19(8.8)	-	-
	More than \$80,000		91(41.8)	-	-
Merrill-Palmer-Revised:		T1			
	Cognitive raw score*		210	56.06	17.95
	Cognitive standard score		201	61.40	24.15
CSS		T1	216	7.70	1.67
BRI raw scores		T5	89	59.47	13.45
		T6	98	58.44	14.74
		T7	81	57.12	13.71

	T8	81	52.84	14.42
MI raw scores	T5	87	91.15	17.03
	T6	93	89.15	20.79
	T7	77	91.71	18.89
	T8	79	83.39	19.55

**Age at T1 was used to account for cognitive raw scores not standardized by age.*

within NSF recommendations (9 to 11 hours). Twelve percent of participants at T4 slept more than the recommended sleep duration, while 6% slept less than recommended. See Table 2.

At T1, 57% of participants were found to ‘sometimes or usually’ have a problem with night awakenings and 50% had delayed sleep onset issues documented more than twice per week. At T4, 50.7% and 46.5% of participants were reported as ‘sometimes or usually’ having night awakenings and sleep onset delay per week, respectively. See Table 3. Correlations among sleep, EF, and covariates can be found in the supplementary materials (Tables S2-S9).

Latent Growth Curve Models

BRI difficulties. The unconditional growth model with a linear growth factor only fit the data best (fit indices are presented in Table 4). The intercept mean was 59.5 (SE = 0.96) and the slope mean was -1.42 (SE = 0.42), indicating that BRI difficulties decreased over time. The mean and variance of both the intercept and slope were significant, the latter indicating significant decrease in the BRI from T5 to T8 (reflecting improvement). Models 1-4 are found in Table S9. Results from Model 1 (see Table 5) showed that a delayed sleep onset significantly predicted lower BRI difficulties at the intercept ($b = -4.14, p = 0.04$). A delayed sleep onset remained a significant predictor of lower difficulties after the inclusion of early cognitive ability and ASD severity in Model 2 and after the addition of T4 sleep variables in Model 3 ($b = -7.18, p = .001$) and early cognitive ability and ASD severity in Model 4 ($b = -8.51, p = .001$).

Table 2. *CSHQ Sleep duration frequencies*

Duration (hours)	*2yrs (T1)		3-4yrs (T1)		6-7yrs (T4)	
	N	%	N	%	N	%
6.50	-	n/a	n/a	n/a	3	1.4
7.50	1	1.5	n/a	n/a	n/a	n/a
8.50	6	8.8	9	6.0	10	4.6
9.50	5	7.4	23	15.4	60	27.6
10.50	10	14.7	55	36.9	91	41.9
11.50	23	33.8	41	27.5	23	10.6
12.50	17	25.0	14	9.4	3	1.4
13.50	4	5.9	3	2.0	n/a	n/a
14.50	3	2.9	4	2.7	n/a	n/a

**Ages based on National Sleep Foundation developmental categories of infants, toddlers and school-age*

Table 3. *CSHQ night awakenings and sleep onset item scores*

	T1		T4	
	N	%	N	%
Night awakenings				
0*	94	43.3	107	49.3
1*	123	56.7	110	50.7
‘awakes more than once’				
<i>Never/Rarely</i>	101	46.5	113	58.2
<i>Sometimes</i>	78	35.9	55	28.3
<i>Usually</i>	38	17.5	26	13.4
‘awakes more than once’				
<i>Never/Rarely</i>	162	74.6	165	85.4
<i>Sometimes</i>	43	19.8	22	11.4
<i>Usually</i>	12	5.5	6	3.10
Sleep onset				
0*	109	50.2	116	53.5
1*	108	49.8	101	46.5
‘child falls asleep after 20mins’				
<i>Never/Rarely</i>	109	50.2	116	53.5
<i>Sometimes</i>	71	31.7	51	23.5
<i>Usually</i>	37	17.1	27	12.4

**Transformed binary variables*

Table 4. *Unconditional BRI and MI models*

	BRI		MI	
	Linear model	Quadratic Model	Linear model	Quadratic Model
χ^2 (df)	8.572(5), $p = 0.12$	5.084(1), $p = 0.02$	9.40 (5), $p = 0.09$	8.744(1), $p = 0.003$
RMSEA (95%CI)	0.053 (0.00- 0.11)	0.126 (0.037-0.243)	0.059 (0.00 - 0.12)	0.174 (.082 -.287)
CFI	0.98	0.98	0.96	0.922

Table 5. *Parameter estimates for behavioral regulation difficulties Model 1-4*

Predictors	Intercept				Slope			
	Estimate (standardized)	95% CI	SE	p	Estimate (standardized)	95% CI	SE	p
Model 1								
Age	0.03 (0.02)	-0.17 - 0.22	0.12	.834	-0.05 (-0.14)	-0.14 - 0.05	0.06	.410
Halifax site	-5.49 (-0.47)	-11.45 - 0.47	3.62	.130	1.13 (0.36)	-1.27 - 3.54	1.46	.438
Montreal site	-6.84 (-0.58)	-11.78 - -1.92	3.00	.022	0.17 (0.05)	-1.98 - 2.33	1.31	.895
Edmonton site	2.29 (0.19)	-3.27 - 7.85	3.38	.498	-0.72 (-0.23)	-3.85 - -2.42	1.90	.707
Vancouver site	-2.39 (-0.20)	-7.27 - -2.39	2.97	.420	1.29 (0.41)	-1.05 - 3.64	1.43	.364
Income	-4.01 (-0.34)	-7.39 - -0.63	2.05	.051	0.97 (0.31)	-0.61 - 2.55	0.96	.313
T1 Sleep onset	-4.14 (-0.35)	-7.54 - -0.75	2.07	.045	1.01 (0.32)	-0.55 - 2.57	0.95	.287

INTERPLAY BETWEEN SLEEP & EF IN ASD

14

T1 Night awakening	1.53 (0.13)	-1.92 - 4.99	2.10	.466	0.01 (0.01)	-1.46 - 1.46	0.89	.999
T1 Sleep duration	-0.80 (0.09)	-2.11 - 0.52	0.80	.317	0.31 (0.14)	-0.35 - 0.97	0.40	.437
Model 2								
Age	0.12 (0.09)	-0.12 - 0.35	0.14	.410	-0.09 (-0.25)	-0.20 - 0.02	0.07	.177
Halifax site	-3.46 (-0.29)	-9.53 - 2.60	3.68	.347	1.15 (0.34)	-1.29 - 3.59	1.48	.438
Montreal site	-4.21 (-0.35)	-9.13 - 0.70	2.99	.159	-0.65 (-0.19)	-2.89 - 1.59	1.36	.633
Edmonton site	5.66 (0.47)	0.03 - 11.29	3.42	.098	-0.99 (-0.29)	-4.30 - 2.33	2.02	.624
Vancouver site	-0.95 (-0.08)	-5.93 - 4.02	3.02	.753	1.19 (0.36)	-1.22 - 3.61	1.47	.415
Income	-3.16 (-0.26)	-6.80 - 0.48	2.21	.153	0.82 (0.25)	-0.92 - 2.56	1.06	.436
ASD Severity	1.45 (0.20)	0.43 - 2.47	0.62	.020	-0.53 (-0.26)	-1.03 - -0.03	0.31	.084
Early Cognition	-0.08 (-0.17)	-0.16 - 0.01	0.05	.082	0.03 (0.21)	-0.01 - 0.07	0.02	.207
T1 Sleep onset	-5.44 (-0.45)	-8.99 - -1.89	2.16	.012	1.26 (0.37)	-0.42 - 2.93	1.02	.217
T1 Night awakening	1.553 (0.13)	-2.04 - 5.15	2.19	.477	0.32 (-0.10)	-1.89 - 1.25	0.95	.736
T1 Sleep duration	-1.48 (-0.17)	-2.96 - -0.01	0.90	.099	0.41 (0.16)	-0.33 - 1.14	0.45	.362
Model 3								
Age	-0.01 (1.03)	-0.23 - 0.21	0.13	.926	-0.01 (-0.02)	-0.12 - 0.10	-0.11	.913
Halifax site	-5.36 (0.46)	12.73 - 2.01	4.48	.231	0.93 (0.29)	-2.16 - 4.09	1.88	.622
Montreal site	-5.10 (-0.44)	-10.13 - -0.08	3.05	.094	-0.03 (-0.01)	-2.32 - 2.25	1.39	.980

INTERPLAY BETWEEN SLEEP & EF IN ASD

15

Edmonton site	0.30 (0.02)	-5.62 - 6.23	3.60	.933	0.21 (0.07)	-3.54 - 3.97	2.27	.925
Vancouver site	-0.69 (-0.06)	-5.36 - 3.98	2.84	.808	1.01 (0.32)	-1.52 - 3.52	1.53	.513
Income	-3.57 (-0.31)	-7.27 - 0.13	2.25	.113	1.16 (0.37)	-0.53 - 2.86	1.03	.259
T1 Sleep onset	-7.19(-0.62)	-10.85 - -3.53	2.22	.001	2.07 (0.66)	0.40 - 3.73	1.01	.041
T1 Night awakening	2.37 (0.20)	-1.69 - 6.44	2.47	.337	-0.38 (-0.12)	-2.07 - 1.30	1.02	.707
T1 Sleep duration	-1.39 (-0.16)	-2.96 - 0.18	0.96	.146	0.22 (0.09)	-0.50 - 0.93	0.44	.620
T4 Sleep onset	7.78 (0.67)	3.69 - 11.87	2.49	.002	-1.47 (-0.47)	-3.22 - 0.28	1.06	.166
T4 Night awakening	3.74 (0.32)	-0.14 - 7.61	2.36	.113	-0.76 (-0.24)	-2.52 - 1.01	1.07	.479
T4 Sleep duration	3.15 (0.26)	1.14- 5.17	1.23	.010	-0.92 (-0.28)	-1.93 - 0.09	0.61	.133
Model 4								
Age	0.02 (0.02)	-0.23 - 0.28	0.16	.883	-0.025 (-0.06)	-0.16 - 0.11	0.08	.753
Halifax site	-5.54 (-0.47)	13.29 - 2.20	4.71	.239	1.654 (0.46)	-1.56 - 4.87	1.95	.398
Montreal site	-3.53 (-0.30)	-8.13 - 1.06	2.79	.206	-0.636 (-0.18)	-3.01 - 1.74	1.44	.660
Edmonton site	2.95 (0.25)	-2.92 - 8.82	3.57	.409	0.297 (0.08)	-3.78 - 4.37	2.48	.905
Vancouver site	0.70 (0.06)	-3.67 - 5.09	2.67	.792	0.85 (0.24)	-1.68 - 3.38	1.54	.581
Income	-1.97 (-0.17)	-5.88 - 1.93	2.374	.406	0.76 (0.21)	-1.14 - 2.66	1.155	.508
ASD Severity	1.43 (0.20)	0.44 - 2.43	0.61	.018	-0.52 (-0.24)	-1.02 - -0.01	0.31	.092
Early Cognition	-0.10 (-0.20)	-0.17 - -0.02	0.05	.045	0.04 (0.25)	-0.01 - 0.08	0.03	.165

T1 Sleep onset	-8.51 (-0.72)	-12.15 - -4.86	2.22	.000	2.37 (0.66)	0.63 - 4.10	1.05	.025
T1 Night awakening	3.05 (0.26)	-1.01 - 7.11	2.47	.216	-1.02 (-0.28)	-2.78 - 0.73	1.07	.337
T1 Sleep duration	-2.05 (-0.24)	-3.74- -0.36	1.03	.046	0.27 (0.10)	-0.51 - 1.05	0.47	.565
T4 Sleep onset	7.85 (0.66)	3.86 - 11.84	2.43	.001	-1.58 (-0.44)	-3.41 - 0.24	1.11	.154
T4 Night awakening	4.47 (0.38)	0.35 - 8.60	2.51	.075	-0.816 (-0.23)	-2.76 - 1.13	1.18	.490
T4 Sleep duration	3.64 (0.30)	1.54 - 5.74	1.28	.004	-1.16 (-0.31)	-2.24 - -0.07	0.66	.079

When T4 sleep variables were entered in Model 3, a delayed T1 sleep onset significantly predicted a worsening slope of BRI difficulties ($b = 2.07, p < .041$), and this remained significant in Model 4 ($b = 2.37, p = .025$). Delayed sleep onset at T4 also significantly predicted higher BRI difficulties at the intercept in Model 3 ($b = 7.78, p = .002$) and in Model 4 ($b = 7.85, p = .001$). In Model 4, shorter sleep duration at T1 was found to predict higher BRI difficulties at the intercept ($b = -2.05, p = .046$). Conversely, a shorter sleep duration at T4 predicted lower BRI difficulties at the intercept in Model 3 ($b = 3.15, p = .010$), and this remained significant in Model 4 ($b = 3.64, p = .004$). Night awakenings at T1 or T4 showed no significant associations with the intercept or slope. For full parameter estimates see Table 5.

MI difficulties. The unconditional latent growth curve model with only a linear growth factor only fit the data best (see Table 4). The intercept mean was 91.2 (SE = 1.29) and the slope mean was -1.3 (SE = 0.06), indicating MI difficulties decreased over time. The mean and variance of both the intercept and slope were significant, the latter indicating significant growth in the MI from T5 to T8. Models 1-4 also had an adequate fit (Table S10). No sleep variables were significantly associated with MI difficulties at the intercept or slope. See Table S11 for full parameter estimates.

Subscale analysis. Post hoc analyses were conducted to further investigate the three subscales of the BRI: *inhibition*, *shifting*, and *emotional control*. Fit indices and parameter estimates of unconditional growth curves and Models 1-4 for each subscale are reported in supplementary materials (Table S11-S17). Multiple comparisons for our three exploratory models were corrected for, with significance set at $p = .017$.

As in the overall BRI models, a delayed sleep onset in Model 1 was associated with lower emotional control difficulties at the intercept ($b = -2.08, p = .004$). This was not found for inhibition or shifting. Upon entering T4 sleep in Model 3, delayed sleep onset at T1 became significantly associated with lower inhibition difficulties at the intercept ($b = -2.28, p = .008$). The addition of ASD severity and early cognitive ability in Model 4 did not significantly alter these associations. In

Model 3, a delayed sleep onset at T1 was significantly associated with a worsening emotional control slope ($b = 0.95, p = .008$), which was not found for shifting or inhibition. Subsequently, with the addition of ASD severity and early cognitive ability in Model 4, T1 delayed sleep onset significantly predicted a worsening inhibition slope ($b = 1.01, p = .009$), but this was not found for shifting.

Similarly to the overall BRI, associations were found between a delayed sleep onset at T4 and higher difficulties at the intercept for all three BRI subscales in Model 3: inhibition ($b = 2.82, p = .004$), cognitive shifting ($b = 2.20, p = 0.01$) and emotional control ($b = 2.77, p = .001$). These results remained significant in Model 4.

Shorter sleep duration at T1, which was found to predict higher overall BRI difficulties at the intercept after the addition of T4 sleep and early cognitive ability and ASD severity, marginally predicted higher cognitive shifting difficulties at the intercept ($b = -0.64, p = .039$) in Model 3. No significant associations were found between T1 sleep duration and other BRI subscales. In model 3, similarly to the overall BRI, longer sleep duration at T4 was associated with lower inhibition ($b = .228, p = .007$) and emotional control difficulties ($b = 1.07, p = .015$) at the intercept, but not cognitive shifting. These results remained in Model 4, but with the addition of early cognitive ability and ASD severity, shorter sleep duration at T4 predicted a worsening inhibition slope ($b = -0.60, p = .011$).

Finally, like the overall BRI, neither night awakenings at T1 or T4 were significantly associated with BRI subscales.

Discussion

In the current study, the association between early childhood sleep and later EF at school age was examined in children with ASD. Our results partially confirm our hypothesis, indicating that sleep quantity and quality are exclusively related to ‘hot’ (BR) rather than ‘cold’ (MC) EF in school-aged children with ASD. Contrary to our prediction, participants with delayed sleep onset at 3.5 years had better BR, as reported by teachers on the BRIEF, at the intercept (7.7 years). Examination of the three BRI subscales showed that this association was only significant for emotional and inhibitory control.

However, as hypothesized, delayed sleep onset at 3.5 years exclusively predicted a worsening BR slope after the more proximal school-age sleep was accounted for, and this same pattern was seen for the BR emotional and inhibitory control subscale slopes. Of the school age sleep variables (assessed at age 6.7), a delayed sleep onset was associated with greater BR difficulties at the intercept. Longer sleep duration at age 6.7 was associated with greater BR difficulties at the intercept, and this was also seen for the three BR subscales. In contrast, a shorter sleep duration at 6.7 years predicted a worsening inhibition slope during school age, but this was not seen for overall BR difficulties or the other two subscales. Neither night awakenings nor shorter sleep duration at 3.5 years of age was related to EF as expected.

Given previous documentation of sleep problems in 40%-80% of children with ASD and evidence suggesting early poor sleep impairs EF development, we hypothesized that poor sleep may serve as a mechanism to exacerbate EF difficulties found in children with ASD. It is difficult to ascertain whether early sleep problems are more prevalent in our ASD cohort compared to normative samples due to measurement differences⁴³⁻⁴⁵. The CSHQ was not developed for children under age 6; hence, questions and scoring differed from what we have documented. For example, previous studies captured the number of night awakenings per night rather than per week as in the CSHQ, whereas sleep onset difficulty was usually set at 30 minutes rather than the 20 minutes on the CSHQ^{43,45}. Up to 28% of TD preschoolers at 3.5 years of age have at least one awakening per night⁴³, whereas 56.7% of our same-aged Pathways cohort had one or more night awakenings between two to seven nights per week. At first glance it may seem as though there are more awakenings in our cohort, but upon examination of the item '*awakes once during the night*' only 17% of Pathways parents responded their child woke up once five to seven nights per week (closer to one night per week). Hence, night awakenings may actually be lower in our cohort, but this cannot be conclusive given the variability of parents' reports. Similarly, 16% of typical 3.5-year-olds have had sleep onset difficulties documented per night⁴³, whereas 49.8% of our same-aged preschool cohort had sleep onset difficulties two to seven nights per week. More comparably, in our cohort, 17% of preschoolers took more than 20 minutes to get to sleep, five to seven night per week. Again, this is compared to the 30-minute cutoff of the TD sample. When school-aged, greater sleep problems on the

CSHQ were found in our ASD cohort compared to a normative North American sample with a similar mean age of 7 years⁴⁶. In the TD cohort 21% ‘sometimes’ or ‘usually’ had sleep onset difficulties, compared to 46.5% in our cohort. 25.1% of typically developing children had one-night awakening ‘sometimes’ or ‘usually’ per week, compared to 41.7% of Pathways children. Although the age range of the normative sample is larger, we can say with more certainty that Pathways youth had more disturbed sleep reported by their parents at school age, in line with estimates from the literature. Interestingly, during both age assessments, our Pathways cohort slept comparably to normative samples and within the recommended sleep duration for their age⁴². Hence, links between EF difficulties and low sleep quantity may be more pronounced in a clinical cohort with greater sleep duration disturbances.

This was the first study to examine growth in EF across multiple time points in middle childhood in ASD. We found significant but small improvement over time in both BR and MC. We did not replicate previous longitudinal associations between sleep and MC documented in TD children⁴⁷. However, our findings do parallel preliminary evidence from two cross-sectional studies reporting no significant relationship between sleep and MC in children with ASD^{28,29}. We also substantiated previous links found between poor sleep and behavioral problems in ASD children^{48,49}, as the BRI subscale shows some overlap with behavioral problems. Overall, our novel findings highlight a non-uniform relationship, whereby age, type of BR, and sleep traits need to be taken into account.

Links between sleep onset and BR. The finding that delayed sleep onset predicted lower BR difficulties at the intercept was unexpected. It is important to take into account that bedtime is more externally determined earlier in childhood; therefore, delayed sleep onset may reflect both internal sleep processes and external parental regulation. One possible explanation for the association may be that toddlers and preschoolers who tolerate being put to bed earlier than their natural circadian rhythm bedtime show improved BR around the start of school age. It has been previously documented that preschoolers whose parentally determined bedtime does not match their internal circadian rhythm have greater bedtime resistance⁵⁰. Sleep problems like delayed onset are thought to arise from a de-synchrony between one’s endogenous circadian rhythm and preferred sleep-wake schedule⁵¹. The proposed

interpretation is in line with previous documentation of circadian rhythm alterations in ASD. This includes atypical levels and synthesis of melatonin, involved in resetting circadian rhythms, and disturbances of circadian genes⁵². Moreover, delayed sleep phase syndrome, a circadian rhythm disorder characterized by sleep that is delayed by at least two hours³⁷, is found in adults with ASD^{53,54}. Suggesting that a mismatch of external bedtimes and internal sleep preferences is an issue in ASD. Hence, young children with delayed sleep onset may be regulating their behaviors based on parental instructions, despite not being ready to sleep. These children may be required to control their emotions (e.g., crying) and inhibit resistant behavior (e.g., getting out of bed) during bedtime; indeed, improved inhibitory and emotional control were the only two subscales linked to early delayed onset at the intercept. However, delayed sleep onset measured more proximally to the EF assessments (age 6.7 years) showed the expected association of delayed onset with increased BR difficulties. It may be that the behavioral impact of delayed sleep onset becomes pronounced during the first years of elementary school, when children are gaining greater independence and are adapting to new school routines and environments. Furthermore, as EF was captured during middle school, marking a period of complex EF acquisition and increasing social intricacies, early delayed sleep onset might inhibit development of complex BR, rather than attainment of basic BR. Curiously, after the inclusion of the more proximal age 6.7 sleep problems in the model, early delayed sleep onset, while continuing to predict improved BR and emotional control at the intercept, was associated with a worsening overall BR and emotional control slope from age 7-11 years. The delayed onset at age 6.7 was not associated with the slope. The present findings do suggest a specific role for delayed sleep onset in later BR difficulties, but the pattern of findings is complex and warrants replication and further investigation to understand the mechanisms involved. Parental report of sleep is likely confounded with both parent and child characteristics, so future studies using objective measures of sleep will be important. Delayed sleep onset is a particularly salient sleep problem in individuals with ASD throughout the lifespan^{53,55} and may be a significant source of stress for parents, underscoring the need for a better understanding of the role of sleep onset delay in the development of later difficulties in individuals with autism.

In contrast to emotional and inhibitory control, cognitive shifting was not significantly linked to sleep onset. Previous findings have found total sleep problems (including sleep onset) from preschool and school-age were not longitudinally associated with experimental or neuropsychological measures of shifting^{56,57}, while decreasing sleep problems across childhood have been correlated with better inhibitory control but not shifting⁵⁶. The latter provides evidence that sleep may better predict inhibitory control outcomes over shifting. As shifting difficulties are consistently documented to be the most impaired EF component in ASD^{58,59}, it consequently may be less malleable to significant developmental changes.

This is the first finding linking delayed sleep onset in early childhood to later emotional control in children with ASD. The finding is unsurprising given extensive documentation that sleep quantity and quality (including insomnia traits) affects mood, affective information processing and the capacity to regulate emotions^{60,61}. It is posited that poor sleep impairs the connectivity between the prefrontal cortex and amygdala, a central neural pathway for affective processing⁶¹. A lack of prefrontal-amygdala connectivity during emotional responses is found in children with ASD⁶²; hence, this may be one possible mechanism by which sleep disturbance further exacerbates emotional regulation impairments in ASD. Finally, inhibitory control was most consistently impacted negatively by all sleep disturbances in the current cohort, not only by sleep onset, mirroring previous findings with restricted sleep duration and night awakenings in TD and children with ADHD^{63,64}.

Links between sleep duration and BR. Interestingly, longer sleep duration at school age was associated with worse BR difficulties during early school age. Twelve percent of these participants slept more than 11 hours, which according to the NSF falls into the *may be appropriate or not recommended* range. Oversleeping is known to have negative consequences for cognitive processes such as EF^{65,66}. Negative outcomes for both extremes of under- or over-sleeping reflect an inverted-U shaped relationship⁶⁵. Weekday oversleeping can also be compounded by school-aged children who tend to sleep more during the weekends⁶⁷. Further investigations of subscales revealed that shorter sleep duration at 6.7 years predicted a worsening inhibition but not overall BR trajectory during school age. As both preschool

and school-aged sleep durations are positively correlated in our sample, children might have accumulated a sleep debt, known to have negative consequences for behavioral modulation.

Links between night awakenings and BR. Frequent night awakenings years did not predict EF difficulties. It is possible that earlier night awakenings at age 3.5 years were not significant predictors as awakenings are commonly found during toddlerhood and may have more impact on EF when they are less developmentally appropriate. This is also supported by previous findings showing night awakening in infants was not associated with later impulse control at 6-months and 1-year follow-ups³².

Strengths and Limitations

A major strength of the current study is the large sample of systematically diagnosed and phenotyped children with ASD. Pathways is a unique and advantageous cohort as the participants had a narrow age range at study entry and have been regularly assessed by multiple respondents. This includes sleep repeatedly reported by parents and EF assessments by various teachers at four time points, limiting responder bias. Multiple assessment points allowed for longitudinal modelling techniques, another major strength, providing the first growth curve analysis of EF in ASD. Controlling for factors including early cognitive ability and ASD severity also provides some confidence that our significant findings are unique to the relationship between sleep and EF.

We did not use psychometric or experimental tasks that may evaluate ‘pure’ EF components; however, performance on these tasks varies based on presentation modality and response type and do not reflect natural everyday demands⁵. Questionnaires like the BRIEF capture EF in multiple everyday scenarios, adding to the generalizability of our results.

Parent reports of sleep have been flagged as a limitation due to their susceptibility to biases and discrepancies with physiological sleep reports⁶⁸. For instance, night awakenings might only be documented if they are significant enough to impair parental sleep, whereas sleep onset concerns may be missed if children do not present with disruptive behavior. This reporting obstacle may be more pronounced in school-age children, when parents might be less involved in monitoring sleep. In fact, previous evidence indicates that electroencephalographic markers of sleep are atypical in ASD even when

parents do not report sleep problems⁶⁹. Reporting biases may also underlie the lack of problems with sleep quantity problems documented in our cohort. Further, the CSHQ it is not optimized for documenting sleep during early childhood periods and a recent review of its psychometric properties suggests that modifications are needed for children with ASD⁷⁰. Although for our study purposes we used specific sleep traits of interest, bypassing psychometric issues, using the CSHQ for a young age group limited our ability to assess sleep differences between our cohort and normative samples. The lack of suitability for capturing early sleep problems also raises methodological concerns about how well these questionnaire items are isolating actual sleep problems, as opposed to varying parent preconceptions of appropriate sleep. The use of objective sleep monitoring is crucial to remove these report biases and may help delineate current sleep onset findings that are difficult to disentangle.

A further limitation of our study is that we did not have access to a control group. Finally, there was attrition from the first assessment point, from which our key sleep measures were taken, to the final four assessment points conducted at school age, at which the EF outcome was measured. Attrition is common with longitudinal studies. In this sample non-response at school-age was associated with lower income and lower child cognitive scores, but not with T1 sleep problems or autism severity. Family income and child cognitive score were both included as covariates in the analysis, which helps to account for any effects of attrition on the analysis. There was some variability in response at the T5 to T8 assessment points; thus, the main analysis used maximum likelihood estimation to include participants with teacher-reported data at any school-age time point to be included in the analysis.

Another study limitation is that concurrent sleep and EF were not documented thus. We only tested a unidirectional relationship (i.e., sleep predicating EF); nevertheless, this does not rule out a bidirectional association. Previous studies have reported that EF problems during preschool and school-age are longitudinally associated with later sleep disturbances in TD children^{71,72}. Finally, as previously flagged⁴, the presence of co-morbid psychiatric conditions (e.g., ADHD or anxiety) or environmental stressors (e.g., parental stress), may also modify the interplay between sleep and EF.

Conclusion

Current findings suggest that poorer sleep in childhood may serve as a risk factor for developing atypical EF outcomes in ASD. The novelty of our findings suggest greater nuance is needed to decipher the relationship between sleep and EF, as independent sleep phenotypes have different age related impacts on selective components of EF. We are the first to report poor sleep specifically impacts BR and more specifically, inhibitory control development, above cold EF in ASD. This information is beneficial for informing possible EF interventions in ASD, by targeting sleep in children. In fact, a randomized controlled trial found that TD adolescents who received treatment for their insomnia had improved EFs after six sessions, compared to waiting list controls⁷³. Parents and clinicians should carefully monitor and consider treatment if children with ASD are having early sleep problems. Current interpretations of our results suggest the need to promote better matching bedtimes, which may require later bedtimes and wake-times for some children. More widespread awareness and dialogue is needed to help parents navigate enforcing bedtimes that are appropriate for their child's internal clock. Further investigations on the interplay between sleep and EF in ASD are needed with both objective and parent report measures to validate current findings.

Disclosures

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