

## The effects of maternal risk factors during pregnancy on the onset of sleep difficulties in infants at three months of age

**Short version:** Maternal problems, pregnancy and infant's sleep

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## **SUMMARY**

Sleep problems in young children are among the most common concerns reported to pediatricians. Sleep is thought to have important regulatory functions, and sleep difficulties in early childhood are linked to several psychosocial and physiological problems. Moreover, several prenatal factors have been found to influence infants' sleep. Among them, most of the studies have been focused on maternal prenatal depression and/or anxiety as potential risk factors for sleep problems in childhood, whereas other relevant psychological factors during pregnancy have not received as much attention. Therefore, we aimed to examine the effect of several psychiatric maternal risk factors during pregnancy (i.e., symptoms of anxiety, depression, insomnia, alcohol use, seasonality, attention deficit and hyperactivity disorder-ADHD, and/or stressful life events) on the onset of some sleep problems related to sleep quality and sleep practices in three months old infants. We examined 1 221 cases from a population-based birth cohort, with subjective measures during pregnancy in mothers, and at three months after birth in the infants. The findings showed that all the maternal risk factors during pregnancy, except for symptoms of alcoholism and sleepiness, were related to sleep difficulties in infants. Interestingly, ADHD symptomatology in mothers during pregnancy was the only variable that predicted more than two sleeping difficulties (i.e., long sleep-onset latency, co-sleeping with parents and irregular sleeping routines) at three months of age. Our results highlight the relevance of maternal risk factors during pregnancy, and not only prenatal depression and/or anxiety, as variables to be considered when examining sleep difficulties in infants.

**Keywords:** pregnancy, maternal risk factors, sleep difficulties, infancy

## **INTRODUCTION**

Infants' sleep problems are highly prevalent and represent one of the most frequent complaints of parents consulting a pediatrician. It is well established that infant sleep quality and development can be modulated by a number of biopsychosocial factors (Touchette *et al.*, 2005), and thus several intrinsic and extrinsic factors can interact with the development of sleep in the childhood. These factors include infant characteristics such as gender, temperament and season of birth (Dauvilliers *et al.*, 2003), and environmental characteristics such as parental stress (Sorondo *et al.*, 2015).

Previous studies have shown the short and long-term negative impact of prenatal stress on both fetal and child development (Graignic-Philippe *et al.*, 2014). Some prenatal factors have also been linked to childhood sleeping problems. For example, women with higher levels of preconceptional psychological distress are more likely to report more night wakings among the offspring at the age of 6 and 12 months (Baird *et al.*, 2009). Moreover, lower birth weight and shorter length at birth have been associated with lower sleep efficiency at the age of 8 years, while alcohol usage during pregnancy has been linked with shorter sleep duration (Pesonen *et al.*, 2009). Accordingly, one study reported that prenatal-early life stress increases risk for insomnia in adulthood (Palagini *et al.*, 2015).

It is also well established that various psychiatric symptoms are common during pregnancy, with maternal depression being the most common (Chandra *et al.*, 2009). Maternal depression and anxiety during pregnancy have been linked to child development and an increased risk for mood and anxiety disorders later in life (Van den Bergh *et al.*, 2017), as well as behavioral and cognitive problems in infants (Monk *et al.*, 2012). Furthermore, one large-scale community study reported that prenatal maternal anxiety and depression were related to infants' sleep difficulties at 18 and 30 months of age (O'Connor *et al.*, 2007). However, there are also several other parental psychiatric disturbances that may play a role in the development of sleeping problems in early childhood, which have not received much attention.

Concerning postnatal factors, various studies have highlighted that maternal depression is associated with adverse child outcomes (Netsi *et al.*, 2018), such as excessive infant crying, feeding or sleeping problems (Golik *et al.*, 2013), as well as with difficulties in infant-parent relationship, such as diminished emotional involvement and neglect and hostility towards the newborn (Stein *et al.*, 1991). In addition, maternal depressive disorders and additionally comorbid anxiety disorders have been associated with infant sleeping problems (Hiscock and Wake, 2001).

Although maternal mental health in the postpartum period is relatively well studied, there is still less research on risks related to mental health problems during pregnancy. In particular, empirical studies on the impact of any of them on infant/child sleep are still quite scarce. Furthermore, different maternal psychiatric disturbances/symptoms might exert differential influence on infant's sleep. In

this paper, we aimed to study how maternal prenatal psychiatric symptoms are related to infant sleep quality at the age of three months. In particular, the aim of this study was to examine the effect of several maternal risk factors during pregnancy (such as symptoms of anxiety, depression and attention deficit and hyperactivity disorder; ADHD or sleep-related problems, alcohol use, seasonality, and stressful life events) on the onset of specific sleep difficulties (such as short sleep, night awakenings, circadian rhythm, difficulties in self-soothing, long sleep-onset latency, co-sleeping with parents and irregular sleeping routines) in infants at three months of age. Following the line of research of prenatal depression and anxiety, we hypothesized that the maternal risk factors during pregnancy would be related to various sleeping difficulties within the infants.

## **METHODS**

### **Participants and procedure**

The study was based on a longitudinal CHILD-SLEEP birth cohort, with several measurement points (Paavonen *et al.*, 2017). The recruitment and the first questionnaire occurred prenatally at 32nd week, and the following questionnaires took place at birth and at the child age of 3, 8, 18 and 24 months, and 5 years. For this study, we only used the information regarding maternal questionnaires during pregnancy (32nd week) and the sleep questionnaires of the infants at three months. Initially, a total of 2 244 parents were approved to receive the prenatal questionnaires during their visits at maternity clinics, from which 1 673 (74.6%) families returned the baseline questionnaires. From this original sample, 1 427 cases were selected for the current study, which were those cases with questionnaires at both pregnancy and 3 months. As we aimed to examine healthy infants, 206 cases with any medical illness and/or condition reported (i.e., mild and/or severe illness, including allergies, infections, use of medication for the child, virus, blood problems, and other diseases) were excluded. Therefore, a final sample of 1 221 was obtained.

The CHILD-SLEEP study protocol was approved by the local Ethical Committee (9.3.2011, ethical research permission code R11032). Written informed consent was obtained from all the parents.

### **Measures**

#### ***Psychiatric measures in mothers during pregnancy***

Basic Nordic Sleep Questionnaire (BNSQ; Partinen and Gislason, 1995) assesses common sleep habits, symptoms and quality during the past three months. The BNSQ also uses quantitative

questions to assess time of the night sleep and sleep latency. For this study we used the BNSQ insomnia score (Paavonen et al., 2017).

Epworth sleepiness scale (ESS; Johns, 1991) is a subjective measure of a patient's sleepiness. There is a list of eight situations in which the tendency to become sleepy is rated in each situation on a scale of 0 to 3. We used in this study the total score.

Alcohol Use Disorders Identification Test (AUDIT; Bohn *et al.*, 1995) is a screening tool to assess alcohol consumption, drinking behaviors, and alcohol-related problems. We used a three-item version to consider amount of alcohol consumed.

The global seasonality score (GSS) is a subscale of the Seasonal Pattern Assessment Questionnaire (SPAQ; Rosenthal *et al.*, 1984). GSS total score is calculated based on responses to the six parameters of seasonality (sleep duration, social activity, mood, weight, appetite, and energy level). Higher scores indicate more pronounced seasonality.

List of Threatening Experiences (LTE; Brugha *et al.*, 1985) consists of 12 questions, with dichotomous responses (yes/no) about the occurrence of 12 prevalent major stressful life events in the preceding 6 months. In this case, the variable used was the total score.

State-Trait Anxiety Inventory (STAI; Spielberg *et al.*, 1983) is a commonly used measure of trait and state anxiety. It can be used in clinical settings to screen for anxiety and it is also often used in research as an indicator of distress. For this study we selected 6 items from the original version of the STAI (Bieling *et al.*, 1998), and these items measured anxiety trait on a four point scale. The variable we used for this study was total sum.

Center for Epidemiological Studies Depression Scale (CESD; Radloff, 1997) is a screening tool for depression and depressive disorders, and the participant is asked to rate how often over the past week symptoms associated with depression were experienced. We used a shortened version of the original CESD comprising 10 items which include four response categories (Andresen, 1994). In this case, we used the CESD total score.

Adult ADHD Self-Report Scale-V1.1 Screener (ASRS-V1.1; Kessler *et al.*, 2005) was designed as a tool to help screen for ADHD in adults. We used a six items version of the ASRS Symptom Checklist, which is the most predictive version to detect ADHD symptoms (Goodman, 2009). We used the ASRS total score.

### ***Sleep measures in infants at three months***

Brief Infant Sleep Questionnaire (BISQ; Sadeh, 2004) was developed to characterize infant sleep quality with 13 items about duration of sleep, settling, night waking, and sleep arrangements. For this study we selected the following variables: i) number of nocturnal sleep hours; ii) number of daytime sleep hours; iii) total number of sleep hours per day; and iv) method for falling asleep (independently vs. parental support).

Infant Sleep Questionnaire (ISQ; Morrell, 1999) is a 10-item questionnaire that assesses infant sleeping habits and parental strategies for managing infant sleep. More specifically, this questionnaire contains questions assessing settling, waking, and sleeping in the caregivers' bed. Parents are asked if they perceive a sleep problem in the child and to report the duration of the possible problem.

In order to examine the main sleeping difficulties in infants at three months, in terms of sleep quality and sleep practices, we created the following variables: for a) sleep quality: i) short sleep in total (cut-off, less than 12 hours of total sleep in 24 hours); ii) slow circadian rhythm development, which was operationalized as high proportion of daytime sleep (cut-off, higher than 41 percent; Sadeh *et al.*, 2009); iii) difficulties in self-soothing, which was obtained from the infants capacity to fall asleep on their own without the parent being present; iv) high frequency of night awakening, with a cut-off of 3 or more times per night; and v) long sleep-onset latency (cut-off, 20 or more minutes); and for b) sleep practices: i) co-sleeping with parents, which was obtained from an additional item concerning the frequency the infant slept in the parent's bed (cut-off, more than 3 times per week); and ii) irregular sleeping routine, which came from an additional item about the frequency of regular routines used.

### **Statistical analysis**

Statistical analyses were performed with SPSS Statistics V22.0. Descriptive statistics were conducted to obtain the means, standard deviations (SD), frequencies and percentages of the variables of interest. Pearson correlations were also calculated. In order to examine the potential effects of maternal problems during pregnancy on infant's sleep at three months, logistic regression analysis was conducted. To control for confounding factors, maternal age during pregnancy, infant's age, gestational age of the time when the mother filled out the questionnaire, number of children in the family, breast feeding, use of pacifier and season of birth were included as covariates. Regarding the season of birth, we chose to divide the year into four seasons: winter (November, December, January), spring (February, March, April), summer (May, June, July), and autumn (August, September, October) (Johnsen *et al.*, 2012). In addition, infants' sleep measures were included as dependent variables, and psychiatric maternal risk factors as independent variables. Dependent variables were treated as dichotomous variables (yes vs. no), and independent variables as continuous (total score).

Each variable of interest, along with the covariates, were studied in different models. Parameters regarding the confounding factors are not reported. Furthermore, a full multivariate logistic regression model was also estimated where all the independent variables and the covariates were entered to the model at the same time. However, as very similar results to the separate logistic regression models were obtained, we did not report in this study the results concerning the full model.

## **RESULTS**

Sociodemographic and psychiatric variables in the mothers during pregnancy, and sociodemographic and sleep variables in infants at three months of age are reported in Table 1.

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The correlation analyses were conducted within maternal risk factors during pregnancy. No significant correlations we observed between ASRS and LTE; between AUDIT and CESD, STAI and ASRS; and between ESS and any of the maternal risk factors. Correlations between maternal risk factors are given in Table 2. Except for the 0.65 correlation between mother's depressive and anxiety symptoms, all correlations were smaller than 0.40 and majority of them smaller than 0.20, albeit some being statistically significant.

### **Maternal psychiatric problems and sleep measures in infants at 3 months**

Our main results showed that i) maternal symptoms of anxiety (i.e., STAI sum) were related to long sleep-onset latency ( $p=0.004$ ) and to co-sleeping with parents ( $p=0.021$ ); ii) seasonality (i.e., GSS sum) was related to co-sleeping with parents ( $p=0.032$ ); iii) maternal depressiveness (i.e., CESD) was related to long sleep-onset latency ( $p<0.001$ ) and to irregular sleep routine ( $p=0.043$ ); iv) maternal ADHD symptoms (i.e., ASRS sum) were related to long sleep-onset latency ( $p=0.047$ ), to irregular sleep routine ( $p=0.019$ ) and to co-sleeping with parents ( $p=0.019$ ); v) stressful life events (i.e., LTE sum) were related to co-sleeping with parents ( $p=0.011$ ); and vi) maternal symptoms of insomnia were related to short sleep duration ( $p=0.012$ ) and long sleep-onset latency ( $p=0.039$ ). There were no significant associations between maternal psychiatric characteristics and infant circadian rhythms, high frequency of night awakenings, or the ability for self-soothing (i.e.,  $p>0.05$  for all measures).

To sum up, sleep difficulties in infants were related to several maternal psychiatric problems during pregnancy. All the significant results are presented in Table 3.

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## DISCUSSION

Our results showed that maternal risk factors during pregnancy were related to certain sleep difficulties in infants at three months of age. More specifically, we obtained that symptoms of insomnia were related to short sleep and long sleep-onset latency. In addition, symptoms of anxiety during pregnancy, symptoms of seasonality, ADHD symptoms and stressful life events were associated each of them with co-sleeping with parents. Interestingly, maternal depressiveness and ADHD symptoms during pregnancy were also related to both long sleep-onset latency and irregular sleeping routines, and symptoms of anxiety were also associated with long sleep-onset latency in the infants.

Previous research supports the notion that prenatal factors may have persisting influences on sleep in the child (O'Connor *et al.*, 2007). In fact, both animal and human studies have found prenatal maternal anxiety and depression to be associated with sleep difficulties at early ages. For instance, experimental animal research shows that prenatal and early postnatal stress are associated with long-lasting structural sleep changes in the offspring mimicking those reported in depression (Santangeli *et al.*, 2016). The underlying mechanism of such long-term effect of prenatal conditions is believed to be the inhibition of the 11 $\beta$ -hydroxysteroid dehydrogenase type 2 (HSD2) placental enzyme, which is responsible for inactivation of excessive maternal glucocorticoids (Harris and Seckl, 2001). When we are stressed, a series of chemical changes is set off in our bodies and brains, such as the release of cortisol and adrenaline (Henry, 1992). Normally, these chemicals help prepare us for danger and are important for our survival; however, if we are chronically stressed and anxious, these stress-related hormones can remain high for too long and harm our bodies (Schneiderman *et al.*, 2005). When a pregnant woman is chronically stressed or experiences extreme stress, like it can happen in women with symptoms of anxiety and/or depression, the infant may be exposed to unhealthy levels of stress hormones, which can impact the infant's brain development (Moon *et al.*, 2001). This leads to permanent impairment of the offspring's hypothalamo-pituitary-adrenal axis, alternations in central nervous system functions and gene expression (Cottrell and Seckl, 2009; Vallée *et al.*, 1999), predisposing the offspring to maladaptive behavior later in life.

Following this line of research, we found in this study that maternal symptoms of anxiety during pregnancy predicted long sleep-onset latency and the prevalence of co-sleeping with parents in infants



at three months of age and maternal prenatal depressiveness was related to long sleep-onset latency and irregular sleeping routines at this age. In addition to this, these prenatal psychiatric symptoms of anxiety and depression in mothers may persist after the infant birth, and thus they may mediate the risk here attributed to prenatal factors. In fact, psychiatric disturbances during pregnancy, such as depression and/or anxiety have been found to be associated with inadequate antenatal care, low-birth weight and preterm delivery (Biaggi *et al.*, 2016). In addition to this, prenatal factors such as depression or anxiety are associated with impairment of maternal-infant bonding (Dubber *et al.*, 2015), which may indicate that infant–caregiver attachment can be affected by prenatal factors, too (Ryan *et al.*, 2017).

In addition to symptoms of anxiety and depression, this study aimed to examine other prenatal maternal risk factors that could exert some negative effects on the infant’s sleep functioning. To this end, sleep problems, alcohol use, ADHD symptoms, and seasonality symptoms in mothers during pregnancy were considered. Our findings showed that ADHD symptoms and symptoms of seasonality predicted separately the prevalence of co-sleeping with parents at three months of age, while symptoms of insomnia were related to short sleep and long sleep-onset latency in early childhood. ADHD symptoms, in addition to co-sleeping with parents, predicted also long sleep-onset latency and irregular sleeping routines. To sum up, these findings support the notion that other prenatal risk factors, and not exclusively anxiety and depression, may underlie the variation in sleeping that appears in the early childhood.

Interestingly, ADHD symptoms in the mothers during the pregnancy period were related to long sleep-onset latency, irregular sleep routines and co-sleeping with parents, and thus further research on this topic might be of great interest, in order to understand the underlying biological and behavioural mechanisms of this association. ADHD has been found to have a highly heritable component (Thapar *et al.*, 2007), and thus this should be also considered when interpreting these results. Therefore, further studies should control for whether ADHD symptoms are also present in the infants and whether they are related to sleep difficulties. Maternal symptoms of insomnia during pregnancy were also related to short sleep and long sleep-onset latency in infants. Therefore, these findings highlight the role of maternal sleeping problems during pregnancy as a potential predictor of sleep difficulties in infants, and thus further studies on this topic would be of great value.

The present study has some limitations. First, only subjective data of sleeping functioning reported by the parents is provided in this study. Additional psychophysiological examination (e.g., actigraphy) would provide useful objective information to validate these initial results. Second, the prevalence rates for short sleep, irregular sleep routines and high frequency of night awakening in

infants were rather small and thus we studied quite deviant cases to represent obvious abnormalities in sleep development in infants. Nevertheless, these prevalence rates are representative of the cases found in this sample of general population. Clearly, further studies are needed to replicate our findings and to study the mechanisms underlying the relationship between prenatal mood problems, stress, tiredness and ADHD symptoms, and infant sleep development. In addition, new studies on postnatal risk factors and infants sleep would be of great interest. Third, the questionnaire used to examine maternal depression was the CESD, instead of the Edinburgh Postnatal Depression Scale (EPDS), which was specifically designed for women who are pregnant or have just had a baby. This current study is a part of a longitudinal study up to 5 years of age, and this is the reason why the use of CESD was preferred in this study.

To sum up, we obtained that prenatal psychiatric factors in mothers may be a risk factor for developing sleep problems in infants. Interestingly, our results showed that symptoms of mood disturbances, ADHD, and stress in mothers during pregnancy were associated with the onset of certain sleep difficulties related to sleep quality and sleep practices in three-months-old infants. To conclude, examining the role of specific prenatal risk factors associated to infant's sleep will be an interesting area of further studies, when considering the best possible way to understand and support the early development of sleep and the well-being of the whole family. Understanding better the large variability in the early sleep development can provide new ways for preventing these problems.

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## **AUTHOR CONTRIBUTIONS**

EJP, OSH, AK, PP, TPH and TP designed the study and wrote the protocol. EJP and IMM conducted literature searches and provided summaries of previous research studies. IMM conducted the

statistical analysis and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

## **CONFLICT OF INTEREST**

No potential conflict of interest was reported by the authors.

## **REFERENCES**

- Andresen, E.M. Screening for depression in well older adults: Evaluation of a short form of the CES-D. *Am. J. Prev. Med.*, 1994, 10:77.
- Baird, J., Hill, C.M., Kendrick, T., and Inskip, H.M. Infant sleep disturbance is associated with preconceptional psychological distress: findings from the Southampton Women's Survey. *Sleep*, 2009, 32: 566-568.
- Biaggi, A., Conroy, S., Pawlby, S., and Pariante CM. Identifying the women at risk of antenatal anxiety and depression: A systematic review. *J. Affect. Disord.*, 2016, 191: 62-77.
- Bieling, P.J., Antony, M.M., and Swinson, R.P. The State-Trait Anxiety Inventory, Trait version: Structure and content re-examined. *Behav. Res. Therapy*, 1998, 36: 777-788.
- Bohn, M.J., Babor, T.F., and Kranzler, H.R. The Alcohol Use Disorders Identification Test (AUDIT): validation of a screening instrument for use in medical settings. *J. Stud. Alcohol.*, 1995, 56: 423-432.
- Brugha, T., Bebbington, P., Tennant, C., et al. The list of threatening experiences - a subset of 12 life event categories with considerable long-term contextual threat. *Psychol. Med.*, 1985, 15: 189-194.
- Chandra, P.S., Herman, H., Fisher, J., et al. *Contemporary topics in womens mental health-Global perspectives*. John Wiley and Sons Ltd, United Kingdom, 2009.
- Cottrell, E.C., and Seckl, J.R. Prenatal stress, glucocorticoids and the programming of adult disease. *Front. Behav. Neurosci.*, 2009, 3:19.
- Dauvilliers, Y., Carlander, B., Molinari, N., et al. Month of birth as a risk factor for narcolepsy. *Sleep*, 2003, 26: 663-665.
- Dubber, S., Reck, C., Müller, M., and Gawlik, S. Postpartum bonding: the role of perinatal depression, anxiety and maternal-fetal bonding during pregnancy. *Arch. Womens Ment. Health*, 2015, 18:187-95.
- Golik, T., Avni, H., Nehama, H., Greenfeld, M., Sivan, Y., and Tauman, R. Maternal cognitions and depression in childhood behavioral insomnia and feeding disturbances. *Sleep Med.*, 2013, 14: 261-265.

- Goodman, DW. ADHD in adults: update for clinicians on diagnosis and assessment. *Prim. Psychiatry*, 2009, 16: 21-30.
- Graignic-Philippea, R., Dayana, J., Chokronb, S., Jacquetb, A-Y., and Tordjmana, S. Effects of prenatal stress on fetal and child development: A critical literature review. *Neurosci. Biobehav. Rev.*, 2014, 43: 137-162.
- Harris, A., and Seckl, J. Glucocorticoids, prenatal stress and the programming of disease. *Horm. Behav.*, 2011, 59: 279-289.
- Henry, JP. Biological basis of the stress response. *Integr. Physiol. Behav. Sci.*, 1992, 27, 66-83.
- Johns, M.W. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, 1991, 14: 540-545.
- Hiscock, H., and Wake, M. Infant sleep problems and postnatal depression: a community-based study. *Pediatrics*, 2001, 107: 1317-22.
- Johnsen, M.T., Wynn, R., and Bratlid, T. Is there a negative impact of winter on mental distress and sleeping problems in the subarctic: the Tromsø Study. *BMC Psychiatry*, 2012, 12:225.
- Kessler, R.C., Adler, L., Ames, M., et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol. Med.*, 2005, 35: 245-256.
- Monk, C., Spicer, J., and Champagne, F.A. Linking prenatal maternal adversity to developmental outcomes in infants: the role of epigenetic pathways. *Dev. Psychopathol.*, 2012, 24: 1361-76.
- Moon, P.F., Ramsay, M.M., Fecci, P.E., and Nathanielsz, P.W. Fetal exposure to magnesium chloride-adenosine triphosphate (MgCl<sub>2</sub>-ATP) results in alterations in cerebral blood flow and a metabolic acidosis. *Pediatr. Crit. Care Med.*, 2001, 2: 74-81.
- Morrell, J.M. The infant sleep questionnaire: a new tool to assess infant sleep problems for clinical and research purposes. *Child Psychol. Psychiatry Rev.*, 1999, 4: 20-26.
- Netsi, E., Pearson, R.M., Murray, L., Cooper, P., Craske, M.G., and Stein A. Association of persistent and severe postnatal depression with child outcomes. *JAMA Psychiatry*, 2018, doi:10.1001/jamapsychiatry.2017.4363.
- O'Connor, T.G., Caprariello, P., Blackmore, E.R., Gregory, A.M., Glover, V., and Fleming P. Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Hum. Dev.*, 2007, 83: 451-458.

- Paavonen, E.J., Saarenpää-Heikkilä, O., Pölkki, P., Kylliäinen, A., Porkka-Heiskanen, T., and Paunio T. Maternal and paternal sleep during pregnancy in the Child-sleep birth cohort. *Sleep Med.*, 2017, 29: 47-56.
- Palagini, L., Drake, C.L., Gehrman, P., Meerlo, P., and Riemann, D. Early-life origin of adult insomnia: does prenatal-early-life stress play a role? *Sleep Med.*, 2015, 16: 446-56.
- Partinen, M., and Gislason, T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J. Sleep Res.*, 1995, 4: 150-155.
- Pesonen, A.K., Räikkönen, K., Matthews, K., et al. Prenatal origins of poor sleep in children. *Sleep*, 2009, 32: 1086-1092.
- Radloff, L.S. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurements*, 1997, 1: 385-401.
- Rosenthal, N.E., Bradt, G.H., and Wehr, T.A. *Seasonal Pattern Assessment Questionnaire (SPAQ)*. National Institute of Mental Health, Bethesda, 1984.
- Ryan, J., Mansell, T., Fransquet, P., and Saffery, R. Does maternal mental well-being in pregnancy impact the early human epigenome? *Epigenomics* 2017, 9: 313-32.
- Sadeh, A. A brief screening questionnaire for infant sleep problems: validation and findings for an Internet sample. *Pediatrics*, 2004, 113: e570-577.
- Sadeh, A., Mindell, J.A., Luedtke, K., et al. Sleep and sleep ecology in the first 3 years: a web-based study. *J. Sleep Res.*, 2009, 18: 60-73.
- Santangeli, O., Lehtikujja, H., Palomäki, E., et al. Sleep and Behavior in Cross-Fostering Rats: Developmental and Sex Aspects. *Sleep*, 2016, 39: 2211-2221.
- Schneiderman, N., Ironson, G., and Siegel, S.D. Stress and health: psychological, behavioral, and biological determinants. *Annu. Rev. Clin. Psychol.*, 2005, 1: 607-628.
- Sorondo, B.M., and Reeb-Sutherland, B.C. Associations between infant temperament, maternal stress, and infants' sleep across the first year of life. *Infant Behav. Dev.*, 2015, 39: 131-135.
- Spielberger, C.D., Gorsuch, R.L., Lushene, R., et al. *Manual for the State-Trait Anxiety Inventory*. Consulting Psychologists Press, Palo Alto, 1983.
- Stein, A., Gath, D.H., Bucher, J., Bond, A., Day, A., and Cooper, P.J. The relationship between post-natal depression and mother-child interaction. *Br. J. Psychiatry*, 1991, 158: 46-52.

- Taylor, A.K., Netsi, E., O'Mahen, H., Stein, A., Evans, J., and Pearson, R.M. The association between maternal postnatal depressive symptoms and offspring sleep problems in adolescence. *Psychol. Med.*, 2017, 47: 451-459.
- Thapar, A., Langley, K., Owen, M.J., and O'Donovan, M.C. Advances in genetic findings on attention deficit hyperactivity disorder. *Psychol. Med.*, 2007, 37:1681–1692.
- Touchette, E., Petit, D., Paquet, J., et al. Factors Associated With Fragmented Sleep at Night Across Early Childhood. *Arch. Pediatr. Adolesc. Med.*, 2005, 159: 242-247.
- Vallée, M., MacCari, S., Dellu, F., et al. Long-term effects of prenatal stress and postnatal handling on age-related glucocorticoid secretion and cognitive performance: a longitudinal study in the rat. *Eur. J. Neurosci.*, 1999, 11: 2906-2916.
- Van den Bergh, B.R.H., van den Heuvel, M.I., Lahti, M., et al. Prenatal developmental origins of behavior and mental health: The influence of maternal stress in pregnancy. *Neurosci. Biobehav. Rev.*, 2017, pii: S0149-7634(16): 30734-5.
- Virring, A., Lambek, R., Thomsen, P.H., Møller, L.R., and Jennum, P.J. Disturbed sleep in attention-deficit hyperactivity disorder (ADHD) is not a question of psychiatric comorbidity or ADHD presentation. *J. Sleep. Res.*, 2016, 25: 333-340.

**Table 1.** Descriptive variables in mother during pregnancy and in infants at 3 months (N=1221).

<b>Sociodemographic variables in mothers</b>		
	<i>Mean</i>	<i>SD</i>
Age (in years)	30.61	4.52
Number of pregnancy weeks	34.71	2.52
Number of children per family	0.74	0.88
<b>Psychiatric history and use of medication in mothers</b>		
	<i>Frequency</i>	<i>%</i>
Depression diagnosis during pregnancy (Yes / No)	21 / 1084	1.90 / 98.10
ADHD diagnosis during pregnancy (Yes / No)	4 / 1079	0.37 / 99.63
Panic disorder diagnosis during pregnancy (Yes / No)	16 / 1075	1.47 / 98.53
Schizophrenia diagnosis during pregnancy (Yes / No)	0 / 1079	0 / 100
Other mental disorders during pregnancy (Yes / No)	4 / 1077	0.37 / 99.63

Use of antidepressants during pregnancy (Yes / No)	11 / 1182	0.92 / 99.08
Use of other medication during pregnancy (Yes / No)	304 / 894	25.38 / 74.62

### Clinical variables in mothers

	<i>Mean</i>	<i>SD</i>
Number of sleeping hours at night	7.90	1.04
BNSQ insomnia score	1.79	1.09
ESS total score	5.53	4.66
AUDIT sum	4.01	1.86
GSS sum	5.41	2.96
LTE total score	0.62	1.11
STAI total score	8.89	2.31
CESD total score	5.08	3.45
ASRS total score	1.13	1.21

### Sociodemographic variables in infants

	<i>Mean</i>	<i>SD</i>
Age (in days)	98.70	16.49
	<i>Frequency</i>	<i>%</i>
Season of birth (Winter/Spring/Summer/Autumn)	335 / 133 / 401 / 351	27.46 / 10.90 / 32.87 / 28.77
Feeding (only breast feeding / breast feeding+milk substitute /only milk substitute)	797 / 262 / 159	65.44 / 21.51 / 13.05
Use of pacifier (Yes / No)	860 / 350	71.07 / 28.93

### Sleep variables in infants

	<i>Mean</i>	<i>SD</i>
Number of sleep hours at night (7pm-7am)	9.00	1.59
Number of sleep hours during the day (7am-7pm)	5.18	1.49
Day-to-night ratio (%)	36.57	8.86
	<i>Frequency</i>	<i>%</i>
Short sleep ( $\leq 12$ hours per day) (Yes / No)	216 / 974	18.2 / 81.8
Day-to-night ratio $> 41$ (Yes / No)	333 / 827	28.71 / 71.29
Difficulties in self-soothing (Yes / No)	489 / 732	40.05 / 59.95
High frequency of night awakenings ( $\geq 3$ times / night) (Yes / No)	217 / 961	18.4 / 81.6
Long sleep-onset latency ( $> 20$ mins) (Yes / No)	496 / 676	34.8 / 47.4
Co-sleeping with parents (Yes / No)	447 / 703	38.87 / 61.13
Irregular sleeping routine (Often or always / No)	54 / 1161	4.44 / 95.56

SD=Standard deviation; BNSQ= Basic Nordic Sleep Questionnaire; ESS= Epworth sleepiness scale (ESS); AUDIT= Alcohol Use Disorders Identification Test; GSS= Global Seasonality Score; LTE= List of Threatening Experiences; STAI= State-Trait Anxiety Inventory; CESD= Center for Epidemiological Studies Depression; ASRS= Adult ADHD Self-Report Scale





**Table 2.** Correlations between maternal risk factors during pregnancy

	<b>GSS</b>		<b>STAI</b>		<b>LTE</b>		<b>ASRS</b>		<b>AUDIT</b>		<b>BNSQ</b>		<b>ESS</b>	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p
<b>CESD</b>	0.285	0.000	0.651	0.000	0.121	0.000	0.347	0.000	0.006	0.884	0.310	0.000	-0.061	0.111
<b>GSS</b>			0.268	0.000	0.074	0.014	0.212	0.000	0.092	0.001	0.113	0.000	0.011	0.704
<b>STAI</b>					0.141	0.000	0.312	0.000	0.006	0.830	0.198	0.000	-0.003	0.912
<b>LTE</b>							0.046	0.111	0.071	0.013	0.052	0.071	0.016	0.569
<b>ASRS</b>									0.049	0.090	0.108	0.000	-0.017	0.545
<b>AUDIT</b>											-0.041	0.155	0.003	0.927
<b>BNSQ</b>													-0.049	0.086

**Table 3.** Logistic regression analysis between prenatal maternal variables and sleep variables in infants at 3 months

<b>Short sleep</b>			
	<b>B</b>	<b>p</b>	<b>AOR (95% C.I.)</b>
AUDIT	-0.002	0.958	0.998 (0.917 to 1.085)
STAI sum	0.039	0.269	1.040 (0.970 to 1.114)
GSS sum	0.026	0.347	1.027 (0.972 to 1.084)
CESD sum	0.037	0.120	1.037 (0.991 to 1.086)
ASRS sum	0.124	0.065	1.132 (0.992 to 1.291)
LTE sum	0.006	0.943	1.006 (0.854 to 1.185)
<b>BNSQ sum</b>	<b>0.185</b>	<b>0.012</b>	<b>1.203 (1.041 to 1.390)</b>
ESS sum	0.002	0.894	1.002 (0.968 to 1.038)
<b>Slow circadian rhythm development</b>			
	<b>B</b>	<b>p</b>	<b>AOR (95% C.I.)</b>
AUDIT	-0.073	0.082	0.930 (0.857 to 1.009)
STAI sum	0.027	0.393	1.027 (0.966 to 1.091)
GSS sum	0.018	0.466	1.018 (0.971 to 1.068)
CESD sum	0.015	0.472	1.015 (0.975 to 1.057)
ASRS sum	-0.008	0.890	0.992 (0.882 to 1.115)
LTE sum	-0.016	0.818	0.984 (0.859 to 1.128)
BNSQ sum	0.090	0.163	1.095 (0.964 to 1.242)
ESS sum	-0.012	0.437	0.988 (0.958 to 1.019)
<b>Difficulties in self-soothing</b>			
	<b>B</b>	<b>p</b>	<b>AOR (95% C.I.)</b>
AUDIT	-0.022	0.547	0.978 (0.910 to 1.051)
STAI sum	-0.021	0.442	0.979 (0.927 to 1.033)
GSS sum	-0.003	0.893	0.997 (0.957 to 1.039)
CESD sum	0.003	0.858	1.003 (0.968 to 1.040)
ASRS sum	-0.005	0.932	0.996 (0.898 to 1.103)
LTE sum	0.007	0.911	1.007 (0.894 to 1.133)
BNSQ sum	0.039	0.501	1.039 (0.929 to 1.163)
ESS sum	-0.014	0.309	0.986 (0.960 to 1.013)
<b>High frequency of night awakening</b>			
	<b>B</b>	<b>p</b>	<b>AOR (95% C.I.)</b>
AUDIT 1-3 items	-0.005	0.902	0.995 (0.916 to 1.081)
STAI sum	0.023	0.501	1.024 (0.956 to 1.096)
GSS sum	-0.006	0.841	0.994 (0.941 to 1.050)
CESD sum	0.024	0.291	1.025 (0.979 to 1.072)
ASRS sum	0.095	0.150	1.100 (0.966 to 1.251)
LTE sum	-0.019	0.809	0.981 (0.839 to 1.147)
BNSQ sum	0.097	0.186	1.101 (0.955 to 1.271)
ESS sum	-0.035	0.065	0.966 (0.931 to 1.002)
<b>Long sleep-onset latency</b>			
	<b>B</b>	<b>p</b>	<b>AOR (95% C.I.)</b>
AUDIT 1-3 items	0.020	0.559	0.981 (0.918 to 1.047)
<b>STAI sum</b>	<b>0.074</b>	<b>0.010</b>	<b>1.077 (1.018 to 1.140)</b>
GSS sum	0.038	0.481	1.039 (0.934 to 1.156)
<b>CESD sum</b>	<b>0.122</b>	<b>0.025</b>	<b>1.129 (1.016 to 1.256)</b>
<b>ASRS sum</b>	<b>0.077</b>	<b>0.001</b>	<b>1.080 (1.034 to 1.128)</b>
LTE sum	-0.004	0.947	0.996 (0.880 to 1.127)
<b>BNSQ sum</b>	<b>0.123</b>	<b>0.039</b>	<b>1.131 (1.006 to 1.271)</b>
ESS sum	0.003	0.843	1.003 (0.975 to 1.031)
<b>Co-sleeping with parents</b>			
	<b>B</b>	<b>p value</b>	<b>AOR (95% C.I.)</b>
AUDIT	0.050	0.204	1.051 (0.973 to 1.136)

<b>STAI sum</b>	<b>0.084</b>	<b>0.003</b>	<b>1.088 (1.028 to 1.151)</b>
<b>GSS sum</b>	<b>0.049</b>	<b>0.032</b>	<b>1.050 (1.004 to 1.098)</b>
CESD sum	0.033	0.088	1.033 (0.995 to 1.073)
<b>ASRS sum</b>	<b>0.129</b>	<b>0.019</b>	<b>1.138 (1.021 to 1.268)</b>
<b>LTE sum</b>	<b>0.172</b>	<b>0.011</b>	<b>1.188 (1.040 to 1.357)</b>
BNSQ sum	0.063	0.297	1.065 (0.946 to 1.199)
ESS sum	-0.012	0.396	0.988 (0.960 to 1.016)
<b>Irregular sleeping routine</b>			
	<b>B</b>	<i>p value</i>	<b>AOR (95% C.I.)</b>
AUDIT	-0.043	0.632	0.958 (0.804 to 1.142)
STAI sum	0.101	0.096	1.107 (0.982 to 1.247)
GSS sum	0.041	0.428	1.042 (0.941 to 1.155)
<b>CESD sum</b>	<b>0.084</b>	<b>0.043</b>	<b>1.087 (1.003 to 1.179)</b>
<b>ASRS sum</b>	<b>0.270</b>	<b>0.019</b>	<b>1.310 (1.045 to 1.643)</b>
LTE sum	-0.142	0.459	0.867 (0.595 to 1.265)
BNSQ sum	-0.064	0.671	0.938 (0.698 to 1.260)
ESS sum	0.001	0.986	1.001 (0.936 to 1.069)

AUDIT= Alcohol Use Disorders Identification Test; GSS= Global Seasonality Score;  
 LTE= List of Threatening Experiences; STAI= State-Trait Anxiety Inventory;  
 CESD= Center for Epidemiological Studies Depression;  
 ASRS= Adult ADHD Self-Report Scale; ESS= Epworth sleepiness