Maternal Depressive Symptoms During the Pre- and Postnatal Periods and Infant Attention to Emotional Faces

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Abstract

We examined how infants' attentional disengagement from happy, fearful, neutral, and phase-scrambled faces at eight months, as assessed by eye-tracking, is associated with trajectories of maternal depressive symptoms from early pregnancy to six months postpartum (decreasing n=48, increasing n=34, and consistently low symptom levels n=280). The sample, (mother-infant dyads belonging to a larger FinnBrain Birth Cohort Study), was collected between 5/2013 – 6/2016. The overall disengagement probability from faces to distractors was not related to maternal depressive symptoms, but fear bias was heightened in infants whose mothers reported decreasing or increasing depressive symptoms. Exacerbated attention to fearful faces in infants of mothers with depressive symptoms may be independent of the timing of the symptoms in the pre- and postnatal stages.

INTRODUCTION

Maternal depressive symptoms of varying severity are common during the pre- and postnatal periods (Andersson, Sundstrom-Poromaa, Wulff, Astrom, & Bixo, 2006; Leight, Fitelson, Weston, & Wisner, 2010), and have consistently been linked to adverse effects on both the mother and developing child (DiPietro, 2012; Field et al., 2010; Murray, Fearon, & Cooper, 2015; Vigod, Buist, & Steiner, 2016). However, depression is a heterogeneous disorder with different subtypes (Goldberg, 2011; Rantala, Luoto, Krams, & Karlsson, 2018), and the time course of symptoms and the degree of chronicity also vary during the pre- and postnatal periods (Amiel Castro et al., 2017; Fredriksen, von Soest, Smith & Moe, 2017; Putnam et al., 2017). Chronic depressive maternal symptoms seem to be more predictive of adverse child outcomes compared to transient symptoms (Grace, Evindar, & Stewart, 2003; Murray, Halligan, & Cooper, 2010; van der Waerden et al., 2015). While past research has mainly focused on the effects of maternal postnatal depression, a recent emphasis has been to understand the specific effects of maternal prenatal depression on child development (Galbally & Lewis, 2017). Importantly, the mechanisms for the effects of pre- vs. postnatal exposures are likely to differ (Galbally & Lewis, 2017) and these exposures should, therefore, be also addressed separately.

Prenatal exposure to maternal psychological stress, such as depression and anxiety, has been associated with alterations in child neurodevelopment and stress regulation systems (Pechtel & Pizzagalli, 2011; Sandman, Class, Glynn, & Davis, 2016; Van den Bergh et al., 2017). Changes in offspring HPA axis function and glucocorticoid receptor sensitivity (Frasch et al., 2017; Loman & Gunnar, 2010), as well as alterations in brain functional and structural development (e.g. cortical thinning, amygdala-prefrontal connectivity), and related problems in attention and emotion regulation have been reported (Dunkel Schetter & Tanner, 2012; Posner et al., 2016; Sandman et al., 2016a; Sandman, Glynn, & Davis, 2016). Moreover, higher rates of symptoms of depression and anxiety as well as attention deficit disorders (ADHD) and conduct disorders have been reported in children with prenatal stress exposure (Glover, 2011; 2015; Van den Bergh et al., 2017). The underlying biological

mechanisms are not well understood (Sandman et al., 2016a, 2016b), but possibly include exposure to inflammatory cytokines and/or excessive levels of cortisol *in utero* (Glover & Capron, 2017) that lead to altered fetal growth and changes in structure and functions of the central nervous systems (Van den Bergh et al., 2017).

In turn, postnatal maternal depressive symptoms, especially if persistent (Sutter-Dallay et al., 2011; van der Wærden, Galéra, Saure-Cubizolles, Melchior, & EDEN Mother-Child Cohort Study Group, 2015) or combined with socio-economic disadvantage (Parsons, Young, Rochat, Kringelbach, & Stein, 2012; Stein et al., 2014), may also influence child social-emotional and cognitive development. This may occur through maternal difficulty responding sensitively and appropriately to a child's needs during early sensitive periods of development (Society CP, 2004; Sohr-Preston & Scaramella, 2006; Sutter-Dallay et al., 2011) leading to dysregulation of child physiological and behavioral responses (Loman & Gunnar, 2010). While there is often some continuity in depressive symptoms from the pre- to postnatal period, the mechanisms through which pre- and postnatal exposures impact the offspring are different. The former acts through shared biological routes between the mother and the fetus, while the latter acts mostly by shaping the psychosocial environment. Pre- and postnatal exposures may also interact so that prenatal exposure programs the offspring development towards increased vulnerability to subsequent postnatal influences (reviewed e.g. by O'Donnell & Meaney, 2017) or so that the adverse effects acquired during prenatal development are exacerbated (or attenuated) by the postnatal environment (Stein et al., 2014).

Of the different aspects of child development that are affected by maternal depression, changes in attention and emotion regulation functions may be particularly consequential for the child's functional outcome. The pathways that regulate attention and stress-responses overlap in the brain, and these developing systems are particularly plastic during pregnancy and in infancy (Loman & Gunnar, 2010). Attention to faces is one of the earliest emerging behavioral traits in infants, and

may reflect a specific form of attention (Haist & Anzures, 2016). While infants orient to faces at birth (Johnson, 2005), the development of this bias and associated specialization of cortical visual systems for face processing are also highly sensitive to postnatal experiences, particularly during the first years of life (Arcaro et al., 2017; Haist & Anzures, 2016; Leppänen & Nelson, 2009; Scerif, 2010). Individual differences in this developmental process and the emerging attentional biases for social signals (e.g., individual differences found in the context of maternal depression) may have important long-term effect on the child's developmental outcome, given the allegedly central role of attention to faces in daily interaction, attachment formation, and interpersonal communication situations (Aktar & Bögels, 2017; Parsons, Young, Murray, Stein, & Kringelbach, 2010).

Newborn infants of mothers with depression have been shown to exhibit cognitive and behavioral markers for self-regulation difficulties (Field, 2010; Luby, Heffelfinger, Mrakotsky, Brown, Hessler, & Spitznagel, 2003), with deviances in their attention processes and interaction in social-emotional situations (Field, Diego, & Hernandez-Reif, 2009; Hernandez-Reif, Field, Diego, & Ruddock, 2006; Sohr-Preston & Scaramella, 2006; Sutter-Dallay, Murray, Glatigny-Dallay, & Verdoux, 2003). These infants seem to be less responsive to faces and voices in general (Field et al., 2009; Field, 2011), and their overall presence is characterized by higher arousal, lower attentiveness, and less "empathy" to social signals (Gentile, 2017; Salisbury et al., 2016). Moreover, these infants show patterns of atypical development such as difficulties discriminating facial expressions and preference for social signals from strangers over their mother's (Bornstein, Arterberry, Mash, & Manian, 2011; Pacheco & Figueiredo, 2012). These behavioral markers may be indicators of delayed attention and cognitive development and/or slower processing of social-emotional information due to exposure to maternal prenatal depression (Field et al., 2009; Figueiredo, Pacheco, Costa, Conde, & Teixeira, 2010; Gentile, 2017).

Early development of attention to faces may continue to be shaped by maternal postnatal symptoms. Mothers with postnatal depression tend to be less sensitive and responsive in their interactions with the infant (Murray, Halligan, & Cooper, 2010; Society CP, 2004; Tronick & Reck, 2009). They use less social speech, touch, and gaze in interaction situations, and express less positive and more neutral or negative affect and intrusiveness during interaction with the infant (Aktar, Colonnesi, de Vente, Majdandžic, & Bögels, 2016; McAndrew, 2017). These problems in maternal communicative behavior during the postnatal period may reflect a longer continuum already present during pregnancy (Pearson, Cooper, Penton-Voak, Lightman, & Evans, 2010). Possibly reflecting infants' sensitivity to these alterations in maternal communicative behaviors, Forssman et al. (2014) showed that infants of mothers with heightened current vs. low depressive symptoms showed relatively reduced disengagement of attention from fearful faces (i.e., enhanced threat bias). Similarly, Morales et al. (2017) reported an association between maternal current anxiety symptoms and infant's heightened bias to angry facial expressions. This hyper-sensitivity of the infant's developing threat-appraisal system may increase vulnerability to environmental stressors.

A number of studies, hence, suggest that infants' attention regulation and face perception is influenced by maternal depressive symptoms (but see Leppänen, Cataldo, Bosquet Enlow, & Nelson, 2018), and that these influences may have their origins in prenatal effects. A conspicuous limitation of the existing studies is, however, that that the evidence for adverse effects is mostly cross-sectional (examining symptoms at one time point) and there have been no studies linking children's attention patterns with more long-term trajectories of maternal symptoms. This question is important given data showing that the child's sensitivity to prenatal influences may be dependent on whether or not the symptoms are carried over to the postnatal phases (Stein et al., 2014).

The Present Study

We examined the processing of emotional faces among eight-month-old infants of mothers with depressive symptoms during the pre- and early postnatal periods. We used eye-tracking combined with an attention disengagement paradigm, previously used in several studies in children at this age-range (e.g. Forssman et al., 2014; Leppänen et al., 2018; Morales et al. 2017, Nakagawa, & Sukigara, 2012; Peltola, Hietanen, Forssman, & Leppänen, 2013) to assess infants' attentional biases for emotional faces, and compared these biases in groups with different trajectories of maternal depression symptoms from pre- to postnatal stages.

Eye-tracking provides a temporally and spatially accurate method for studying attention and emotional processing in pre-verbal infants. At the age of eight months, infants are both able to engage to and disengage attention from faces (Hunnius, Geuze, & Geert, 2006; Hunnius, 2007). Infants at this age orient preferentially to faces and when presented with a face to central visual field, suppress reflexive saccades to other competing stimuli in the visual periphery (Leppänen, 2016). This attentional bias for faces is significantly modified by the emotional content and valence of the face. Infants' preference for faces over non-face patterns is more evident when faces display fearful expressions (Bayet et al., 2017). Moreover, the probability of disengaging attention from faces to competing stimuli is reduced (and the latency increased) in the context of fearful as compared to other emotional expressions (Leppänen & Nelson, 2009; Nakagawa, & Sukigara, 2012; Peltola, Leppänen, Palokangas, & Hietanen, 2008; Peltola et al., 2013). Individual differences in these age-typical attentional patterns may provide information about the personal salience of different emotions at this early age.

To our knowledge, our study represents the first effort to relate infants' attention disengagement from emotional faces with longitudinal data on maternal pre- vs. postnatal depressive symptoms. We examined whether infants' attention to emotional faces, and particularly threat-alerting cues (i.e.,

fearful faces) are associated with maternal depressive symptoms during pregnancy, and whether this association would be sensitive to the trajectory of maternal symptoms from pre- to postnatal stages, as determined by growth modelling. We predicted that infants of mothers with predominantly prenatal symptoms might be more distractible generally (thus disengaging from all central facial stimuli) in the attention-distraction task (as compared to infants with no exposure to maternal depressive symptoms), possibly indicating higher arousal level, weaker endogenous attention control, and less attention to social-emotional stimuli (Field et al., 2009; Huizink et al., 2003; Sohr-Preston & Scaramella, 2006; Van den Bergh et al., 2017). We also hypothesized that maternal depressive symptoms would be associated with heightened bias to threat (i.e. difficulty disengaging from fearful faces), although this bias may be limited to infants of mothers with postnatal depressive symptoms, as reported by Forssman et al. (2014).

METHOD

Participants and design

The participants, all Caucasian, for this study (n=363 mother-infant dyads) were drawn from an ongoing FinnBrain Birth Cohort Study (N=3808 families), a general population pregnancy cohort located in South-Western Finland. The Cohort population represents well the source population of Finland (Karlsson et al., 2018). Recruitment for the whole Cohort took place at the first ultrasound visit at the gestational week (gwk) 12 at three maternal welfare clinics that performed ultrasound scans for the women giving birth at Turku University Hospital in the Southwest Finland Hospital District and the Åland Islands in Finland between December 2011 and April 2015. The inclusion criteria were 1) an ultrasound-verified pregnancy and 2) sufficient knowledge of Finnish or Swedish (the official languages of Finland). The subjects for the present study belonged to a nested case-control population embedded in the main Cohort, i.e. the Focus Cohort, designed to investigate the effects of maternal prenatal stress (PS) on child development. The inclusion for the Focus Cohort required scoring in the highest or lowest approximately 25th percentiles on depression, anxiety, and/or pregnancy-related anxiety symptom questionnaires across pregnancy (see Karlsson et al. 2018 for details of the Cohort). The Ethics Committee of the Hospital District of Southwest Finland approved the study protocol. The study was conducted in full compliance with the Helsinki Declaration.

Infant Neurodevelopmental study

At 8 months postpartum, between May 2013 and June 2016, the Focus Cohort mother-infant dyads were invited to take part in a laboratory visit, where infants' attention to faces expressing different emotions and to non-face patterns was assessed with eye-tracking, along with a laboratory assessment of infant temperament and mother-child interaction during free play. The visits of 1 to 1.5 hours were conducted by psychologists or advanced psychology students in the FinnBrain laboratories at the University of Turku. The parents gave informed consent on behalf of their infant. Parents were

informed about the study details and their option to withdraw from the testing at any time without providing a specific reason.

A total of 908 families in the high- or low–symptom groups were contacted about the participation in the current study. Of these, 694 (76.4%) were reached, and 488 (70.3%) accepted the invitation. Finally, 437 (63.0% of reached, 89.5% of initially agreed) families participated in the laboratory visit; altogether 421 eye-tracking, 427 temperament, and 197 mother-infant-interaction measurements were conducted. The recruited mothers differed from declined mothers in terms of education level (years of education: <12 years, 30.3% vs. 41.4%, 12-15 years, 32.1% vs. 31.6%, >15 years, 37.7% vs. 27.0%, respectively; $\chi^2(2) = 9.02$, $p = .01$, effect size $\eta_p^2 = 0.12$). The declined mothers were more likely multiparous than those who participated (56.9% vs. 45.2%; $\chi^2(1) = 7.06$, $p < .01$, $\eta_p^2 = .10$).

Of the initial 421 infants assessed in the laboratory, 31 (7.4%) failed to either provide data (i.e. were too fussy) or their data was invalid due to technical problems. For the remaining participants, 363 (93.1%; 46.0% girls) provided ≥3 valid trials per each stimulus condition, and were included in the sample. The mean length of gestation in this sample was 39.9 (range 34.4 – 42.3), and the mean age of infants at the time of study visit (from due date) was 8.1 months (range (7.2 – 9.1). The mean age of the participating mothers at the time of delivery was 30.8 years (SD 4.3), 58.3% were primiparous. Educational level (missing information 2.8%) was distributed as follows: 28.1% (< 12 years), 36.2 % (12-15 years), and 33.7% (> 15 years).

Measure of maternal pre- and postnatal depression

Maternal depressive symptoms were assessed three times during pregnancy (gwk 14, 24, 34) and twice postpartum (3 and 6 months) with the Edinburgh Postnatal Depression Scale (EPDS). EPDS is a widely-used questionnaire (see e.g., Gibson et al., 2009), sensitive to both pre- and postnatal

depression, and consists of 10 questions scored on a 4-point Likert scale (from 0 to 3) (Cox et al., 1987). Mothers completed the EPDS along with other questionnaires covering a wide range of information related to maternal well-being during perinatal period and early child development. The questionnaires were either mailed to the participants or filled out on-line. The EPDS showed good internal consistency in our study (α = 0.82 - 0.89).

Trajectories of maternal depressive symptoms

To model the trajectories of maternal pre- and postnatal depressive symptoms we used Latent Growth Mixture Modelling (LGMM; Muthén & Muthén, 2000). In this approach growth curves of depressive symptoms are estimated for each individual, and then prototypic growth curves are identified for the whole sample. The aim is to select the latent curves (i.e. the developmental patterns in symptoms) that most optimally describe the data. Moreover, the interpretability of the latent curves is also used to determine the optimal model. Participants with missing data on depressive symptoms were incorporated in the analyses to minimize bias (Nagin, 2005) by using maximum likelihood under the missing-at-random assumption (Graham, 2009), allowing us to retain data from 362 participants.

First, the factor structure of maternal self-reported depressive symptoms in EPDS during pre- and postnatal period was examined using structural equation modeling. The longitudinal Confirmatory Factor Analysis of the EPDS showed good fit with the data (χ^2 [1050] = 1620.152, p < .001, CFI = 0.92, RMSEA = 0.039, SRMR = 0.066. Consecutive items 1 and 2, 4 and 5, 8 and 9 were allowed to correlate to improve model fit. Second, measurement invariance in EPDS was tested by investigating χ^2 difference between the first and second model with the constrained factor loadings of CFA. The difference in χ^2 between the first and second model was significant, χ^2_{diff} [36] = .01, but the difference between CFI (ΔCFI) was .003, demonstrating adequate invariance in measures across the measurement points (Cheung & Rensvold, 2002).

Then, the number of latent growth curves was established by increasing the number of subgroups in the LGMM models and comparing fit indexes of the outputs with an increasing number of subgroups. Decision about the optimal number of groups was based on Bayesian Information Criteria (BIC, where lower value indicates better model fit; Nylund, Asparouhov, & Muthén, 2007), the posterior probability (i.e., the probability of an individual belonging to a group) for each trajectory group (a score of .80 or above is preferred; Nagin, 2005), and Entropy rate indexing classification accuracy (> .80 indicating excellent accuracy; Lubke, 2007).

The BIC scores continued to improve up to a 5-group model (8931.349 – 8806.672). However, the posterior probability scores as well as Entropy rate improved only up to the 3-group model (posterior probability scores for 3-group model .85/.83/.96; Entropy .85, indicating a good model; Muthén et al., 2002), so we adopted this solution. Moreover, with this solution we were able to retain satisfactory latent group sizes. Thus, the following groups were formed: "Increasing symptoms" (n = 34, Estimate of intercept = 7.75, Estimate of slope = 1.50, p = 0.008), "Decreasing symptoms" (n = 48, Estimate of intercept = 12.19, Estimate of slope = -1.38, p = 0.002), "Consistently low symptoms" (n = 280, Estimate of intercept = 3.23, Estimate of slope = -0.11, p = 0.22).

Eye tracking of infant attention to facial expressions

Procedure

During eye-tracking, the infant sat on his/her parent's lap at the distance of 50–70cm from the eye-tracker (EyeLink1000+, SR Research Ltd, Toronto, Ontario, Canada). A sampling frequency of 500Hz was used. A five-point calibration procedure, with an audiovisual animation sequentially presented in five locations on the screen, was used before every measurement. This could be repeated at least two times before actual testing and also during measurement when necessary. Small breaks were allowed during measurement, if necessary. The researcher sat in the same, dimly lit room as the

infant and parent but was separated by a curtain to avoid interference. The researcher used another independent computer to manage the measurement.

Gaze acquisition and raw data processing

The overlap paradigm (Aslin & Salapatek, 1975; Peltola et al., 2008) was used to study infant attention disengagement from a centrally presented face or a scrambled face control stimulus to a lateral distractor. The infants were shown photographs of two different women portraying happy, fearful, and neutral faces together with scrambled non-face control pictures (Peltola et al., 2008). Altogether, a set of 48 trials were presented, including 12 trials per condition (each emotion and the control picture) and comprising 18 photographs of each woman, and 12 non-face control pictures, in a semi-random order.

During the experiment, the infants were first shown a picture of a face (or a non-face control stimulus) in the center of the screen for 1000ms (Figure 1). Then, a lateral distractor (black and white checkerboard or circles) appeared on either left or right side of the face (a visual angle of 13.6°) for 3000ms, simultaneously with the face. One trial lasted for 4000ms. The sizes of the emotion-depicting pictures and distractor stimuli were 15.4° x 10.8° and 15.4° x 4.3°, respectively. A brief animation was shown after each trial to capture the attention of the infant to the center of the screen. Once the infant's gaze was in the middle of the screen, the next trial was presented by the researcher. The order of the central stimuli was semi-randomized, with a constraint that the same stimulus was not presented more than three times in a row. The lateral stimulus was selected and presented randomly for each trial.

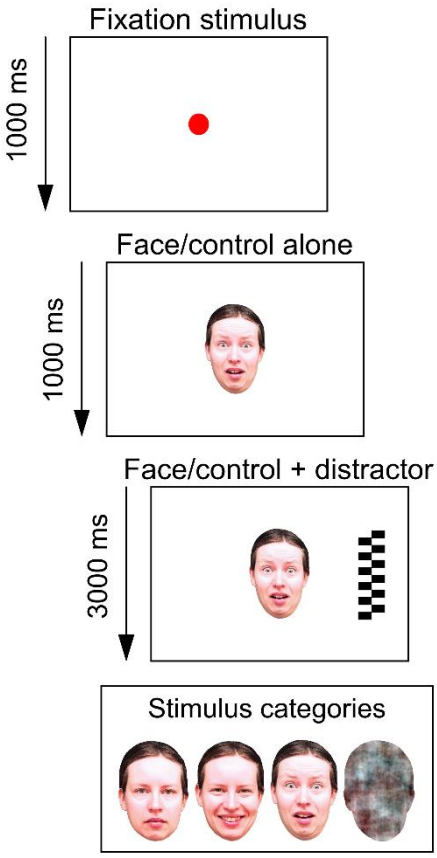


Figure 1 The overlap paradigm. A face or a control stimulus was presented in the center of the screen after the infant fixated on a fixation stimulus. A distractor appeared to the right or to the left side of the central stimulus after 1000ms from face/control onset. The central stimulus was presented until the end of each trial (4000ms), overlapping in time with the distractor. (Figure reproduced from Yrttiaho et al., 2014, https://doi.org/10.1371/journal.pone.0100811.g001 under the terms of the creative commons attribute license.)

The trial data, comprising of timestamps for the onset times of central and lateral pictures and the xy coordinates of the participants' gaze position (500 samples/second) were stored as text files, and analyzed offline using a library of Matlab (Mathworks, Natick, MA) scripts (Leppänen, Forssman, Kaatiala, Yrttiaho, & Wass, 2015). We used the following quality control criteria based on prior studies (Leppänen et al., 2015) to retain trials for the analysis. First, trials had to have sufficiently long fixation on the central stimulus (i.e., >70 % of the time) during the time preceding gaze disengagement or the end of the analysis period (i.e., 1000ms from the appearance of the lateral distractor). Secondly, trials had to have a sufficient number of valid samples in the gaze data (i.e., no gaps >200 ms). Thirdly, trials had to have valid information about the eye movement from the central to the lateral stimulus (i.e., the eye movement did not occur during a period of missing gaze data).

Eye-tracking variables

Only the retained trials were included in the statistical analysis. A binary disengagement variable, indicating whether there was an attention disengagement from the central to the lateral stimulus or not, was used in our statistical models as the response variable when the disengagement probabilities (DPs) were estimated. The average number of scorable trials in the eye-tracking tests (8.7–9.4/condition) did not have statistically significant difference ($p > 0.05$) across the EPDS symptoms groups.

Statistical methods for modeling the disengagement probabilities

The possible differences in DPs were investigated in the three groups of infants, with the infants of mothers with consistently low symptoms as the reference group. All the statistical models are presented as Appendix. The results of these analyses are presented in Results section.

As there were large individual differences in the infants' overall DPs in our sample (Figure S1), we decided to model the DPs using mixed effects logistic regression (MELR) models with random intercept for each infant.

The DPs were dependent on the trial number (Figure S2) so trial number was included in our MELR models. Furthermore, due to the possibility that the trial number dependency would vary by condition, we modeled the trial number dependency by fitting a natural cubic spline with one cut-point between trials 24 and 25, separately for each condition. That is, we included main effects of trial number spline and condition with their interaction in our first model (Model 1). We also compared Model 1 to a model without the interaction terms (Model 0), using likelihood ratio test (as in all the following model comparisons), to find out if the trial number by condition- interaction was statistically significant.

Next, we constructed Model 1.1 by adding latent EPDS growth curve group (EPDS group) main effect to Model 1 and Model 2 by adding EPDS group main effect and its interaction with condition to Model 1. Model 1.1 was then compared to Model 1 to test the main effect of EPDS group, i.e. to test if the overall DPs are different in different EPDS groups. Furthermore, Model 2 was compared to Model 1.1 to test the interaction of condition and EPDS group. We also constructed Model 3 by adding all possible interactions with trial number spline to Model 2 (see Appendix for the details). By comparing Model 3 to Model 2, we were then able to test if the trial number dependency was different for different EPDS groups. Finally, we constructed Model 4, by adding child gender main effect and all interactions between gender, condition, and EPDS group to Model 2, and then compared it to Model 2 to find out if the effect of EPDS group on the DPs was different for boys and girls.

We also carried out comparable analyses to previous studies (e.g. Forssman et al., 2014; Peltola et al., 2015), where the trial number dependency has not been taken into account. That is, we constructed Models 1b, 1.1b and 2b which were similar to Models 1, 1.1 and 2, respectively, but without the trial

number terms. Models 2b and 1.1b were then compared to Model 1b to find out if EPDS group was associated with the DPs when the trial number effect was not taken into account..

Next, we performed post-hoc tests with Models 1.1b and 2b to analyze our hypotheses 1 and 2. That is, we contrasted overall DPs and fear bias between the EPDS groups of Increasing vs. Decreasing, Increasing vs. Low, Decreasing vs. Low and Increasing and Decreasing vs. Low, i.e. we made four post-hoc tests concerning each hypothesis. Holm-Bonferroni method (Holm, 1979) was used to control the family wise error rate when assessing the statistical significance of the post-hoc tests.

The fear bias was defined here as the difference between infants' tendency to disengage from fearful condition and their tendency to disengage from neutral/happy condition (i.e. infants who had [much] higher probability to disengage from happy/neutral condition than from fearful condition had high fear bias). Technically, the fear bias was defined as the ratio of the odds to disengage from the happy/neutral condition to the odds to disengage from fearful condition.

As the exclusion of infants born < 37 gwk (n=15, data from national birth registries, National Institute for Health and Welfare, www.thl.fi) from the full sample (N=362) did not alter the results, the final analyses were conducted with the full sample. The analyses were run using R (R Core Team, 2017) with package lme4 (Bates et al, 2015). Figures 3-4 were made using R package ggplot2 (Wikham, 2009).

RESULTS

The mean level of maternal depressive symptoms in the three latent groups based on the trajectories of EPDS symptoms

The mean level of maternal depressive symptoms in each depressive symptom group (Decreasing, n=48, Increasing, n=34, Consistently low, n=280) at each assessment point is presented in Figure 2. The symptom levels differed across the three groups in all assessment points (Bonferroni corrected p

values < 0.01) except at gwk 34 where the mean level of symptoms was equal between the decreasing and increasing symptoms groups (p = 0.25).

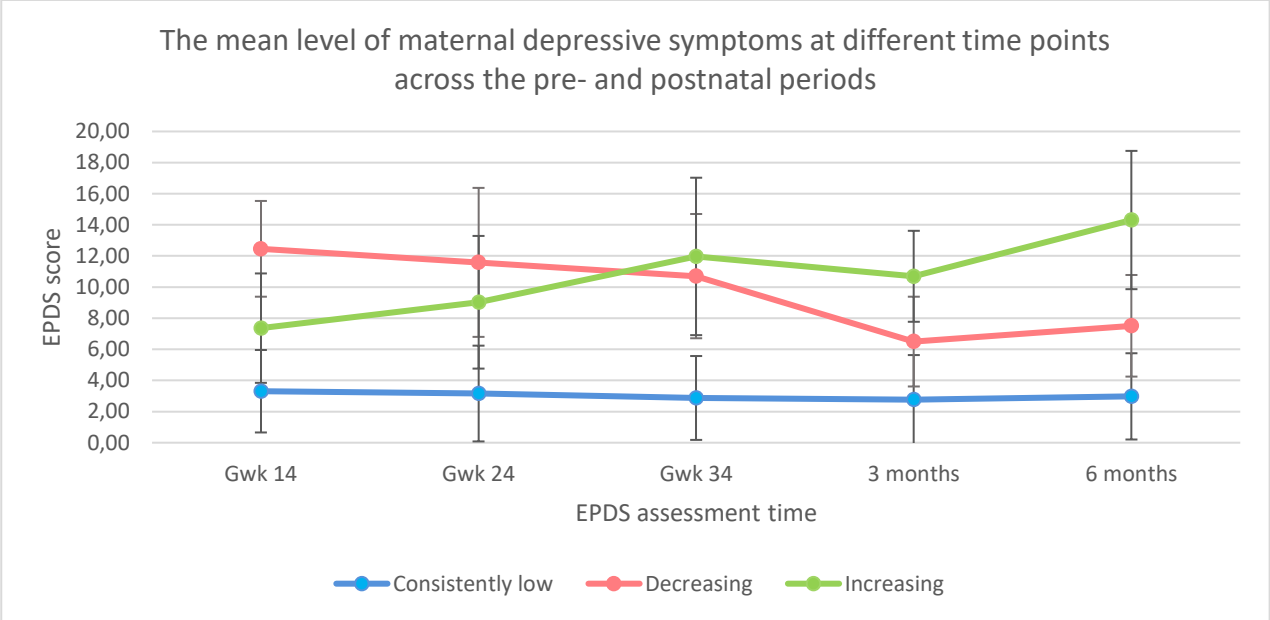


Figure 2 The mean level of maternal depressive symptoms (EPDS) for the three groups of infants classified according to the maternal depressive symptom trajectories. Error bars represent standard deviations.
Note. The correlations (Spearman *r*s) between maternal depressive symptoms at consecutive time points varied between .60–.71 (p < .001).

The overall DPs in the whole infant sample and their dependence on trial number

The predicted values from Model 1 are shown in Figure 3a. The DPs were highest for the control stimulus and lowest for the fearful condition. The DPs for the happy and neutral conditions were between those and approximately equal to each other.

Similarly to Peltola et al. (2008), the reaction times (i.e. latency [ms] for gaze shift to the lateral distractor after its appearance excluding trials with no gaze shift) were longest for fearful (M =

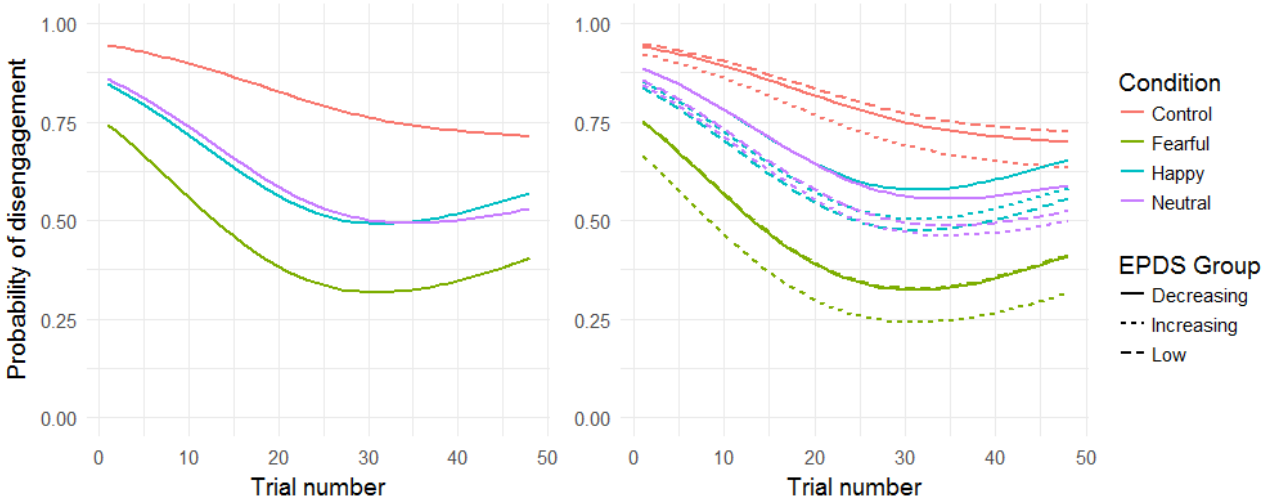
411.63, SD = 172.81), following happy (M =382.02, SD = 158.36) and neutral (M =388.48, SD = 159.83) faces, and shortest for control stimuli (M = 338.76, SD = 138.71).

Figure 3a also shows the trial number dependency of the DPs (i.e., a clear decline in DP until the midpoint of the experiment). Comparing Model 1 to Model 0 yielded a significant interaction between stimulus condition and trial number (χ_6^2 = 13. 317, p = 0.038), reflecting the fact that the DPs for non-face patterns continued to decrease even after the midpoint of the experiment whereas the DPs of the three face conditions started to slightly increase towards the end of the experiment. The three face conditions did not differ in trial-number effects.

The overall DPs for the three different groups of infants

Comparison of Model 3 and Model 2 showed that there was no evidence of the association between EPDS group and trial number dependency of the DPs (χ_{16}^2 = 12.42, p = 0.71).

Figure 3b shows the predicted values for Model 2. We first tested our hypothesis 1. Comparing Model 1.1 to Model 1 showed that the overall DPs were not different for different EPDS groups when trial number was controlled for (χ_2^2 = 1.71, p = 0.43). And similarly comparing Model 1.1b to Model 1b showed that the difference was not significant when trial number was not included in the models (χ_2^2 = 1.67, p = 0.43). Although the infants of mothers with increasing symptoms seemed to have overall lower DPs than the infants of mothers with decreasing symptoms (Figure 4), post-hoc comparisons between the groups showed that the difference was not statistically significant (Table 1).



Figures 3a (left) and 3b (right) The predicted DPs for the whole sample (Model 1; 3a) and for the three different groups of infants (Model 2; 3b) when trial number spline and condition main effects and their interaction are included in the model.

The DPs in different stimulus conditions and fear bias in the three different groups of infants

Comparing Model 2 to Model 1.1, and Model 2b to Model 1b, showed that the interaction between the EPDS group and condition was statistically significant when trial number was controlled for (χ^2_6 = 19.32, p = 0.0037) and when not (χ^2_6 = 18.08, p = 0.0060), respectively. However, the significant interaction was not driven by any of the individual conditions (see Table 2 for post-hoc comparisons between the three groups of infants in different stimulus conditions, and Figure 4 for illustration of the predicted DPs) .

All predicted DPs from Model 2 are given in Figure 3b, and predicted DPs for one selected trial [25] in the middle of the experiment are given in Figure 4a. Figure 4b shows the predicted DPs from Model 2b.

Then we tested our hypothesis 2 by comparing the fear bias between the EPDS groups. The infant groups of symptomatic mothers (the EPDS groups of “Decreasing” and “Increasing” symptoms)

showed greater fear bias than the reference group (p = 0.015 and p = 0.016, respectively, and the results were statistically significant after applying Holm-Bonferroni method). All comparisons are presented in Table 1. Figure 4c illustrates the fear bias in three different groups of infants.

Finally, we compared Model 4 to Model 2 but observed no sex difference in the DPs (χ^2_{12} = 3.98, p = 0.98).

Table 1 The results (OR, p values) of the post-hoc comparisons of the overall disengagement probabilities (DPs) and Fear bias between the three different groups of infants (EPDS groups of Increasing, Decreasing, and Low symptom levels)

EPDS Group	**Overall**		**Fear bias**	
	OR[1)]	p value[2)]	Ratio of ORs[3)]	p value[2)]
Increasing vs. Decreasing	0.73	0.20	1.05	0.80
Increasing vs. Low	0.85	0.42	1.49	0.016*
Decreasing vs. Low	1.04	0.36	1.41	0.015*
Increasing and Decreasing vs. Low	1.00	0.99	1.45	0.0013*

[1)] Ratio between the overall disengagement odds in the first and the second group.

[2)] All p-values are uncorrected.

[3)] Ratio of fear bias (odds) between the first and the second group.

The p-values of the tests where null hypothesis was rejected after applying the Holm-Bonferroni method are marked with asterisk (*)

Table 2
The results (OR, p values) of the post-hoc comparisons of the disengagement probabilities (DPs) in different face conditions between the three different groups of infants (EPDS groups of Increasing, Decreasing, and Low symptom levels)

	Control		**Neutral**		**Happy**		**Fearful**	
EPDS Group	OR[1)]	p-value[2)]	OR[1)]	p-value[2)]	OR[1)]	p-value[2)]	OR[1)]	p-value[2)]

Increasing vs. Decreasing	0.75	0.35	0.71	0.23	0.75	0.33	0.69	0.20
Increasing vs. Low	0.69	0.13	0.91	0.70	1.15	0.55	0.69	0.11
Decreasing vs. Low	0.91	0.68	1.30	0.20	1.52	0.04	1.00	0.99
Increasing and Decreasing vs. Low	0.80	0.19	1.09	0.60	1.32	0.08	0.83	0.25

[1] Ratio between the overall disengagement odds in the first and the second group.
[2] All p-values are uncorrected for multiple comparisons.

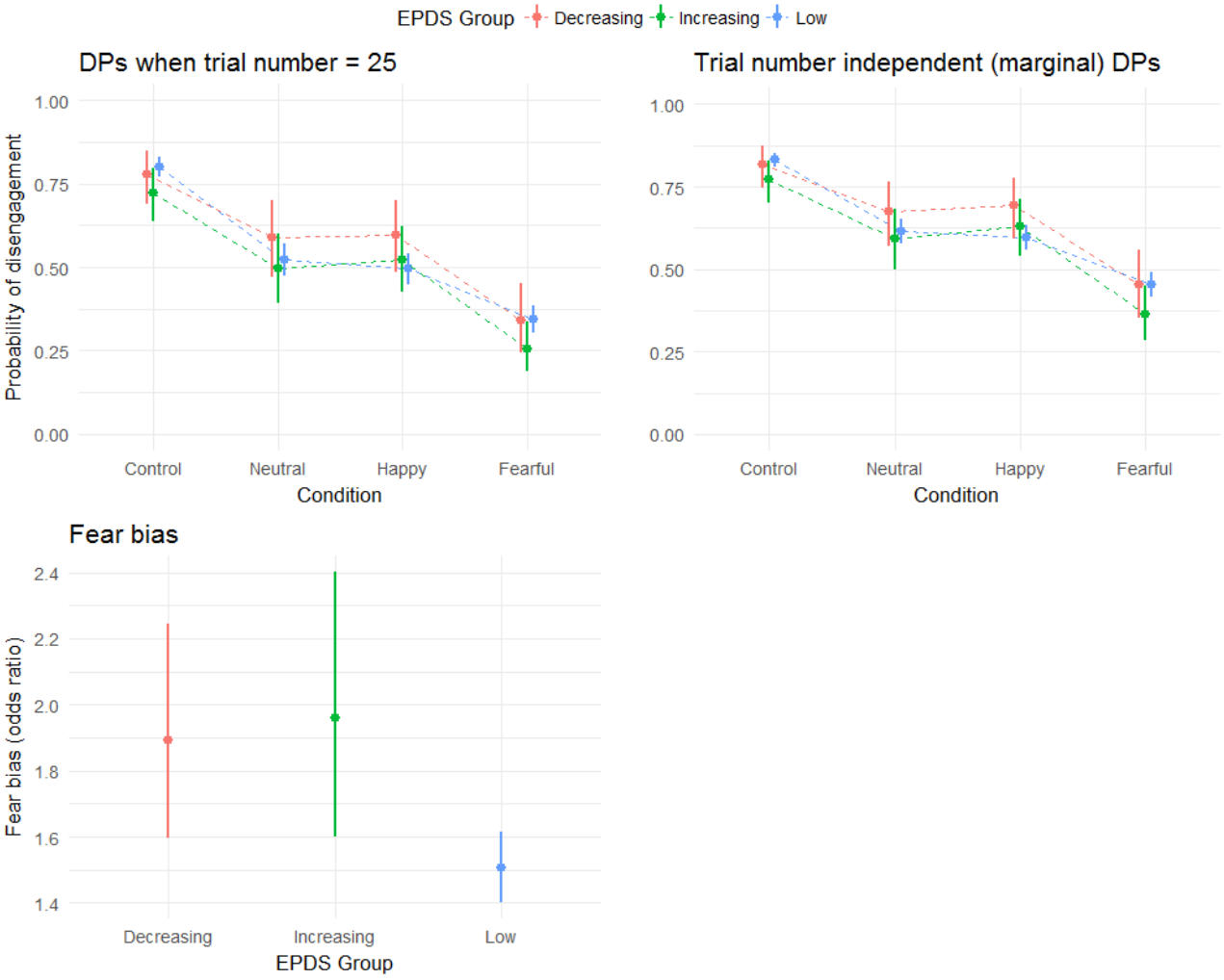


Figure 4a (upper left) and 4b (upper right) The predicted DPs (for infants for whom the random effect is zero) in three different groups of infants when the trial number is 25 (Model 2; 4a) and trial number independent (marginal) DPs predicted by Model 2b (4b). The predicted probabilities are presented with 95% confidence intervals (uncorrected for multiple comparisons). *Note*. We chose trial 25 in the middle of the experiment to illustrate the predicted DPs when the trial number is taken into account, because the overall DPs were roughly at an average level on this trial, making it easier to compare the predictions of the models with and without the trial number. *Figure 4c* (lower panel) illustrates the fear bias in three different groups of infants

DISCUSSION

In this study, we examined the processing of emotional faces among eight-month-old infants of mothers with increasing, decreasing, or low depressive symptom levels (i.e. three latent groups based on the trajectories of EPDS symptoms) during the pre- and early postnatal periods. Based on earlier literature, we first hypothesized that infants exposed to maternal prenatal depressive symptoms would show more attention distractibility (thus disengaging from all central facial stimuli) in the attention-distraction task. Second we hypothesized that maternal depressive symptoms would be associated with heightened bias to threat, but that this bias would be limited to infants of mothers with postnatal depressive symptoms.

We did not find support for our first hypothesis. Although the estimated DPs appeared to be higher for the infants of the decreasing symptoms group (thus exposed predominantly to prenatal symptoms; Figure 4b), this difference was not statistically significant. However, our second hypothesis was supported by the current results. The infants of symptomatic mothers, that is increasing and decreasing symptoms groups, showed heightened fear bias (the ratio of odds to disengage from the happy/neutral condition / the odds to disengage from fearful condition) as compared to the infants of mothers with consistently low symptom levels. This finding supports earlier studies showing that maternal depression may alter infant social-emotional processing by exacerbating threat processing. However, we extend previous research by showing that this heightened bias for threat may also be related to exposure to maternal prenatal symptoms.

Interestingly, Leppänen et al., (2018) did not find a relation between moderate variations in maternal depressive or anxiety symptoms and infant threat biases. The authors concluded that the sample characteristics (high SES, low variability in symptoms) as well as methodological differences in assessing maternal symptoms might have led to the discrepancy between their and previous study results.

In earlier studies, prenatal exposure to maternal psychological distress has been associated with adverse development of the child's stress regulation systems, higher order cognitive abilities, and general attention regulation (Sohr-Preston & Scaramella, 2006; van den Bergh et al., 2017). These infants have been characterized as 'fussier' and less attentive in general, but also when processing social-emotional information or interacting with the parent or stranger (Field et al, 2006; Field, 2011). Higher stress reactivity (as indicated by autonomic nervous system arousal) seems to lead to a faster, more stimulus-driven attention profile in infancy (de Barbaro, Clackson, & Wass, 2016; Wass, de Barbaro, Clackson, & Leong, 2018) and/or problems in habituating to repeated visual stimuli (de Barbaro, Chiba, & Deak, 2011). We expected that in the overlap paradigm this might be manifested as higher tendency to disengage attention from the central stimulus to a lateral distractor. This was not supported by the current results. So, therefore, it may be that face processing represents a specific form of attention in infancy. Disruption in the general control of attention or problems in regulating overall arousal levels might not be manifested in the overlap paradigm with emotional faces and distractors. Alternatively, it may be that our sample was underpowered to detect small differences in the general DPs of the infant groups, due to relatively small groups of infants of mothers with pre- or postnatal depressive symptoms. Further studies could test our hypothesis in larger infant samples, and also in samples with more severe levels of maternal prenatal depression.

Our second hypothesis was that infants of mothers with postnatal depressive symptoms would show heightened threat bias, as some, but not all (Leppänen et al., 2018), earlier studies have found that postnatal maternal depressive (Forssman et al., 2014) and anxiety (Morales et al., 2017) symptoms exacerbate infant's attention bias to threat. Extending previous research, we found that the infants of the increasing symptoms group (exposed predominantly to postnatal maternal depressive symptoms) and also the infants of the decreasing symptoms group (exposed to prenatal maternal depressive symptoms) showed higher bias for fearful faces as compared to the infants of the mothers with consistently low symptoms. Future studies should test whether underlying genetic factors explain

maternal symptoms of depression (both pre- and postnatal) and infant attention for threat, irrespective of the timing of exposure to maternal symptoms. Alternatively, there may be independent prenatal and postnatal effects but both lead to similar outcomes in the child, in this case heightened attention bias to threat. Disentangling the pre- and postnatal exposures remains an important aspect of future studies on infant attention development.

It should be noted that in our sample, the infants of the decreasing symptoms group were exposed predominantly to maternal prenatal depressive symptoms and the infants of the increasing symptoms group predominantly to postnatal symptoms. However, as can be seen from Figure 2, the level of maternal symptoms was actually equal in late pregnancy assessment between these two groups, although the long-term symptom courses appeared distinct. Moreover, the symptom level of the decreasing group remained elevated also postnatally, compared to the reference group (consistently low symptoms). These identified trajectories of maternal depressive symptoms (i.e. decreasing and increasing symptom levels, but not explicitly "prenatal-only" and "postnatal-only" symptoms) in our sample might have prevented us from detecting a significant relation between prenatal exposure to maternal depressive symptoms and infant's general distractibility of attention (hypothesis one). Alternatively, there is a possibility that exposure to maternal prenatal symptoms does not affect the distractibility of attention at least in infancy, and in specific situations where faces are being processed.

The early-life environment, and especially the caregiving received, significantly contributes to how the child's stress and attention regulation systems and their interconnections develop (Loman & Gunnar, 2010). One may speculate that maternal symptoms of depression at some stages of pregnancy and postnatal period are associated with changes in her caregiving, and constitute a source of repeated stress to the infant. This may push the development of threat detection systems towards hypersensitivity to environmental threats (Feldman et al., 2009; Loman & Gunnar, 2010). For

instance, the unpredictable, less positive interactive style found among mothers with depression, changing erratically from negative and intrusive to withdrawn, may enhance child vigilance towards social signals and threat. Later, this bias in the attention systems, especially if combined with certain temperament styles or genetic predispositions (Papageorgiou & Ronald, 2017) may predispose the child to a risk for later self-regulation problems and psychopathology. Evaluating parent-child–interaction patterns and also different parenting components that might be impaired by maternal depressive affect among these mother-infant pairs might shed more light on our findings.

Based on earlier studies, children at high familial risk for depression seem to show early patterns of depressotypic information processing style with abnormal patterns of neural activation and brain structure development (Gotlib, Joormann, & Foland-Ross, 2014; Pagliaccio, Pine, Barch, Luby, & Leibenluft, 2018). These findings may be generalized to more general emotion perception in children at high risk for depression. Our results indicate that children at risk for self-regulation problems and mental health disorders based on their mothers' history of depressive symptoms may show very early deviances from their peers in how they attend to emotional faces. Long-term follow-up of the same infants is needed in order to understand the relevance of our findings and their implications for child social-emotional and mental health development.

Finally, consistent with prior studies (e.g., Ahtola et al., 2014; Leppänen et al., 2011), the current results showed that infants' probability of disengaging from the central to the lateral stimulus declined over the course of the experiment, possibly reflecting habituation or learning. These changes tended to be more pronounced in the three face conditions (as compared to the non-face, control condition). Given these effects, we investigated the possibility that the differences in attention patterns between the groups would be due to differential trial-related changes during the experiment (for example, instead of an attentional bias towards fearful faces, reduced disengagement from fear in infants of mothers with increasing symptoms may reflect differential changes in attention to faces over the

course of the experiment). However, we did not find evidence for this, as there was no difference across the infant groups between disengagement probability and trial number (Figure 3b). This suggests that the differential attention disengagement patterns between the three groups of infants reflect genuinely attentional phenomena, not differential "trial effects" or changes in behavior during the experiment.

Conclusions

In the current study we found that infants exposed to maternal pre- or postnatal depressive symptoms compared to continuously low symptoms levels showed heightened fear bias (lower probability of disengagement from fearful faces as compared to other faces). This supports earlier findings where the postnatal environment or maternal symptoms of depression or anxiety have been found to exacerbate infant threat processing. This study extends previous research in showing that threat bias may be also prevalent among infants exposed to prenatal symptoms, in addition to postnatal exposure. However, contrary to what we hypothesized, the infants exposed predominantly to maternal prenatal depressive symptoms did not differ in their overall disengagement probability, that is in distractibility on the attention-distraction paradigm. It may be that face processing, in its importance for our survival and well-being (Haist & Anzures, 2017), override the possible general attention related problems and difficulties in regulating overall arousal levels at this age. This could be tested in the future in larger samples of infants, and with more severe maternal symptoms levels.

Limitations

In this study, maternal depressive symptoms were self-reported. Nevertheless, questionnaires, and moreover continuous measures of maternal symptoms of distress are consistently used in similar developmental studies (Dunkel Schetter & Tanner, 2012; Stein et al., 2014). We used repeated assessment of the same symptoms, strengthening our measure of maternal mood during pre- and

postnatal periods. While we were able to show a clear relationship between maternal depressive symptom trajectories and infant attention outcomes, we cannot elucidate the mechanisms and possible moderating and mediating factors between the two. For instance, it may be that maternal depressive symptoms, combined with anxiety, may change the interactive patterns between the mother–infant dyads and also alter infant attention to faces (reviewed in: Aktar & Bögels, 2017), and may explain part of our results of the differential attention patterns of the infants. However, here we decided to restrict the scope only to maternal depressive symptoms, as depression and anxiety seem to have differential impacts on face and threat processing (Armstrong & Olatunji, 2012). Finally, the magnitudes of associations were small, and long-term follow-ups are needed to evaluate the functional relevance of our findings for child development.

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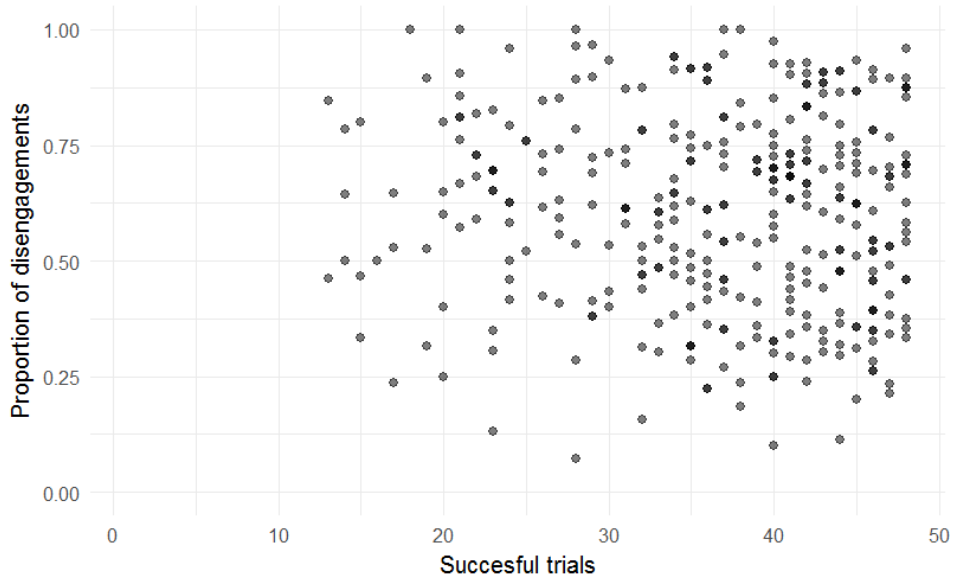
SUPPLEMENTARY MATERIAL



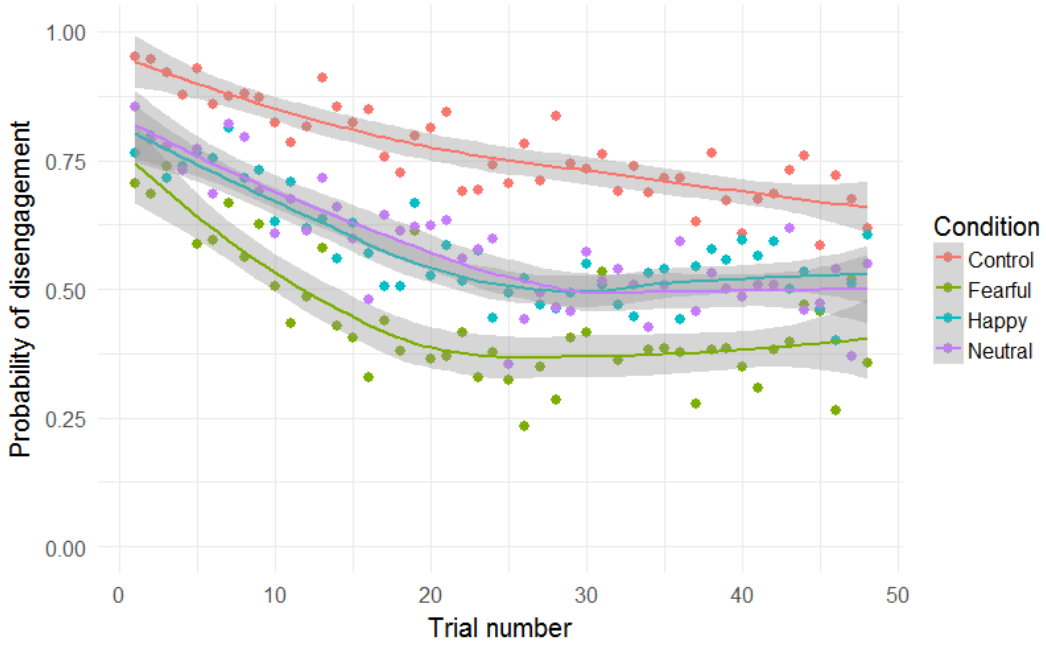


Figure S1 Each infant's observed disengagement proportions plotted against the number of valid trials, illustrating the large individual differences in the infants' overall DPs. Figure S2 The observed proportions of disengagements (for the whole sample) plotted as a function of trial number for each condition, illustrating the dependence of the DPs on the trial number.

APPENDIX

Fixed effects in the mixed effects logistic regression models

All the mixed effects logistic regression models used to analyze the DPs included a random intercept for each infant as the only random effect. The fixed effects used in each model are given below:

Model 0: Condition + TNS

Model 1: Condition + TNS + Condition×TNS

Model 1.1: Condition + TNS + EPDSG

Model 2: Condition + TNS + Condition×TNS + EPDSG + Condition×EPDSG

Model 3: Condition + TNS + Condition×TNS + EPDSG + Condition×EPDSG + TNS×EPDSG + Condition×TNS×EPDSG

Model 4: Condition + TNS + Condition×TNS + EPDSG + Condition×EPDSG + Sex + Condition×Sex + EPDSG×Sex + Condition×EPDSG×Sex

Model 1b: Condition

Model 1.1b: Condition + EPDSG

Model 2b: Condition + EPDSG + Condition×EPDSG

Explanations:

Condition = Categorical variable with four levels (Control, Happy, Neutral and Fearful)

TNS = Trial number spline terms, i.e. s*um of two* natural cubic spline terms.

EPDSG = EPDS growth curve group; categorical variable with three levels (Decreasing, Increasing and Low)

Sex = Categorical variable with two levels (Boy and Girl)