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Regular Article

Exclusive breastfeeding mitigates the association between prenatal maternal pandemic-related stress and children sleep problems at 24 months of age

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Abstract

Infant sleep quality is increasingly regarded as an important factor for children long-term functioning and adaptation. The early roots of sleep disturbances are still poorly understood and likely involve a complex interplay between prenatal and postnatal factors. This study investigated whether exclusive breastfeeding during the first 6 months moderated the association between maternal prenatal pandemic-related stress (PRS) and sleep problems in 24-months children born during the COVID-19 pandemic. We also explored the potential contribution of maternal postnatal anxiety in these relations. Seventy-eight infants (50% males) and their mothers provided complete data from birth to 24 months. Between 12 and 48 h from birth, maternal PRS during pregnancy was retrospectively reported as well as maternal anxiety and exclusive breastfeeding. Maternal anxiety and exclusive breastfeeding were also reported at 3 and 6 months after childbirth. Children sleep disturbances were reported at 24 months. Bayesian analyses revealed that maternal PRS was positively associated with sleep problems in children who were not exclusively breastfed from birth to 6 months. Findings add to the growing literature on the lasting impact of early pre- and postnatal experiences on child well-being and development.

Keywords: anxiety; breastfeeding; child; pandemic; parent; sleep; stress

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Introduction

Background

Sleep quality plays a crucial role in brain development and adaptation from early in life to adulthood. Children sleep disruptions might increase the risk for a range of adverse outcomes, including cognitive and socio-emotional domains (Astill et al., 2012) as well as undermine academic achievements (Dewald et al., 2010). Noteworthy, sleep disruptions in childhood have been found to predict mental health outcomes later in life, including behavioral and emotional problems in adolescence (Sadeh et al., 2014). Understanding the factors that underlie the early onset of sleep problems in childhood is critical for developing prevention and intervention strategies that might support healthy sleep patterns and enhance long-term developmental outcomes.

The etiology of sleep disturbances is complex and poorly understood. Besides genetic factors, mounting evidence suggests the role of pre- and postnatal environmental exposures. For example, prenatal exposure to maternal stress might impact infant bio-behavioral regulation, including sleep behaviors (Van den Bergh et al., 2020). Likewise, exclusive breastfeeding and postnatal maternal mood are often regarded as non-negligible contributors to the onset of sleep disturbances in the youngests (Galbally et al., 2013). However, how prenatal and postnatal environmental exposures act together to shape infant sleep behaviors in humans is still unknown. This study investigates, for the first time, whether exclusive breastfeeding from birth to six months moderates the association between maternal prenatal COVID-19 pandemic-related stress (PRS) exposure and infant sleep regulation at 24 months, taking also into account the potential contribution of maternal postnatal anxiety. Delving into the complex interplay between pre- and postnatal environmental influences of infant sleep quality becomes a paramount endeavor in unraveling the multifaceted determinants of healthy child development.

Prenatal maternal stress and child sleep behaviors

The impact of prenatal exposure to maternal stress on child development is an area of growing interest and research. Maternal stress during pregnancy exceeds the confines of gestation, influencing various aspects of a child's growth and development

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(for a review see Van den Bergh et al., 2020). Amassing evidence indicates that prenatal exposure to maternal stress is associated with cognitive and emotional developmental outcomes in the offspring, such as poorer cognitive development (e.g., Nazzari et al., 2020), altered emotional regulation (e.g., Nolvi et al., 2016), and more "difficult" temperament (e.g., Nazzari et al., 2023b). Additionally, maternal stress during pregnancy has been shown to be related to a number of biological alterations early in life, encompassing structural (e.g., Buss et al., 2010; Lehtola et al., 2020) and functional (e.g., van den Heuvel et al., 2021) brain alterations, stress regulation (e.g., Davis et al., 2011), immune function (e.g., Veru et al., 2014), and DNA methylation patterns (e.g., Provenzi et al., 2021; Nazzari et al., 2023a) with possible long-term implications for children health and development (Van Den Bergh et al., 2018). An intriguing area of exploration is its potential effect on the sleep patterns of infants. Higher maternal prenatal stress has been found to be associated with greater sleep difficulties at 3 months (Morales-Muñoz et al., 2018), increased sleep disturbances at 18 and 30 months (O'Connor et al., 2007), greater parents' sleep concerns at 3 years of age and disturbed sleep physiology at 5 years (van den Heuvel et al., 2021). Furthermore, it was recently showed in a large population-based cohort that greater prenatal stressful life events predicted not only higher rates of sleep problems at 1.5 years of age, but also their persistence over time (at 3, 5, 7 and 11 years) (Ksinan Jiskrova et al., 2022). Interestingly, Simcock and colleagues (2019) investigated the prospective association between prenatal exposure to a natural disaster and children's sleep. They reported more severe objective flood-related hardship, but not maternal subjective stress, to be associated with greater children's sleep problem scores at 2.5 years of age. However, few studies suggested that prenatal maternal stress may not be associated with sleep characteristics in 4–6 years old children (e.g., Chatterjee et al., 2018; Liu et al., 2020). The lack of consistency in findings across studies may partly be due to methodological heterogeneity in sleep assessments and to an inconsistent consideration of relevant postnatal maternal factors. For example, findings from Morales-Muñoz et al. (2018) were adjusted for breastfeeding, whereas some studies accounted for postnatal maternal mood (e.g., O'Connor et al., 2007; van den Heuvel et al., 2021; Simcock et al., 2019). In contrast, few studies did not include postnatal confounders (e.g., Chatterjee et al., 2018; Ksinan Jiskrova et al., 2022). Thus, further research is clearly needed to explore these relationships with a more comprehensive approach to postnatal factors.

Exclusive breastfeeding: a buffer for child sleep?

Exclusive breastfeeding, defined as feeding an infant solely with breast milk without any other liquids or solids, has well-known multifaceted benefits, acting as a cornerstone of early childhood nutrition and immunological protection (Victora et al., 2016). Beyond its advantages in bolstering the infant's immune system and promoting optimal growth, recent research illuminates a potential link between breastfeeding and enhanced sleep patterns. The rich composition of breast milk, containing a host of bioactive compounds including tryptophan and melatonin precursors, suggests it may function as a natural sedative, potentially augmenting the infant's capacity for consolidated and restorative sleep (e.g., Engler et al., 2012). On another account, qualitative research indicated that new mothers often perceive breastfeeding as being associated with more night-waking and poorer sleep quality in infancy, due to the faster digestion of breast milk (Cloherty et al., 2004; Rosenbaum et al., 2022). In contrast, they perceive formula feeding as offering more opportunity to rest. As maternal perception of the relationship between breastfeeding and infant sleep might influence the decision to initiate/terminate breastfeeding (Bay et al., 2023), more empirical evidence is needed. While several studies reported that exclusive breastfeeding is associated with increased sleep disturbances in the first year of life (e.g., Galbally et al., 2013; Nakagawa et al., 2021), null associations has also been found (Demirci et al., 2013; Figueiredo et al., 2017a). Furthermore, conflicting evidence exists of longer sleep duration in breastfed infants as compared to formula-fed infants (e.g., Engler et al., 2012). A recent systematic review concluded that although more fragmented sleep and more waking are reported in breastfed infants, the total sleep duration does not differ between breastfed and formula-fed infants (Manková et al., 2023). Interestingly, while few studies reported different results according to the infant's age (Figueiredo et al., 2017; Jafar et al., 2021; Rudzik et al., 2018), more night awakenings and similar or longer night sleep duration in breastfed infants were found in the majority of works regardless of infant's age (Mankova et al., 2023). Noteworthy, beyond the nutritional and hormonal content of breast milk, several psychosocial factors have been hypothesized to underline the association between breastfeeding and infant's sleep, including sleep environments (Quante et al., 2022), bed arrangements (Mankova et al., 2023) or the quality of the dyadic relationship between the mother and child (for a review see Dias & Figueiredo, 2019). For example, a secure attachment has been associated with more regulated sleep-wake behavior, characterized by longer night sleep duration and less night wakings (Pennestri et al., 2015; Zentall et al., 2012). Longer duration of breastfeeding, in turn, has been associated with the security of attachment in some studies (reviewed in Linde et al., 2020), thus possibly highlighting an additional pathway for the effects of breastfeeding on sleep behaviors.

As exclusive breastfeeding is often regarded as a protective factor for many domains of child growth and development, an important aspect that is yet to be determined is whether it can act as a buffer for the effect of prenatal stress on infant's sleep behaviors.

Postnatal maternal anxiety: a risk factor for child sleep?

Alongside, postnatal maternal anxiety is an emerging risk factor for sleep problems in infants (Goldberg et al., 2013). The pervasive influence of maternal anxiety on the mother-infant dyad has the potential to disrupt the establishment of healthy sleep routines and patterns. Heightened maternal anxiety may result in increased infants' nocturnal awakenings and fragmented sleep, ultimately compromising the quality and duration of restorative sleep (Tikotzky et al., 2021). Notwithstanding, the association between maternal postnatal anxiety and infants' sleep is likely to be bi-directional with insufficient or fragmented sleep negatively affecting maternal mood and potentially increase the risk for maternal postnatal anxiety symptoms (Okun et al., 2018). To further complicate the picture, more anxious mothers are more likely to misinterpret their infants' behaviors, possibly providing biased perceptions of infant sleep behaviors (Davies et al., 2022). This intricate interplay underscores the needs to account for maternal postnatal mood when investigating factors underpinning the early establishment of infant sleep disturbances.

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The COVID-19 pandemic: an unprecedented emergency and opportunity

In this context, the recent COVID-19 pandemic, an unparalleled global crisis, provides a framework for examining these complex dynamics. Pregnant women, already navigating the complexities of gestation, found themselves contending with an unprecedented level of uncertainty and stress. The pandemic, with its far-reaching influence on daily life, constitutes a critical period during which prenatal stressors may have been amplified (Tomfohr-Madsen et al., 2021), potentially heightening the risk or prevalence of sleep problems in offspring. Early reports suggest that maternal prenatal PRS during pregnancy, understood as the emotional and psychological stress response related to the COVID-19 emergency, is associated with several early infants' socio-emotional developmental outcomes (Buthmann et al., 2022; López-Morales et al., 2022; Nazzari et al., 2023c, 2024; Provenzi et al., 2021), including sleep difficulties (Maccarini et al., 2024). To the best of our knowledge, nearly nothing is known for what pertains the possible moderating role of postnatal factors, such as breastfeeding or anxiety, in the observed associations. Understanding the nuanced interplay between maternal prenatal PRS, postnatal influences and infant sleep outcomes is crucial to elucidate the potential intergenerational impact of the pandemic.

The present study

Based on these premises, this study aimed at investigating whether exclusive breastfeeding from birth to 6 months of age may act as a potential moderator of the association between prenatal maternal PRS and the risk of emerging sleep problems in 24-months children born during the COVID-19 healthcare emergency in Italy. Given the extensive changes in sleep development during the first two years of life, including the maturation of sleep-wake rhythms, the development of self-regulation skills, and the reduction in sleep needs, with significant inter-individual variability (e.g., Paavonen et al., 2020), we assessed infant sleep behaviors at 24 months of age. This age was chosen to provide a clearer picture of infants who establish patterns of sleep difficulties. Due to the constraints imposed by the pandemic, maternal stress experiences related to the pandemic during pregnancy were reported retrospectively soon after childbirth (i.e., between 12 and 48 hr postpartum), following previous studies (e.g., Provenzi et al., 2021). Continuous exclusive breastfeeding, defined as no other forms of food or liquids being introduced, was assessed from birth to 6 months of age, in line with World Health Organization recommendations (WHO, 2021). In line with emerging literature on the buffering role of the postnatal environment in the association between maternal stress and infant outcomes (Grande et al., 2021; Nazzari et al., 2022a), we tested both the independent and interactive effects of maternal PRS and exclusive breastfeeding on infant sleep disturbances. We hypothesized that continuous exclusive breastfeeding at 6 months of age would buffer the magnitude of the association between maternal PRS and infant's sleep problems, reducing the effect of prenatal stress exposure in breastfed infants. In contrast, we anticipated greater sleep problems to occur in infants prenatally exposed to greater maternal stress and not exclusively breastfed in the first 6 months of life. Additionally, as maternal anxiety might further confound the observed associations, we further explored whether maternal postnatal anxiety would also modify the relations between prenatal maternal PRS, exclusive breastfeeding, and children sleep problems. To this aim, maternal postnatal anxiety was assessed soon after childbirth, at 3 and 6 months of age to track the trajectory of maternal mental health across the early perinatal period. A three-way interaction among maternal PRS, breastfeeding and postnatal anxiety was included in our exploratory model. Due to the exploratory nature of this latter analysis, no specific a-priori hypotheses were made.

Methods

Participants and procedures

Mother-infant dyads were recruited from May 2020 to February 2021 in ten neonatal units in Northern Italy as an extended follow-up of a longitudinal multi-centric research project, the MOM-COPE Study (for full details see Provenzi et al., 2020). Inclusion criteria were: maternal age over 18 years, absence of prenatal and perinatal diseases or injuries, and term delivery (i.e., from $37 + 0$ to $41 + 6$ weeks of gestation). As the data collection occurred during the COVID-19 health emergency, a negative PCR test for SARS-CoV-2 at delivery was an additional inclusion criterion. All infants (50% males, mostly White) were born full-term (37–42 weeks' gestation) and had normal birth weight (> 2500 g). Most women were well-educated (averaged years of education = 15.79, $SD = 2.9$) and employed at the time of the data collection. For more information on sample characteristics see Table 1. Within 48 hr from infant birth, mother-infant dyads were recruited from a diverse urban environment including the metropolitan and suburban areas of major cities of Northern Italy such as Pavia, Lodi, Piacenza, Brescia, Milano and Monza. Socio-demographic (i.e., age, educational level, occupational status) and neonatal (i.e., gestational age, birth weight, head circumference, length, Apgar scores, breastfeeding at birth, and mode of delivery) data were obtained from medical records. Between 12 and 48 h after childbirth (T0), women retrospectively reported on their PRS experience during pregnancy, as well as on their current anxiety levels and breastfeeding practices. Maternal anxiety and breastfeeding were also assessed at 3 (T1) and 6 (T2) months after childbirth. Infants' sleep disturbances were reported 24 months after childbirth (T3). An initial sample of 320 mother-infant dyads were recruited at birth. From this sample, 220 dyads (around 69%) completed the T1 assessment, whereas 85 mothers (around 26,5%) provided data at the 24-months follow-up assessment (T3). Given the presence of missing-data for some of the study measures in the T3 sample, we decided to use a listwise deletion approach (i.e., dropping observations in the dataset for which the values of at least one variable are missing) resulting in a final analytic sample of 78 participants. While sample attrition at the postnatal follow-up phases was a significant issue, it is noteworthy that we did not observe any meaningful difference between participants and those who withdrew from the postnatal phases in demographic, PRS, anxiety and depression scores, suggesting no systematic patterns of attrition (Section 3 in Supplementary Material).

The study was approved by the Ethics Committees of the IRCCS Mondino Foundation and the participating hospitals. All the procedures were performed in accordance with the 2018 Declaration of Helsinki for studies conducted with human participants. All parents provided written informed consent to participate to the study.

Measures

Maternal PRS. At delivery (T0) mothers retrospectively reported on their PRS during pregnancy through an ad hoc questionnaire

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Table 1. Descriptives of the included subjects

	n	mean	sd	min	max	skew	kurtosis
Gestational age (weeks)	78	39,78	1,14	37	42	−0,26	−0,49
Birth weight (grams)	78	3327,51	412,47	2580	4270	0,15	−0,61
Apgar at minute 5	78	9,87	0,37	8	10	−2,89	8,19
Maternal age (years)	78	33,21	4,17	21	43	0,06	0,08
Maternal education (years)	78	15,79	2,90	8	21	−0,76	−0,29
Maternal anxiety at T0	78	35,57	11,68	20	74	0,99	0,55
Maternal anxiety at T1	78	34,23	12,14	20	69	1,15	0,66
Maternal anxiety at T2	78	32,83	10,43	20	70	1,16	1,10
Maternal anxiety factor score (f1)	78	−0,01	7,58	−10,25	24,92	1,06	0,80
Maternal pandemic-related stress (PRS)	78	2,53	0,69	1	4,5	0,56	0,47
Infants' sleep problems at T3	78	49,31	4,89	42	68	1,17	1,70

(Provenzi et al., 2020; Section 2 in Supplementary Material). The questionnaire included six 5-point Likert scale items (1, not at all; 5, very much) on the emotional stress response to the COVID-19 emergency during pregnancy. An average maternal antenatal PRS score was obtained, ranging from 1 (low) to 5 (high). The Cronbach's α of this scale was .88, 95% CI [0.62, 0.98].

Maternal postnatal anxiety. The 20-item Italian version of the State anxiety subscale (STAI-S) of the State-Trait Anxiety Inventory (Pedrabissi & Santinello, 1989) was employed to assess maternal postnatal anxiety symptoms at delivery (T0), 3 (T1) and 6 (T2) months postpartum. Each item is rated on a 4-point Likert scale with the total continuous score ranging from 20 (low) to 80 (high). The Cronbach's α of this scale was .98, 95% CI [0.96, 0.99] at T0 and T1 and .97, 95% CI [0.94, 0.99] at T2.

Exclusive breastfeeding. Mothers were asked to complete an ad hoc form to assess whether they were using exclusive breastfeeding, maternal milk from a bottle, formula or mixed feeding methods at delivery (T0), 3 (T1) and 6 (T2) months of infants' age.

Children sleep behavior. Mothers filled in the Italian adaptation of the 33 items Children's Sleep Habits Questionnaire (Borrelli et al., 2021) at 24 months after childbirth (T3). The frequency of sleep-related behaviors in the last previous week was rated on a 3-point scale as "usually" (5 to 7 times per week, scored as 3 points), "sometimes" (2 to 4 times per week, scored as 2 points) or "rarely" (0 to 1 time per week, scored as 1 point). The total Sleep Disturbance Scale results from the sum of the responses obtained on each item, with higher scores indicating greater sleep disturbances. The Cronbach's α of this scale was .77, 95% CI [0.63, 0.87].

Data analysis

Statistical analyses were performed using R software (R Core Team, 2018) including brms (Bürkner, 2017) and ggplot2 (Wickham, 2016) packages, and using STAN to implement MCMC sampling (Stan Development Team, 2018). In preliminary analyses, we explored data distribution. Then, we computed descriptive statistics (Table 1) and bivariate correlations among our study variables (Figure S4 and S5). We subsequently evaluated our hypothesis by fitting and comparing a series of linear models (Table 2) using a full Bayesian approach for estimating parameters. Model comparison allows for the selection of the most plausible models given the data and a set of candidate models. Specifically, we compared the following models: model 0 (M00), i.e., a model assuming that there were no associations among the study variables; model 1 (M01), including only exclusive breastfeeding as predictor; model 2 (M02), including only maternal PRS; model 3 (M03), including both exclusive breastfeeding and maternal PRS main effects and, lastly, model 4 (M04), testing the interactive effect between maternal PRS and exclusive breastfeeding. Models were compared in terms of statistical evidence (i.e. support by the data) using information criteria, which enables the evaluation of models considering the tradeoff between parsimony and goodness-of-fit. Here, models were compared using the following criteria: Bayesian R2 (Gelman et al., 2019), Leave-one-out Cross Validation information criterion (Vehtari et al., 2017), where models with lower values indicate higher predictive capability, and model weights, with high values indicating a better model. Considering that the sample size is relatively small, we used the following weak informative priors (for prior specifications see Section 5 Supplementary Materials): for exclusive breastfeeding effect Student's *t* (3, −5, 5), for maternal PRS effect Student's *t* (3, 0, 1), and for interaction effect between the two predictors Student's *t* (3, −2, 3). For all models, estimates were based on 4000 samples extracted from the posteriors with 4 chains. MCMC convergences were assessed by means of the Potential Scale Reduction Statistic (PSRF or Rhat; Gelman & Rubin, 1992). We also checked model diagnostics for residuals. Once identified, the best model was analyzed in detail. We analyzed the model predictions based on the parameters' posterior distributions and the Posterior Predictive Distribution (i.e. the distribution of possible unobserved values conditional on observed data and model parameters, PPD). In order to obtain further information on the extent to which infants' sleep problems may differ in relation to the interaction between maternal PRS and breastfeeding, we computed the degree of overlap of the posterior distribution of parameters (eta; Pastore & Calcagnì, 2019). The eta index measures the degree of overlap between two empirical densities and ranges between 0 (when the distributions are completely disjoint) and 1 (when the distributions completely overlap). Values within this range quantify the similarity/difference of the values in the two groups (no-exclusive breastfeeding, exclusive breastfeeding). Finally, we addressed our exploratory research question by including maternal anxiety factor score (i.e., estimated values for maternal anxiety assessed at 0, 3 and

Table 2. Linear models definition

	Formula	description
M00	Infants' sleep problems ~ 1	Null model
M01	Infants' sleep problems ~ breastfeeding groups	Group comparison
M02	Infants' sleep problems ~ maternal PRS	Effect of maternal PRS
M03	Infants' sleep problems ~ breastfeeding groups + maternal PRS	Additive effect of group and PRS
M04	Infants' sleep problems ~ breastfeeding groups * maternal PRS	Interaction effect between group and PRS

Note. Infants' sleep problems: infants' sleep problems assessed at 24 months of age, breastfeeding groups: exclusive breastfed vs. no- exclusive breastfed infants; maternal PRS: maternal pandemic-related stress.

Table 3. Model comparison

Model	LOO	SE	W	R2
M04	462.8	19.5	0.998	0.158
M03	466.5	19.5	< .001	0.109
M01	474.2	19.5	< .001	0.033
M02	465.5	18.7	0.002	0.082
M00	475.2	18.7	< .001	< .001

Note. LOO, leave-one-out cross-validation information criterion; SE, standard error; W, model weight; R2, Bayesian R2. M00 is the null model, M01 is the model with breastfeeding group comparison, M02 is the model with the effect of maternal PRS, M03 is the model with the additive effect of breastfeeding groups and PRS, M04 is the model with the interaction effect between breastfeeding groups and PRS.

6 months of infant age) in our statistical model. Again, to obtain information on the extent to which infants' sleep problems may differ in relation to the interaction between maternal PRS, breastfeeding and anxiety, we computed the degree of overlap of the posterior distribution of parameters. In this case, the eta index allows to quantify the similarity/difference of the values in the two groups concerning maternal anxiety level.

Results

Preliminary analysis

In Table 1 are reported the univariate statistics for the quantitative study variables. Exclusive breastfeeding was reported by 65.4% of the sample at T0, 55.1% at T1, and 48.7% at T2. At six months 38.5% of the sample had continuative exclusive breastfeeding since birth, while 61.5% had discontinued.

Figure S4 represents bivariate associations between variables of interest while Figure S5 represents distributions and bivariate associations between participants descriptives (i.e., the descriptives reported in Table 1) in exclusive breastfeeding groups.

Main analyses

Table 3 shows the results of the Bayesian model comparison. The best performing model was model M04 (i.e., the model with the interaction between exclusive breastfeeding and maternal PRS). Importantly, continuous exclusive breastfeeding from birth up to 6 months of age interacted with maternal PRS in predicting infants sleep problems at 24 months ($B = 2.46$, with a 90% Highest posterior density interval (HPDI) [0.35; 4.54], corresponding to an $\eta 2$ of 0.03 with a 90% HPDI [.00; .10]).

Specifically, as illustrated in Figure 1 [B], infants who do not received continuous exclusive breastfeeding from birth to 6 months showed higher sleep problems at 24 months of age at higher (+1SD) levels of maternal PRS. Figure 2 represents the overlapping of PPD of the expected values of infants' sleep problems assessed at 24 months of age as a function of maternal PRS (x-axis) and exclusive breastfeeding (colors). Between non-continuosly breastfed and continuosly breastfed infants, those with mothers with lower (1) PRS scores showed a very small overlap (0.05), indicating a large difference in means, while those with PRS scores equal to 3 showed a higher overlap (0.84). When mothers reported the maximum level of PRS (5), the overlapping index between breastfed and non-breastfed infants was very small (0.16), indicating a large difference in means.

Exploratory analysis

To address our exploratory research question concerning the potential role of maternal anxiety in the observed associations, we included maternal anxiety factor score to our best model identified from the analyses described above. We computed 2 different levels of maternal anxiety corresponding to its mean ± the standard deviation (i.e., −7.58, 7.58). For each maternal anxiety level * maternal PRS * group (breastfed vs non-breastfed) interaction, we sampled 4000 posterior draws of the expected values from PPD of the model (Figure 3 [A]). We represented the obtained posteriors in Figure 4 and for each pair (−7.58 vs 7.58 and breastfed vs. non-breastfed) we computed the eta. Figure 3 [A] represents the posterior predictive check while Figure 3 [B] represents the expected values of the model testing the triple interaction between group (i.e., breastfed vs. non-breastfed), maternal PRS and maternal anxiety. Figure 4 represents the PPD of the expected values in interaction model as a function of maternal PRS (x-axis), breastfeeding groups (panels), and maternal anxiety (colors). Among breastfed infants, those with mothers with lower (1) PRS scores showed an high overlap (0.84), while those with higher (5) PRS showed a small overlap (0.24), indicating a large difference in means. Among non-breastfed infants, those with lower (1) PRS showed a small overlap (0.34) which becomes lower and lower until it is equal to 0.19 for those with higher (5) PRS scores. This highlight that the effect of maternal anxiety (i.e., f1) on the association between PRS and infants' sleep problems at 24 months of age seems to impact similarly in breastfed and non-breastfed infants. It should also be noted that the triple interaction is rather weak and poorly supported by the data.

Discussion

With amassing evidence of an association between maternal prenatal stress and infants' developmental outcomes (Van den Bergh et al., 2020), there is now a growing focus on identifying

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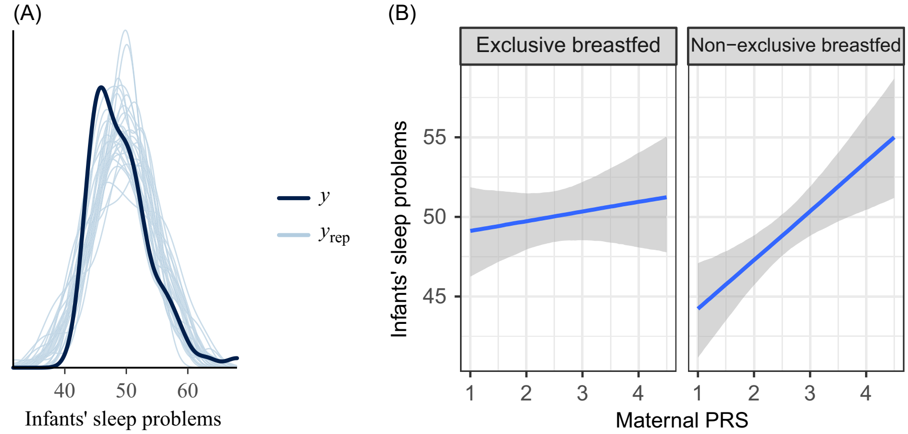

Figure 1. Model M04 posterior predictive check [a] and expected values of infants sleep problems at T3 (*y*-axis) as a function of maternal PRS assessed at T0 (*x*-axis) and exclusive breastfeeding groups [b].

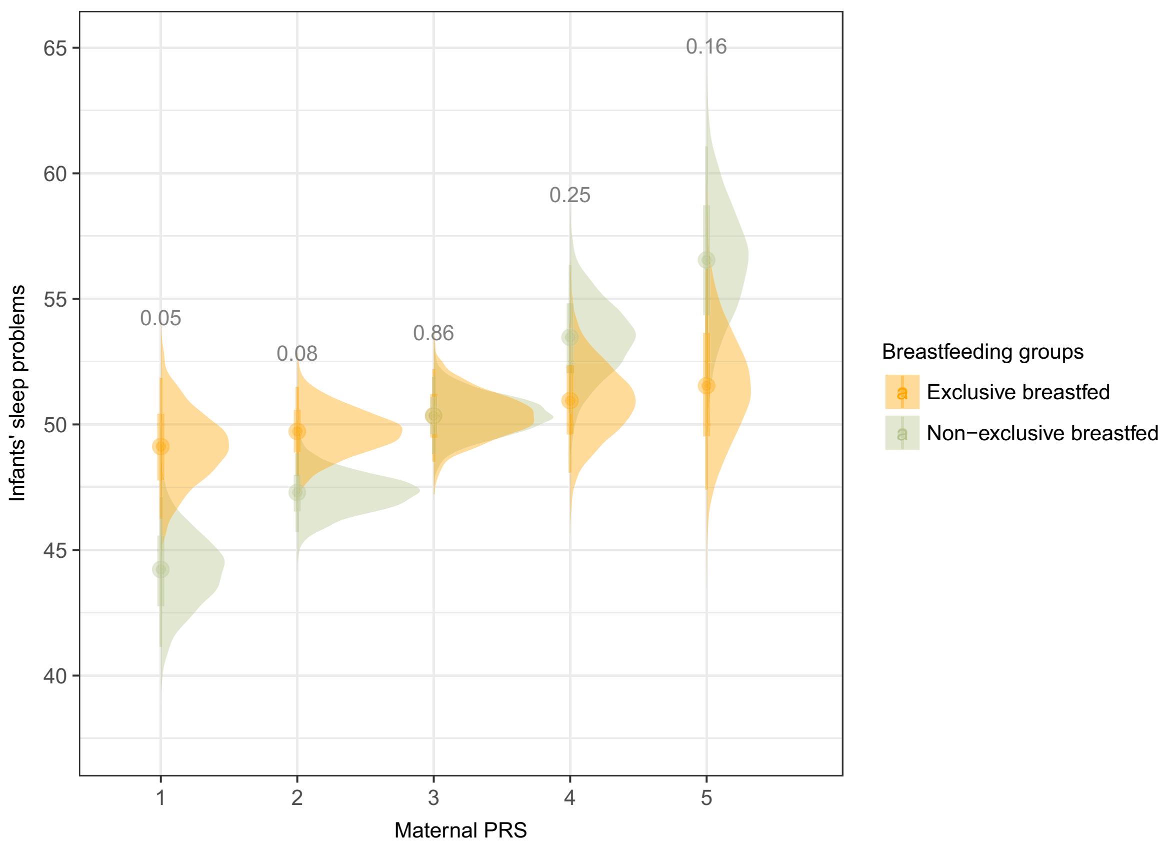

Figure 2. Overlapping index for M04. Expected values of infants sleep problems at T3 (*y*-axis) as a function of maternal pandemic-related stress assessed at T0 (*x*-axis) and exclusive breastfeeding groups represented in yellow and green respectively.

relevant postnatal factors that might buffer these effects. One potential candidate is breastfeeding, considering its beneficial effects that extend beyond maternal and infant health, encompassing maternal sensitivity and mother-infant bonding (Kim et al., 2011; Tharner et al., 2012). The current study provides novel evidence suggesting that exclusive breastfeeding might buffer the association between antenatal exposure to maternal PRS and sleep disturbances in infants born during the COVID-19 pandemic. Specifically, in line with our broad hypothesis, higher levels of maternal PRS during pregnancy were associated with greater children's sleep problems at 24 months of age only among infants that were not exclusively continuously breastfed until 6 months of age, while the association became non-significant among infants that were exclusively continuously breastfed until 6 months of age. Interestingly, exploratory analyses indicate that maternal postnatal anxiety might not represent a substantial modifier of these effects.

The COVID-19 pandemic, along with the related restriction measures, has been an extraordinary and highly stressful situation for many families on a global scale, with a carry-over negative impact on people's mental well-being, particularly in vulnerable groups like expectant mothers (Tomfohr-Madsen et al., 2021). There is a growing literature showing that maternal stress experience related to the pandemic (i.e., PRS) might have

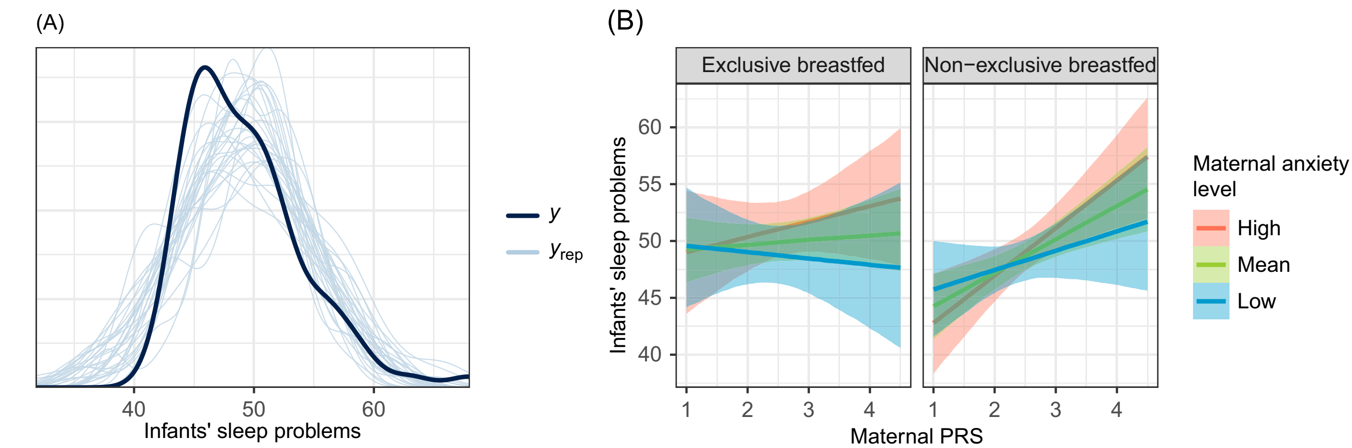

Figure 3. Triple interaction model posterior predictive check [a] and expected values of infants sleep problems at T3 (*y*-axis) as a function of maternal pandemic-related stress assessed at T0 (*x*-axis), breastfeeding groups and different levels of maternal anxiety [b].

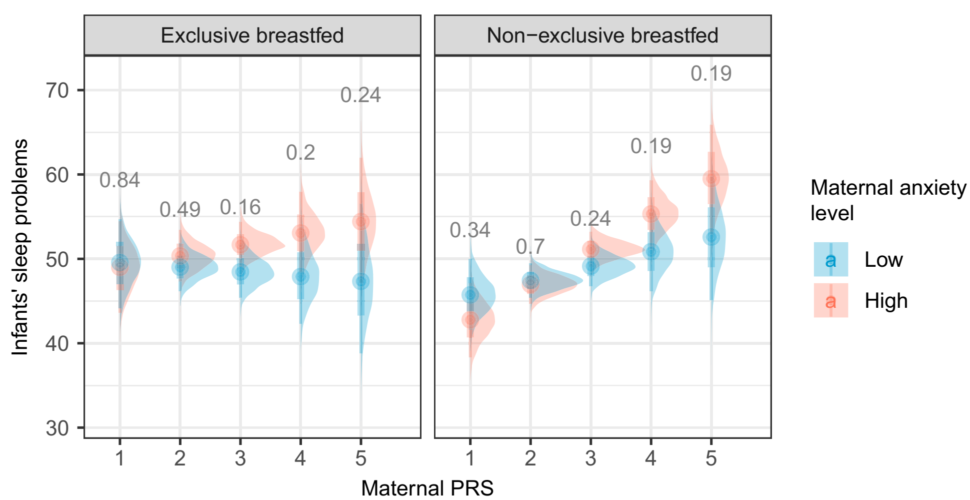

Figure 4. Triple interaction model overlapping index. Expected values of infants sleep problems at T3 (*y*-axis) as a function of maternal pandemic-related stress assessed at T0 (*x*-axis), exclusive breastfeeding groups (panels) and maternal anxiety level (colours).

significant implications for both maternal and fetal outcomes. Elevations in maternal PRS during pregnancy have been found to be associated with early infant temperament (e.g., Buthmann et al., 2022; López-Morales et al., 2022), socio-cognitive outcomes (Nazzari et al., 2023c) and sleep problems (Maccarini et al., 2024). Furthermore, prenatal exposure to the lockdown has been linked with patterns of DNA methylation of gene involved in stress regulations in the newborns (Nazzari et al., 2022b, 2023a; Provenzi et al., 2021), thus suggesting that maternal prenatal PRS might have a broad impact on infant's bio-behavioral development. The current findings critically extend available literature by showing that continuous exclusive breastfeeding from birth to 6 months of age might be able to mitigate some of these effects. These results align with mounting evidence showing that the association between maternal prenatal stress and infants' bio-behavioral outcomes might be at least partly over-ridden by the quality of the postnatal rearing environment (Frigerio & Nazzari, 2021; Nazzari et al., 2022a), raising important conceptual and clinical implications.

It is acknowledged that an altered prenatal environment can have enduring impacts on the functioning of physiological systems, including the regulation of circadian rhythms (Palagini et al., 2015). For example, prenatal exposure to stress-related elevations in maternal cortisol might alter the development of fetal stress response systems leading to disturbances in the hypothalamic-pituitary-adrenal (HPA) axis functioning (Nazzari et al., 2019), such as a hyper-responsivity of the HPA axis, which in turn have been associated with several sleep problems, such as chronic insomnia (Bonnet & Arand, 2010). Interestingly, maternal emotional distress during pregnancy have been found to be associated with fetal activity and sleep patterns. For example, foetuses of depressed women spent a greater percentage of time being active, as compared to the offspring of non-depressed women (Dieter et al., 2008). In contrast, fetuses of anxious mothers were found to spend more time in "quiet sleep" and to be less active in "active sleep" than fetuses of mothers without high anxiety (Groome et al., 1995). Furthermore, growing research is showing an association between maternal prenatal stress and altered fetal brain activity in areas that might be involved in sleep regulation (e.g., van den Heuvel et al., 2021), possibly suggesting a mediating role of these alterations in the onset of early sleep problems. While the mechanisms underlying the association between maternal prenatal stress and infant's sleep disturbances required further investigation, the current work suggests that exclusive breastfeeding can reverse these effects. Specifically, we showed that the association between maternal PRS and 24-month sleep problems was not significant in dyads that reported continuous exclusive breastfeeding until 6 months of life.

Exclusive breastfeeding is widely acknowledged as an important bio-behavioral protective factor, exerting widespread beneficial effects on infant health and development (Victora et al., 2016). The current findings align with initial human's evidence showing that exclusive breastfeeding can buffer the association between maternal prenatal or postnatal distress and infants' outcomes. For example, Miller-Graff & Scheid (2020) recently showed that breastfeeding mitigated the effects of prenatal exposure to intimate partner violence on infant temperament. Likewise, the typical frontal asymmetry patterns often found in infants of depressed mothers has not been observed in infants of depressed mothers who breastfed (Jones et al., 2004). Biological and/or psychosocial mechanisms might underline these effects. Maternal milk has important nutritional properties, including high levels of long-chain polyunsaturated fatty acids, which are known to directly impact on neural and cognitive development in offspring (Larque et al., 2002). In addition, maternal milk contains a broad range of biologically active hormones, such as glucocorticoids, which might provide important biochemical signals to the offspring about the quality of the postnatal environment. Interestingly, a positive association has been reported between milk cortisol levels and an enhanced performance on the Autonomic Stability cluster of the Neonatal Behavioral Assessment Scale in one-week-old newborns, indicating a better homeostatic adjustment of the central nervous system (Hart et al., 2004). Furthermore, aspects of maternal microbiome might be transmitted through breastmilk and further influence infant's health and development (Kordy et al., 2020). Besides purely biological factors, breastfeeding has been found to have a beneficial impact on maternal mood, sensitivity and mother-infant bonding (Kim et al., 2011; Tharner et al., 2012), promoting close physical contact and emotional connection. In this light, the moderating effects of maternal breastfeeding on the association between maternal PRS during pregnancy and children sleep might be mediated by maternal postnatal behaviors, such as greater maternal sensitivity. However, this hypothesis needs to be explicitly addressed in future studies including observative direct measure of the quality of maternal caregiving. While the precise mechanisms of the observed effects deserve further investigation, the current results underscore the holistic benefits of breastfeeding, which not only provide essential nutrients but also extend to positively influencing the sleep architecture of infants. Recognizing the potential role of exclusive breastfeeding in mitigating the intergenerational transmission of stress-related disturbances provide further empirical leverage for supporting and promoting this practice as part of pre- and postnatal care systems. Importantly, current findings suggest that extra efforts to promote breastfeeding should be directed toward mothers experiencing stressful situations or higher levels of distress across pregnancy as this may be especially beneficial in promoting long-term outcomes in the offspring.

Lastly, current findings suggest that the observed associations between maternal PRS, exclusive breastfeeding and children sleep are not substantially modified by maternal postnatal anxiety. It is important to acknowledge that the limited sample size might have reduced the chance to observe a significant 3-way interaction in the current sample, thus further replication in larger samples is required. Nevertheless, the lack of a substantial effect of maternal postnatal anxiety, if true, suggests that the observed effect of breastfeeding on the association between maternal prenatal stress and infant sleep is not confounded by postnatal maternal mood so that it is fairly comparable among mothers with high versus low levels of anxiety across the first months of life. Maternal anxiety can negative impact breastfeeding duration (Fallon et al., 2016) and is bidirectionally linked with children's sleep, with greater anxiety either influencing or resulting from early difficulties in children's establishment of healthy sleep patterns (Goldberg et al., 2013; Okun et al., 2018). Furthermore, maternal anxiety might influence the accurate reporting of children sleep behaviors (Davies et al., 2022). Although caution is needed in interpreting the current results due to the limited statistical power, our exploratory analyses seem to further corroborate the current findings showing that the observed interaction between maternal PRS during pregnancy and breastfeeding in influencing children sleep problems is not significantly modified by maternal postnatal mood.

Some limitations are noteworthy. First, results are based on a small middle-high SES community sample of healthy women and infants, and assessments were made during an extraordinary stressful period, thus limiting generalizability to different time and high-risk populations. Secondly, the longitudinal and observational nature of the project, especially during the pandemic time, resulted in remarkable sample attrition. Nevertheless, potential systematic patterns of missingness were not detected in the current study. Third, we selected specific time points for assessing infant sleep, exclusive breastfeeding and maternal stress, which may not fully capture the dynamic changes and variability in these parameters over the early years of life. While these time points were chosen based on theoretical and practical considerations, including constraints imposed by the pandemic, this may limit the generalizability of the findings to other developmental periods and contexts. Fourth, the prenatal stress questionnaire was developed ad hoc for this study, prioritizing sensitivity to the specific and unprecedented nature of COVID-19 emergency over measure standardization. Lastly, the reliance on maternal reports for measures of maternal PRS, breastfeeding status and infant sleep produces shared method variance and potentially leads to an overestimation of the effects of maternal predictors on infant sleep outcomes. Further replication of these findings is needed using more objective and structured assessment of infant sleep problems. Future work would also benefit from the inclusion of direct measures of breastmilk cortisol as well as of maternal sensitivity to elucidate the biological and/or relational mechanisms that might underlying the buffering effect of breastfeeding. Lastly, although findings of a prospective association between maternal prenatal stress, breastfeeding until 6 months of age and offspring sleep at 24 months were in the expected direction and it is tempting to interpret them as suggestive of causative pathways, they are based on correlational analyses and no causal conclusions should be drawn.

Conclusions

The present study suggests that continuous exclusive breastfeeding from birth to 6 months of age might be able to reverse the effects of prenatal exposure to maternal PRS on children sleep problems at 24 months in a sample of infants born during the pandemic. Around 40% of mothers reported continuous exclusive breastfeeding from birth to 6 months in the current sample, generally in line with the global trend observed in high-income countries (Cai et al., 2012). As empirical support accumulates for a critical protective role of breastfeeding in promoting infant and children's developmental trajectories, a call for action is needed to enhance the rates of exclusive breastfeeding during the first 6 months of age. Going beyond the well-known "breast is best" motto, this overarching goal need to be accomplished by spreading a nurturing culture that prioritize the mother-infant dyad well-being. Instead of leaving women who do not wish or are unable to breastfeed navigating the stigma and guilt, new mothers should be empowered to make informed choices and receive the necessary physical, psychological, social and economic support. Together these factors may not only increase the duration of breastfeeding, but ultimately strengthen mother-infant relationship, setting the stage for healthier generations to come.

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