Prenatal sleep health and risk of offspring ADHD symptomatology and associated phenotypes: a prospective analysis of timing and sex differences in the ECHO cohort

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Summary

Background Sleep difficulties are common in pregnancy, yet poor prenatal sleep may be related to negative long-term outcomes for the offspring, including risk for attention-deficit/hyperactivity disorder (ADHD). Existing studies are few and have not examined timing of exposure effects or offspring sex moderation. We thus aimed to test the hypotheses that poor sleep health in pregnancy is associated with increased risk for ADHD symptoms and offspring sleep problems at approximately 4 years of age.

Methods Participants were 794 mother-child dyads enrolled in the NIH Environmental Influences on Child Health Outcomes Study (ECHO). Participants self-reported on sleep duration, quality, and disturbances during pregnancy and on children's ADHD symptoms and sleep problems on the Child Behaviour Checklist.

Findings Pregnant participants were 32.30 ± 5.50 years and children were 46% female. 44 percent of pregnant participants identified as Hispanic or Latine; 49% identified as White. Second-trimester sleep duration was associated with offspring ADHD symptoms (b = –0.35 [95% CI = –0.57, –0.13], p = 0.026), such that shorter duration was associated with greater symptomatology. Poorer sleep quality in the second trimester was also associated with increased ADHD symptomatology (b = 0.66 [95% CI = 0.18, 1.14], p = 0.037). Greater sleep disturbances in the first trimester were associated with offspring ADHD (b = 1.03 [95% CI = 0.32, 1.03], p = 0.037) and in the second trimester with sleep problems (b = 1.53 [95% CI = 0.42, 2.92], p = 0.026). We did not document substantial offspring sex moderation.

Interpretation Poor prenatal sleep health, particularly quality and duration in the second trimester, may be associated with offspring risk of neurodevelopmental disorders and sleep problems in early childhood. Further research is needed to understand mechanisms, yet our study suggests that prenatal maternal sleep may be a modifiable target for interventions aimed at optimizing early neurodevelopment.

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Research in context

Evidence before this study

The correlates and consequences of poor sleep health in pregnancy remain underexamined. We searched MEDLINE, PsycINFO, PubMed, and ClinicalTrials.gov for human studies of prenatal maternal sleep health and offspring neurodevelopment published from January 1, 1980, March 17th, 2023. We used the search terms: "pregnancy, "prenatal", "in utero", "antenatal", "perinatal", "sleep" and "ADHD", "neurodevelopment", "offspring". We found no reviews or meta-analyses, and only five studies of prenatal sleep and child neurodevelopment. All converge in suggesting poor sleep during pregnancy increases risk for neurodevelopmental disorders in offspring, particularly attention-deficit/hyperactivity disorder (ADHD) and associated phenotypes and are reviewed in detail in the introduction yet are limited by not examining timing of exposure (e.g., trimester in pregnancy) and offspring sex effects.

Added value of this study

We present novel evidence that, among 794 mother-child dyads, shorter maternal sleep duration and poorer sleep quality in the second trimester were associated with all outcomes of interest in 4-year-old offspring with no significant moderation by offspring sex. For the first time we identify a period of pregnancy where sleep may be most important to offspring neurodevelopment, raising the possibility that the second trimester may be most important to interventions aimed at protecting offspring well-being.

Implications of all the available evidence

Prenatal maternal sleep health–particularly duration and quality in the second trimester of pregnancy–may be important for offspring neurodevelopment, although mechanistic studies are needed to inform interventions.

Introduction

Sleep difficulties are common in pregnancy, yet poor prenatal sleep may be related to negative outcomes for the parent-infant dyad, including pregnancy complications and poor birth outcomes (e.g., preterm birth, low birth weight[1]). Moreover, the impact of poor prenatal sleep may extend beyond pregnancy and birth outcomes, as rodent studies have shown that comprised sleep health during gestation increases prenatal maternal inflammation and HPA axis activation, which may impact fetal neurodevelopment.[2] Prenatal maternal sleep difficulties may thus represent a risk factor for offspring neurodevelopmental disorders, yet human research is scarce.

The existing five studies of prenatal sleep and child neurodevelopment converge in suggesting poor sleep during pregnancy increases risk for neurodevelopmental disorders in offspring, particularly attention-deficit/hyperactivity disorder (ADHD) and associated phenotypes. A study of 3634 dyads documented that compared to offspring of mothers without sleep disorders, offspring of mothers with prenatal sleep disorders had 40% more ADHD symptoms as preschoolers, particularly hyperactive/impulsive symptoms,[3] even when controlling for prenatal depression and anxiety. Another study of 111 dyads demonstrated that prenatal maternal daytime sleepiness — which is distinct from, but related to poor sleep health — was associated with ADHD symptoms in preschoolers.[4] A third study of 103,062 pregnancies documented associations between poor self-reported prenatal sleep quality with irritable infant temperament at one month,[5] and poorer gross motor and communication development at one year of age.[6] This study also found that shorter prenatal maternal sleep duration and later bedtimes were associated with worse offspring sleep at both timepoints. This is noteworthy, given that prospective birth cohorts have documented that poor sleep in infancy is associated with increased likelihood of future childhood ADHD, suggesting sleep difficulties at this age could precede the development of the disorder.[7] Finally, a study of 155 dyads found that poorer maternal sleep quality at 24 weeks gestation was associated with newborns' event-related potentials (ERP) in response to auditory emotional stimuli, specifically reduced ERP amplitude to happy stimuli and enhanced responses to sad stimuli.[8] Although the functional significance of these results remains unclear, this study suggests that prenatal sleep health may impact early brain development.

While this emerging work supports an association between prenatal sleep health and risk of offspring ADHD symptoms and sleep problems, it is limited in critical ways. First, studies have been inconsistent in which index of sleep health in pregnancy is examined (quality, duration, etc). Studies have also not examined timing of exposure effects, as studies have either included a single assessment of sleep during pregnancy or averaged across timepoints. Understanding potential timing of exposure effects is critical to developing and

timing interventions. Further, studies have not considered possible offspring sex effects, despite research repeatedly identifying sexually dysmorphic outcomes related to prenatal exposures.[9] Of the five aforementioned studies, only one[4] tested offspring sex effects and did not find significant sex interactions, yet maternal sleep health was operationalized only as daytime sleepiness without attention paid to overnight sleep health.

We aimed to test associations between three indicators of prenatal maternal sleep health (duration, quality, sleep disturbances) and offspring ADHD symptoms and sleep problems in early childhood (at ~4 years). While ADHD symptoms are our primary outcome of interest, we also examined offspring's own sleep problems, as studies show prenatal maternal sleep may be associated with early difficulties with offspring sleep,[5] which have in turn been associated with the development of ADHD.[7] We examined these associations in a large, racially/ethnically diverse sample from the NIH Environmental Influences on Child Health Outcomes (ECHO) Program. This represents the first study on this topic in the US, a country where self-reported sleep duration is declining[10] and one-third of adults report getting insufficient sleep.[11] We examined trimester-specific maternal report of sleep quality, duration, and disturbances and test moderation by offspring sex. We hypothesized poorer sleep health in pregnancy will be associated with worse offspring outcomes but make no hypotheses regarding sex and timing of exposure given the lack of prior research.

Methods

Procedures

The data for this study come from the NIH ECHO Program.[12] Established in 2016, the ECHO Program is a collaborative research initiative aimed at advancing our understanding of the effects of early environmental exposures on children's development. We combine data from five ECHO cohorts in the present analysis, collected from September 2016 to November 2022, including all mother-child dyads with available prenatal sleep and offspring ADHD symptomatology or sleep problem assessments. Pregnant participants completed self-reports of sleep health at least once during their pregnancy, up to three times total (one per trimester). A caretaker reported on children's symptoms and behaviours when children were 3.96 ± 0.9 years of age. Participants provided consent, and Institutional Review Boards—either the ECHO single IRB or each cohort's local IRB—approved all study procedures.

Participants

Participants included 794 mother-child dyads. Pregnant participants were 32.3 ± 5.5 years old at the time of enrolment, and children included 363 (46%) females, 430 (54%) males, and <5 missing offspring sex data. 44 percent of pregnant participants identified as Hispanic or Latine, and 49% as White, 26% identifying as multiple races, 9% as Black, and 9% as Asian (see Table 1). eTables S1 and S2 (Supplemental Materials) display the demographic characteristics, separately for each cohort and by trimester, of sleep reports and eFigure S1 display flowcharts summarizing sample selection.

Measures

Demographic characteristics

Maternal demographic characteristics included maternal age at enrolment, self-reported race and ethnicity, household income, education, and pre-pregnancy body mass index (BMI). Child demographic characteristics included caretaker reported race, ethnicity, age at assessment, and sex assigned at birth.

Prenatal maternal sleep health

Prenatal maternal sleep health was assessed via two self-report instruments, the Pittsburgh Sleep Quality Index (PSQI) and/or the ECHO Maternal Sleep Health in Pregnancy Questionnaire (MSHP). The PSQI is a widely used measure of subjective sleep quality[13] and has been previously validated in pregnant populations.[14] The MSHP was specifically developed by the ECHO Program. In line with prior work conducted with the ECHO cohort examining sleep disparities in pregnancy,[15] we used both instruments to yield three indices of sleep health: 1) duration, 2) overall quality (higher scores index poorer quality), and 3) disturbances (e.g., felt too cold/hot). The Supplement provides details.

Offspring outcomes: ADHD symptoms and sleep problems

Offspring ADHD symptoms and associated phenotypes were assessed using the Child Behaviour Checklist Preschool Version (Ages 1.5–5; CBCL[16]), a widely used parent report. We examined T-scores for two subscales: Attention Deficit/Hyperactivity Problems-DSM5 and Sleep Problems. Emotionally Reactivity (ER), was examined in supplemental analysis at ADHD is associated with ER,[17] results are reported in the Supplement and in eTable S8.

Prenatal maternal depression

Prenatal maternal depression was assessed using a harmonised variable created by the ECHO consortium. See the supplement material for details.

Prenatal maternal tobacco, alcohol, and/or substance use

A dichotomous variable was created harmonising the different instruments used across cohorts, where any endorsement of tobacco, alcohol, or psychoactive substance (e.g., cannabis) use during pregnancy resulted in classification as positive for use (see Supplemental Materials).

Prenatal health problems

A dichotomous variable was created as an index of common pregnancy health problems across cohorts

Variable	Mean (SD) or n (%)	Missing (n)
Sex of Child		<5
Female	363 (46%)	
Male	430 (54%)	
Household Income		194
<$30k	140 (23%)	
$30k–50k	66 (11%)	
$50k–75k	54 (9%)	
$75 k+	340 (57%)	
Age of Child (at CBCL)	3.96 (0.93)	0
Ethnicity of Child		37
Hispanic	368 (49%)	
Not Hispanic	389 (51%)	
Race of Child		66
White	386 (49%)	
Black	69 (9%)	
Asian	68 (9%)	
Other/Multiracial	14 (2%)	
Native Hawaiian/Pacific Islander	8 (1%)	
American Indian/Alaska Native	31 (4%)	
Multiple Race	205 (26%)	
Maternal Age	32.3 (5.5)	<5
Maternal Pre-pregnancy BMI	26.0 (6.1)	122
Maternal Ethnicity		0
Hispanic	350 (44%)	
Not Hispanic	444 (56%)	
Maternal Race		10
White	386 (49%)	
Black	69 (9%)	
Asian	68 (9%)	
Other/Multiracial	14 (2%)	
Native Hawaiian/Pacific Islander	8 (1%)	
American Indian/Alaska Native	31 (4%)	
Multiple Race	205 (26%)	
Maternal Education		
Less than High School Diploma	75 (9%)	36
HS/GED	145 (18%)	
Some college/Associates degree/Trade school	134 (17%)	
Bachelor's degree	163 (21%)	
Master's degree	241 (30%)	

Notes: n = 794; BMI = Body mass index; CBCL = Child Behavior Checklist; SD = Standard Deviation, HS = High School, GED = Graduate Equivalency Degree.

Table 1: **Demographic characteristics.**

(gestational diabetes, preeclampsia, or gestational hypertension; see Supplement).

Statistical analysis

Mixed effects linear regression models were fit using SAS (v9.4) featuring random intercepts for cohort. A separate set of models was fit for each combination of maternal sleep health predictor (sleep duration in hours, sleep quality, or average sleep disturbance score) and CBCL outcome (ADHD symptoms, Sleep Problems) during each trimester. First, a model including all mother-child pairs was fit to estimate the overall association between the maternal sleep health predictor and the CBCL outcome for each trimester of pregnancy, separately. Models were adjusted for the sex of the child; maternal age; pre-pregnancy BMI; household income; maternal tobacco, alcohol, and/or substance use; prenatal depression, and prenatal health problems. There were no missing values for the CBCL. Participants missing covariate values were excluded from analysis, except for BMI and income, where a "missing" category was included to minimise the number of excluded dyads. Next, effect moderation by child sex was explored by adding an interaction term for child sex and maternal sleep health. Finally, when maternal sleep X offspring sex interactions were detected, the initial model was repeated stratified by sex. Residual diagnostic plots were produced for each of these models and were examined for goodness-of-fit. The Benjamini-Hochberg method[18] was used to adjust *p*-values for model main effects, to maintain a false discovery rate of 5%.

Sensitivity analyses

To test possible non-linear maternal sleep duration effects, models with sleep duration as the predictor were refit with a categorized sleep duration variable (<6 h vs. 6–10 h vs. >10 h). Because prenatal health problems could represent an intermediate downstream effect of prenatal maternal sleep on offspring neurodevelopment, models were also performed without controlling for prenatal health. Finally, to assess the effect of cohort on the results, two analyses were carried out. First, models were refit including only participants from the largest cohort, and consequently removing the random intercept for cohort. Second, models were re-fit excluding each of the smaller cohorts, one-by-one. Excluding the largest cohort did not leave a large enough sample for analysis.

Role of the funding source

The funding source contributed to study design.

Results

Out of the 794 pregnant participants included, 394 completed assessments of sleep health in the first trimester of pregnancy, 564 in the second, and 117 in the third. As expected, pregnant participants reported shorter sleep duration in the later trimesters of pregnancy, with participants reporting 8.62 ± 1.58 h in the first trimester, 8.40 ± 1.41 h in the second, and 7.66 ± 1.88 h in the third (Fig. 1). The quality of sleep also declined across trimesters (Table 2). Similarly, participants reported slightly more sleep disturbances in the third trimester compared with the first two (1st: 0.85 ± 0.47, 2nd: 0.86 ± 0.45; 3rd: 0.98 ± 0.56; eTable S3). Across all trimesters, the most widely reported sleep disturbances were having to get up to use

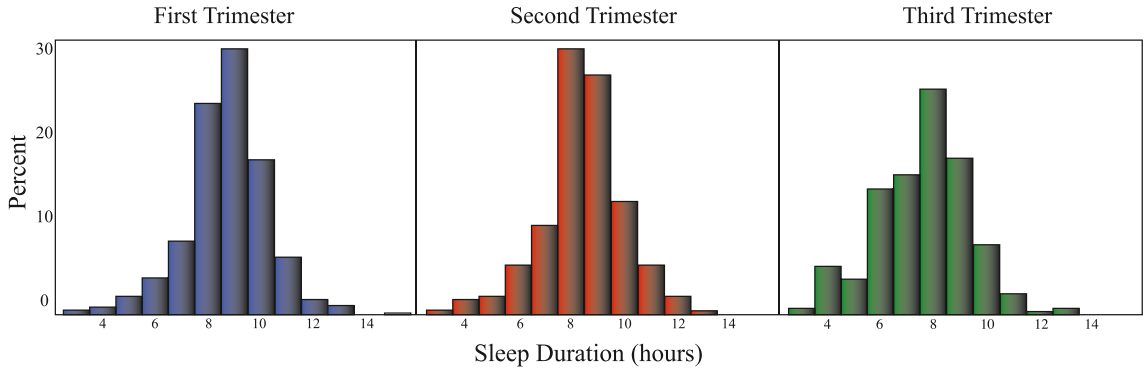

Fig. 1: Sleep duration and disturbances across pregnancy.

the bathroom and waking up in the middle of the night. These were endorsed by roughly 65% and 46% of the sample as occurring more than three times per week, respectively, and were endorsed in similar numbers across all trimesters.

Offspring ADHD symptoms

Mixed effects linear regression models testing the main effect of maternal sleep duration demonstrated that prenatal maternal sleep duration in the second trimester was negatively associated with offspring ADHD symptom scores, such that longer sleep duration in the second trimester was associated with fewer ADHD symptoms in offspring (b = –0.35 [95% CI = –0.57, –0.13], p = 0.026; Table 3). Poorer sleep quality scores in the second trimester were associated with greater offspring ADHD symptomatology (b = 0.66 [95% CI = 0.18, 1.14], p = 0.037; Fig. 2). In the first trimester, models detected a significant interaction between maternal sleep quality and offspring sex (p = 0.034 [95% CI = –1.76, –0.07]; eTable S4), such that first trimester sleep quality was marginally positively associated with ADHD symptomatology for male, but not female offspring (males: b = 0.59 [95% CI = –0.02, 1.19], p = 0.06; females b = –0.46 [95% CI = –1.10, 0.19], p = 0.17). Finally, greater sleep disturbances in the first trimester of pregnancy were associated with greater offspring ADHD symptomatology (b = 1.03 [95% CI = 0.32, 1.03], p = 0.037). This association was not found for second trimester sleep disturbances, while for third trimester sleep disturbances the statistical significance of the association was attenuated upon FDR correction (b = 1.35 [95% CI = 0.10, 2.61], p = 0.12). No statistically significant interactions were detected between offspring sex and prenatal maternal sleep duration or disturbances.

Maternal assessment of their overall sleep quality in the last month	1st Trimester n (%)	2nd Trimester n (%)	3rd Trimester n (%)
Very good	99 (23%)	116 (17%)	28 (15%)
Fairly good	233 (54%)	396 (60%)	101 (54%)
Fairly bad	90 (21%)	131 (20%)	47 (25%)
Very bad	12 (3%)	22 (3%)	10 (5%)

Table 2: **Distribution of maternal sleep quality reports across the three trimesters.**

Offspring sleep problems

Second trimester sleep duration and quality were both associated with offspring sleep difficulties, such that shorter duration and poorer quality were associated with more offspring sleep problems, although the statistical significance was attenuated upon FDR correction (duration: b = –0.29 [95% CI = –0.56, –0.02], p = 0.12; quality b = 0.70 [95% CI = 0.12, 1.28], p = 0.068). Sleep disturbances during all trimesters were associated with sleep difficulties in offspring, although the statistical significance remained after FDR adjustment only for the second trimester (1st trimester: b = 1.00 [95% CI = 0.02, 1.99], p = 0.12; 2nd trimester: b = 1.53 [95% CI = 0.62, 2.45], p = 0.026, 3rd trimester: b = 1.04 [95% CI = –0.01, 2.08], p = 0.12). No statistically significant interactions with offspring sex were detected for any of the three sleep health indicators.

Sensitivity analyses

Sensitivity analyses testing potential non-linear sleep duration effects showed that for the first and second trimesters of pregnancy, short (<6 h), but not long (>10 h), sleep was significantly associated with offspring ADHD symptoms, as compared with average sleep duration (6–10 h; eFigure S2). Analyses including only the largest cohort mostly replicated multi-cohort findings, showing that shorter sleep duration in the second trimester was associated with ADHD symptoms and sleep problems in offspring. Sleep disturbances in the first trimester were associated with greater ADHD symptomatology and poorer second trimester sleep quality was associated with offspring sleep problems.

Prenatal sleep health variable	Offspring outcome	Trimester	N	Unstandardized estimate (95% CI)	Error	DF	t-Value	*Raw p* value	*FDR-adjusted p* value
Sleep duration	ADHD symptoms	1	385	−0.199 (−0.401, 0.003)	0.103	375	−1.93	0.054	0.122
		2	559	−0.351 (−0.571, −0.131)	0.112	547	−3.12	0.0019	0.026
		3	115	−0.062 (−0.438, 0.314)	0.192	101	−0.32	0.748	0.880
	Sleep Problems	1	385	−0.221 (−0.491, 0.049)	0.138	375	−1.60	0.111	0.231
		2	559	−0.286 (−0.556, −0.016)	0.138	547	−2.07	0.039	0.117
		3	115	−0.041 (−0.349, 0.267)	0.157	101	−0.26	0.796	0.880
Poor sleep quality	ADHD symptoms	1	394	0.130 (−0.309, 0.569)	0.224	384	0.58	0.563	0.761
		2	556	0.660 (0.184, 1.136)	0.243	546	2.72	0.0068	0.037
		3	113	−0.038 (−0.981, 0.905)	0.481	101	−0.08	0.936	0.936
	Sleep Problems	1	394	0.196 (−0.412, 0.804)	0.310	384	0.63	0.529	0.752
		2	556	0.701 (0.123, 1.279)	0.295	546	2.38	0.018	0.068
		3	113	−0.045 (−0.815, 0.725)	0.393	101	−0.11	0.910	0.936
Average sleep disturbances score	ADHD symptoms	1	394	1.028 (0.317, 1.739)	0.363	384	2.83	0.0049	0.037
		2	558	0.469 (−0.288, 1.226)	0.386	548	1.22	0.225	0.379
		3	113	1.354 (0.098, 2.610)	0.641	101	2.11	0.037	0.117
	Sleep Problems	1	394	1.004 (0.016, 1.992)	0.504	384	1.99	0.047	0.122
		2	558	1.535 (0.622, 2.448)	0.466	548	3.29	0.0011	0.026
		3	113	1.043 (−0.015, 2.080)	0.529	101	1.97	0.051	0.122

Notes: ADHD = attention deficit hyperactivity disorder; DF = degrees of freedom. Models were adjusted for the sex of the child; maternal age; pre-pregnancy BMI; household income; maternal tobacco, alcohol, and/or substance use; prenatal depression, and prenatal health problems.

Table 3: **Associations between sleep health in pregnancy and offspring ADHD symptoms and sleep problems.**

Sleep disturbances across all trimesters were associated with offspring sleep problems (eTable S5). Leave-one out analyses showed similar findings across iterations, with the most variability documented on estimates of poor sleep quality effects on offspring sleep in the third trimester (eTable S6). Finally, results did not change in analyses where prenatal health was not included as a covariate (eTable S7).

Discussion

The present study examined associations between self-reported prenatal maternal sleep health and offspring ADHD symptoms in early childhood in a sociodemographically diverse sample in the US and US territories, including Puerto Rico. We document significant associations between shorter sleep duration, poorer sleep quality, and greater number of sleep disturbances with offspring ADHD symptoms and sleep problems in early childhood, controlling for maternal depression in pregnancy and other sociodemographic characteristics.

This is the first human study to test timing of exposure effects and we most consistently observed associations between second-trimester sleep duration and quality with offspring ADHD and sleep problems. Although findings require replication, they are in line with prior studies documenting disturbances in sleep during pregnancy are associated with children's ADHD symptoms and sleep problems. Similarly, our findings are in line with the one study to date in failing to document significant offspring sex effects.

Human studies that address timing of exposure, mechanism, and offspring brain development are critically needed. However, rodent work has shown that

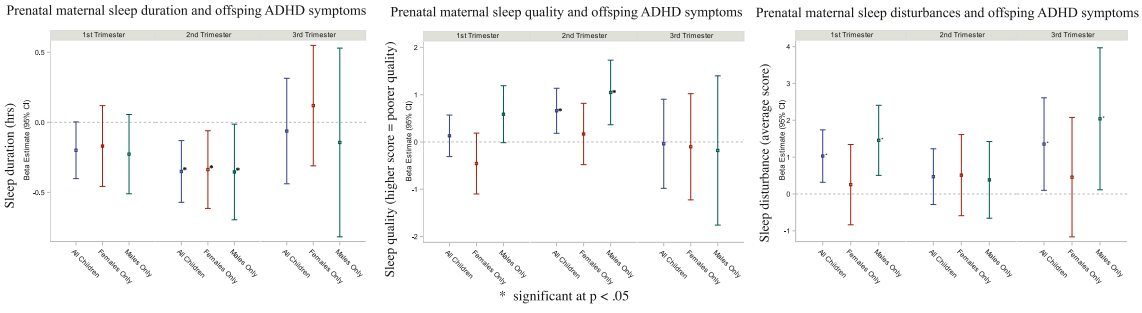

Fig. 2: Associations between prenatal maternal sleep health and offspring ADHD symptoms. Models were adjusted for the sex of the child; maternal age; pre-pregnancy BMI; household income; maternal tobacco, alcohol, and/or substance.

rapid eye-movement (REM) deprivation during gestational days 15–20 (equivalent to mid-gestation in humans[19]) is associated with atypical sleep patterns in pups, which is in turn suggestive of delayed brain maturation.[20] Similarly, offspring of sleep-deprived dams (days 14–19) demonstrate greater risk-taking behaviour and higher overall mobility (i.e., hyperactivity[21]), phenotypes often seen in the context of ADHD. Animal studies also document that prenatal REM deprivation—specifically on gestational day 18–was associated with decreased hippocampal neurogenesis in offspring.[22] This study also documented increased pro-inflammatory and decreased anti-inflammatory cytokines in offspring hippocampi, suggesting microglial activation and associated neuroinflammatory processes may mediate transmission of maternal sleep disruptions to the offspring brain, particularly the hippocampus.[23] This is of interest, as hippocampal structure is closely related to emotion regulation abilities, including in children.[24] Prenatal sleep might thus increase risk of emotion regulation difficulties (often seen in ADHD) by impacting maternal immune function and inflammation. Disrupted sleep may also act as a stressor that activates the maternal HPA axis[25] and in doing so, may unravel a self-perpetuating cycle that disrupts fetal brain development, including the hippocampus.[26] Longitudinal studies need to address biological mechanisms and examine interactions between maternal immune and HPA axis activation, examining brain regions specifically implicated in sleep and sleep regulation.

Interestingly, reports of sleep duration and subjective estimation of overall sleep quality seemed to be equally predictive of offspring outcomes. It may be that both are reflective of stress-related sleep disruption processes that could thus result in the activation of the same prenatal programming pathways (e.g., maternal HPA axis activation, inflammatory alterations[27]). On the other hand, we documented associations between sleep disturbances and offspring outcomes across all trimesters, with no clear trimester-specific pattern emerging. Because our measure included an array of disturbances (e.g., difficulty falling asleep, needing to use the bathroom), future studies examining individual disturbances are needed. It may be that sleep disturbances are associated to other mechanisms (e.g., changes in body temperature could be associated to fluctuations in hormones like progesterone and adiponectin[28]) that would alter fetal development differentially. Further studies should consider employing clustering methodologies to understand common and diverging associations across different sleep indicators.

Our analyses suggest maternal sleep is similarly associated with outcomes among male and female offspring. This is of note, as many prenatal programming studies suggest early brain insults associated with maternal immune and HPA axis activation have differential effects depending on offspring sex. It is worth highlighting that children in our sample were, on average, 4 years old at the time parents reported symptoms, an age when neurodevelopmental disorders like ADHD begin to arise but have yet to peak. It may be that with increasing offspring age, sex-specific associations could emerge, which would be in line with the pronounced male bias seen in ADHD at older ages. Therefore, longitudinal studies that follow children through childhood and adolescence will be needed to fully understand development of risk.

The present study relied on maternal self-reported sleep health, which may not align well with objectively assessed metrics.[29] We also had a smaller sample size for the third trimester, which may have resulted in reduced power. Additionally, by relying on a self-report for maternal sleep and offspring outcomes measures, bias may have been introduced (e.g., from maternal mood), highlighting the need for the inclusion of actigraphy and alternative outcome measures (e.g., teacher reports). Further, lack of information about familial risk for ADHD precluded consideration of the role of shared familial genetic risk for ADHD, which may be associated with both poor sleep and offspring ADHD. Future studies should consider the role of perinatal anxiety, as well as postnatal maternal mood, as prenatal sleep difficulties might exacerbate risk for postnatal depression, which could in turn impact children's neuro- and socioemotional development.[30] Information on maternal sleep disorders (e.g., sleep apnoea) were also not available in the current dataset, which may be important confounders. Missing covariate data could also introduce bias. Finally, our study documented that maternal sleep problems were associated with difficulties in children's own sleep. Although the present assessments of offspring sleep and ADHD occurred concurrently, prior work has documented sleep difficulties in infancy may precede the onset of neuropsychiatric disorders.[7] More work is needed to understand the role of offspring sleep in the prenatal maternal sleep–offspring ADHD association, as it could prove to be an important target for interventions aimed at deterring transmission.

In conclusion, our study documents that poor prenatal maternal sleep health, particularly duration and quality during the second trimester, is associated with offspring risk of neurodevelopmental and sleep problems in early childhood. Although research is needed to understand the underlying mechanisms, our study suggests prenatal maternal sleep may be a future modifiable target for interventions aimed at optimizing fetal neurodevelopment. Efficacious interventions for the management of sleep difficulties, exist.[31] Research on these interventions' effectiveness in pregnant populations has lagged, yet preliminary evidence supports their usefulness.[32] In non-pregnant populations, interventions for depression and anxiety – which often co-occur with sleep disturbances—have shown mixed

success in improving sleep outcomes,[33,34] yet it is still to be determined whether these treatments may be beneficial for pregnant people's sleep in the context of a comorbid depression or anxiety disorder. Although our findings require replication, they may suggest that optimising sleep in the second trimester may be maximally effective, highlighting the need for the screening of sleep health in early pregnancy, particularly for pregnant people with a history of preconception sleep difficulties or mood disorders, as these have been associated with increased risk for sleep problems in pregnancy.[35] Overall, our study highlights the need to better understand the role prenatal sleep plays in the health of both the pregnant person and the developing foetus.

Contributors

CLC, JP, CD, and CM conceived and planned the present manuscript. All authors (CLC, JP, CD, CM, GC, TH, SL, ML, ASA, LK, CB, TOC, AG, AP, JA, SD, AM) were involved in conducting the study in their respective cohorts. CLC, TH and SL analysed the data. CLC interpreted the data and drafted the initial manuscript. All authors (CLC, JP, CD, CM, GC, TH, SL, ML, ASA, LK, CB, TOC, AG, AP, JA, SD, AM) significantly contributed to manuscript revisions. CLC, TH and SL accessed and verified the data. All authors (CLC, JP, CD, CM, GC, TH, SL, ML, ASA, LK, CB, TOC, AG, AP, JA, SD, AM) approved the final text. All authors (CLC, JP, CD, CM, GC, TH, SL, ML, ASA, LK, CB, TOC, AG, AP, JA, SD, AM) take responsibility for the decision to submit for publication. The funding source contributed to study design.

Data sharing statement

Data that underlie the results reported in this Article is available in de-identified form to the public the Data and Specimen Hub, a centralized resource established by the National Institute of Child Health and Human Development (NICHD). Researchers can request access to these data via a Data Request Form.

Declaration of interests

All authors declare no competing interests. CLC, CD, JA and AM all report funding from NIH. CD reports funding form Morgan Stanley, Saks Foundation, payments from WT Grant Foundation and UC Davies College of Biological Sciences and a leadership role in the American Psychopathological Association. JA reports honoraria from IPOKRaTES Neonatology Conference and holding a leadership position in National Board of Trustees: March of Dimes. SD reports payment or honoraria from Nestle Nutrition, Wyeth. Nutrition and Mead Johnson Nutrition.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2023.100609.

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