9-30-2019

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Publication Statement
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Olsavsky, A. K., Stoddard, J., Erhart, A., Tribble, R., & Kim, P. (2019). Neural processing of infant and adult face emotion and maternal exposure to childhood maltreatment. *Social Cognitive and Affective Neuroscience, 14*(9), 997-1008. https://doi.org/10.1093/scan/nsz069

Social Cognitive and Affective Neuroscience, 2019, 997–1008

doi: 10.1093/scan/nsz069
Advance Access Publication Date: 4 November 2019
Original article

Neural processing of infant and adult face emotion and maternal exposure to childhood maltreatment

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Abstract

Face processing in mothers is linked to mother–infant social communication, which is critical for parenting and in turn for child development. Neuroimaging studies of child maltreatment-exposed (CME) mothers are sparse compared to studies of mothers with postpartum depression, which have suggested blunted amygdala reactivity to infant stimuli. We expected to see a similar pattern in CME mothers. Based on broader studies in trauma-exposed populations, we anticipated increased amygdala reactivity to negative adult face stimuli in a comparison task in CME mothers given heightened evaluation of potential threat. We examined Neuroimaging studies of mothers with childhood maltreatment exposure (CME) (18–37 years old), who performed infant ($N = 45$) and/or adult ($N = 46$) face processing tasks. CME mothers exhibited blunted bilateral amygdala reactivity to infant faces. There was no between-group difference in amygdala reactivity to adult faces. In infant and adult face processing tasks regardless of CME, superior temporal gyrus activation was increased for negative-valence stimuli. Our preliminary findings suggest that childhood maltreatment alters maternal processing of infant social cues, a critical skill impacting infant socioemotional development.

Key words: childhood maltreatment; mother; infant; amygdala; face

Introduction

Trauma exposure is common, with lifetime prevalence of 50–60% in epidemiological samples (Kessler *et al.*, 1995; McLaughlin *et al.*, 2013). Childhood maltreatment exposure (CME), a specific type of trauma exposure, is known to increase risk for adult psychopathology and for poor outcomes (Green *et al.*, 2010; McLaughlin *et al.*, 2010; Nanni *et al.*, 2012). Human and animal studies have demonstrated the impact of mothers' early-life adverse experiences on their parenting behaviors (Champagne & Meaney, 2001; Maestripieri *et al.*, 2006; Gonzalez *et al.*, 2012; Schwerdtfeger *et al.*, 2013; Juul *et al.*, 2016). Studying maternal CME is important, as it may affect a broad array of mother–child outcomes beyond maternal psychopathology, including infant stress reactivity (Brand *et al.*, 2010; Jovanovic *et al.*, 2011), infant brain development (Moog *et al.*, 2017) and parent and child behavioral outcomes (Schwerdtfeger *et al.*, 2013; Zalewski *et al.*, 2013; Smith *et al.*, 2014; Cross *et al.*, 2016). In our study, we focus on CME in new mothers (e.g. physical or emotional abuse, witnessed domestic violence). Specifically, given evidence for effects of maternal CME on two generations, we are interested in how these exposures affect parenting behaviors and thereby child development.

Defining CME, we consider direct adverse experiences involving conflict and aggression in households of mothers as children, as opposed to a broader array of family dysfunction (e.g.

Received: 8 March 2019; **Revised:** 7 August 2019; **Accepted:** 19 August 2019

divorce), which prior studies suggest have distinct outcomes *vs* maltreatment (Felitti *et al.*, 1998; Repetti *et al.*, 2002; Narayan *et al.*, 2017). We focused on active maltreatment, including physical or verbal abuse and witnessed domestic violence, given its inclusion in prior maltreatment studies and potential for negative outcomes (Teicher *et al.*, 2006; Bailey *et al.*, 2012; Scott *et al.*, 2012).

To understand the impact of CME on parenting, we examined how CME mothers process infant faces. Specifically, attribution of importance and appropriate responses to offspring cues are critical for instantiation and maintenance of motivated maternal behaviors, which have been well characterized in animal and human studies (Lonstein *et al.*, 2015; Lomanowska *et al.*, 2017). In prior work, amygdala has been shown to respond to important social stimuli (Davis & Whalen, 2001; Adolphs, 2003), particularly in the context of mother–child relationships (Leibenluft *et al.*, 2004; Tottenham *et al.*, 2012). In one study of healthy comparison mothers without psychopathology, amygdala was part of a broader network activated when viewing their own and other infant's faces (Lenzi *et al.*, 2009). We thus chose to focus on amygdala activation in our study.

While there has been significant work examining neural circuitry of parenting in mothers with depression (Moses-Kolko *et al.*, 2011, 2014; Laurent & Ablow, 2012, 2013; Webb & Ayers, 2015), fewer studies address the impact of CME on mothers' neural response to infants and its relationship to parenting (Pawluski *et al.*, 2017). An initial study in one cohort demonstrated that mothers responded in amygdala more to happy *vs* distressed faces of their own infant (Strathearn & Kim, 2013), i.e. that responsivity to infant faces is influenced by personal relevance of the stimulus. A follow-up study in a partially overlapping sample of new mothers, some of whom had unresolved attachment-related trauma (i.e. which constitutes difficult early interactions with parent but not CME *per se*), demonstrated blunted amygdala activation to own child's distressed *vs* happy faces compared to mothers without this exposure (S. Kim *et al.*, 2014). Interestingly, this finding is parallel to previous findings in women with postpartum depression demonstrating decreased reactivity to infant faces in salience network areas other than amygdala (i.e. anterior cingulate cortex, insula; Laurent & Ablow, 2013). A third study in mothers with PTSD found greater limbic activation to mother–child separation *vs* play videos (Schechter *et al.*, 2012). Discrepant study findings are likely due to stimuli (e.g. photographic *vs* video, baby age), population (e.g. PTSD, trauma-exposed) and trauma–definition differences. To address this gap, we utilize previously validated infant face stimuli and examine specific exposures—childhood maltreatment—to increase ease of interpretation.

Furthermore, we sought to understand whether differences in CME mothers' face processing were specific to infant stimuli by including a comparison adult faces task. Specifically, it is important to consider whether CME mothers attend more to environmental threats at the expense of attention to infant cues. In other emotional contexts, salience processing allocates attention to significant stimuli and is perturbed in anxiety disorders, with increased threat bias and avoidance (Paulus & Stein, 2006; Etkin *et al.*, 2009; Geng *et al.*, 2015; Uddin, 2015). Another study in adults without lifetime psychopathology demonstrated that increased amygdala response to negative *vs* neutral adult faces was associated with Childhood Trauma Questionnaire score (Dannlowski *et al.*, 2013). This study is relevant to our non-clinical population as it focuses on trauma exposure without significant psychopathology, suggesting that exposure alone may affect face processing. Furthermore, one study found increased amygdala reactivity across emotions in a sample of CME participants (van Harmelen *et al.*, 2013).

Conceivably, attention to threat might interfere with maternal behaviors, which aligns with data regarding associations of maternal trauma exposure with harsh parenting (Smith *et al.*, 2014; Powers *et al.*, 2015; Cross *et al.*, 2016). Subtle changes in parenting including increased neutral affect (Juul *et al.*, 2016), distorted maternal mental representations of the child (Schechter *et al.*, 2008), and differences in prenatal attachment (Schwerdtfeger & Goff, 2007) have been associated with maternal CME. Additionally, in a related sample to our current study, P. Kim *et al.*, 2017 found a relationship between socioeconomic status and maternal intrusive behaviors toward the child—an indirect effect of amygdala activation to infant distress distr faces. Given our interest in the intersection between maternal behavior outside the scanner and neural response to infant faces, we included a mother–infant observation, coding for maternal sensitivity and intrusiveness using the Emotional Availability Scale (EAS; Biringen & Easterbrooks, 2012; Saunders *et al.*, 2015).

We hypothesized that mothers with CME would have blunted amygdala reactivity to distressed infant faces and that they would have increased amygdala reactivity to negative-valence adult faces. Further, we predicted that blunted amygdala reactivity to distressed infant faces would be associated with decreased maternal sensitivity, whereas, increased amygdala reactivity to negative-valence adult faces would be associated with greater maternal intrusiveness, both during mother–infant behavioral observation.

Methods

Participants/Study Procedure

English-speaking first-time mothers between 18–40 years of age were recruited via University of Denver Psychology Department volunteer pool, Denver Health Obstetric Clinic, local advertisements, Prenatal Plus and Women, Infants and Children clinics. Mothers were excluded from the Infant Development, Emotion and Attachment study based on having any history of pregnancy-related illnesses, having an infant who stayed in the Neonatal Intensive Care Unit (>1 night), taking psychotropic medications (excluding antidepressants) or neurological or psychiatric illness (except depression/anxiety). The research protocol was approved by the University of Denver IRB, and informed consent was administered to all participants.

Home Visit Measures

Demographic data including age, time postpartum, partner status, breastfeeding, ethnicity, medications and self-reported illness and drug/alcohol use were collected. Socioeconomic status was assessed with income-to-needs ratio (P. Kim *et al.*, 2017). Beck Depression Inventory (Beck *et al.*, 1961) and Spielberger State and Trait Anxiety (Spielberger *et al.*, 1970) were administered to assess psychological symptoms. Participants completed the Risky Families Questionnaire (RFQ) to assess mothers' childhood adverse experiences (Repetti *et al.*, 2002) and to determine study group assignment. We created a subscale from three relevant RFQ questions representing verbal/emotional or physical abuse and witnessed domestic violence: (1) How often did a parent or other adult in the household swear at you, put you down or act in a way that made you feel threatened? (2) How often did a parent or other adult in the household push, grab,

Table 1. Demographics of infant faces task participants

	HC	CME	Significance1
N	19	26	
Mean Age at Scan (y)	26	24	NS
Mean Prenatal Income to Needs Ratio	2.74	2.53	NS
Mean Days Postpartum	130	139	NS
Ethnicity other than Caucasian (N)	12	15	NS
Scanner (N)			NS
3T Siemens Trio	17	20	
3T Siemens Prism	2	6	
History of breastfeeding (N)	19	25	NS
Peripartum medication use (N)	13	18	NS
Peripartum medical illness (N)	5	8	NS
Peripartum alcohol or drug use (N)	5	5	NS
Long-term relationship/marriage (N)2	14	22	NS
Mean WASI Full Scale IQ3	96	102	NS
History of psychiatric disorder (N)4	3	12	CME>HC; p=0.07
Spielberger Trait Anxiety mean score	31	38	CME>HC; p<0.05
Spielberger State Anxiety mean score	29	32	NS
Beck Depression Inventory mean score	6	8	NS
Direct Sensitivity mean score	5	5	NS

Notes. Continuous variables tested with independent sample *t*-tests for between-group differences and categorical variables tested with Pearson chi-square tests. Relationship status missing data: NE, 0; CME, 1. WASI Full Scale IQ missing data: NE, 3; CME, 11. History of psychiatric disorder missing data: NE, 5; CME, 3.

Table 2. Demographics of adult face task participants

	HC	CME	Significance[1]
N	18	28	
Mean Age at Scan (y)	27	27	NS
Mean Prenatal Income to Needs Ratio	2.97	3.05	NS
Mean Days Postpartum	140	132	NS
Ethnicity other than Caucasian (N)	12	15	NS
Scanner (N)			NS
3T Siemens Trio	13	14	
3T Siemens Prism	5	14	
History of breastfeeding (N)	18	28	NA[2]
Peripartum medication use (N)	10	15	NS
Peripartum medical illness (N)	4	7	NS
Peripartum alcohol or drug use (N)	8	15	NS
Long-term relationship/marriage (N)[3]	15	23	NS
Mean WASI Full Scale IQ[4]	94	101	NS
History of psychiatric disorder (N)[5]	2	14	CME>HC; p<0.05
Spielberger Trait Anxiety mean score[6]	29	39	CME>HC; p<0.001
Spielberger State Anxiety mean score[6]	28	32	CME>HC; p<0.05
Beck Depression Inventory mean score	4	8	CME>HC; p<0.005
Direct Sensitivity mean score	5	5	NS

Notes. Continuous variables tested with independent sample *t*-tests for between-group differences and categorical variables tested with Pearson chi-square tests. History of breastfeeding: all were breastfeeding so chi square was unable to be performed due to empty cell. Relationship status missing data: NE, 0; CME, 1. WASI Full Scale IQ missing data: NE, 5; CME, 13. History of psychiatric disorder missing data: NE, 4; CME, 2. STAI State and Trait Anxiety Inventory missing data: NE, 1; CME, 0.

shove or slap you? (3) How often would you say that a parent or other adult in the household behaved violently toward a family member or visitor in your home? Questions are scored utilizing a Likert scale with four options: 0, 'never;' 1, 'a little;' 2, 'most of the time;' and 3, 'all the time.' We assigned participants by dichotomous criterion (Hardt & Rutter, 2004). If participants endorsed any CME experience, they were assigned to the CME group (*N* = 26) with the remaining to the non-exposed (NE) group (*N* = 19). Participant characteristics and group comparisons are presented in Tables 1 and 2. In the CME group, 12 participants endorsed all three types of maltreatment, while 5 endorsed two types and 9 experienced one type of maltreatment.

fMRI Visit

Mothers participated in fMRI protocol at the Intermountain Imaging Consortium at CU Boulder. Please see Figure 1 for schematic of participants who completed the task(s). Infant task was performed prior to adult task due to increased relevance for mothers. Additionally, there were other non-face tasks (e.g. infant cry, emotion regulation, resting state) performed prior to adult faces task; thus adult faces task did not directly follow infant faces task. Thirty-three mothers completed both face tasks. Infant data (*N* = 39) have been previously reported to address questions related to poverty, but adult data have not been published (P. Kim *et al.*, 2017).

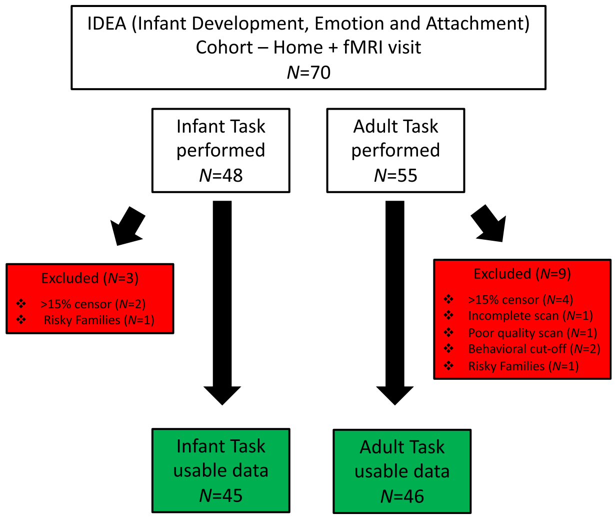

Fig. 1. Schematic of participant flow in study.

Maternal Behaviors

Mother–infant dyads engaged in a 15 min free-play videotaped observation, coded by two trained coders (ICC = 0.84) utilizing the EAS, a macro-coding scale assessing mother–child interactions across a broad range of child development (Biringen, 2000; Biringen & Easterbrooks, 2012). Mothers are instructed to interact with their child as they would at home. EAS measures four maternal dimensions, including maternal sensitivity, structuring, non-hostility and non-intrusiveness. Sensitivity is the extent to which mothers respond appropriately to their infant's cues, encompassing attunement to child's affect, timing of responses and incorporation of child feedback (Saunders *et al.*, 2015). We focused on maternal sensitivity because it has been shown to both moderate the effect of maternal psychiatric diagnoses and to have its own effects on child social engagement and stress reactivity (Feldman *et al.*, 2009). Maternal non-intrusiveness is defined as the mother's ability to participate in the child's play while not interfering with a developmentally appropriate level of child independence (Saunders *et al.*, 2015). We examined this construct given prior findings in an overlapping sample reflecting an association between income-to-needs ratio and maternal non-intrusiveness, mediated via right amygdala activation to negative infant faces (P. Kim *et al.*, 2017), as well as our thoughts that intrusiveness might correlate with mother's response to negative adult faces.

Infant face Task

The infant face task included previously standardized photographic stimuli (Strathearn *et al.*, 2008; Strathearn *et al.*, 2009; Strathearn & Kim, 2013; S. Kim *et al.*, 2014; P. Kim *et al.*, 2017) of one male and one female Caucasian baby (10 photos/baby, happy, neutral and distressed). We did not match for baby race due to insufficient availability of stimuli. Since we included mothers at 0–6 months postpartum, we utilized standardized rather than custom infant stimuli, given that younger babies lack social smile. Mothers were instructed to view photos and experience their thoughts and feelings without any required response. The event-related paradigm included 90 2000 ms trials (30/emotion) in randomized order with fixation between trials (average 1250 ms; 500–5350 ms). Afterwards, mothers were asked these questions about stimuli (9 point Likert scale): (1) 'How does the picture make you feel?' (2) 'How do you think the baby in the picture is feeling?'

Adult face task

The adult task included standardized photographs (six female, four male) with varied emotions (angry, fearful, happy, neutral; Ekman & Friesen, 1976). Mothers were instructed to identify stimulus gender with button-press. The event-related paradigm was similar to a previously used paradigm, with 120 2000 ms trials in randomized order (30/emotion; average 1250 ms inter-trial fixations; 500–6000 ms; P. Kim *et al.*, 2012).

fMRI acquisition

fMRI scans were performed utilizing a 3T Siemens Trio or Prisma scanner, and thus scanner is included in analyses. Groups were balanced for scanner. fMRI parameters were similar for scanners and tasks as follows: 3 × 3 × 3 mm voxels, TR = 2300 ms, TE = 27 ms, FOV = 192 mm, flip angle = 73. T1 anatomical scans were collected with slice-thickness: 1.0 mm (Trio); 0.8 mm (Prisma). fMRI and post-task paradigms were administered with E-Prime (Psychology Software Tools, USA).

fMRI preprocessing

Images were analyzed with Analysis of Functional Neuroimages (AFNI; Cox, 1996) as follows: remove four pre-steady-state volumes, slice-timing correction, registration to Talairach template, non-linear warping and smoothing (FWHM kernel = 6 mm). Volumes were censored (motion >0.5 mm or >10% of brain voxels outliers (>4 SD), with participants with >15% censoring excluded. Single-subject models were checked for behavioral response rate and quality, including amygdala coverage and activation in visual areas to all faces *vs* fixation at uncorrected $P < 0.001$ threshold. Please see Figure 1 for schematic of task completion/exclusion of participants. For infant task, 48 mothers were scanned (3 excluded): missing RFQ ($N = 1$), censoring > 15% ($N = 2$). For adult task, 55 mothers were scanned (9 excluded): missing RFQ ($N = 1$), censoring > 15% ($N = 4$), incomplete scan ($N = 1$), poor scan quality (i.e. no activation in all-faces-*vs*-fixation contrast, $P_{uncorr} < 0.001$, $N = 1$) or response accuracy < 65% ($N = 2$; P. Kim *et al.*, 2012). There were no group differences in exclusion ($P < 0.05$).

fMRI single subject models.

Anatomical images were skull-stripped using FreeSurfer (Segonne *et al.*, 2004), followed by non-linear co-registration with AFNI TT_N27 Taliarach-space template. Single-subject GLM were constructed modeling hemodynamic response function with emotion relative to implicit baseline for all conditions (infant—happy/distressed/neutral; adult—happy/angry/fearful/neutral), cubic polynomial for drift, six framewise displacement motion regressors (three translational, three rotational). For the adult task, there was an additional incorrect-trial regressor.

fMRI group anatomical region-of-interest analyses

Anatomical region-of-interest (ROI) analysis for amygdala was performed using intersection map of DD_Desai_MPM maximum probability map amygdala and activation map for each participant (Desikan *et al.*, 2006). We extracted average percent signal change and performed secondary analyses in R (*R: A language and environment for statistical computing*, 2017). We constructed linear mixed effects (LME) models with fixed effects of emotion, scanner, side (right *vs* left), maternal race (Caucasian *vs* non-Caucasian), CME group and random-effect of participant separately for the infant face task and the adult face task. In each analysis, we first examined three-way and two-way interactions of CME group, emotion and side, and we removed non-significant higher-order interactions to preserve power. Pearson chi-square (categorical) or independent sample *t*-tests (dimensional) were performed to assess between-group differences in demographics and psychological scales. Variables that differed between groups were included in models barring significant collinearity concerns. Finally, we performed regression diagnostics to examine potential collinearity (examination of variance inflation factors, VIF < 2 for all factor main effects in all models), model residuals and effect of removing potentially influential points (Cook's $d > 0.1$, as determined by the equation $4/(N\text{-}k\text{-}1)$). We also tested dimensional effects of the RFQ-reported CME severity in each model with identical factors to primary analyses. As an extra safeguard for quality control given the passive nature of infant task, we constructed similar models for both tasks for fusiform gyrus (bilateral, with effect of side) to assess for differences in visual attention between groups. We also combined tasks in participants who performed both ($N = 33$) into one anatomical ROI model which also included fixed effect of stimulus type (infant/adult). Given that our groups did not overlap entirely and the two tasks having significant differences (passive *vs* active, differing stimulus characteristics), this analysis is exploratory in nature, with similar approach to covariates/cofactors and interactions as primary ROI analyses. Further, in order to perform this analysis we needed to collapse fearful and angry stimuli in the adult faces task into negative valence stimuli in order to have a parallel analysis structure to the infant task (which had positive, neutral and negative stimuli).

fMRI group whole-brain analyses.

We performed whole-brain analyses separately for infant and adult tasks via using AFNI *3dLME*. Fixed effects were emotion, group, side, maternal race and scanner, with random effect of participant with relevant covariates/factors differing between groups barring collinearity concerns as described above. Interactions between factors were assessed similarly to ROI analyses above. To determine cluster threshold for tasks, we utilized AFNI 3dClustSim (ACF option) with NN = 3, primary voxel-wise significance threshold of $P < 0.001$ and cluster-forming threshold for alpha < 0.05: k = 42 (infant) and k = 32 (adult).

fMRI associations with maternal behaviors

Given our interest in whether maternal sensitivity was associated with higher maternal amygdala response to infant faces we performed exploratory analyses adding either sensitivity or non-intrusiveness separately into amygdala ROI analyses with identical factors/covariates (sensitivity and non-intrusiveness analyzed in separate models due to collinearity).

Subjective stimulus ratings associated with CME

Mothers performed a post-scan infant face rating task. Two NE mothers' post-scanner ratings data were missing. Mothers rated stimuli on 9 point Likert scales: (1) 'How does the picture make you feel?' (2) 'How do you think the baby in the picture is feeling?' Results were analyzed utilizing LME with identical fixed and random factors to imaging analyses except for side and scanner to test for differences in subjective ratings of pictures associated with CME. We also tested whether adding subjective ratings to imaging models affected results.

Results

Participants

Usable data included $N = 45$ for infant and $N = 46$ for adult task. Given that groups were not entirely overlapping ($N = 33$ overlapping), we present separate demographic data for each task (Tables 1 and 2). Infant task CME mothers had higher trait anxiety ($t_{1,43} = -2.6$, $P < 0.05$) and trend for higher lifetime psychiatric diagnoses (CME > NE, $\chi 2 = 3.4$, $P = 0.07$). Adult task CME mothers had greater lifetime psychiatric diagnoses (CME > NE, $\chi 2 = 5.4$, $P < 0.05$), greater trait ($t_{1,42} = -3.7$, $P < 0.005$) and state anxiety ($t_{1,42} = -2.7$, $P < 0.05$) and depression ($t_{1,43} = -3.2$, $P < 0.005$) scores. In our model for adult task we included trait rather than both state and trait anxiety, as this was the more significant effect and due to concerns for collinearity.

Infant task group ROI analysis

We constructed LME model with main effects of emotion, side, group, maternal race (Caucasian *vs* not Caucasian), scanner and factors/covariates which differed between groups (STAI Trait, lifetime psychiatric diagnoses) and random effect of participant. In initial analyses we examined interactions of group with emotion and side (*P*s > 0.05), prior to removing them from model. Our models revealed between-group difference in amygdala ($F_{1,38} = 12.0$, $P < 0.005$, CME < HC; Figure 2) and main effect of side ($F_{2,222} = 6.7$, $P < 0.05$, R > L; Supplementary Figure S2), with no other significant effects. Amygdala findings were robust to regression diagnostic analyses. Control ROI analysis in bilateral fusiform gyrus with identical factors/covariates revealed no between-group differences in infant task (Supplementary Figure S3). There was no dimensional dose effect of CME load in the model.

Adult task group ROI analysis

We utilized LME model with identical initial factors (emotion, side, group, race, scanner), along with interactions related to group, side and emotion, adding in factors/covariates with between-group differences sequentially, in order to examine collinearity issues (BDI, STAI-Trait, lifetime psychiatric diagnoses). There were no significant effects including interactions in amygdala model ($F_{1,38} = 0.01$, $P > 0.05$; Figure 2). Given our surprise at the lack of a finding in the amygdala for the adult task, in addition to amygdala coverage checks which we performed, we also examined all faces *vs* fixation contrast and were able to confirm that there was indeed bilateral amygdala activation at $P < 0.001$ threshold (uncorrected). Control ROI analysis in bilateral fusiform gyrus with identical factors/covariates revealed no between-group differences in adult task (Supplementary Figure S3). There was no dimensional dose effect of CME load in the model.

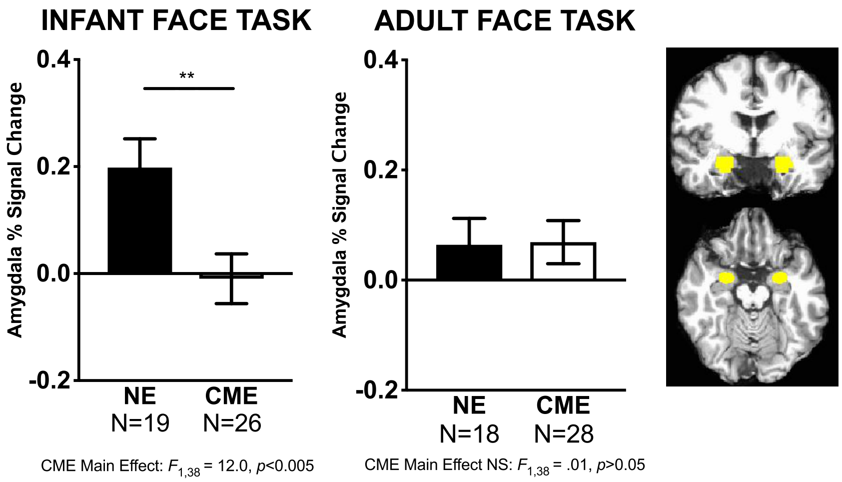

Fig. 2. Bilateral amygdala activation—infant and adult face tasks.

Table 3. Whole-brain analyses for infant and adult face tasks

	Coordinates(RAI)	Cluster Size (k)	Significance	Post hoc tests
Infant Picture				
E3 motion				
Right Superior Temporal Gyrus	-44 35 6	95	$F_{2,88}$=17.4; p<0.001	Distress>Happy (p<0.001) Distress>Neutral (p<0.001)
Adult Picture				
Emotion				
Left Brodmann Area 17	11 95 3	121	$F_{3,135}$=12.0; p<0.001	Happy>Angry (p<0.001) Happy>Neutral (p<0.001) Happy>Fear trend (p=0.05)
Right Brodmann Area 18	-29 92 3	78	$F_{3,135}$=10.3; p<0.001	Happy>Angry (p<0.001) Fear>Angry (p<0.001) Happy>Neutral (p<0.005)
Right Superior Temporal Gyrus	-47 38 6	39	$F_{3,135}$=9.5; p<0.001	Angry>Neutral (p<0.001) Fear>Neutral (p<0.001) Happy>Neutral trend (p=0.05)
Group				
Right Middle Frontal Gyrus	-29 -26 45	41	$F_{1,38}$=24.6; p<0.001	CME>NE (p<0.001)
Scanner				
Left Middle Frontal Gyrus	41 -29 36	33	$F_{3,135}$=24.2; p<0.001	Prisma>Trio scanner (p<0.001)

Exploratory analysis—adult and infant tasks in combined overlapping sample

Combined model in overlapping participants ($N = 33$) revealed two significant interactions—Stimulus Class × Group and Valence × Group (Supplementary Figure S4). Stimulus Class × Group ($F_{1,286} = 6.8$, $P < 0.01$) interaction was driven by there being a Group effect within infant but not adult faces task ($F_{1,20} = 6.6$, $P = 0.01$, CME < NE). Valence × Group effect ($F_{2,286} = 3.3$, $P < 0.05$) was driven by CME mothers having lower amygdala activation compared to NE to neutral ($P < 0.05$) and a trend for lower response to positive faces ($P = 0.06$). There were no other main effects or interactions.

Infant picture task group whole-brain analysis

Whole-brain analysis including similar factors/covariates to amygdala ROI analysis for infant task described above (Table 3) revealed main effect of emotion in R superior temporal gyrus (STG; [−44 35 6],k = 95, $F_{2,88} = 17.4$, $P < 0.001$;Figure 4A), driven by higher activation to distressed *vs* happy or neutral faces (Ps < 0.001). There were no significant interactions.

Adult face task group whole-brain analysis

Whole-brain analysis including similar factors/covariates to amygdala ROI analysis for adult task described above (Table 3) revealed main effect of emotion in areas associated with vision, face processing and social cognition: LBA17 ([11 95 3], $k = 121$, $F_{3,135} = 12.0$, $P < 0.001$); RBA18 ([−29 92 3], $k = 78$, $F_{3,135} = 10.3$, $P < 0.001$); R superior temporal gyrus ([−47 38 6], $k = 39$, $F_{3,135} = 9.5$, $P < 0.001$). The findings in visual areas (BA17/18) were driven primarily by higher activation to happy *vs* neutral/negative emotions (Ps < 0.05). In STG, the finding was driven by negative (fearful/angry) faces eliciting greater activation *vs* neutral (Ps < 0.001; Figure 4B). There was also a group effect in right middle temporal gyrus ([−29–26 45], $k = 41$, $F_{1,38} = 24.6$, $P < 0.001$; CME > NE), as well as an effect of scanner in right middle temporal gyrus ([41–29 36], $k = 33$, $F_{3.135} = 24.2$, $P < 0.001$; Prisma > Trio). There were no significant interactions.

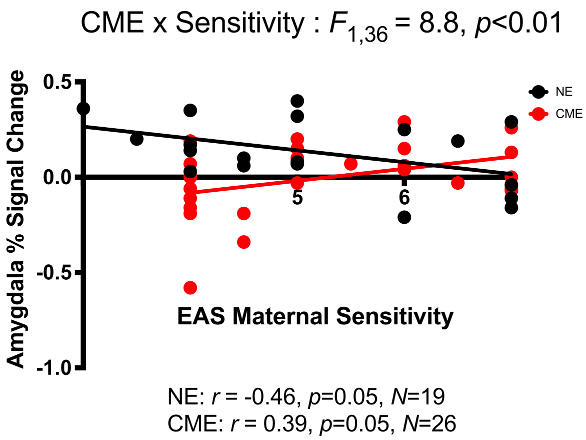

Fig. 3. Bilateral amygdala activation *vs* maternal sensitivity—infant faces.

fMRI associations with maternal behaviors

Sensitivity and non-intrusiveness were correlated in both task samples (infant: $r = 0.53$; adult: $r = 0.42$, Ps < 0.005). The overall group difference in amygdala activation for the infant task was robust to adding maternal sensitivity to the model, but was qualified by a Group × Sensitivity interaction ($F_{1,36} = 8.8$, $P < 0.01$), driven by trends for a negative association between amygdala activation to infant faces in NE ($r = -0.46$, $p = 0.05$, $N = 19$) and the opposite in CME mothers ($r = +0.39$, $P = 0.05$, $N = 26$; Figure 3). There were neither significant effects in infant task of non-intrusiveness, though the main effect of CME was robust to its addition to model. There was no significant effect in the adult task of either maternal behavior measure.

Subjective stimulus ratings associated with CME

Model of mother's feelings about infant pictures revealed main effects of emotion ($F_{2,82} = 239$, $P < 0.001$; Happy > Neutral > Distress, all Ps < 0.001) and group ($F_{1,37} = 4.8$, $P < 0.05$), with CME mothers experiencing decreased positive feelings *vs* NE (Supplementary Figure S1A). Mothers' ratings of babies' emotional state revealed similar effects, include main effect of emotion ($F_{2,82} = 510$, $P < 0.001$; Happy > Neutral > Distress, Ps < 0.001), and of group ($F_{1,37} = 8.0$, $P < 0.01$), with CME mothers rating babies' feelings less positively *vs* NE (Supplementary Figure S1B). There were no Group × Emotion interactions of ratings. Regression analysis revealed that neither rating was correlated with amygdala activation to infant faces or maternal behaviors (sensitivity/intrusiveness).

Discussion

We examined differences in neural processing of infant and adult faces in CME and NE mothers. We found that CME mothers exhibited blunted bilateral amygdala reactivity to infant faces regardless of emotion. Further, there was a Group × Sensitivity interaction, which was driven by two trends, with higher amygdala activation to infant faces associated with increased maternal sensitivity during mother–infant interaction in CME, and the opposite relationship in NE mothers. Furthermore, in a post-scan rating task, mothers with CME *vs* NE reported both that baby face stimuli made them feel less positive and that they had less positive perception of infants' emotional states, though there were no Group × Emotion interactions in subjective stimulus ratings. Adult face task revealed no between-group differences in amygdala activation. There were no Group × Emotion interactions in amygdala in either task, which may be related to power limitations. There were no relationships between amygdala activation during infant or adult tasks and maternal non-intrusiveness. Whole-brain analyses of infant and adult face tasks revealed that in both tasks, right superior temporal gyrus preferentially activated to negative-valence stimuli. Lastly, in a combined exploratory analysis of both tasks, we found that specifically in the infant task, mothers with CME tended to distinguish less between different baby emotions, particularly that unexposed had increased amygdala activation to positive ($P = 0.06$) and neutral ($P < 0.05$) infant faces compared to CME mothers but no difference between groups in response to negative baby faces.

Understanding the significance of the amygdala findings is complex as the amygdala plays a variety of roles in processing socioemotional and threat stimuli (Fareri & Tottenham, 2016). Furthermore, the finding must be interpreted cautiously and contextualized with respect to other findings to avoid reverse inference (Poldrack, 2011). Amygdala activation has been demonstrated to play an important role in processing of infant stimuli by mothers (Leibenluft *et al.,* 2004; Strathearn *et al.,* 2008; Strathearn & Kim, 2013). Others have suggested a broader function for amygdala in social interactions, suggesting it may play a role in motivational aspects of social stimuli (Adolphs, 2003), which is consistent with data suggesting that amygdala is connected with motor areas of the brain as well, which are involved in executing motivated behaviors (Rizzo *et al.,* 2018). In this context, we interpret blunted amygdala activation across infant face emotion stimuli in CME as suggestive of diminished affective or motivational significance of infant faces. The finding in the primary amygdala analyses is similar to findings in mothers with unresolved trauma who were found to have lower amygdala response to their own infant's distressed *vs* happy faces (S. Kim *et al.,* 2014). The finding in the primary amygdala analyses is similar to findings in mothers with unresolved trauma who were found to have lower amygdala response to their own infant's distressed *vs* happy faces (S. Kim *et al.,* 2014). However, the exploratory analysis utilizing the overlapping sample of mothers who performed both tasks suggests that differences in face processing in mothers with CME in the postpartum period may reflect diminished attentiveness to infant cues that are neutral or positive, which may have important implications for maternal responsiveness and reward processes in the context of the mother–infant relationship.

We further found that among CME mothers, higher amygdala response to infant faces was associated with more sensitive maternal interactions with one's own infant at the trend level, while the relationship was reversed for NE mothers. One PET-fMRI study found that dopaminergic response in an extended amygdala network in mothers was related to synchronous behaviors with one's own infant during behavioral observation (Atzil *et al.,* 2017). Maternal sensitivity has been linked to child outcomes via multiple pathways, with one study revealing that sensitivity mediated the effect of maternal depressive symptoms on child social engagement and exerted separate effects on child stress reactivity (Feldman *et al.,* 2009). The opposite result in NE mothers is more difficult to explain, and of course these findings are both trend-level (though the interaction was significant) in a small sample size. Perhaps in mothers with CME, amygdala response to infant faces may be of particular importance for promoting sensitive maternal

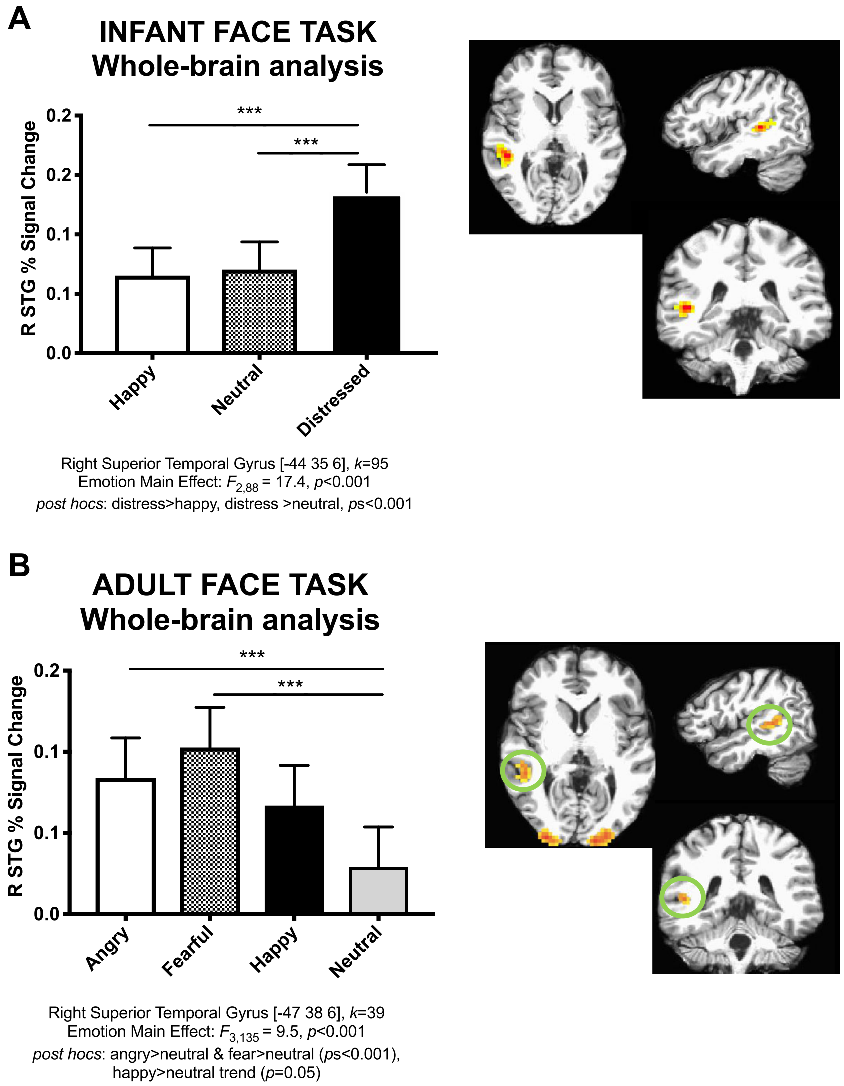

Fig. 4. Infant and adult faces task—common whole-brain findings. (**A**) Infant task—main effect of emotion—right STG. (**B**) Adult task—main effect of emotion—right STG.

behaviors and may serve as a resilience factor for affected dyads. The lack of findings with regard to intrusive maternal behaviors are different from prior findings in an overlapping sample where there was a relationship between higher amygdala activation to infant faces and maternal intrusiveness (P. Kim *et al.*, 2017). The discrepancy may relate to maternal CME perhaps having distinct mechanisms *vs* children who suffer from the different challenges encountered by children with lower socioeconomic status. Interestingly, this question could be answered if one were to recruit within a lower socioeconomic population of families for mothers with and without exposure to childhood maltreatment.

Interestingly, there was no between-group difference in amygdala activation based on infant emotion, which is different from studies which have found a specific effect of emotion in different maternal populations (S. Kim *et al.*, 2014; Strathearn & Kim, 2013). This discrepancy in finding might be due to the use of personalized stimuli in other studies. Furthermore, though there was not an effect of emotion within amygdala, there was an effect in the STG, an area which has been associated with social cognition and mentalization (Gallagher & Frith, 2003). Mothers exhibited higher activation in STG when processing neutral and distressed *vs* happy infant facial expressions, and when processing negative-valence (anger, fear) stimuli for adult faces, both regardless of CME. The parallel findings in STG across tasks suggest common mechanisms in responding to adult and infant faces, as this area has been associated with social cognitive processes including perspective-taking and cognitive empathy (Allison *et al.*, 2000; Mackes *et al.*, 2018). Furthermore, in a related study focused on maternal functional connectivity to infant cry, amygdala to superior temporal sulcus (a nearby area) connectivity was found to be associated with both maternal anxiety symptoms and maternal sensitivity (Guo *et al.*, 2018). Though we did covary for maternal anxiety symptoms and did not find any effect of anxiety symptoms in our study, the groups were nonetheless consistently different in regard to this variable, though the range of STAI scores in our population was below the ranges found in clinical populations. This association of connectivity between these two areas with caregiving behaviors is also consistent with the greater response in STG to distressed infant faces, which would preferentially prompt for motivated maternal behaviors.

Finally, the lack of a group effect in amygdala ROI and whole-brain analysis of the adult faces task is somewhat surprising. Of course, one needs to be highly cautious about interpreting a negative finding given that there is always the possibility of it being a case of insufficient power. Additionally, it is possible that order of tasks (infant first, adult faces last, with other non-face tasks in between) may have contributed to this lack of an effect. Given these caveats, we would nonetheless like to speculate a bit in order to guide follow-up studies. The negative finding is not consistent with one prior study of male and female adults having experienced childhood maltreatment and representing a spectrum of psychiatric diagnoses and healthy comparisons, wherein the authors found enhanced amygdala reactivity to adult faces regardless of emotion (van Harmelen *et al.*, 2013). The negative finding in amygdala in our sample may suggest that there is something particular to infant *vs* adult faces that is sensitive to maternal CME. Much has been written about dynamic changes occurring in the peripartum brain, including alterations in gene expression, hormonal processes and neural circuitry (Numan & Woodside, 2010; Barrett & Fleming, 2011; Swain *et al.*, 2012; Feldman, 2015; Lonstein *et al.*, 2015; P. Kim *et al.*, 2016; Lomanowska *et al.*, 2017). For instance, there tends to be an increase in anxiety symptoms and parental preoccupations during pregnancy, but a decrease in stress reactivity in the postpartum period (Hillerer *et al.*, 2012; P. Kim, 2016; P. Kim *et al.*, 2016). Thus, perhaps the lack of differing responses to adult faces may relate to this decline in stress reactivity.

Limitations

Our findings must be taken to be preliminary given the small sample. Additionally, our trauma assessment questionnaire did not include sexual abuse, which is an important form of childhood maltreatment to consider, particularly since the rates are higher in females. The cross-sectional study design limits our ability to make any inferences about the directionality of effects, including whether maternal amygdala activation influences the nature of the mother–infant relationship. Further, our population was a community sample without severe psychiatric symptomatology. Thus, our results may not apply to clinical populations. Furthermore, we did not assess substance use or psychiatric diagnoses including PTSD utilizing a structured clinical interview. We chose to utilize tasks that were validated previously in the literature, which has the consequence that unfortunately, these tasks are not exactly the same. The differences in tasks (particularly passive *vs* identifying gender of stimuli) or in the order of task administration may contribute to the findings of a group difference in infant but not adult task. Furthermore, we cannot state whether our results would be similar with customized own baby stimuli. Additionally, race was not able to be matched between stimuli and mother; thus, maternal race (Caucasian mothers *vs* non-Caucasian mothers) was included in analyses. We would like to use baby stimuli closely matched to mothers' babies in future studies, as we believe that implicit face processing differences with respect to race and ethnicity are important to consider based on prior work (Kubota *et al.*, 2012).

Lastly, we did not include non-facial stimuli in our design. Though we can test for differences between facial stimuli classes, we cannot assess the contribution of facial features that are more involved in emotion processing (i.e. eyes, mouth) from those that are less involved (Wegrzyn *et al.*, 2017). Additionally because AFNI models utilize an implicit baseline, we cannot rule out the possibility of higher amygdala activation at baseline in CME mothers contributing to the findings, though this question may be answered with future studies utilizing resting state MRI techniques.

Conclusions

Our study investigates CME mothers' infant and adult face processing. Our findings include blunted amygdala activation to infant faces across emotions in CME mothers. The amygdala reactivity–CME association was specific to infant faces. In CME mothers, higher amygdala activation to infant faces was associated with greater sensitivity during mother–infant interaction. Future studies with larger samples might include tasks linking face processing directly to maternal behaviors, deeper clinical phenotyping and larger connectivity analyses of salience and reward networks.

Funding

This work was supported by National Institutes of Health (grants R21 HD078797A1, R21DA046556 and R01 HD090068 all to P.K.) and NARSAD (to P.K.). A.K.O. is supported by Developmental Psychobiology Research Group Postdoctoral Fellowship T32MH015442 and the National Institutes of Health Loan Repayment Program. For disclosure, A.K.O. is the recipient of additional non-governmental funding sources which did not support this research project (American Academy of Child and Adolescent Psychiatry Pilot Award and Developmental Psychobiology Endowment Fund small grant award), and A.K.O.'s husband works for Thermo Fisher Scientific, a biomedical company unrelated to this line of research. J.S. is supported by National Institute of Mental Health (K23 MH113731).

Supplementary data

Supplementary data are available at *SCAN* online.

Conflict of interest.

None declared.

Acknowledgments

We would like to thank the participants and their families as well as the members of the Family Child Neuroscience Lab for their important contributions to this study. We appreciate the contributions of Alexandra Jensen, M.S. and Susan Mikulich-Gilbertson, Ph.D., for their roles in statistical consultation. Thanks to Amy Anderson, Lindsay Blanton, Christian Capistrano, Christina Congleton, Tanisha Crosby-Attipoe, Alexander Dufford, Victoria Everts, Melissa Hansen, Rachel Gray, Leah Grande, Hana Gulli, Claire Jeske, Laura Jeske, Mallory Kruse, Daniel Mason, Miriam Nowrouzi, Mathias Smrekar and Nanxi Xu for their help in recruitment, data collection and data entry.

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