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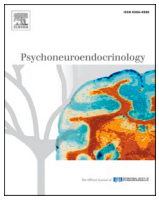

Neural processing of cry sounds in the transition to fatherhood: Effects of a prenatal intervention program and associations with paternal caregiving

Sandra Thijssen [a,*], Kim Alyousefi-van Dijk [b], Noor de Waal [c], Marinus H. van IJzendoorn [d], Marian J. Bakermans-Kranenburg [e,f]

[a] Behavioural Science Institute, Radboud University Nijmegen, the Netherlands
[b] Anna Freud National Centre for Children and Families, 4-8 Rodney St, London N1 9JH, UK
[c] Department of Developmental Psychology, Tilburg University, Tilburg, the Netherlands
[d] Department of Psychiatry, Monash University, Melbourne, Australia
[e] ISPA - University Institute of Psychological, Social and Life Sciences, Lisbon, Portugal
[f] Department of Psychology, Personality, Social and Developmental Psychology, Stockholm University, Stockholm, Sweden

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ABSTRACT

This study examined whether neural processing of infant cry sounds changes across the transition to fatherhood (i.e., from the prenatal to postnatal period), and examined whether an interaction-based prenatal intervention modulated these changes. Furthermore, we explored whether postnatal activation in brain regions showing transition or intervention effects was associated with sensitive care and involvement. In a randomized controlled trial, 73 first-time expectant fathers were enrolled, of whom 59 had at least 1 available fMRI scan. Intervention and transition effects on cry processing were analyzed in the amygdala and superior frontal gyrus (SFG) using linear mixed effect models with all available data and with intent-to-treat analyses. Further, exploratory whole-brain analyses were performed. ROI analyses suggest that the transition to fatherhood is characterized by *decreasing* activation in response to cry vs control sounds in the amygdala but not SFG. Exploratory whole-brain analyses also show a *decrease* in activation over the transition to fatherhood in the sensorimotor cortex, superior lateral occipital cortex, hippocampus, and regions of the default mode network. In the putamen and insula, larger decreases were found in fathers with more adverse childhood caregiving experiences. In regions showing transitional changes, *higher* postnatal activation was associated with more concurrent parenting sensitivity. No effects of the intervention were found. The decrease in activation from the pre- to postnatal period may reflect fathers' habituation to cry sounds over repeated exposures. The positive association between postnatal neural activation and paternal sensitive care suggest that continued sensitivity to cry sounds may be conducive to parenting quality.

1. Introduction

Over the last decades, the role of fathers has significantly changed. From relatively uninvolved bread winners in the 1970's, in many families fathers now make a significant contribution to child care. Despite their significant role in caretaking, support for fathers-to-be is still in its infancy. While many programs exist to support woman in their transition to motherhood, few prepare men for their role as father. As the first 1000 days in the life of the child are particularly important in shaping their development (Berg, 2016), guiding fathers in their transition to parenthood may significantly support child development. In order to help expectant fathers improve their parenting skills and to stimulate paternal involvement, we developed a prenatal video-feedback intervention for fathers-to-be (Alyousefi-van Dijk et al., 2022). Here we examined the effects of this interaction-based intervention program on changes in the neural processing of infant crying from the prenatal to postnatal period.

The Video-feedback Intervention to Promote Positive Parenting-Prenatal (VIPP-PRE) is a brief and interaction-focused intervention for expectant fathers based on the evidence-based postnatal intervention program VIPP (Juffer et al., 2017). VIPP is grounded in attachment theory (Ainsworth, Bell, and Stayton, 1974; Bowlby, 1982) and aims to

* Correspondence to: PO Box 9104, Nijmegen 6500 HE, the Netherlands.
E-mail address: sandra.thijssen@ru.nl (S. Thijssen).

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enhance caregiver sensitivity using videotaped recordings of parent–child interactions. VIPP-PRE is the adapted program for men in the transition to fatherhood. In VIPP-PRE, fathers are encouraged to interact with their unborn babies. The babies' reactions are visualized using ultrasound imaging, and both father and child are videotaped to allow reviewing and feedback in later sessions (for two case studies, see de Waal et al., 2022). Compared to the control condition, fathers taking part in VIPP-PRE reported more insight into the relationship with their baby and the feelings of their baby, (Alyousefi-van Dijk et al., 2022), and importantly, showed increased sensitive parenting from the pre- to postnatal period (Buisman et al., 2022).

Parental sensitivity refers to caregivers' abilities to accurately observe and interpret the signals of a child, and to react promptly and appropriately to such signals (Ainsworth et al., 1974). In the early postnatal phase, infants' crying is one of their few signals to communicate distress. It is, however, a two-sided coin. Besides eliciting sensitive care, crying can also elicit aversion and anger, and even trigger child abuse and neglect (Barr et al., 2006). How parents process infant crying may be an important predictor of their behavioral response. As VIPP-PRE has been shown to affect parental sensitivity across the transition into parenthood, we hypothesize that VIPP-PRE may also affect neural processing of infant crying.

A meta-analysis of studies on cry processing suggests that the neural response to crying may involve at least four neural circuits: an auditory circuit, the thalamocingulate pathway, a salience network, and a motor network (Witteman et al., 2019). According to this model, cry processing starts with the auditory cortex performing an acoustic analysis of infant cries. Second, the thalamocingulate pathway may shift attention to this potentially salient signal. Third, the dorsal anterior insula may further support salience detection and the focusing of attention while the medial superior frontal gyrus, the triangular and orbitofrontal cortex may assist in evaluating the emotional information and mentalizing. Last, a motor network including the basal ganglia, the medial superior frontal gyrus and the lateral motor areas may initiate, plan, and execute the parental response. To our knowledge, no studies have examined the change in neural cry processing from the prenatal to the postnatal period, but studies comparing parents to non-parents suggest that parents show a stronger neural response to infant crying (Witteman et al., 2019).

Individual differences in cry processing are related to parental behaviors. In mothers, greater activity in the superior frontal cortex and amygdala to her own baby's cry (versus control baby's cry) was associated with higher sensitivity (Kim et al., 2011). Moreover, in fathers, negative emotional reactions to crying were associated with decreased activation in the thalamus and caudate nucleus, as well as increased activation in the hypothalamus and dorsal anterior cingulate cortex (Li et al., 2018). Swain et al. (2017) found increased precuneus activation and connectivity for mothers who took part in an attachment-based parenting intervention to decrease maternal distress. Finally, maternal mental state talk (i.e., a mother's proclivity to attribute mental states and intentionality to her infant) has been found related to increased activity in the right frontoinsular cortex, thalamus, amygdala, hippocampus and putamen during own infant crying (Hipwell et al., 2015).

Attachment-based interventions may be particularly powerful for individuals at risk for displaying lower levels of parental sensitivity, such as adults who have experienced maltreatment. As a history of maltreatment has been associated with greater behavioral and autonomic response to infant crying (Buisman et al., 2018; Verhees et al., 2021), aberrant processing of crying may be one of the mechanisms linking maltreatment history to current maladaptive parenting. Indeed, history of maltreatment has been associated with neural cry processing, i.e. divergent amygdala activation and connectivity (Olsavsky et al., 2021; Riem et al., 2021), and cingulate, insula, precentral, and parietal activation (Wright et al., 2017).

The present study examined whether neural processing of infant cry sounds changes across the transition to fatherhood, and examined whether VIPP-PRE influences these changes. Moreover, we examined whether transition and intervention effects depend on fathers' adverse childhood care experiences. Finally, we explored whether postnatal activation in brain regions showing significant transition or intervention effects was associated with paternal sensitivity and involvement. Because cry processing in the amygdala and superior frontal cortex has previously been associated to observed parental sensitivity (Kim et al., 2011), initial analyses were performed in these regions. These region-of-interest (ROI) analyses were supplemented by exploratory whole-brain analyses. We expected that fathers would show greater activation in neural networks involved in cry processing during the postnatal compared to the prenatal phase. Moreover, we expected larger changes in the intervention condition, and greater intervention effects for individuals reporting adverse caregiving experiences. Finally, we expected that higher postnatal activation in regions showing an increase in neural activation to cry sounds over the pre- to postnatal transition would be associated with more sensitive interaction or more involvement with the infant.

2. Methods

2.1. Participants and procedure

Participants were recruited via midwives and (online) advertisements. Participants had to be first-time expectant fathers and had to cohabitate with first-time expectant partners, as well as speak Dutch; they were excluded if they self-reported current psychiatric symptoms or medication. Partners had to have an uncomplicated pregnancy of a singleton with a pregnancy duration of 18–31 weeks at the time of inclusion. Fathers were excluded when their partners used alcohol, tobacco, or illicit drugs during the pregnancy or had a BMI over 30 before pregnancy. Additionally, participants were excluded when abnormalities were found during the 20-week ultra-sound examination or in case of known birth defects in the families of either parent that caused excessive worry for the current pregnancy. Fathers were invited to participate in a study examining the effect of the time before birth on fatherhood. To explain the different conditions, fathers were told we were interested in examining the differential effect of talking about your child (control condition) and talking with your child (VIPP-PRE). Using a computer-generated randomization sequence, included fathers (N = 73) were randomly assigned to the intervention or control group based on their study identification number. The intervention preferably took place between 20 and 30 weeks prenatally. Participants took part in three imaging sessions: a prenatal pre-intervention scan, a prenatal post-intervention scan about 2 weeks after the intervention, and a postnatal follow-up scan when the child was approximately 10 weeks old. Parenting was observed at the parent's home when the child was om average 9 weeks old. For the current study, we use data from all three imaging sessions in the ROI analyses. In the exploratory whole-brain analyses, the prenatal pre-intervention and the postnatal scans are used to determine the transition to parenthood.

Figure S1 depicts a flow diagram of enrollment, intervention allocation, follow-up, and data analysis. Of the 73 included fathers, 60 fathers had available MRI data, of whom 59 had at least one good quality fMRI scan. Included fathers did not differ from excluded fathers on age, education, race, child (gestational) age, child sex, reported adverse caregiving experiences.

The study was approved by the Ethics Committees of the Leiden University Medical Centre (NL62696.058.17, P17.216) and of the Department of Education and Child studies at Leiden University (ECPW2017/170). All participants and their partners gave informed consent.

2.2. Intervention

The VIPP-PRE intervention has been described more extensively

elsewhere (Alyousefi-van Dijk et al., 2022; de Waal et al., 2022). Briefly, the VIPP-PRE consists of three prenatal sessions in which the intervener discusses the following themes with the expectant father: 1) attachment and exploration; 2) speaking for the child; and 3) sensitivity chains. During each session one or two video recordings are made while the father performs interaction-based tasks specific to the current session (e.g., reading, touching, singing, talking). These videos are used at the next appointment to provide feedback based on the interactions. During the recordings, sonographers are asked to create a recognizable live image of the fetus using ultrasound images (Philips Lumify 2017, Best, the Netherlands) and to interfere as little as possible. Each father is seated next to the mother's abdomen, where he is close to the child and can see the ultrasound images. The resulting recordings contain both the ultrasound images as well as a frontal view of the father's upper body. During the interactions between the father and his unborn child, the mother is asked not to interfere and read a magazine. At the start of each session, ultrasound images are viewed with both parents in order to meet mothers' wishes to see their unborn babies as well.

During the recordings of fathers' interactions with their unborn children, interveners provide live feedback in line with the current theme being discussed, while an effort is made not to disrupt ongoing interactions but subtly support the father to read the child's signals. Additional effort is put into encouraging fathers to let the babies lead the interactions; each father is encouraged to act according to his child's current behavior (e.g., active when the child is active, but softly supporting the child when he/she is resting). After the recordings, the father is invited to review the recordings of the previous session together with the intervener and is provided with feedback on these recordings as prepared by the intervener in the period between the sessions. Fathers are also encouraged to interact with their unborn child at home for at least 5–10 minutes per day.

Ideally, the VIPP-PRE sessions were scheduled at a prenatal screening facility between 20 and 30 weeks of gestation when fetal behavior can be easily visualized by use of ultrasound, with 1–2 weeks in between sessions.

Fathers in the control group received phone calls from a researcher during the same period and with the same frequency as fathers receiving the intervention. Fathers were asked, for example, about the development of the pregnancy, and their preparations for birth and fatherhood. In both groups, current fetal development was discussed.

2.3. Measures

2.3.1. fMRI cry paradigm

The fMRI paradigm consisted of the presentation of six cry sounds and six control sounds matched on duration, frequency and volume. Duration of the sounds was 10 s. Cry sounds were derived from six infants (three boys, three girls, maximum age 5.5 months). For each cry sound, a neutral auditory control stimulus was created by calculating the average spectral density over the entire duration of the original sound. See Supplemental Text 1 for a detailed description of the sounds. Fathers were instructed to attend to the sounds presented in the MRI scanner. The six cry and six control sound were presented in three blocks in random order. Interstimulus Interval (ISI) was calculated using NeuroDesign in order to optimize design efficiency. ISI was jittered (mean ISI = 4.5 s, range 3.5–8). Blocks of six trials were separated by rest periods of 15 s. During the ISI and rest periods a fixation cross remained visible. In blocks 1 and 3, fathers were asked to evaluate the cry sounds. Using VAS scales, they indicated the perceived urgency of the cry and control sounds and the extent to which the sounds were perceived as annoying. VAS scales ranged from 0 (not at all) to 100 (very much).

2.3.2. Adverse caregiving experiences

One week after the pre-intervention session, participants completed the Conflict Tactics Scale – Parent Child (CTS), a questionnaire assessing maltreating behaviors that occur in a parent-child relationship (Straus et al., 1998) as well as a questionnaire measuring love withdrawal (Huffmeijer et al., 2011). All questionnaires were self-completed through an online link. In the present study, participants were asked whether one or both of their parents behaved in an abusive way towards them during their childhood. The CTS consists of 18 items (e.g. "My mother shouted, yelled or screamed at me") answered on a 7-point scale (0 = 'never', 1 = 'once', 2 = 'twice', 3 = '3–5 times', 4 = '6–10 times', 5 = '11–20 times', 6 = 'more than 20 times') which were combined in a total score. In the love withdrawal questionnaire (11 items), participants rated how well each of the statements described their mother's or father's behavior (e.g., "My mother is a person who, when I disappoint her, tells me how sad I make her") on a 5-point scale ranging from 1 (not at all) to 5 (very well). Total CTS and love withdrawal scores were standardized and averaged to obtain the Adverse Caregiving Experiences score ($\alpha = 0.89$ across all items).

2.3.3. Postnatal sensitivity

Father–infant interactions were observed at home during a 10-min play session when the child was on average 9 weeks old. Participants were instructed to engage in their usual routines of play, the first 5 min without play material and the last 5 min with play material. All videotaped father–infant interactions were coded by independent coders using the Ainsworth Sensitivity scale (Ainsworth et al., 1974) with scores ranging from 1 (insensitive) to 9 (sensitive). Five coders were trained to code the infant–father interactions (ICC single measurement, absolute agreement = 0.68–0.76).

2.3.4. Postnatal involvement

Hours spent with the infant were measured via an online self-reported questionnaire that participants received at home in the week following the postnatal lab session. They were asked to indicate the number of hours they spent with their infant for all days of the week separately, counting only time that father and child were both awake. Mean scores were calculated to indicate paternal involvement per day in hours.

2.4. Statistical analysis

Information on fMRI acquisition and preprocessing can be found in Supplemental Text 2.

After preprocessing, statistical analyses were performed at the single-subject level using the general linear model (GLM) within FSL's FEAT (FMRI Expert Analysis Tool). These analyses were performed for the pre-intervention scan, prenatal post-intervention scan, and the postnatal follow-up scan. A total of three EVs (explanatory variables) were created, one for cry sounds, one for control sounds and one referring to the stimulus evaluation phase of the task. All EVs were modeled as a square-wave function and then convolved with a double gamma hemodynamic response function. Temporal derivatives of the EVs were added to the model as well as standard motion parameters. To examine regions involved in cry processing, a cry vs control sound contrast was examined. Results of these single-subject analyses were transformed to standard space.

2.4.1. ROI analyses

Based on results reported by Kim et al. (2011), ROI analyses were performed in the amygdala and superior frontal cortex. Using the Harvard Oxford Subcortical Atlas within FSL, a bilateral amygdala mask was created including voxels with a probability of =>0.90 of belonging to the left or right amygdala. As the superior frontal gyrus (SFG) is a large gyrus, for this ROI we included voxels within a 3.5 mm sphere radius surrounding the coordinates reported in Kim et al. (2011) (23,50,28). Using FSL, for both ROIs and for each data wave, average Z-scores were extracted from the cry vs control sound contrast to allow analysis in R.

Intervention and pre-to postpartum effects were examined using linear mixed effect modeling in R (lme4; Bates et al., 2014). We

modelled time effects, intervention x time interaction effects as well as time x adverse caregiving experience, and intervention x time x adverse caregiving experience interaction effects. The afex package was used to compute statistical significance. The linear mixed effect models were performed with all available data ($n = 59$, total of 157 observations). Further, in order to estimate the effect of the intervention according to the intent-to-treat principle, ROI data was imputed for participants with missing imaging data (predictive mean matching method, 20 datasets). Analyses were repeated with the total sample of randomized participants ($N = 73$) using the 20 imputed datasets. Of these analyses, pooled statistics are reported.

2.4.2. Exploratory whole-brain analyses

In order to examine intervention and pre-to postpartum effects, whole-brain mixed effect ANOVAs were performed comparing the prenatal pre-intervention and postnatal follow-up scans. Specifically, intervention effects were examined using a 2 [prenatal vs. postnatal scan] x 2 [intervention vs control] whole-brain mixed effect ANOVA using Randomise (5000 iterations) in FEAT. We examined whether intervention and session effects depended on adverse experiences in separate mixed effect models examining a session x group x adversity interaction. For all comparisons of interest, both positive and negative t-tests were performed as well as an overarching F-test to account for two-sided testing. Statistical maps were thresholded using clusters determined by $Z > 3.1$ and a cluster corrected significance threshold of $p < .05$.

In order to further probe significant effects, featquery was used to extract average z-values per significant cluster for the pre-intervention scan, post-intervention prenatal scan and postnatal follow-up scan. To rule out the possibility that differences between the prenatal pre-intervention and postnatal follow-up session already existed in the late prenatal phase (and thus are not true prenatal-postnatal differences), activation in significant clusters were extracted for all three data waves: the prenatal pre-intervention, prenatal post-intervention, and postnatal follow-up sessions. Data were compared using repeated measures ANOVA in SPSS. Because, to our knowledge, whole-brain data cannot be imputed, for these exploratory analyses no intent-to-treat analyses have been performed.

2.4.3. Associations with paternal care

For ROIs or clusters showing significant intervention or pre-to postpartum effects, average z-scores for the cry vs control contrast during the postnatal session were associated to postnatal parental sensitivity and involvement using linear regression analyses controlling for paternal age, age of the child, sex of the child and paternal education (years following primary school). These analyses were performed with complete cases ($n = 46$), but were additionally conducted using imputed imaging data (multiple imputation, 20 datasets, $N = 73$). Regression analyses were FDR corrected for multiple testing across the different clusters.

Time and intervention effects on the fathers' perception of the cry stimuli are reported in Supplemental Text 3.

3. Results

For an overview of characteristics of the sample, see Table 1. For correlations between main variables, see Table S1.

3.1. Session and intervention effects on cry processing

3.1.1. ROI analyses

For results of the linear mixed effects models, see Tables 2–3. For the amygdala ROI, a significant pre-to postnatal effect was found ($b = -0.42$, $p = .005$, and $b = -0.62$, $p < .001$ for the pre- vs post-intervention session, and the pre-intervention vs. postnatal session, respectively), but there was no evidence for an intervention effect or effects of adverse caregiving. Compared to the pre-intervention session, activation in response to cry vs control sounds decreased in later sessions. For the SFG, a significant difference between the prenatal pre-intervention and post-intervention (irrespective of intervention type, $b = -0.44$, $p = .035$) but not the pre-intervention and postnatal ($b = -0.35$, $p = .144$) sessions was found. No intervention or caregiving effects were found. Results of the intent-to-treat analyses can be found in Tables S2–3 and were similar to the main results.

Table 1
Sample characteristics.

	Total (N=73)	Analytic sample (N=59)	Intervention (N=31)	Control (n=28)
Age father pre-intervention	32.62 (3.27)	32.78 (3.03)	32.88 (2.70)	32.67 (3.39)
Education father (years following primary school)	8.79 (1.44)	8.95 (1.34)	8.61 (1.49)	9.32 (1.06)
Ethnicity father (% Caucasian)	70 (95.9%)	57 (96.6)%	29 (93.5%)	28 (100%)
Male infant (%)	28 (38.4%)	23 (39.0%)	13 (41.9%)	10 (35.7%)
Gestational age pre-intervention (weeks)	24.95 (2.81)	24.96 (2.73)	24.70 (2.58)	25.25 (2.91)
Gestational age post-intervention (weeks)	34.44 (2.09)	34.38 (2.23)	34.55 (2.03)	34.19 (2.45)
Age infant postnatal (weeks)	10.82 (6.11)	10.88 (6.16)	12.60 (7.16)	9.16 (4.47)*
Adverse childcare experiences	0.00 (0.83)	-0.03 (0.84)	0.20 (0.91)	-0.28 (0.68)
Paternal sensitivity	5.76 (1.57)	5.77 (1.55)	5.91 (1.48)	5.63 (1.64)
Paternal involvement (hrs per day)	6.02 (3.23)	6.10 (24.96)	6.38 (4.35)	5.82 (2.44)

Note.* Due to the outbreak of COVID-19, postnatal assessment was delayed for several participants, resulting in a difference in postnatal age between intervention and control groups

3.1.2. Exploratory whole- brain analyses

The 2 [pre-intervention prenatal vs. postnatal scan] x 2 [intervention vs control] mixed effect ANOVA provided significant effects for time, but not for the intervention or for the interaction between time and intervention. Significant differences between the pre-intervention and postnatal session were found in nine clusters, see Table 5 and Fig. 1. For all clusters, activation decreased from the prenatal to the postnatal session.

Clusters included the right pre- and postcentral gyrus, superior and middle frontal gyrus, and supramarginal gyrus (cluster 1) as well as the left pre- and postcentral gyrus, supramarginal gyrus, superior parietal lobule and superior frontal gyrus (cluster 4). Cluster 2 included bilateral the paracingulate gyrus, anterior cingulate gyrus, medial frontal cortex and frontal pole. Cluster 3, 5 and 7 included the right lateral occipital cortex and angular gyrus (cluster 3); the right superior parietal lobule, superior lateral occipital cortex, precuneus and postcentral gyrus (cluster 5); and the left superior lateral occipital cortex (cluster 7). Two clusters included the left (cluster 8) and right (cluster 6) hippocampus and amygdala, and extended to the parahippocampal gyrus, lingual gyrus and fusiform gyrus. The ninth cluster included the bilateral posterior cingulate gyrus, extending to the anterior cingulate gyrus, the precentral and postcentral gyrus, the precuneus and juxtapositional lobule cortex.

Follow-up analyses examining activation in significant clusters during the prenatal post-intervention session, suggest that for cluster 1, 3, 5, 6, 7, and 8, activation decreased linearly from the first prenatal session to the postnatal session. For cluster 2, 4 and 9, no difference was found between the second prenatal session and the postnatal session. See Table S4 for average z-values for the different sessions. For all clusters, z-

Table 2
Intervention and transition effects in the amygdala.

	Session		Session x intervention		Session x adversity		Session x intervention x adversity	
	b (SD)	*p*	*b (SD)*	*p*	*b (SD)*	*p*	*b (SD)*	*p*
Prenatal post-intervention session	-0.42 (0.15)	.005	-0.26 (0.21)	.215	-0.42 (0.15)	.004	-0.31 (0.23)	.172
Postnatal session	-0.62 (0.15)	<.001	-0.49 (0.22)	.026	-0.60 (0.15)	<.001	-0.23 (0.24)	.341
Intervention			-0.08 (0.21)	.691			-0.01 (0.22)	.969
Post-intervention x condition			-0.28 (0.29)	.336			-0.23 (0.30)	.453
Postnatal x condition			-0.24 (0.31)	.432			-0.52 (0.11)	.110
Adverse caregiving					-0.11 (0.12)	.364	-0.26 (0.22)	.249
Post-intervention x adverse caregiving					-0.11 (0.17)	.524	-0.10 (0.31)	.736
Postnatal x adverse caregiving					0.22 (0.19)	.236	0.79 (0.33)	.019
Condition * adverse caregiving							0.22 (0.27)	.412
Post-intervention x intervention x adverse caregiving							0.06 (0.37)	.881
Postnatal x intervention x adverse caregiving							-0.76 (0.41)	.065

Table 3
Intervention and transition effects in the SFG.

	Session		Session x intervention		Session x adversity		Session x intervention x adversity	
	b (SD)	*p*	*b (SD)*	*p*	*b (SD)*	*p*	*b (SD)*	*P*
Prenatal post-intervention session	-0.44 (0.21)	.035	-0.41 (0.30)	.175	-0.44 (0.21)	.039	-0.27 (0.33)	.418
Postnatal session	-0.35 (0.22)	.114	0.04 (0.31)	.906	-0.39 (0.22)	.078	-0.09 (0.35)	.793
Intervention			0.52 (0.30)	.079			0.58 (0.31)	.065
Post-intervention x condition			-0.09 (0.42)	.826			-0.28 (0.44)	.535
Postnatal x condition			-0.75 (0.44)	.088			-0.63 (0.47)	.185
Adverse caregiving					0.01 (0.18)	.951	-0.22 (0.32)	.503
Post-intervention x adverse caregiving					0.27 (0.24)	.286	0.49 (0.45)	.277
Postnatal x adverse caregiving					-0.26 (0.27)	.334	-0.29 (0.49)	.549
Condition * adverse caregiving							0.20 (0.39)	.615
Post-intervention x intervention x adverse caregiving							-0.28 (0.55)	.610
Postnatal x intervention x adverse caregiving							0.22 (0.60)	.713

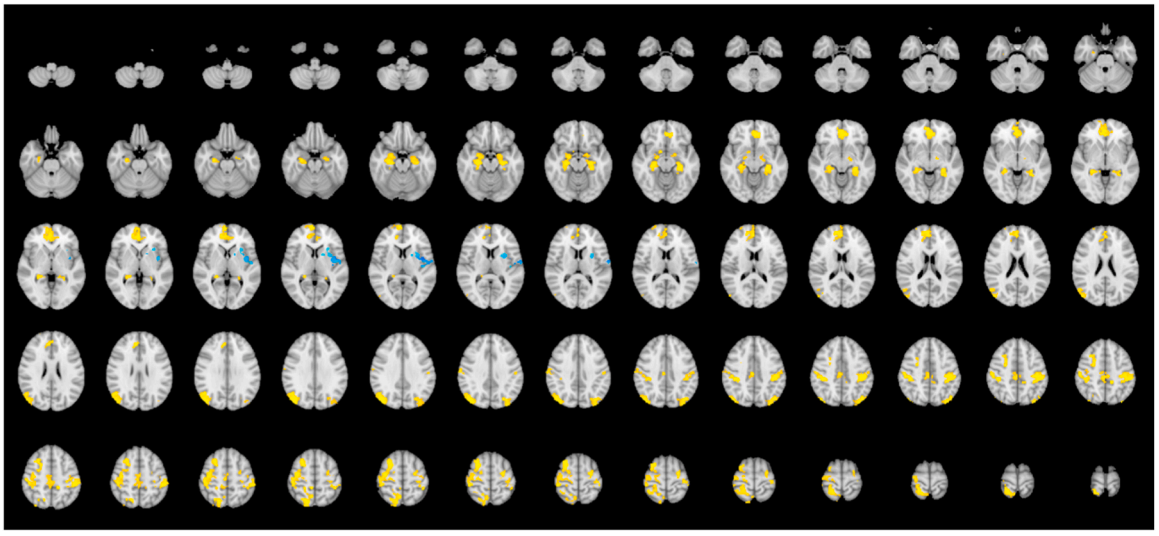

Fig. 1. Increased activation in the prenatal session compared to the postnatal session. Yellow: main effect of session, blue: interaction between session and adverse caregiving experiences.

scores were positive during the prenatal pre-intervention session (cry > control), but negative for the prenatal post-intervention and postnatal session (control > cry).

The whole-brain analyses examining the moderating effect of early caregiving adversity provided a significant effect in the left putamen, insula and opercular cortex, suggesting a stronger decrease in fathers who experienced more adversity, see Table 4. Early caregiving adversity did not moderate the effect of the intervention.

3.2. Associations with caregiving

Analyses on the available data ($n = 46$) showed that higher activation during the postnatal session was positively associated with parental sensitivity in six out of eleven ROIs (whole-brain clusters 1, 2, 7, 8, 9 and the session x adversity cluster). However, only three clusters (cluster 2, left medial prefrontal cortex, cluster 7, left superior lateral occipital cortex, and cluster 9, posterior cingulate gyrus) remained significant after correction for multiple testing, see Table 5. More activation in these clusters at the postnatal session was associated with higher

Table 4
Difference between pre-intervention and postnatal follow-up sessions.

	Cluster		# of voxels	p	x	y	z
$Pre_{cry>control} > post_{cry>control}$	1	R postcentral gyrus	2004	.003	66	-18	34
	2	L paracingulate gyrus/frontal medial cortex	1486	.006	-2	36	-14
	3	R inferior lateral occipital cortex	1428	.006	54	-80	8
	4	L postcentral gyrus	1124	.008	-52	-20	34
	5	R superior lateral occipital cortex	955	.010	16	-64	50
	6	R hippocampus	786	.014	28	-14	-26
	7	L superior lateral occipital cortex	731	.017	-26	-74	32
	8	L hippocampus	653	.020	-20	-10	-22
	9	R posterior cingulate gyrus	453	.032	6	-20	38
Session x adversity	1	L insula, putamen	337	.041	-28	18	0

Table 5
Associations between postnatal neural activation and caregiving.

		Sensitivity				Paternal involvement: average hours of care per day			
	Cluster	B (95% CI)	β	p	p_{adj}	B (95% CI)	β	p	p_{adj}
Amygdala		.364 (-0.18–0.91)	.27	.182	.182	0.49 (-0.90–1.88)	.11	.482	.969
Pre > post	1	0.69 (0.07–1.30)	.31	.031	.066	0.28 (-1.36–1.92)	.06	.730	.969
	2	0.72 (0.21–1.22)	.42	.007	.026	0.01 (-1.37–1.39)	.00	.987	.969
	3	0.57 (-0.03–1.17)	.39	.060	.094	1.47 (-0.06–3.00)	.31	.060	.987
	4	0.54 (-0.13–1.20)	.27	.113	.124	0.39 (-1.38–2.17)	.08	.657	.330
	5	0.52 (-0.13–1.16)	.25	.112	.124	0.13 (-1.52–1.79)	.03	.873	.969
	6	0.55 (-0.05–1.15)	.28	.069	.095	1.54 (0.02–3.01)	.31	.047	.330
	7	0.80 (0.30–1.30)	.44	.003	.017	0.11 (-1.32–0.09)	.02	.881	.969
	8	0.75 (0.05–1.44)	.33	.036	.066	1.03 (-0.76–2.83)	.18	.277	.969
	9	0.97 (0.45–1.50)	.53	<.001	.007	0.20 (-1.39–1.79)	.04	.798	.969
Session x adversity	1	0.59 (0.06–1.30)	.35	.029	.066	-0.54 (2.05–0.97)	-.12	.474	.969

Note. All analyses were corrected for paternal age and education, and child age and sex.

observed caregiving sensitivity. To rule out the explanation that fathers showing higher prenatal activation (but equal change) drove the positive association with sensitive parenting, we repeated the analyses controlling for activation during the first session. Controlling for prenatal activation did not change the results, see Table S5.

Only cluster 6 was associated with paternal involvement. However, this association did not survive correction for multiple testing.

The analyses on the imputed datasets showed large variation between imputations (e.g. cluster 8: β's range from.02–.40). However, all associations were positive, indicating that greater postnatal neural activation was related to more paternal sensitivity. Only the association between cluster 9 and paternal sensitivity remained significant (see Table S6).

4. Discussion

The present study examined the neural response to cry sounds in the transition to fatherhood, and examined whether a prenatal interaction-based parenting intervention modulated those changes. We further examined whether transition and intervention effects depended on childhood adverse caregiving experiences. Results suggest that neural activation in response to cry (vs control) sounds decreases in the transition to fatherhood in regions including the amygdala, bilateral sensorimotor cortex, superior parietal lobule, angular gyrus, superior lateral occipital cortex, hippocampus, medial prefrontal cortex, precuneus and cingulate cortex. These transitional changes were not influenced by the intervention. However, larger decreases in the left putamen and insula were found for fathers with greater adverse childhood caregiving experiences. Interestingly, for several of the regions showing transitional decreases in activation, postnatal activation was positively associated with paternal sensitivity (but not involvement).

Contrary to our expectations, the transition to fatherhood was characterized by a decrease of neural activation in response to cry sounds. The difference between neural activation in response to cry versus control sounds was positive in the prenatal session and negative in the postnatal session (although average z-scores representing the cry vs control difference during a single session were not significant for any cluster). Many of the regions reported here correspond to regions found in other studies examining the neural response to infant crying. The sensorimotor cortex, cingulate, medial prefrontal cortex, and amygdala have repeatedly been associated to cry processing (for a meta-analysis, see Witteman et al., 2019). Activation in these regions during cry processing has been suggested to assist in salience detection (amygdala, cingulate), perspective taking (medial prefrontal cortex), and responding (sensorimotor) to the cry sound. The lateral occipital cortex is not often reported in studies examining cry processing. However, a study on consoling in response to infant crying in fathers reported decreased activation in the lateral occipital cortex (Rilling et al., 2021). Compared to passive listening, consoling was also associated with decreased activation in other regions reported here, such as the amygdala and hippocampus, precuneus, anterior and posterior cingulate cortex and parts of the sensorimotor cortex. Speculatively, these results may explain the negative trend described here, as fathers in the transition to parenthood may increasingly have tried to mentally console the crying infant.

In addition to these pre-to postnatal transitional changes found in the entire sample, results suggest that fathers with adverse childhood caregiving experiences show larger changes in the left putamen and insula. Prior studies on cry processing have reported activation in the insula and suggest that this activation is related to salience detection and emotional empathy (Rilling, 2013; Witteman et al., 2019). The putamen may support motor preparation (Provost et al., 2015). In a prior study examining neural processing of infant crying in mothers who experienced neglect, greater insula activation was reported with increasing neglect experiences (Wright et al., 2017). The insular response to cry sounds, therefore, may be specifically sensitive to early negative caregiving experiences.

Prior work in the same sample suggests that paternal sensitivity decreases from the prenatal to early postnatal period, at least in the

control group of the randomized controlled trial (Buisman et al., 2022). Although counterintuitive, this finding may be unsurprising. Adjusting to the new paternal role may be stressful—especially given the fatigue and high amount of infant crying that characterizes the postpartum period—and may result in a temporary decrease in sensitive paternal behavior. Our findings paint a similar picture: the transition from the pre- to postnatal period results in a decrease in neural activation in response to cry vs control sounds, while higher postnatal activation is associated with increased postnatal sensitive behavior. The differences in neural activation reported here, however, may not be the (sole) consequence of child birth. Our analyses examining neural activation in an intermediate prenatal session suggest that the shift in activation already started prenatally, but—with the exception of the medial clusters and one of the sensorimotor clusters—further change occurred in the transition to fatherhood. Our results, therefore, suggest that care should be taken when linking prenatal to postnatal differences to child birth, as changes may already occur during the partner's pregnancy.

Indeed, previous research suggests that biological changes in fathers already occur during their partner's pregnancy (e.g. decreasing testosterone, Saxbe et al., 2017). Fathers' decrease in neural activation during pregnancy may reflect increasing adjustment to parenthood. However, this interpretation contrasts with our finding of a positive association between postnatal neural activation and paternal sensitivity. Therefore, as an alternative explanation, the decreased activation in the transition to fatherhood may reflect habituation to the cry sounds as a consequence of the repeated exposure to the cry sounds. Our finding of a positive association between postnatal activation and sensitive parenting, despite the general negative trend in activation, then suggests that fathers who show a smaller decrease over sessions—and thus less habituation—are more sensitive towards their child. This effect is specific to the quality of fathers' parenting (sensitivity), not quantity (involvement), which aligns well with our interpretation. Of course, not all infants cry equally frequently. Research shows that exposure to excessive crying is a risk factor for negative parenting practices (Barr et al., 2006). If, as we suggest, neural habituation to cry sounds does occur, this may explain why excessive crying might lead to lower parenting quality. Future studies may examine how neural processing of cry sounds relates to intensity and frequency of crying behavior of their infant, and assess associations between cry behavior, neural processing of cry sounds, and parental sensitivity. Of note, the associations with paternal sensitivity were not found in the analyses using imputed data (37% of sample) and thus should be interpreted with caution.

We did not find an intervention effect on the neural processing of infant crying. As crying elicits a caregiving response from the parent, and cry processing has been associated with variation in caregiving behavior (this study, Kim et al., 2011; Li et al., 2018; Swain et al., 2017), cry processing could be one of the mechanisms linking the VIPP-PRE intervention to changes in parental behavior. In the same sample, the VIPP-PRE intervention was associated with an increase in parental sensitivity over the transition to parenthood, while the control group showed a decrease in sensitivity (Buisman et al., 2022). However, this effect seems to be independent of cry processing. The absence of associations between the intervention and cry sound processing suggests that other mechanisms are responsible for the intervention effect on parental sensitivity. Alternatively, given the significant number of fathers with missing imaging data, the current study may have been underpowered to find significant intervention effects on cry processing. Moreover, fathers reporting psychiatric symptoms were excluded from participation. As individuals with current mental health problems are at greater risk for poor parenting quality and may show differences in neural reactivity to cry sounds (Kim et al., 2020; Wilson and Durbin, 2010), intervention effects on cry processing may have been limited by a ceiling effect and might be greater in a more diverse sample.

Despite considerable strengths, such as the randomized controlled design of the study, limitations of the present study should be noted. First, the study has a modest sample size, and, therefore, is at increased risk for false negative and positive findings. Further, the study was performed in a relatively homogeneous group of well-educated, white participants. Consequently, results may not generalize to individuals with a lower socioeconomic status or with a different ethnic background. Finally, as this study is a developmental study, prenatal vs postnatal sessions could not be counterbalanced. Further, cry processing was not examined in a childless control group. Therefore, it is unclear whether changes reported here are specific to the transition to parenthood.

In all, our results suggest that the transition to fatherhood is characterized by a *decrease* in activation in response to cry vs control sounds in the amygdala, bilateral sensorimotor cortex, superior lateral occipital cortex, hippocampus, as well as regions that are part of the default mode network. In these same regions, *higher* postnatal activation was associated with more concurrent parenting sensitivity. Results may reflect fathers' increasing adjustment to parenthood over the course of their partner's pregnancy or habituation to cry sounds over repeated exposure. Although the design of the current study does not ascertain whether our findings are specific to the transition to fatherhood, our findings do suggest that continued sensitivity to cry sounds may be conducive to parenting quality.

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CRediT authorship contribution statement

Sandra Thijssen: Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Kim Alyousefi-van Dijk:** Data curation, Project administration, Writing – review & editing. **Marian Bakermans-Kranenburg:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing – review & editing. **Noor de Waal:** Data curation, Writing – review & editing. **Marinus van IJzendoorn:** Conceptualization, Funding acquisition, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2024.107005

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