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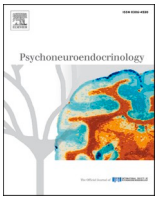

A soft baby carrier intervention enhances amygdala responses to infant crying in fathers: A randomized controlled trial

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ABSTRACT

New fathers may grow into their parental role through active involvement in childcare. Spending time in physical contact with the child may promote an adaptive transition to fatherhood. In this randomized controlled trial, we tested the effects of a baby carrier intervention on fathers' hormonal and neural functioning. Using functional magnetic resonance imaging (fMRI), we examined whether infant carrying affects neural reactivity to infant crying in first-time fathers, taking into account the role of the hormone oxytocin as a mediating mechanism and fathers' own childhood experiences as a potential moderating factor. Sixty first-time fathers (infant age M = 11.18 weeks, SD = 2.08) were randomly assigned to a baby carrier intervention group (n = 32 fathers) or a control group (n = 28 fathers). Fathers in the intervention group were instructed to use a baby carrier for three weeks, whereas fathers in the control group were instructed to use a baby seat. Before and after the intervention salivary oxytocin was measured and neural reactivity to infant crying was assessed using fMRI. Results showed that the infant carrier intervention increased amygdala reactivity to infant crying compared to the infant seat users. This effect was most pronounced in fathers with experiences of childhood abuse. The carrier intervention did not affect fathers' oxytocin levels. Our findings indicate that spending time in physical contact with the infant may promote attention to and accurate perception of infant signals, in particular in fathers with more adverse childhood experiences. Soft baby carriers may, therefore, facilitate an adaptive transition to fatherhood.

1. Introduction

Research on parenting has predominately focused on mothers and neglected the role of fathers for a long time. Consequently, little is known about the development of caregiving behaviors in fathers. In contrast to mothers who undergo strong hormonal changes during pregnancy and labor, fathers may adapt to their new parental role more slowly through active involvement in childcare (Abraham et al., 2014). Spending time in physical contact with the child may therefore promote an adaptive transition to fatherhood. In the current randomized controlled trial (RCT), we examined the effects of a baby carrier intervention on fathers' hormonal and neural functioning. Using fMRI, we aim to test whether carrying an infant for at least six hours per week, for three weeks, affects neural reactivity to infant crying in first-time fathers, examining the role of the hormone oxytocin as a potential mediating mechanism and fathers' own childhood experiences as a potential moderating factor.

Research has provided ample evidence for a role of hormones in regulating caregiving behaviors. In particular the hormone oxytocin has been associated with sensitive parenting behaviors (Feldman et al., 2007; Feldman and Bakermans-Kranenburg, 2017). Endogenous oxytocin levels have also been associated with typical maternal and paternal behaviors during parent-infant observations. In mothers, oxytocin levels are related to affectionate touch during infant interaction, while paternal oxytocin levels are related to stimulatory touch (Feldman et al., 2010). Consistent with correlational studies, intranasal

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oxytocin administration experiments have shown that an oxytocin nasal spray increases sensitive paternal behaviors, e.g. (Naber et al., 2010). In addition to oxytocin, vasopressin has also been suggested to be an important regulator of paternal parenting (Thijssen et al., 2018; Witte et al., 2019). Here we focus on oxytocin because the oxytocin system may be especially responsive to infant carrying given prior findings showing parental oxytocin system reactivity to touch and infant contact (Feldman et al., 2010).

Oxytocin-enhancing effects of touch and physical contact have not only been found in parent-child dyads, but also in individuals without children. Consistent with previously reported oxytocin-enhancing effects of massage (Morhenn et al., 2012), we found that massage applied by a seat cover elevates salivary oxytocin levels in men and women without children (Riem et al., 2017). Importantly, in men, high oxytocin levels after mechanically-delivered massage were related to reduced handgrip force during exposure to infant crying and laughter, indicating that massage promotes a more sensitive response to infant signals through stimulating oxytocin release. Hence, physical contact with an infant may be an important mechanism triggering the biological basis of fathering during the first months of fatherhood. A question that follows from these findings is whether a physical contact intervention, such as a baby carrier intervention, can boost oxytocin levels in fathers and subsequently stimulate more sensitive paternal caregiving responses. Stimulating oxytocin release through physical contact may be an effective intervention for enhancing sensitive responsiveness to infant signals, and may be particularly important for fathers who find it difficult to adjust to their parental role, in particular fathers with adverse caregiving experiences during their own childhood.

The experience of adverse childhood events, including childhood physical and emotional abuse, can trigger changes in neural and hormonal systems important for regulating later parental behaviour, including the oxytocin system. These physiological changes may be one of the mechanisms underlying risk for insensitive parenting in these individuals (van IJzendoorn et al., 2020). Parents with experiences of childhood abuse tend to perceive signals of their child, such as infant crying, in a more negative way (Beckerman et al., 2018) and respond less sensitively. They show physiological hyporeactivity during exposure to infant crying, possibly reflecting disengagement from the caregiving context (Reijman et al., 2014). Physiological hyperreactivity to infant crying has also been observed in individuals with experiences of child abuse. Olsavsky et al. (2021) found that maltreated mothers who were exposed to cry sounds showed hyperreactivity to crying in the amygdala, a brain region important for anxiety and the processing of social stimuli (Pessoa and Adolphs, 2010). Maternal amygdala activation has been shown to be particularly relevant in a caregiving context and has been related to sensitive parenting (Kim et al., 2011), although amygdala hyperreactivity to infant crying may reflect emotion dysregulation and may interfere with sensitive caregiving (Olsavsky et al., 2021). Interestingly, fMRI studies using visual infant cues found amygdala hypo-reactivity in maltreated mothers, suggested a blunted response possibly reflecting disengagement from a caregiving context (Kim et al., 2014; Olsavsky et al., 2019).

Although abused fathers may be most in need of an intervention to stimulate adjustment to parenthood, it is unclear whether a physical contact intervention would be effective. On the one hand, boosting oxytocin levels through physical contact may be particularly beneficial for abused fathers, because experiences of child abuse have been associated with lower endogenous oxytocin levels (Ellis et al., 2021). Hence, abused fathers may gain the most from stimulation of endogenous oxytocin release. On the other hand, a recent meta-analysis shows that individuals with untoward childhood experiences are less responsive to intranasal administration of oxytocin (Ellis et al., 2021) and increased oxytocin levels after massage were absent in men with negative childhood experiences (Riem et al., 2017). Hence, oxytocin system dysregulation after childhood adversity may impede beneficial effects of infant physical contact. In the current study, we therefore examine whether fathers' experiences of child abuse moderate the effectiveness of the carrier intervention.

We aimed to examine the effects of the infant carrier intervention on fathers' neural reactivity to infant crying using fMRI. Infant crying is highly salient and motivates parental care, but can also trigger harsh responses from parents who perceive the sound as aversive (Soltis, 2004). Examining how physical infant contact influences fathers' neural reactivity to infant crying is, therefore, particularly relevant for understanding adaptation to fatherhood. Previous neuroimaging studies on cry perception indicate that exposure to crying activates the parental brain network, including the amygdala, frontal regions, supramarginal gyrus, regions involved in auditory perception (the middle and superior temporal gyrus), and empathy-related regions (insula, inferior frontal gyrus) (Swain, 2011; for a meta-analysis see Witteman et al., 2019). However, most studies have been conducted with mothers or individuals without children. Parental status and gender make a difference in the pattern of activation (Witteman et al., 2019), possibly due to changes in hormonal levels that accompany the transition to fatherhood.

This study is the first RCT with a baby carrier in fathers. Based on a previous study showing positive effects of a baby carrier on maternal caregiving (Anisfeld et al., 1990) and positive effects of infant carrying on parents and parenting skills (Pisacane et al., 2012; Williams, 2020), we expected that the baby carrier would enhance activity in parental network regions. Furthermore, we expected that the effects of the carrier would be mediated by salivary oxytocin levels, with increased oxytocin levels after using the infant carrier stimulating more activity in the parental brain network. Lastly, we expected that the effects of the baby carrier would be moderated by fathers' adverse childhood experiences. More specifically, we examined the moderating role of experiences of physical and emotional abuse.

2. Materials and methods

2.1. Participants

A total of 63 first-time fathers participated in the current study, which was a randomized controlled trial testing the effect of paternal use of a soft baby carrier. The original sample of fathers who participated in the randomized trial was $N = 80$, but not all fathers were eligible to undergo an fMRI scan, due to diabetes or metallic foreign objects in body or claustrophobia, and a few fathers withdrew or cancelled post-test participation. See Fig. S1 for a flow chart. Participants were recruited via municipal records, infant welfare centers, midwife practices, and social media, see (Lotz et al., 2020). Participants were screened on inclusion criteria during telephone interviews. To be eligible for participation in the study, participants had to be cohabitating with their partner, have a healthy infant and be able to read and speak Dutch. Exclusion criteria included non-removable metallic parts in their body, self-reported neurological, neuroendocrine and psychiatric disorders, claustrophobia, or alcohol/substance abuse. Additionally, included fathers reported not to use a baby carrier over 5 h per week at the time of inclusion. Fathers with premature babies (born before 37 weeks) were also excluded. One infant was born at 36 weeks and 6 days, but was considered healthy and did not receive medical care. One father was not the biological father of the infant, but had been cohabitating with the mother since mid-pregnancy. Two fathers dropped out for the current analyses due to technical problems during MRI scanning, one father had corrupt data and was therefore excluded from analyses. Thus, a total sample 60 first-time fathers with complete data were included in the analyses. Mean age of the fathers was 33.09 years (SD = 4.92). Mean age of the infant was 11.18 weeks (SD = 2.80). See Table S1 for background characteristics. Participants received a monetary incentive for participation. The study was approved by the Ethics Committees of the Department of Education and Child Studies at Leiden University and the Leiden University Medical Centre (P17.215; NL62692.058.17). The study was carried out in accordance with the declaration of Helsinki and

all participants gave written informed consent prior to the start of the first session.

2.2. Procedure

The experimental procedure is visualized in Fig. 1. Fathers were randomly assigned to the baby carrier intervention group (n = 32 fathers) or a control group (n = 28 fathers). The procedure started after informed consent with fMRI session 1 (pre-test), followed by saliva collection on two consecutive days at the fathers' home in the same week. After the first fMRI session, fathers were visited at home and received a soft baby carrier (intervention group) or a baby seat (control group) and were instructed on the use. The average number of days between pre-test fMRI session and start of the intervention was 12.22 (SD = 4.99). The duration of the intervention was three weeks. The post-test fMRI session and second saliva collection was scheduled in the week following the intervention. fMRI sessions took place at the Leiden University Medical Centre where the participants completed questionnaires, performed behavioral tasks for other purposes. Participants were asked to refrain from alcohol and caffeine 24 h prior to the visit.

2.3. Baby carrier intervention

The intervention group received an ergonomic soft baby carrier. The intervention aimed at increasing the amount of physical contact between father and infant through the use of the carrier. Infants in the carrier were chest to chest with their father, supported by the father's upper torso. During a home visit, fathers were given the opportunity to try out two different baby carriers (Ergobaby adapt or Kokadi flip) using a doll with the weight of an infant and were asked to choose the carrier that was most comfortable. They were instructed how to use the carrier and were given the opportunity to practice. Fidelity regarding the use of the carrier was measured using a temperature data logger fixed to the baby carrier. Mean total recorded time of use of the infant carrier during the three weeks was 11.72 h (SD = 8.31). Fathers in the control group received a Doomoo seat. This control condition can induce proximity between father and infant without increasing physical contact. Fathers were instructed on how to use the seat and received suggestions on when it could be used, for example during playful interactions. Fathers were requested to use the baby carrier or the Doomoo seat for at least six hours per week, spread over a minimum of four days, for three weeks. Fathers in the carrier and control group did not differ in father's age ($t(58) = -0.43$, $p = .67$), infant's age ($t(57) = -1.31$, $p = .20$), education ($t(58) = 0.12$, $p = .91$), or depressive symptoms ($t(55) = 0.77$, $p = .45$) (see Supplemental Material).

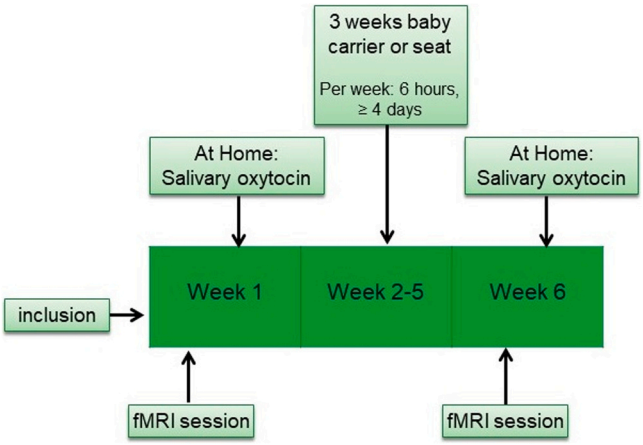

Fig. 1. Timeline of the study.

2.4. Measures

2.4.1. Salivary oxytocin

Saliva samples were collected at fathers' home. Four saliva samples were collected: in the morning and evening of two consecutive days before the intervention (four pre-test samples) and after the intervention (four post-test samples). Fathers were instructed to collect saliva after waking up in the morning and before going to bed in the evening, but before they brushed their teeth. Fathers were also instructed not to eat or drink (other than water), smoke, chew gum, or have excessive physical exercise during the last 30 min prior to saliva assessment. An application was installed on fathers' smartphones reminding them of the start of the saliva collection the evening before they started, as well as on the morning and evening of the two collection days itself. Via this app, fathers were guided through the saliva collection process and reported on the time of saliva collection and indicated whether they adhered to instructions. Saliva was collected using cotton swabs (Salivettes). All samples were stored as soon as possible at −20 °C at fathers' home and were picked up by the researchers after the intervention. Samples were placed on ice for transportation. Oxytocin was assayed at RIAgnosis (Sinzing, Germany). After centrifugation of the salivettes at 4 degrees Celsius for 30 min with ca. 5000 *g* centrifugal force, 0.3 ml of saliva was pipetted into a vial. Oxytocin was quantified using radioimmunoassay. The detection limit of oxytocin was 0.1 pg/ml. Inter-assay and intra-assay variability was <10%.

Oxytocin samples of six fathers were partly missing. One father did not collect saliva samples during both evenings at the pretest and the first evening at the post-test. One father missed one evening saliva sample on the second day of the post-test. Oxytocin samples of a third father were missing on the second day (morning and evening) of the pre- and post-test. Missing evening samples were imputed based on the regression equation predicting the oxytocin values in the evening by morning data from the same day. For one father, all oxytocin values of the post-test were missing. These missing values were replaced by pre-test data (last observation carried forward). For two fathers with all oxytocin values missing mean scores on the corresponding timepoints were used.

For each father, we calculated the area under the curve (AUC) with respect to the ground according to the procedure described by Pruessner et al. (2003) using the four samples before and after the baby carrier or control intervention, resulting in an oxytocin AUC for the pre and post-test (OT-AUC_{pre} and OT-AUC_{post}). AUC takes into account variations in fathers' oxytocin levels assessed in the morning and evening at the two consecutive days. Fathers' reported time of saliva collection was entered in the formula in order to account for differences in timing of saliva collection between fathers. OT-AUC pre (M = 49.00, SD = 9.47) and OT-AUC post (M = 44.47, SD = 7.13) were significantly correlated ($r = 0.40$, $p = .002$). One outlier on OT-AUC_{post} was winsorized. An oxytocin AUC difference score (OT-AUC_{change}) was calculated by subtracting OT-AUC_{pre} from OT-AUC_{post}, reflecting change in OT-AUC across time.

2.4.2. Adverse childhood experiences

In the current study, adverse childhood experiences included experiences of physical and emotional abuse, measured with the Conflict Tactics Scale—Parent Child (CTS, Straus et al., 1998). Fathers completed the subscales Psychological aggression, Minor physical assault, Severe physical assault, and Neglect (18 items). Participants were asked to indicate how often parental behaviors occurred during their childhood on a scale ranging from 0 (never) to 6 (more than 20 times). A recent meta-analysis suggest that the oxytocin system is differently impacted by different dimensions of childhood trauma (Ellis et al., 2021). We therefore differentiated between the neglect and abuse subscales. Results of analyses with abuse are reported because prevalence of neglect was very low in the current sample (M = 0.28, SD = 0.77). A total score for Abuse was calculated by averaging the Psychological aggression,

Minor physical assault, and Severe physical assault scales (13 items). Mean abuse was 1.18 (SD = 1.01). Reliability was good (α = 0.85). Average abuse scores did not differ between fathers in the control and baby carrier intervention groups (t(58) = 1.16, p = .25), see Table S1.

2.4.3. 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 Material for a detailed description of the sounds. Fathers were instructed to attend to the sounds they would hear 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 hair 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) (see Supplemental Material).

2.4.4. MRI data acquisition

Whole brain fMRI data was obtained on a 3 T Philips Achieva TXMRI system (Philips Medical Systems, Best, the Netherlands) at Leiden University Medical Centre. Functional scans were obtained with a T2 weighted gradient-echo echo-planar imaging (EPI) sequence. Functional data was collected using the following sequences; TR = 2200 ms, TE = 30 ms, flip angle = 80°, 38 transverse slices, and voxel resolution of 2.75 × 2.75 × 3.03 mm (345 volumes). A T1-weighted anatomical scan was obtained with repetition time (TR) = 7.9 ms, echo time (TE) = 3.5 ms, flip angle = 8°, 155 transverse slices, voxel size 1.0 × 1.0 × 1.1 mm.

2.4.5. fMRI analyses

Preprocessing of the imaging data was performed using fMRIPrep 1.5.2 (Esteban et al., 2018), which is based on Nipype 1.3.1 (see Supplemental material). For preparation purposes, all data was converted to a Brain Imaging Data Structure (BIDS) standard format to be able to be recognized by the fMRIPrep programming tool. We used this pre-processing pipeline in standard format because it automatically detects the optimal preprocessing workflow for the data and has a focus on reproducibility of methods (Esteban et al., 2018). Preprocessed images were motion correct using mcflirt (FSL v5.0.9, Jenkinson et al., 2002) and loaded into FSL 6.0. fMRI data analyses were carried out using FEAT Version 6.0 (Woolrich et al., 2004), part of FMRIB's Software Library. High-pass temporal filtering (high-pass filter cut-off = 90 s) and spatial smoothing (Gaussian kernel of full-width-at-half-maximum 5.0) was applied using FEAT as these preprocessing steps were not included in fMRIPrep. Preprocessed fMRI data was checked for excessive head motion (>3.0 mm, similar to Lotz et al., 2020), but no fathers with excessive head motion were identified.

Functional activity was examined with general linear model analysis. Cry versus control sound was modeled separately as a square-wave function and then convolved with a double gamma hemodynamic response function. The ratings of the sounds were also modeled. Temporal derivatives were added to the model, giving 6 predictors. To identify regions involved in the perception of infant crying we assessed the cry > control contrast. This first-level contrast image and the corresponding variance image were transformed to standard space and submitted to second-level mixed-effects group analyses. ROI analyses were conducted with the following brain regions that are part of the parental brain network involved in infant cry perception: amygdala, insula, inferior frontal gyrus (IFG), middle frontal gyrus (MFG), middle- and superior temporal gyrus, and the supramarginal gyrus (Swain, 2011; Witteman et al., 2019). These brain regions were anatomically defined using the Harvard–Oxford (Sub)cortical Atlas. Additionally, whole brain analysis was conducted in order to explore effects of the intervention on other brain regions.

Mean activation in the control and carrier group at pre and posttest was calculated using one-sample t-tests. Group means were assessed non-parametrically using FSL's Randomise tool (Winkler et al., 2014), incorporating threshold-free cluster enhancement (TFCE), with 5000 iterations. We used TFCE, embedded in randomise in FSL, because this method gives generally better sensitivity than cluster-based thresholding over a wide range of test signal shapes and signal-to-noise values (Smith and Nichols, 2019). A 2-way Mixed Effect ANOVA was carried out to test the effect of the intervention, again using FSL's Randomise tool. Following the FSL userguide, paired within-subject differences were computed for each father via fslmaths and a two-sample t-test was used to test whether the changes across time differed between the two groups. All statistical maps were family-wise corrected and thresholded at $p < .05$. Father's age and educational level were added to the model as confound regressors in all analyses. Featquery was used to extract z values for the contrast Cry > Control from regions that were significantly affected by the baby carrier intervention.

2.4.6. Statistical analyses

Moderated-mediation analysis was performed to explore to moderating role of childhood experiences and the mediating role of oxytocin in the effects of infant carrying. Extracted z values of neural reactivity to crying compared to control at the post-test as entered as outcome measure, condition as predictor, pre-post difference in OT-AUC as mediator, and adverse childhood experiences (CTS abuse) as moderator. $\text{OT-AUC}_{\text{change}}$ was entered as mediator, because we aimed to test whether change in oxytocin level after the use of the baby carrier mediated the effect of the intervention on neural reactivity. Mediated-moderation analysis was performed using the process script (Hayes, 2013). We used model 8 to test the influence of adverse childhood experiences (CTS abuse) on the association between 1) condition and $\text{OT-AUC}_{\text{change}}$, 2) condition and neural reactivity to crying. Moderated-mediation was tested using a bootstrap estimation approach with 5000 samples. Following the moderated-mediation analysis, an ANCOVA with neural reactivity to infant crying at post-test as dependent variable, group (baby carrier or control intervention) as between-subject factor, and adverse childhood experiences as covariate was conducted. Neural reactivity to crying at pre-test, age and educational level were included as covariates in all analyses. In order to estimate the effect of the infant carrier intervention according to the intention to treat principle, the ANCOVA was repeated with the total sample of randomized participants (N = 80), with imputed data for participants with missing pre- or posttest data. Multiple imputation was carried out separately for the infant carrier and control group, as recommended by Sullivan et al. (2018). See Supplementary Materials for a power analysis showing adequate power of our design.

3. Results

3.1. ROI analyses

ROI analyses revealed that fathers in the control and carrier group showed significant activity in the amygdala, IFG, insula, middle and superior temporal gyrus, and MFG during exposure to crying compared to control sounds at the pre-test as well as the post-test, TFCE-family-wise error corrected, see Table 1 and Fig. 2. There was no significant main effect of time across the control and baby carrier intervention group. However, a significant time x group interaction was observed in the ROI analysis of the amygdala, TFCE-family-wise error corrected, indicating a significant intervention effect. Fathers in the carrier group

Table 1
Brain coordinates (MNI) of the peak average z-value for the contrast cry > control for fathers in the carrier and control group (excluding clusters < 20 voxels).

	Clusters	Nr voxels	Max Z	x	y	z
Control - pre	L amygdala	62	6.61	-16	-4	-16
	R amygdala	55	4.09	24	-6	-16
	L insula / frontal orbital cortex	737	5.98	-32	26	-6
	R insula / IFG	594	7.3	48	22	-2
	R IFG / frontal orbital cortex	2578	7.89	50	24	-6
	L IFG	2317	7.6	-50	20	14
	L supramarginal gyrus / superior parietal lobule	996	4.97	-42	-50	60
	R supramarginal gyrus / postcentral gyrus	491	4.39	48	-24	34
	L superior temporal gyrus	5541	8.32	-56	-18	-2
	R middle temporal gyrus	5442	9.52	60	-22	-14
	L MFG / superior frontal gyrus	6342	7.77	-16	34	48
	R precentral gyrus / MFG	5585	8.15	58	-4	44
Control - post	R planum polare / insula	943	5.45	50	-6	-8
	L insula	666	6.38	-28	20	-2
	R IFG / frontal orbital cortex	1114	5.17	46	24	-6
	L IFG / frontal operculum cortex	509	4.88	-36	28	4
	R IFG / frontal pole	32	3.27	44	36	22
	R middle temporal gyrus	4321	9.44	60	-10	-8
	L superior temporal gyrus	3135	7.25	-52	-14	-4
	R MFG / precentral gyrus	147	5.66	54	-2	40
	R IFG / MFG	30	4.26	56	18	22
Carrier-pre	R amygdala	172	5.67	22	-4	-14
	R amygdala/hippocampus	31	5.05	30	-16	-14
	R planum polare / insula	1255	7.58	50	-4	-8
	L insula	980	7.11	-44	16	-6
	R frontal orbital cortex / IFG	1707	7.4	36	30	-6
	L insula / IFG	1147	7.11	-44	16	-6
	R superior temporal gyrus / supramarginal gryus	24	6.27	66	-18	6
	R superior temporal gyrus	4410	10.4	48	-18	-4
	L superior temporal gyrus	4317	8.6	-60	-6	-4
	R MFG / precentral gyrus	257	5.53	56	-2	46
	R IFG / MFG	75	4.02	54	16	18
	R MFG	37	3.96	42	20	26
Carrier - post	L amygdala	66	4.52	-18	-2	-10
	R insula / frontal orbital cortex	498	5.06	36	28	-4
	R planum polare / insula	62	6.95	50	-6	-6
	L heschl's Gyrus / insula	21	5.15	-46	-18	4
	R IFG / frontal orbital cortex	260	5.06	36	28	-4
	R supramarginal gyrus/ middle temporal gyrus	17	6.44	70	-38	4
	R superior temporal gyrus	3817	9.58	60	-18	-2
	L superior temporal gyrus	2941	7.92	-66	-10	0
Carrier: post > pre	L amygdala	61	4.19	-22	-10	-16
$Carrier^{post > pre} > control^{post > pre}$	L amygdala	70	3.54	-28	-4	-20

showed increased activity in the amygdala when exposed to crying during the post-test compared to the pre-test, whereas no significant change in amygdala reactivity to crying was observed in the control group, see Fig. 3. No time x group interactions were observed for other ROI's.

3.2. Whole brain analyses

Whole brain analysis was conducted in order to explore effects of the intervention on brain regions that are not part of the parental brain network, but no significant time x group interaction was observed.

3.3. Oxytocin and childhood abuse

Mean z values of significantly activated voxels of the amygdala at the pre- and post-test were extracted. Mean z values of amygdala reactivity at post-test was entered as dependent variable in the exploratory moderated-mediation analysis, with group as independent variable, OT-AUC_{change} as mediator, adverse childhood experiences (CTS abuse) as moderator, and age, educational level and amygdala reactivity at pretest as covariates. Moderated-mediation analyses showed that there was no significant main effect of group on amygdala reactivity to crying ($b = -0.78$, $SE = 0.42$, $t(52) = -1.86$, $p = .068$). Neither were there significant main effects of OT-AUC_{change} ($b = -0.01$, $SE = 0.01$, $t(52) = -1.18$, $p = .24$). However, there was a significant effect of adverse childhood experiences ($b = -0.47$, $SE = 0.19$, $t(52) = -2.48$, $p = .016$) on amygdala reactivity and a significant interaction between adverse childhood experiences and group ($b = 0.72$, $SE = 0.26$, $t(52) = 2.75$, $p = .008$), indicating that the effect of the intervention was dependent on adverse childhood experiences. The model with amygdala reactivity as outcome variable approached significance ($F(7,52) = 2.08$, $p = .062$, $R^2 = 0.22$). There was no significant effect of group on the mediator OT-AUC_{change} ($b = 1.32$, $SE = 5.48$, $t(54) = 0.242$, $p = .810$). Neither was there a significant adverse childhood experiences x group interaction in the prediction of OT-AUC_{change} ($b = 1.58$, $SE = 3.43$, $t(54) = 0.46$, $p = .647$). The index of moderated mediation was −0.02 ($SE = 0.07$) and not significant (95% CI [−0.29 0.07]). See Fig. 4.

Analyses were repeated with total CTS score (including the neglect subscale) as independent variable, controlling for the same set of covariates (age, educational level and amygdala reactivity at pretest), and this did not change the results. The interaction between total CTS score and group was significant ($b = 0.75$, $SE = 0.35$, $t(52) = 2.11$, $p = .039$). Analyses were repeated with fathers' average number of hours involved in childcare, number of hours using the carrier as recorded with the thermologger, and depressive symptoms (see Supplemental material) as covariates in addition to age, educational level and amygdala reactivity at pretest, but the results did not change. Moderated-mediation analysis again revealed a significant interaction between adverse childhood experiences and group ($b = 0.73$, $SE = 0.27$, $t(46) = 2.68$, $p = .010$) in the prediction of amygdala reactivity.

The ANCOVA with amygdala reactivity at post-test as dependent variable, group (carrier, control) as between-subject factor, and adverse childhood experiences (CTS abuse), age, educational status and amygdala reactivity at pre-test as covariates showed a significant two-way interaction between group and adverse childhood experiences ($F(1,53) = 7.13$, $p = .010$, partial $\eta^2 = .12$). Adverse childhood experiences was dichotomized using median split in order to interpret and visualize the interaction, see Fig. 5. Compared to the control intervention, the baby carrier intervention increased amygdala reactivity in fathers with higher adverse childhood experiences, whereas the intervention resulted in lower amygdala reactivity in fathers with lower adverse childhood experiences. The effect of group approached significance for fathers with relatively higher levels of adverse childhood experiences ($F(1,25) = 3.49$, $p = .073$, partial $\eta^2 = .12$), but not for fathers with lower adverse childhood experiences ($F(1,25) = 0.63$, $p = .435$, partial $\eta^2 = .03$).

The Benjamini Hochberg (BH) procedure (Macdonald, 2014) was applied in order to correct significance levels for Type I error because of repeated testing of intervention effects on six ROIs. The interaction between abuse and group remained significant after applying the BH procedure.

3.3.1. Intent-to-treat analysis

For an intent-to-treat analysis with the original sample ($N = 80$), we performed multiple imputation modelling and repeated the ANCOVA. Multiple imputation modelling was performed for intervention and control group separately, as recommended by Sullivan et al. (2018). Little's MCAR test was not significant, indicating that missing was

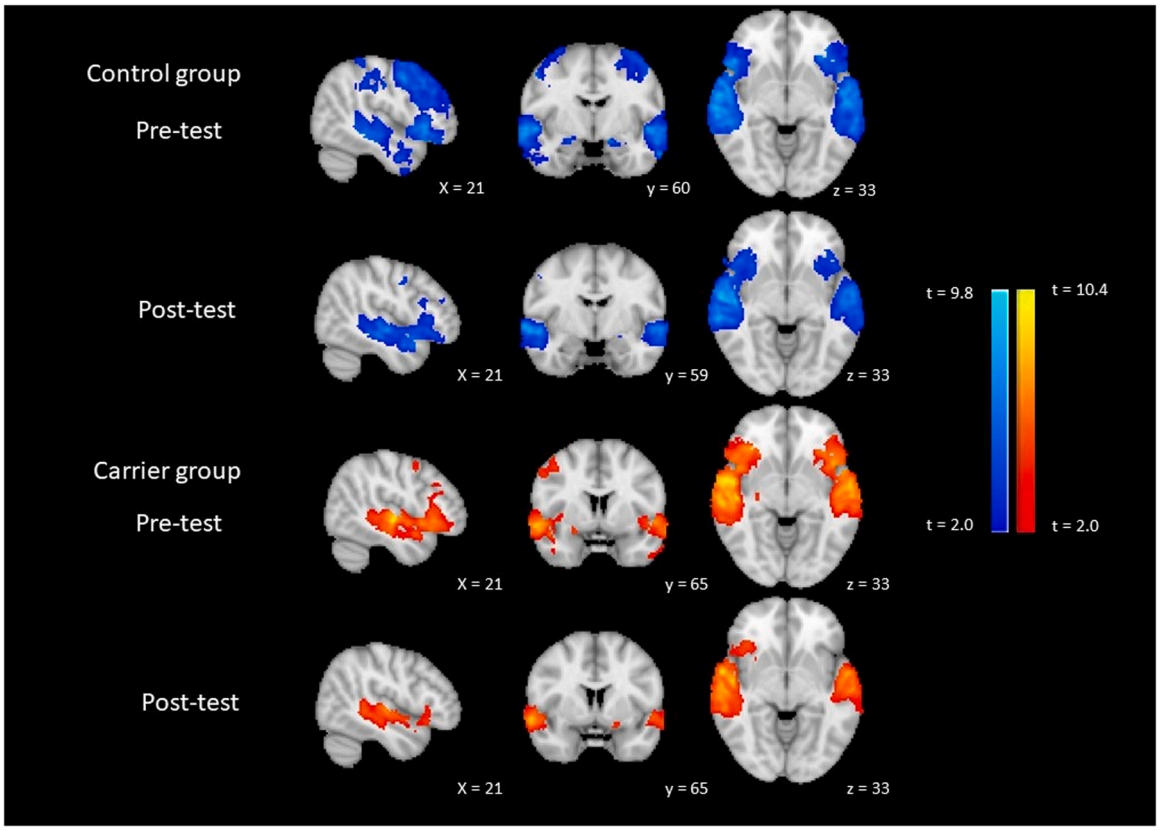

Fig. 2. Significant brain activity during infant crying compared to control sounds in the control and carrier group at the pre- and post-test. Images are t-statistics, TFCE, FWE corrected, $p < .05$, controlled for age and educational level, overlaid on the MNI-152 standard brain. The left hemisphere of the brain corresponds to the right side in this image.

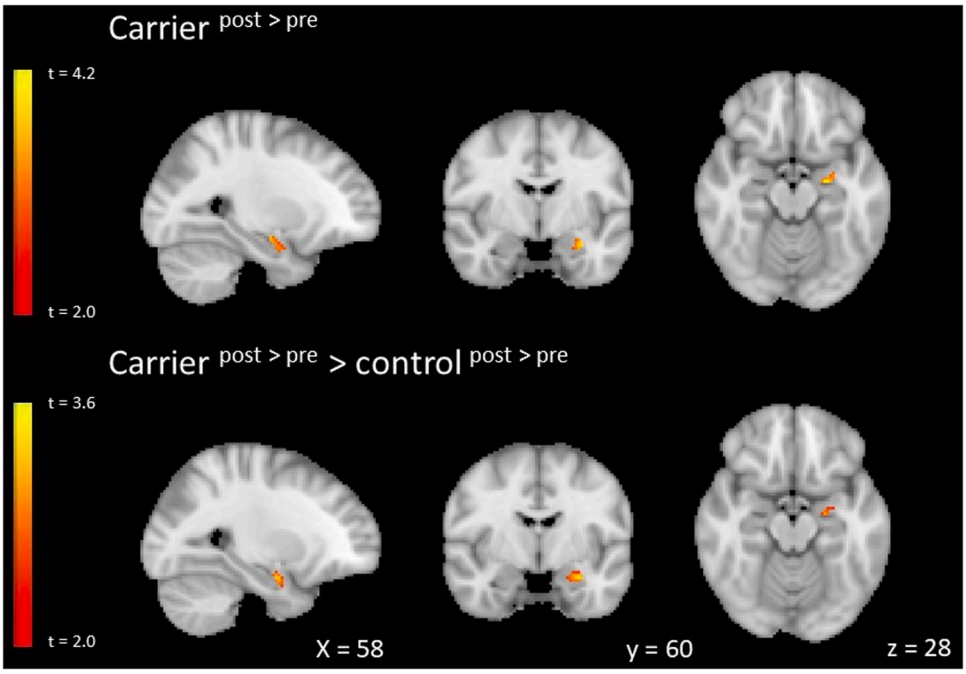

Fig. 3. Significant time x group interaction, indicating increased left amygdala activity during infant crying compared to control sounds in fathers who received the carrier intervention compared to fathers in the control group. Images are t-statistics, TFCE, FWE corrected, $p < .05$, controlled for age and educational level, overlaid on the MNI-152 standard brain. The left hemisphere of the brain corresponds to the right side in this image.

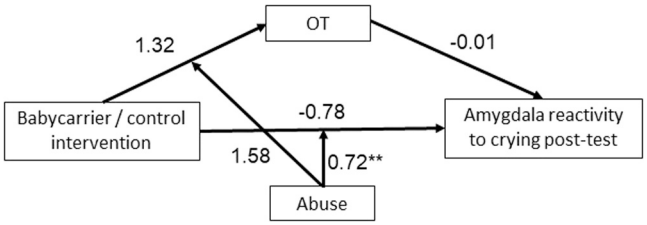

Fig. 4. Results of the moderated-mediation model. $^{**}p < .01$.

completely at random (Chi-square = 172.06, p = .63). We included paternal age and education, child age and sex, father-reported abuse and total maltreatment, paternal depression, father-reported hours spent with infant (average), pretest and posttest amygdala reactivity, pretest and posttest father-reported daily hassles, and pretest and posttest OT as variables in the imputation. Ten imputed data sets were created. After merging the imputed data sets for the intervention and control conditions, the ANCOVA was repeated, with condition and abuse and the interaction between condition and abuse as predictors, and pretest amygdala reactivity, paternal age and education as covariates. Results were pooled using the R package meta 4.18–0, since SPSS does not provide a pooled outcome for ANCOVA in multiply imputed data sets. The combined outcome for the ten imputed datasets showed a significant main effect of condition, Hedges' g = 0.81, (95% CI 0.66, 0.95), p < .01, and a significant interaction effect for condition*abuse, Hedges' g = 0.82 (95% CI 0.67, 0.96), p < .01.

4. Discussion

In the current RCT, we examined the effects of a baby carrier intervention on fathers' hormonal and neural reactivity. We tested whether infant carrying affects neural reactivity to infant crying in first-time fathers, taking into account the role of the hormone oxytocin as a mediating factor and fathers' own childhood experiences as a moderating factor. FMRI analyses revealed that fathers who received the infant carrier intervention showed increased amygdala reactivity to infant crying compared to fathers who received the control interaction. Interestingly, this effect was most pronounced in fathers with adverse childhood experiences. The effect of infant carrying on neural reactivity to crying was not mediated by enhanced oxytocin levels. The carrier intervention did not affect fathers' oxytocin levels, but impacted directly on amygdala reactivity to crying.

We found that fathers in the carrier and control group showed reactivity to crying in parental brain network regions, including the amygdala, frontal regions, supramarginal gyrus, regions involved in auditory perception (the middle and superior temporal gyrus), and empathy-related regions (insula, inferior frontal gyrus), which is consistent with a meta-analysis on neural regions involved in cry perception (Witteman et al., 2019). Interestingly, the infant carrier intervention impacted only on amygdala reactivity to crying and no effects on other parental brain network regions were found. The amygdala has been linked to vigilance and attention (Pessoa, 2010) and is particularly relevant in the context of parent-child relationships because of its role in processing of infant cues (Feldman et al., 2019; Ho and Swain, 2017). Several neuro-imaging studies have demonstrated amygdala activation in mothers viewing their own child versus an unknown child (Gobbini and Haxby, 2007; Leibenluft et al., 2004), which is interpreted to indicate mother's vigilant protectiveness toward her own child. Maternal amygdala activation to infant cries has been related to sensitive parenting (Kim et al., 2011) and the development of infant attachment (Laurent and Ablow, 2012), indicating that amygdala function is an important factor in the quality of parenting. Indeed, animal studies show that disruptions of the basolateral amygdala are related to deficits in parental behavior (Kirkpatrick et al., 1994), especially in males (Lee and Brown, 2007). Other neuro-imaging studies found blunted amygdala reactivity to child signals in mothers with negatively valenced parenting attitudes (Barrett et al., 2012) and in parents at risk for insensitive parenting, including mothers with postpartum depression (Moses-Kolko et al., 2010) and experiences of childhood maltreatment (Kim et al., 2014; Olsavsky et al., 2019), although a recent study points to amygdala hyper-reactivity to infant crying in maltreated mothers (Olsavsky et al., 2021).

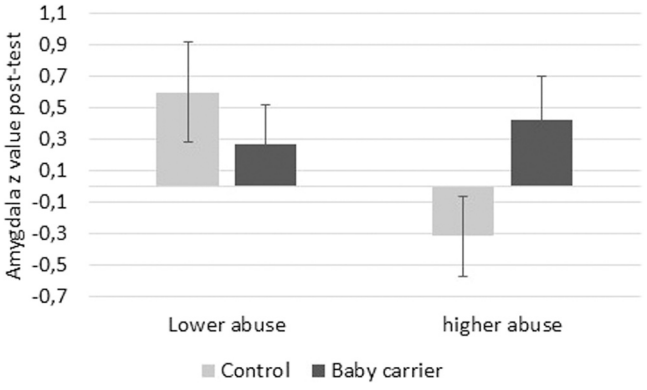

Fig. 5. Amygdala z values for the contrast cry > control in fathers with lower and higher adverse childhood experiences (abuse) in carrier (lower abuse N = 18, higher abuse N = 14) and control group (lower abuse N = 12, higher abuse N = 16) at post-test, adjusted for age, educational level, and amygdala reactivity at pre-test.

Fathers are, however, very much underrepresented in this line of research. In expectant fathers (van 't Veer et al., 2019) and first-time fathers (Lotz et al., 2020), amygdala activity has been related to the identification of potential threats for the child's safety, suggesting that the amygdala plays a role in paternal protective behaviors. Our study adds to these findings and indicates, for the first time, that an infant carrier intervention stimulates amygdala reactivity to infant crying in first-time fathers, possibly reflecting a heightened state of alertness and promoting more acute perception of infant signals. Interestingly, the effect of the carrier intervention was most pronounced for fathers with adverse childhood experiences. Fathers with higher levels of adverse childhood experiences who received the control intervention showed decreased amygdala activity over time, whereas the carrier intervention resulted in enhanced amygdala activity to infant crying in fathers with adverse childhood experiences. Given prior studies reporting amygdala hypo-reactivity to infant cues after experiences of maltreatment in mothers (Kim et al., 2014; Olsavsky et al., 2019), stimulating amygdala activity may be particularly important in maltreated fathers who may disengage from infant distress.

The effect of infant carrying on neural reactivity to crying was not mediated by enhanced oxytocin levels and no effects of infant carrying on fathers' oxytocin levels were found. This contrasts with previous studies showing oxytocin-enhancing effects of touch and physical contact (Feldman et al., 2010; Morhenn et al., 2012; Riem et al., 2017). One explanation could be that we tested the effects of the carrier intervention on fathers' baseline oxytocin levels, but did not assess reactivity. Previous research has shown that fathers exhibiting high levels of stimulatory contact with their infant showed an oxytocin increase after interacting with their infant (Feldman et al., 2010). Future studies should therefore also examine whether increased reactivity of the oxytocin system to infant-parent interaction underlies the effect of the infant carrier intervention on the amygdala. Alternatively, the carrier intervention may not have resulted in enhanced oxytocin levels because we tested the effects in a non-clinical sample of fathers with at most only mild experiences of child abuse. Fathers with more severe experiences of abuse may benefit more from an infant carrier intervention because they have lower baseline oxytocin levels (Ellis et al., 2021).

We cannot rule out that other hormonal mechanisms underlie the

effect of the infant carrier intervention, such as changes in the levels of vasopressin. In addition to oxytocin, vasopressin is considered an important hormonal regulator of parental behavior (Thijssen et al., 2018; Witte et al., 2019). Vasopressin has been related to stimulatory infant contact in parents (Apter-Levi et al., 2014) and is suggested to underlie fathering by increasing vigilance to protection (Carter, 1998). In a study of Atzil et al. (2012) a trend towards a positive amygdala correlation with vasopressin levels in fathers exposed to own infant videos was reported. In addition, vasopressin administration has also been shown to affect fathers' behavioral responding to infant crying (Alyousefi-van Dijk et al., 2019). Hence, vasopressin may be a potential other candidate mediating neural effects of an infant carrier intervention.

Some limitations should be noted. First, not all fathers adhered to the instruction to use the infant carrier for at least six hours per week, spread over a minimum of four days, for three weeks, as indicated by the fidelity check with the thermologger. Moreover, the duration of infant carrying was relatively short compared to previous studies. We determined the timing and use of the baby carrier in close consultation with practitioners in the field. Most of the fathers were non-users at the start of the study, and the duration of 6 h per week (over a minimum of 4 weeks) would strike the balance between feasibility, acceptability, and effectiveness. A previous study showed that maternal use of an infant carrier during a period of 8.5 months was related to infant-mother attachment security (Anisfeld et al., 1990). An infant carrier intervention with a longer duration or higher intensity of carrying may have a more pronounced effect on fathers' oxytocin levels. In the current context it should however be noted that controlling for the number of hours using the carrier did not change the results. Second, childhood abuse was measured with a retrospective self-report questionnaire, which may have resulted in underestimation of maltreatment (Fergusson et al., 2000). It should be noted that retrospectively measured subjective experience of child abuse is a more important predictor of developmental outcomes compared to prospective or objectives measures of the actual event (Danese and Widom, 2020; Latham et al., 2020). Additionally, the distinction between subtypes of maltreatment may be important for neurobehavioral sequelae and different subtypes may relate to specific oxytocin system changes (Ellis et al., 2021). Because in our sample the prevalence of neglect was very low, we did not assess differential effects of abuse and neglect. Future studies with clinical samples may examine the neurobiological effects of infant carrier intervention in parents with more severe maltreatment experiences, taking into account type of maltreatment. Furthermore, our sample size was relatively small. However, it should be noted that our sample was larger than samples of previous fMRI studies on cry perception. Samples of studies included in a recent meta-analyses on neural responding to crying ranged from $n = 11$ to $n = 44$ (Witteman et al., 2019). Another limitation is that the rating of the cry sounds in the fMRI paradigm may have affected neural responses to cry sounds. Cry ratings were, however, modelled as a regressor in fMRI analyses. Lastly, we did not examine how the carrier intervention impacts on fathers' behavior.

An important question that should be addressed in future work is how enhanced amygdala reactivity to infant crying relates to fathers' caregiving behaviors. Enhanced amygdala reactivity may reflect vigilance and alertness to threat. This heightened state of alertness may promote accurate perception of infant signals and may particularly impact on the perception of and responding to infant crying, because crying is a highly salient signal of distress. A previous study showed that elevated amygdala reactivity to own infant crying in mothers with a history of maltreatment was related to maternal non-intrusiveness during infant interactions, indicating that amygdala reactivity may represent an adaptive response related to increased sensitivity toward the infant (Olsavsky et al., 2021). Future studies should examine whether infant carrying also affects the perception of non-distressed infant signals, such as auditory or visual cues of infant laugher, and whether increased neural responding to infant signals facilitate sensitive caregiving behaviour.

Our finding that an infant carrier intervention enhances amygdala activity in particular in fathers with adverse childhood experiences extends previous studies showing positive effects of a baby carrier on parental caregiving in mothers. In a randomized control study, Anisfeld et al. (1990) showed that low-income mothers who used a soft infant carrier were more responsive to infants' vocalization and their infants were more often securely attached compared to a control group, suggesting that increased physical contact promotes attachment security between infant and mother. Similarly, infant carrying has been related to increased parent-infant dyadic conversations and infant-imitated speech (Mireault et al., 2018). Hence, research points to some benefit to infant carrying to the mother and infant relationship, although it should be noted that studies are still scarce and underpowered. The practice of infant carrying may be a potential intervention for parents with problematic infant relationships or parenting problems, such as parents with adverse childhood experiences. Infant carrying may be particularly important for fathers who may be physiologically less prepared for parenthood than mothers and may adapt to their new parental role more slowly through active involvement in childcare.

5. Conclusions

In conclusion, this study is the first RCT to examine the effects of a baby carrier intervention on fathers' hormonal and neural functioning. Infant carrying enhanced amygdala reactivity to infant crying and this effect was most pronounced in fathers with adverse childhood experiences. Our findings indicate that spending time in physical contact with the infant may promote attention to infant signals, in particular in fathers with adverse childhood experiences. Soft infant carriers may facilitate an adaptive transition to fatherhood.

CRediT authorship contribution statement

Madelon M.E. Riem: Methodology, Validation, Formal analysis, Data curation, Writing – original draft, Visualization. **Anna M. Lotz:** Validation, Investigation, Supervision, Resources, Data curation, Writing – review & editing, Project administration. **Lisa I. Horstman:** Data curation, Investigation, Formal analysis, Project administration. **Kim Alyousefi-van Dijk:** Investigation, Resources, Data curation, Supervision, Writing – review & editing. **Martine Verhees:** Methodology, Data curation, Writing – review & editing. **Maaike Cima:** Methodology, Writing – review & editing. **Marinus H. van IJzendoorn:** Conceptualization, Methodology, Formal analysis, Writing – review & editing, Supervision, Funding acquisition. **Marian J. Bakermans-Kranenburg:** Conceptualization, Methodology, Formal analysis, Validation, Writing – review & editing, Supervision, Funding acquisition, Project administration.

Declaration of interest

The authors report no competing interest with regard to the use of the baby carriers. The manufacturers of the baby carriers were not involved in the sponsoring, the design, or any other stage of the study.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2021.105380.

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