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Maternal antenatal daytime sleepiness and child neuropsychiatric and neurocognitive development

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Original Article

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Abstract

Background. The prevalence of sleep problems among pregnant women is over 50%, and daytime sleepiness is among the most common sleep problems. Previous studies have associated antenatal sleep problems with adverse maternal health and neonatal outcomes, but the consequences of antenatal sleep problems and particularly daytime sleepiness on child psychological development have not been assessed prospectively.

Methods. In this prospective cohort study including 111 mother-child dyads, we examined the associations of maternal daytime sleepiness during pregnancy, assessed at 17 and 28 weeks of gestation using the Epworth Sleepiness Scale, with child neuropsychiatric problems and neuropsychological development, assessed with mother-rated questionnaires and individually administered neuropsychological tests, at child age 2.6–5.7 years (mean = 4.3 years).

Results. Independently of sociodemographic and perinatal covariates and maternal depressive and anxiety symptoms during and/or after pregnancy, maternal antenatal daytime sleepiness was associated with increased total [unstandardized regression coefficient (B) = 0.25 standard deviation (S.D.) units; 95% confidence interval (CI) 0.01–0.48] and internalizing (B = 0.25 S.D.s: 95% CI 0.01–0.49) psychiatric problems and ADHD symptoms (B = 0.27 S.D.s: 95% CI 0.04–0.50) in children, and with poorer executive function, particularly in the areas of attention, working memory and inhibitory control (B = −0.39 S.D.s: 95% CI −0.69 to −0.10).

Conclusions. Maternal antenatal daytime sleepiness carries adverse consequences for offspring psychological development. The assessment of sleep problems may be an important addition to standard antenatal care.

Introduction

Sleep problems are very common among pregnant women, with 45–50% of women experiencing sleep problems during pregnancy (Abbott *et al.*, 2014; Mindell *et al.*, 2015; Sedov *et al.*, 2018). Daytime sleepiness, defined as persistent sleepiness and general lack of energy even during the day, is among the most common sleep problems, with especially high prevalence rates during pregnancy (Izci *et al.*, 2005; Facco *et al.*, 2010; Signal *et al.*, 2014; Mindell *et al.*, 2015; Paavonen *et al.*, 2016). Daytime sleepiness can either be a symptom of other sleep disorders including insomnia, hypersomnia, narcolepsy, and difficulties in initiating and maintaining sleep (Johns, 1991; Dickinson *et al.*, 2018), or of other disorders/conditions including depression and anxiety (Dickinson *et al.*, 2018), or be considered its own sleep problem condition (Paavonen *et al.*, 2016).

Maternal antenatal sleep problems are associated with maternal obesity and depressive symptoms during and after pregnancy (D⊘rheim *et al.*, 2012; Mellor *et al.*, 2014; Palagini *et al.*, 2014; Paavonen *et al.*, 2016; Sarberg *et al.*, 2016) and with an increased risk of gestational diabetes (Palagini *et al.*, 2014), preterm birth and suboptimal fetal growth (Micheli *et al.*, 2011; Abbott *et al.*, 2014; Palagini *et al.*, 2014).

Previous studies have repeatedly shown that preterm birth, suboptimal fetal growth, and maternal obesity, gestational diabetes and depressive symptoms during and after pregnancy may each predict an increased risk of psychiatric problems and poorer neurocognition in the offspring (Van Batenburg-Eddes *et al.*, 2013; Betts *et al.*, 2014; 2015; Korhonen *et al.*, 2014; O'Donnell *et al.*, 2014; Tarabulsy *et al.*, 2014; Walder *et al.*, 2014; Sandman *et al.*, 2015; Xiang *et al.*, 2015; Edwards and Hans, 2016; Pearson *et al.*, 2016; Gjerde *et al.*, 2017; Lahti *et al.*, 2017; Mina *et al.*, 2017; Pyhälä *et al.*, 2017; Van den Bergh *et al.*, 2017). In turn, maternal

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sleep problems during pregnancy have been associated with increased sleep problems in children at a mean age of 11 years in a retrospective case-control study of 97 participants (Armstrong *et al.*, 1998), but the effects of maternal sleep problems or particularly daytime sleepiness during pregnancy on child neurocognitive or neuropsychiatric development have, to our knowledge, not been previously studied using a longitudinal design.

We hypothesized that maternal daytime sleepiness during pregnancy predicts offspring neuropsychiatric symptoms and/or neurocognitive development in early childhood. In the current study, we tested this hypothesis in a cohort of women in whom daytime sleepiness was recorded prospectively during pregnancy and their children followed-up at a mean age of 4.3 years [range 2.6–5.7 years; standard deviation (S.D.) = 0.6 years].

Methods

The participants

Our study sample comprised participants of the Hormones and Inflammation in Parents and Young longitudinal pregnancy cohort of 357 women with very severe obesity [body mass index (BMI) $\geqslant$ 40 kg/m^2] and lean controls (BMI $\leqslant$25 kg/m^2) living in Midlothian, Scotland, UK (Mina *et al.*, 2015). The participants were recruited at their first appointment during pregnancy between gestational weeks 8 and 12. We obtained ethical approval for the study from the local research ethics committee (REC: 14/WS/1046, R&D: 2014/0278). The study was conducted in the Wellcome Trust Clinical Research Facility, the Royal Hospital for Sick Children, Edinburgh.

We screened the 357 pregnancy study participants for follow-up participation eligibility. Of these, 90 (25.2%) cohort members declined participation and 57 (16.0%) were uncontactable. We also excluded mothers who had moved out of Midlothian [n = 13 (3.6%)] and mothers whose child was under a child protection register alert [n = 9 (2.5%)], families where there had been a community intervention [n = 12 (3.4%)] and mother-child dyads who were unfit for medical reasons [n = 8 (2.2%)] (Mina *et al.*, 2017). Of the recruited 153 mother-child dyads for the childhood follow-up, 37 (24.2%) did not complete the follow-up although they had verbally agreed to complete study questionnaires at home (Mina *et al.*, 2017). Hence, we obtained written informed consent to participate in the childhood follow-up from 116 mother-child dyads with term-born offspring. As shown previously, the 116 women who participated in the follow-up were less often severely obese in early pregnancy, and they had less often high socioeconomic deprivation, and lower depressive and anxiety symptoms during pregnancy (Mina *et al.*, 2017), but they did not differ in daytime sleepiness during pregnancy (p = 0.38). Of the 116 mother-child dyads who participated in the follow-up, three had missing data on maternal antenatal sleepiness and two on child neuropsychiatric and neurocognitive development.

The current study sample thus comprises 111 mother-child dyads with data on maternal prenatal daytime sleepiness and child neuropsychiatric symptoms and/or neurocognitive development. Compared with the current study participants, the cohort mothers who did not participate had more depressive [mean difference (MD) = 0.36 S.D. units, 95% confidence interval (CI) 0.14–0.59, p = 0.002)] and anxiety (MD = 0.31, 95% CI 0.08–0.53, p = 0.01) symptoms across pregnancy, a significantly higher proportion of severe obesity (69.9% *v.* 45.0%, p < 0.001), and of high socioeconomic deprivation (58.8% *v.* 37.8%, p < 0.001) but did not differ in terms of maternal antenatal daytime sleepiness, age, parity, gestational diabetes, smoking status or child sex (p values $\geqslant$0.32).

Maternal daytime sleepiness during pregnancy

The mothers rated their daytime sleepiness during pregnancy with the Epworth Sleepiness Scale (ESS). The ESS assesses the levels of daytime sleepiness in eight different everyday situations with the question *How likely are you to doze off in the following situations, in contrast to feeling just tired* (Johns, 1991). The ESS shows good psychometric properties (Johns, 1991; Baumgartel *et al.*, 2013; Jaussent *et al.*, 2017) and has been validated among patient populations including patients with narcolepsy, hypersomnia, and snoring (Johns, 1991; Kendzerska *et al.*, 2014; Maurovich-Horvat *et al.*, 2014; Nishiyama *et al.*, 2014), and also among pregnant women (Izci *et al.*, 2005; Baumgartel *et al.*, 2013). Acceptable internal consistency (Cronbach's α = 0.75) for the ESS has been reported among pregnant women (Baumgartel *et al.*, 2013). The mothers completed the ESS up to two times at 17 and 28 weeks of gestation. We used the mean scores of these two assessments, indicating mean levels of daytime sleepiness during pregnancy, as independent variables in our analysis.

Child neuropsychiatric symptoms

The mothers rated child neuropsychiatric symptoms with the Conner's Hyperactivity Scale (Erhart *et al.*, 2008), the *Children's Sleep Habits Questionnaire* (CSHQ)- adopted for preschool children (Goodlin-Jones *et al.*, 2008), Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), and Preschool Version of Child Behavior Checklist (CBCL 1½−5) (Achenbach and Rescorla, 2000). The CBCL (Achenbach and Rescorla, 2000), SDQ (Theunissen *et al.*, 2013; Croft *et al.*, 2015), Conner's Hyperactivity Scale (Erhart *et al.*, 2008; Westerlund *et al.*, 2009) and CSHQ (Owens *et al.*, 2000; Goodlin-Jones *et al.*, 2008) are each validated questionnaires with good psychometric properties. Higher scores on each scale indicate increased neuropsychiatric problems.

The Conner's Hyperactivity Scale includes 10 items assessing ADHD symptoms of emotional lability, hyperactivity, and inattention. While two subscales of hyperactivity and emotional lability can be derived from the Conner's scale, we use only the total Conner sum-score as a dependent variable (Westerlund *et al.*, 2009). The CSHQ contains 45 items on child sleep problems and sleep behaviour. Here we examine CSHQ sleep problems as an outcome. The CBCL1½−5 comprises 99 items and SDQ 25 items on child psychiatric problems (Goodman, 1997; Achenbach and Rescorla, 2000). The SDQ yields a total difficulties scale on general psychiatric problems and four more specific symptom scales (hyperactivity, emotional, conduct, and peer problems) and one subscale on child's strengths. The CBCL/1½−5 yields scores for three main (internalizing, externalizing, and total problems), eight syndrome and five Diagnostic and Statistical Manual for Mental Disorders-oriented scales. Due to limited statistical power on their subscales, we focus here on the SDQ Total Difficulties and the three CBCL broadband scale t-scores (Achenbach and Rescorla, 2000) as outcomes.

Previous studies have reported excellent internal consistency for the Conner's Hyperactivity scale (Cronbach's α = 0.90) (Westerlund *et al.*, 2009). Also in our study sample, the scale showed good internal consistency (α = 0.86). Previous evidence also shows good to excellent internal consistencies for the CBCL internalizing, externalizing, and total problems scales (α:s varying

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between = 0.89 and = 0.95) (Achenbach and Rescorla, 2000), and acceptable internal consistencies for SDQ total difficulties (α = 0.79) (Theunissen *et al.*, 2013), and CSHQ sleep problems (α:s between = 0.68 and = 0.78) (Owens *et al.*, 2000).

Child neurocognitive development

Neurocognitive development in children was assessed with mother-rated neurodevelopmental questionnaire Ages and Stages Questionnaire (ASQ) and two individually administered neuropsychological tests on executive functioning, the Head Toes Knee Shoulders (HTKS) and Marshmallow–Tests. The ASQ, HTKS, and Marshmallow are all commonly used measures of neurodevelopment with good psychometric properties (Squires *et al.*, 1997; Kerstjens *et al.*, 2009; Ponitz *et al.*, 2009; Mischel *et al.*, 2011).

The ASQ assesses the completion of neurocognitive and psychomotor developmental milestones in children (Squires *et al.*, 1997). It is a series of age-specific questionnaires including 5–6 questions on communication, gross motor, fine motor, problem-solving, and personal-social development (Squires *et al.*, 1997). We used a sum score of these subscales with scores from 0 to 300 as an outcome to index global neurodevelopment; higher scores indicate better neurodevelopment (Kerstjens *et al.*, 2009). ASQ has acceptable internal consistency (α = 0.79) (Kerstjens *et al.*, 2009).

The Marshmallow test assesses child executive function aspects of self-regulation and inhibition, specifically the ability to delay immediate self-gratification for higher rewards subsequently (Mischel *et al.*, 2011). The child is presented with a marshmallow and told that s/he can eat it immediately or wait and receive a larger reward later. Maximum test length is 15 min. The duration of test performance was used as the outcome. A longer duration indicates better self-control.

The HTKS evaluates the child's executive functioning aspects of attention, working memory, and inhibitory control (Ponitz *et al.*, 2009). In the HTKS, the children must respond the opposite way to that instructed. The HTKS has three difficulty levels each including 10 tasks. Overall scores range from 0 to 60. Higher scores indicate better executive functioning.

Covariates

The mothers rated their depressive symptoms at 17 and 28 weeks of gestation and again at the childhood follow-up with the 12-item version of the General Health Questionnaire (Goldberg and Blackwell, 1970; Lundin *et al.*, 2016). According to previous evidence (Lundin *et al.*, 2016) the General Health Questionnaire shows good internal consistency (α = 0.83–0.89) and validity in detecting depressive disorders. At the same timepoints, the mothers rated their anxiety symptoms with the state version of the Spielberger State-Trait Anxiety Inventory (Spielberger, 1987), a widely use anxiety scale with high internal consistency (α = 0.91) (Barnes *et al.*, 2002). In our analyses, we used a mean score of the prenatal assessments to indicate antenatal depressive and anxiety symptoms and the follow-up symptom scores to indicate maternal depressive and anxiety symptoms concurrently to rating the child.

Maternal BMI was measured by midwives (Mina *et al.*, 2015), and maternal age, smoking, parity, and infant sex was extracted from perinatal records. The most recent maternal postcode was used to assess socioeconomic deprivation levels of the family, which were grouped into low (score <3) and high (score ⩾4) (Mcloone, 2004). The mothers reported their education level (university level *v.* lower) at the follow-up, and the child's age was recorded at the visit.

Statistical analysis

To achieve normal distributions, the right-skewed maternal ESS and GHQ, and child Conner's, and CBCL Internalizing, Externalizing, and Total Problems scales were square-root transformed. The right-skewed maternal STAI and child SDQ Total Difficulty, CSHQ and left-skewed ASQ scale and Marshmallow test scores were rank-normalized according to Blom's formula. HTKS test scores were normally distributed and did not require transformations. All independent and dependent variables were then standardized and are expressed in S.D. units (Mean = 0, S.D. = 1) to facilitate the comparison of effect sizes. The standardizations were done based on the means and standard deviations of the current study sample.

The associations of the covariates with child neurocognitive development and neuropsychiatric problems were examined with Pearson correlation analysis and Student's *t* tests. Online Supplementary Table S1 shows the associations of these covariates with maternal antenatal daytime sleepiness. Online Supplementary Table S2 shows the associations of the covariates with child neuropsychiatric problems and neurodevelopmental questionnaires and tests. For our regression analyses, we included child sex and age and covariates that had significant associations with both maternal antenatal daytime sleepiness and child neuropsychiatric problems and/or neurodevelopment in our sample. As shown in online Supplementary Tables S1 and S2, these covariates associated both with maternal antenatal daytime sleepiness and child developmental outcomes included maternal obesity in early pregnancy, maternal depressive and anxiety symptoms during pregnancy and maternal depressive symptoms at the follow-up, but not maternal age, parity, smoking status, education level, socioeconomic deprivation level nor anxiety symptoms at the follow-up.

Linear regression analyses were run using mean maternal prenatal daytime sleepiness score as the independent variable in all the regression models and children's neuropsychiatric and neurodevelopmental scores as the dependent variables. The first regression models (Model 1) were adjusted for child sex and age-at-follow-up. Model 2 also included maternal depressive symptoms concurrently to rating the child to adjust for possible rater bias and familial confounding by maternal mental health. In Model 3, we added maternal obesity status in early pregnancy. In the final Model 4, we included Model 3 covariates as well as maternal depressive and anxiety symptoms during pregnancy, to assess whether any effects of maternal daytime sleepiness were independent of other forms of psychological distress during pregnancy. Furthermore, we also examined interactions of maternal daytime sleepiness by child sex on child psychological development with linear regression analyses adjusting for child age.

From all the regression models, we present unstandardized regression coefficients (in S.D. units) and their 95% confidence intervals. From the final regression models (Model 4), we also present estimates of effect size (r^2) of the independent effects of maternal antenatal daytime sleepiness on child neuropsychiatric and neurocognitive outcomes, after adjustment for the covariates in Model 4.

Results

Table 1 shows the characteristics of the current study sample. Maternal daytime sleepiness at 17 and 28 weeks of gestation

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Table 1. The characteristics of the study sample

Maternal demographics	N	Mean (s.d.)/N (%)
Age in early pregnancy (years)	111	32.5 (5.1)
Socioeconomic deprivation level	111	
Low		69 (62.2%)
High		42 (37.8%)
Education level	107	
University level		77 (72.0%)
Lower		30 (28.0%)
Maternal perinatal health and characteristics		
Obesity in early pregnancy	111	
Very severe obesity (BMI ⩾ 40)		50 (45.0%)
Lean (BMI < 25)		61 (55.0%)
Parity	111	
Primiparous		63 (56.8%)
Multiparous		48 (43.2%)
Smoking during pregnancy	111[a]	
Current smoker		4 (3.6%)
Quit smoking		48 (43.2%)
Never smoked		59 (53.2%)
Gestational diabetes	111	
Yes		12 (10.8%)
No		99 (89.2%)
Maternal sleep and psychological well-being		
ESS on daytime sleepiness		
17th week of gestation	100	6.9 (3.5)
28th week of gestation	101	6.8 (3.3)
Mean score across pregnancy	111	6.9 (3.1)
GHQ on Depressive Symptoms		
17th week of gestation	98	2.0 (2.0)
28th week of gestation	99	2.1 (1.8)
Mean score across pregnancy	111	2.1 (1.9)
At childhood follow-up	108	2.1 (2.6)
STAI on State Anxiety		
17th week of gestation	98	29.9 (9.0)
28th week of gestation	99	29.4 (7.6)
Mean score across pregnancy	111	29.8 (8.0)
At childhood follow-up	107	30.6 (9.3)
Child characteristics		
Age at follow-up	111	4.3 (0.6)
Sex	111	
Boys		52 (46.8%)
Girls		59 (53.2%)
Child neuropsychiatric problems		
CBCL total problems t-score	104	42.2 (9.0)
CBCL internalizing symptoms t-score	104	43.0 (9.5)
CBCL externalizing symptoms t-score	104	42.9 (9.0)
SDQ total difficulties	106	7.3 (4.7)
Conner's ADHD symptoms	107	7.5 (4.8)
CSHQ sleep problems	108	44.5(9.5)
Child neurodevelopment scores		
ASQ sumscore	98	271.3 (26.3)
HTKS executive function score	75	28.9 (19.6)
Marshmallow test score (seconds)	77	406.7 (393.0)

s.d., standard deviation; ESS, Epworth Sleepiness Scale; GHQ, General Health Questionnaire; STAI, State-Trait Anxiety Scale; BMI, Body Mass Index; CBCL, Child Behaviour Checklist; SDQ, Strength and Difficulties Questionnaire; ADHD, Attention Deficit Hyperactivity Disorder; CSHQ, Children's Sleep Habits Questionnaire; ASQ, Ages and Stages Questionnaire; HTKS, Head Toes Knees Shoulders Test.

[a]Due to the low number of participating mothers who smoked throughout pregnancy, women who quit smoking during pregnancy or who smoked throughout pregnancy were classified into the same group in all statistical analyses.

showed high intra-individual stability ($r = 0.77$, $p < 0.001$), and there was no within-individual change in the levels of daytime sleepiness across gestation (MD = 0.03 s.d.s, $p = 0.55$). Mean antenatal ESS score was 6.9 (s.d. = 3.1), and 8.1% of participating women reported excessive daytime sleepiness during pregnancy (ESS ⩾ 11).

Maternal antenatal daytime sleepiness and child neuropsychiatric symptoms and seurocognitive development

Figure 1, Fig. 2, and Table 2 show the results of the linear regression analyses of maternal daytime sleepiness during pregnancy as a predictor of child neuropsychiatric problems and neurocognitive development. In models adjusted for child sex and age, higher maternal daytime sleepiness during pregnancy was associated with significantly higher child scores on SDQ Total difficulties, CBCL Internalizing, Externalizing, and Total Problems on general psychiatric problems, Conner's Hyperactivity Scale on ADHD symptoms, and CSHQ on child sleep problems. Of the neurocognitive tests and questionnaires, maternal antenatal daytime sleepiness was also associated with significantly poorer ASQ neurodevelopment and HTKS executive function but not with Marshmallow Test scores.

Adjustment for maternal concurrent depressive symptoms in Model 2 did not markedly influence the associations; the association with CBCL Externalizing Problems was now marginal but all other previously significant associations remained significant. Furthermore, adjustment for maternal prenatal obesity in Model 3 attenuated the association with CBCL externalizing problems to non-significance, but higher maternal daytime sleepiness during pregnancy still predicted significantly higher child scores on SDQ Total Difficulties, CBCL Internalizing, and Total Problems, Conner's Hyperactivity Scale, significantly lower child HTKS executive function scores, and marginally higher child CSHQ Sleep Problems and marginally lower ASQ neurodevelopment scores.

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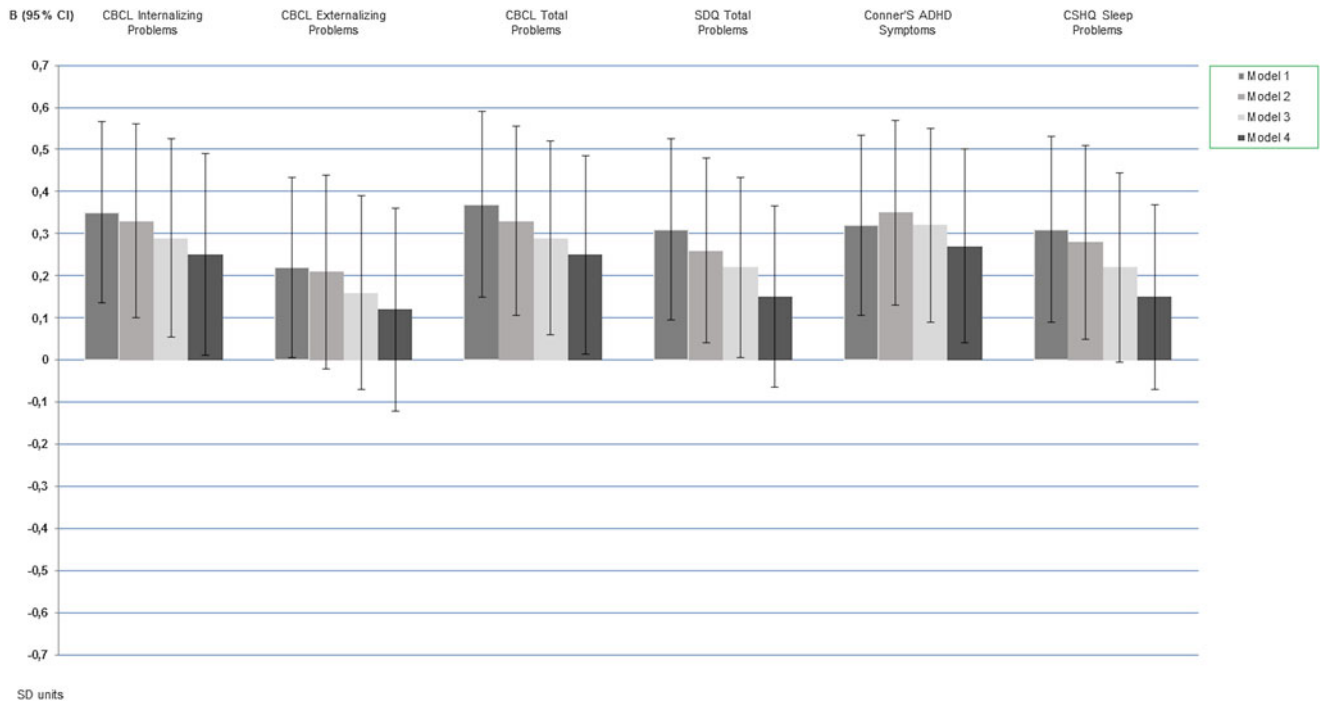

Fig. 1. Maternal antenatal daytime sleepiness and child neuropsychiatric problems. Regression coefficients (*B*) and their 95% confidence intervals (CI) of linear regression analyses where maternal antenatal daytime sleepiness score was used to predict child neuropsychiatric problems. All independent and dependent variables are expressed in standard deviation (S.D.) units. Model 1 is adjusted for child sex and age. Model 2 included Model 1 covariates and maternal depressive symptoms concurrently to rating the child. In Model 3, we added maternal obesity status in early pregnancy as a covariate. In Model 4, we included Model 3 covariates and maternal depressive and anxiety symptoms during pregnancy.

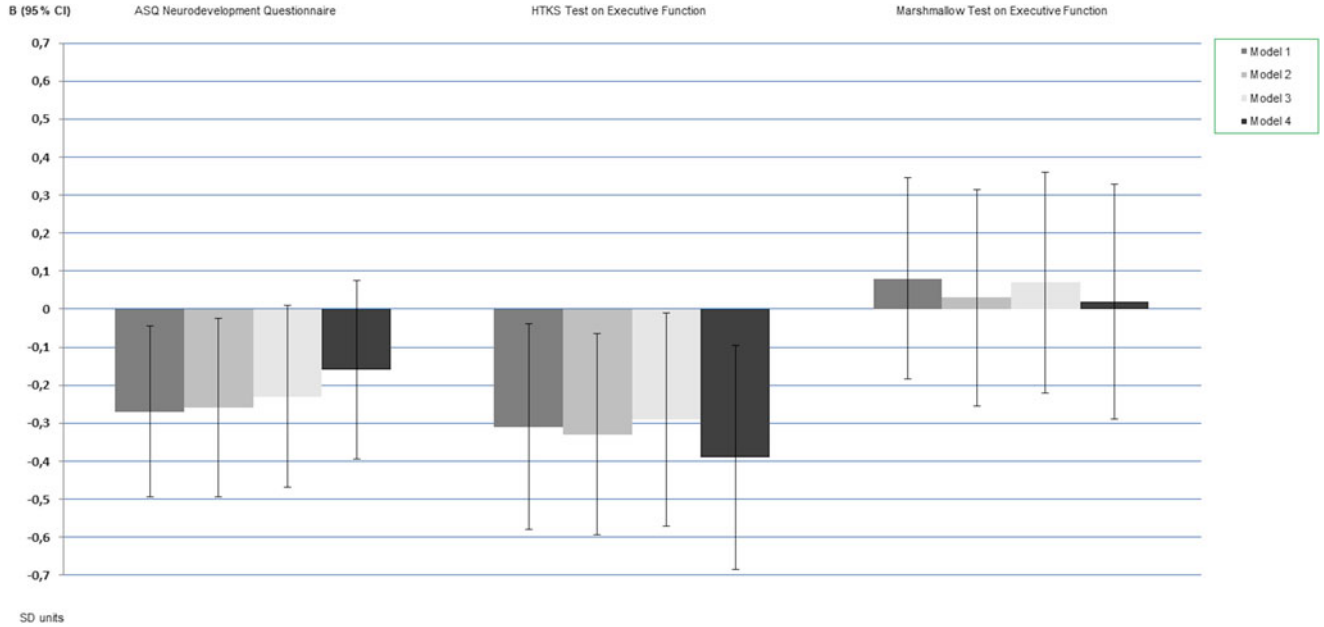

Fig. 2. Maternal daytime sleepiness during pregnancy and child neurocognitive development. Regression coefficients (*B*) and their 95% confidence intervals (CI) from linear regression models where maternal antenatal depressive symptoms was used to predict child neurocognitive development. All independent and dependent variables are expressed in standard deviation (S.D.) units. Model 1 is adjusted for child sex and age. Model 2 also included maternal depressive symptoms concurrently to child follow-up. In Model 3, we added maternal early pregnancy obesity status as a covariate. In Model 4, we included Model 3 covariates and maternal antenatal depressive and anxiety symptoms.

Finally, while the associations with child SDQ Total Difficulties, CSHQ Sleep Problems, and ASQ neurodevelopment scores were non-significant in Model 4 (adjusting also for maternal antenatal anxiety and depressive symptoms), higher maternal antenatal daytime sleepiness was still independently associated with significantly higher CBCL Internalizing and Total Problems, Conner's ADHD symptoms and lower HTKS executive function test scores in children.

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Table 2. Maternal daytime sleepiness during pregnancy and child neuropsychiatric symptoms and neurocognitive development

	Model 1				Model 2				Model 3				Model 4				
	N	*B*	95% CI	*p*	*N*	*B*	95% CI	*p*	*N*	*B*	95% CI	*p*	*N*	*B*	95% CI	*p*	r^2 (%)[a]
Child neuropsychiatric scale																	
CBCL total problems	104	0.37	0.15–0.59	0.001	103	0.33	0.11–0.56	0.005	103	0.29	0.06–0.52	0.01	103	0.25	0.01–0.48	0.04	3.6
CBCL internalizing problems	104	0.35	0.13–0.56	0.002	103	0.33	0.10–0.56	0.01	103	0.31	0.07–0.54	0.01	103	0.25	0.01–0.49	0.04	3.9
CBCL externalizing problems	104	0.22	0.01–0.44	0.04	103	0.21	−0.02 to 0.44	0.07	103	0.16	−0.07 to 0.39	0.16	103	0.12	−0.12–0.36	0.31	0.9
SDQ total difficulties	106	0.31	0.09–0.52	0.01	106	0.26	0.04–0.48	0.02	106	0.22	0.00–0.43	0.047	106	0.15	−0.07–0.36	0.18	1.3
Conner's ADHD symptoms	107	0.32	0.11–0.54	0.003	107	0.35	0.13–0.57	0.002	107	0.32	0.09–0.54	0.01	107	0.27	0.04–0.50	0.02	4.5
CSHQ sleep problems	108	0.31	0.09–0.53	0.01	108	0.28	0.05–0.51	0.02	108	0.22	−0.00 to 0.45	0.053	108	0.15	−0.07 to 0.37	0.18	1.4
Child neurocognitive development scale/test																	
ASQ neurodevelopment	98	−0.27	−0.49 to −0.04	0.02	97	−0.26	−0.50 to −0.03	0.03	97	−0.23	−0.47 to 0.01	0.06	97	−0.16	−0.39 to 0.08	0.19	1.5
HTKS executive function	75	−0.31	−0.58 to −0.04	0.03	75	−0.33	−0.61 to −0.05	0.02	75	−0.29	−0.57 to −0.01	0.04	75	−0.39	−0.69 to −0.10	0.01	7.9
Marshmallow test executive function	77	0.08	−0.18 to 0.35	0.53	75	0.03	−0.25 to 0.32	0.83	75	0.07	−0.22 to 0.36	0.64	75	0.02	−0.29 to 0.33	0.89	0.02

CI, confidence interval; CBCL, Child Behaviour Checklist; SDQ, Strength and Difficulties Questionnaire; ADHD, Attention Deficit Hyperactivity Disorder; CSHQ, Children's Sleep Habits Questionnaire; ASQ, Ages and Stages Questionnaire; HTKS, Head Toes Knees Shoulders Test

Model 1 is adjusted for child age and sex

Model 2 is adjusted further for maternal depressive symptoms concurrently to rating the child

Model 3 is adjusted for Model 2 covariates + maternal obesity status during pregnancy

Model 4 is adjusted for Model 3 covariates and maternal depressive and anxiety symptoms during pregnancy

[a]r^2 refers to the amount of variance explained independently by maternal antenatal daytime sleepiness in regression Model 4, adjusting for child age and sex, maternal depressive symptoms concurrently to child ratings, maternal obesity in pregnancy and maternal depressive and anxiety symptoms during pregnancy

There were no significant interactions of maternal daytime sleepiness during pregnancy by child sex on child psychiatric problems or child neurodevelopment (p values $\geqslant 0.12$).

Discussion

In this prospective cohort study, maternal antenatal daytime sleepiness was associated with increased psychiatric problems and poorer neurodevelopment in young children. Maternal obesity confounded the association with child externalizing behaviour, but maternal daytime sleepiness during pregnancy predicted higher psychiatric problems among children on multiple scales and poorer child executive function even after this adjustment. While the associations were independent of maternal concurrent depressive symptoms when rating the child, many of them were attenuated to non-significance after adjustments for anxiety and depressive symptoms during pregnancy. However, maternal antenatal daytime sleepiness still predicted significantly increased internalizing and total psychiatric problems on the CBCL, increased mother-rated ADHD symptoms and poorer executive function in a neuropsychological test independently of maternal antenatal affective symptoms.

Our findings support those of previous large-scale studies where the maternal prenatal emotional state was associated with child psychiatric problems independently of all assessed covariates including maternal postnatal emotional state (Loomans *et al.*, 2011; Van Batenburg-Eddes *et al.*, 2013; Betts *et al.*, 2014; Lahti *et al.*, 2017). Our findings also correspond with a recent animal study that showed that antenatal circadian rhythm disruption may predict anxiety- and hyperactivity-related behavioural phenotypes in adult mice (Smarr *et al.*, 2017) and with the previous retrospective human study suggesting that maternal sleep problems during pregnancy are associated with offspring sleep problems in late childhood (Armstrong *et al.*, 1998). In our prospective study with a relatively similar sample size and with a follow-up extending to young childhood, maternal sleep problems, particularly daytime sleepiness during pregnancy showed significant independent associations with a wide range of neuropsychiatric and neurocognitive problems in children. Our novel findings hence suggest that maternal daytime sleepiness during pregnancy may contribute to psychological development in children. We found that maternal antenatal daytime sleepiness also showed independent associations with lower scores on an objective experimental measure of executive functioning, in particular, a test measuring attention, working memory and inhibitory control. Interestingly, maternal antenatal daytime sleepiness was also independently associated with significantly increased ADHD problems in children, also suggesting deficits in executive function as a consequence of maternal antenatal sleep problems. Associations were present also with several other types of psychiatric problems, especially with child internalizing psychiatric problems. While previous evidence suggests effects of maternal antenatal psychological distress on child internalizing problems (O'Donnell *et al.*, 2014; Lahti *et al.*, 2017; Van den Bergh *et al.*, 2017), our findings extend these by showing that maternal antenatal daytime sleepiness also predicts child internalizing problems, independently of maternal mood during and after pregnancy.

Neurobiological mechanisms underlying the associations found may include possibly epigenetic functional changes in the neurobiological stress system, including hypothalamus-pituitary-adrenal (HPA) axis and related brain areas, maternal inflammatory milieu and autonomic nervous system, as a consequence of the maternal antenatal sleep problems. Inflammatory levels are associated with sleep disorders (Nishiyama *et al.*, 2014) and maternal inflammation during pregnancy is associated with psychopathology risk in the offspring (Brown *et al.*, 2013; Canetta *et al.*, 2015; Gilman *et al.*, 2016; Zerbo *et al.*, 2016; Murphy *et al.*, 2017). Altered structure and/or functioning of HPA axis is found in sleep disorders (van Dalfsen and Markus, 2018), and maternal HPA axis function has been associated with psychiatric problems in the offspring (Buss *et al.*, 2012), and structural changes of brain areas implicated in HPA axis functioning have been shown to mediate the effects of maternal antenatal psychological distress on child psychiatric problems (Sandman *et al.*, 2015). Epigenetic changes in genes regulating HPA axis glucocorticoid functioning have been shown as a consequence of maternal antenatal psychological distress (Braithwaite *et al.*, 2015; Palma-Gudiel *et al.*, 2015; Mansell *et al.*, 2016), and in children with psychiatric, particularly internalizing problems (Van Der Knaap *et al.*, 2015; Parade *et al.*, 2016). On the other hand, although we controlled for the effects of maternal concurrent mental health, we can neither rule out genetic or shared familial postnatal environmental factors as explanations for our findings. Genetic risk for psychopathology is well-established (Smoller *et al.*, 2013; Stein *et al.*, 2014), and some recent evidence suggests that genetic or shared postnatal environmental factors may confound or mediate the associations between maternal prenatal emotional distress and child psychiatric problems (Plant *et al.*, 2015; Gjerde *et al.*, 2017; Kuckertz *et al.*, 2018). These environmental factors may include child maltreatment and altered parenting practices in families with maternal psychological distress (Plant *et al.*, 2015; Kuckertz *et al.*, 2018). Maternal sleep problems may also have continued postpartum, and affected parenting practices. It may be that mothers who are sleepy antenatally, continue to have high daytime sleepiness postnatally and thus the child's environment, stimulation and interaction with other humans might be adversely affected. Hence, whether the effects we found reflect prenatal programming of the developing nervous system and/or associations mediated by changes in the postnatal environments or confounded by genetics, needs to be solved in further studies.

The strengths of this study include the longitudinal design and use of multiple validated scales on child psychological development. We also had data from individually administered neuropsychological tests. The maternal daytime sleepiness measures, although self-reported, were average scores from up to two measurements, increasing the reliability of the measures. In contrast, the limitations of this study include the relatively small sample size, the relatively high attrition rates at the childhood follow-up, the use of only maternal reports of child psychiatric problems and the case-control design of the cohort in terms of maternal severe obesity in pregnancy. The case-control design meant that the mothers were more often severely obese than women in the general population. As obese pregnant women mothers have higher rates of daytime sleepiness (Amador-Licona and Guízar-Mendoza, 2012), socioeconomic disadvantage (Heslehurst *et al.*, 2007) and their children have more psychiatric problems (Mina *et al.*, 2017), our sample can be considered a high-risk subsample with possibly limited generalizability of the findings to the general population. However, maternal obesity did not explain the effects of daytime sleepiness in our cohort. Furthermore, while having reports from both parents and/or from child's nursery caretakers would have yielded a more precise picture of the associations and eluded the risk of shared method variance inflating the associations, it is important to note the effects of maternal sleep problems were

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independent of maternal depressive symptoms when rating the child. Another limitation is that we did not have measurements of maternal sleep problems at child follow-up, only assessments of maternal affective symptoms. Neither did we have data on other maternal sleep problems during pregnancy than daytime sleepiness available. We do not know, for example, whether mother's sleepiness during the day was due to lack of sleep, other sleep problems, or feelings of fatigue due to other reasons such as depression or other psychological distress. We also had no data on paternal daytime sleepiness or other indices of paternal psychological well-being available. Further studies are needed to compare the effects of maternal and paternal daytime sleepiness and of different types of parental sleep problems antenatally and in childhood on child psychological development.

In conclusion, higher maternal antenatal daytime sleepiness was independently and longitudinally associated with increased neuropsychiatric problems and poorer executive function in early childhood. These effects suggest that antenatal sleep problems carry adverse consequences both for the pregnant woman and her offspring, and suggest their assessment may be an important addition to standard antenatal care.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S003329171800291X.

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