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An intergenerational family study on the impact of experienced and perpetrated child maltreatment on neural face processing

Lisa J.M. van den Berg[a,b,*], Marieke S. Tollenaar[a,b], Laura H.C.G. Compier-de Block[c], Marian J. Bakermans-Kranenburg[c], Bernet M. Elzinga[a,b]

[a] Clinical Psychology Unit, Leiden University, PO Box 9555, 2300 RB Leiden, the Netherlands
[b] Leiden Institute for Brain and Cognition (LIBC), Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, the Netherlands
[c] Department of Child and Family Studies, Leiden University, PO Box 9555, 2300 RB Leiden, the Netherlands

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ABSTRACT

Altered processing of emotional faces due to childhood maltreatment has repeatedly been reported, and may be a key process underlying the intergenerational transmission of maltreatment. The current study is the first to examine the role of neural reactivity to emotional and neutral faces in the transmission of maltreatment, using a multi-generational family design including 171 participants of 51 families of two generations with a large age range (8–69 years). The impact of experienced and perpetrated maltreatment (abuse and neglect) on face processing was examined in association with activation in the amygdala, hippocampus, inferior frontal gyrus (IFG) and insula in response to angry, fearful, happy and neutral faces. Results showed enhanced bilateral amygdala activation in response to fearful faces in older neglected individuals, whereas reduced amygdala activation was found in response to these faces in younger neglected individuals. Furthermore, while experienced abuse was associated with lower IFG activation in younger individuals, experience of neglect was associated with higher IFG activation in this age group, pointing to potentially differential effects of abuse and neglect and significant age effects. Perpetrated abusive and neglectful behavior were not related to neural activation in any of these regions. Hence, no indications for a role of neural reactivity to emotional faces in the intergenerational transmission of maltreatment were found.

1. Introduction

Exposure to childhood maltreatment (i.e. abuse and neglect) is associated with a cascade of negative consequences that impairs psychological, social and biological development, which can persist throughout the life span (e.g., McCrory et al., 2011a; Norman et al., 2012). One of the striking consequences of experienced childhood maltreatment is the increased risk for maltreating own offspring. Around 30% of maltreated individuals maltreat their own children, a percentage that is significantly lower in non-maltreated individuals (e.g., Dixon et al., 2005; Berlin et al., 2011). Unravelling the mechanisms behind this intergenerational transmission of childhood maltreatment is crucial for the design of effective preventive interventions. Our study, using a multi-informant, multi-generational family design including 171 participants with a wide age range (8–69 years), is the first to examine directly the role of neural reactivity to emotional faces in the intergenerational transmission of abuse and neglect within two generations of families. Changes in emotional face processing due to maltreatment are characterized by hypervigilance to (negative) emotional facial cues. For example, maltreated children exhibited selective attention to angry faces (Pollak and Tolley-Schell, 2003). Physically abused children were found to be hypervigilant to hostile cues (Dodge et al., 1995) and needed less visual information to accurately identify facial displays of anger (e.g., Pollak and Sinha, 2002). On the other hand, maltreated children were less accurate in recognizing positive emotional states of others (Koizumi and Takagishi, 2014). Attentional and interpretation biases have also been found in older maltreated individuals. For example, abused young adults displayed preferential attention to angry faces and increased sensitivity in the detection of angry facial expressions (Gibb et al., 2009). From an evolutionary perspective it is useful to process facial expressions rapidly when growing up in a maltreating environment, because they can provide signs of either threat or safety. However, in the course of time enhanced reactivity to negative emotional faces may put maltreated individuals at increased risk to develop a persistent vigilance for threat-related facial expressions and an attentional bias towards threatening or negative

* Corresponding author at: Clinical Psychology Unit, Leiden University, PO Box 9555, 2300 RB Leiden, the Netherlands.
E-mail address: l.j.m.van.den.berg@fsw.leidenuniv.nl (L.J.M. van den Berg).

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information in general, which is often associated with psychopathology such as anxiety and depressive disorders (e.g., Gibb et al., 2009). From a parenting perspective, infant facial cues are crucial to elicit nurturing behaviors from parents. Deficits in recognizing and responding to these emotional face cues may therefore affect parenting behavior. Indeed, deficits in emotional face processing were found to be associated with parental insensitivity (e.g., Thompson-Booth et al., 2014). Also, parents at high risk for physical child abuse made more errors in recognizing pictures of emotional faces (Asla et al., 2011). This puts one of the possible consequences of experienced childhood maltreatment, i.e., deviances in emotional face processing, on the list of possible risk factors for parental maltreating behavior, and hence this may be a possible mediator in the transmission of maltreatment (e.g., Asla et al., 2011; Wagner et al., 2015). Altered emotional face processing following experienced childhood maltreatment may be reflected in chronic functional alterations in the brain. The amygdala plays a central role in the processing of emotional faces (e.g., Davis and Whalen, 2001). In line with enhanced sensitivity to facial expressions, adults with a history of childhood (emotional) maltreatment showed enhanced bilateral amygdala reactivity to neutral and emotional faces (McCrory et al., 2011b; Dannlowski et al., 2012; Van Harmelen et al., 2013). Differential neural processing of facial stimuli in maltreated individuals has also been observed in other brain areas, particularly the hippocampus and insula. Maltreated children for example showed increased reactivity in the left anterior insula in response to angry faces (McCrory et al., 2011b), and neglected youths displayed significantly higher activation in the left amygdala and left anterior hippocampus while viewing angry and fearful faces (Maheu et al., 2010). In adults, experienced childhood maltreatment has been associated with higher activity in face processing areas (fusiform gyri and left hippocampus) while novel compared to familiar adult faces were presented (Edmiston and Blackford, 2013). The IFG is also considered as one of the core regions of emotional face processing (e.g., Haxby et al., 2002; Sabatinelli et al., 2011). Several studies show that IFG activation is associated with expressive face processing (e.g., Carr et al., 2003; Fusar-Poli et al., 2009). Moreover, physically maltreated adolescents showed higher IFG activation while fearful faces were presented compared to healthy controls (Hart et al., 2018). However, whether the impact of childhood maltreatment on neural responsivity in these brain areas is also associated with caregiving behavior in adulthood is still unknown. The neural alterations following child maltreatment span across brain regions (including the amygdala, hippocampus, insula and IFG) that are also involved in caregiving behavior (DeGregorio, 2012; Rilling and Mascaro, 2017; Swain and Ho, 2017). Of note, intrusive mothers exhibited higher activation in the right amygdala while watching videos of their own versus an unfamiliar child (Atzil et al., 2011), and greater activation to their own infant's cry in the left anterior insula and temporal pole (Musser et al., 2012). However, research on the neural correlates of maltreating parenting behavior is scarce, and the current study is the first to examine whether altered neural reactivity to emotional faces is involved in the intergenerational transmission of child maltreatment using a family design. Furthermore, as different types of maltreatment, i.e., abuse and neglect, may have specific effects on emotion processing and recognition (Compier-de Block, 2017; Van den Berg et al., 2018), our study design also allows for a differentiation of effects of (experienced and perpetrated) abuse and neglect. To investigate intergenerational transmission of maltreatment in our sample, we investigated whether maltreated individuals were more likely to show maltreating behavior towards their children. To examine whether alterations in neural reactivity to emotional faces in the amygdala, hippocampus, IFG and insula are involved in the intergenerational transmission of abuse and neglect we investigated whether a history of abuse and/or neglect was associated with altered brain reactivity in response to emotional and neutral faces in these areas. Next, we investigated whether abusive and neglectful behavior was associated with altered activation in these same brain regions. Furthermore, we examined whether abuse and neglect showed differential effects. Lastly, given the large age range in our sample, we investigated whether age moderated associations between neural reactivity to emotional and neutral faces and experienced and perpetrated maltreatment.

2. Method

2.1. Participants

Participants in the current study were part of a larger sample from the 3G parenting study, a family study on the intergenerational transmission of parenting styles, stress and emotion regulation (see also Compier-de Block, 2017; Van den Berg et al., 2018). The current sample was recruited via three other studies that included instruments to assess caregiving experiences (Penninx et al., 2008; Scherpenzeel, 2011; Joosen et al., 2013). From two of these studies we recruited only participants who reported that they had experienced some form of childhood maltreatment. All participants from the third study were recruited. Thus, participants with an increased risk of experienced maltreatment were oversampled. Only those participants who indicated to be willing to participate in other research, and with at least one child of 8 years or older were approached. After their consent for participation, we invited their family members (parents, partners, offspring, adult siblings, nephews, nieces and in-laws) to participate. For the current study, all participants from the 3G study who participated in the functional magnetic resonance imaging (fMRI) part were included. In total, we included 171 participants (n = 73 men and n = 98 women) from two generations (parents and their offspring) of 51 families. The mean age of the parents (n = 100; 45 men and 55 women) was 46.6 years (SD = 10.72, age range: 26.6–69.7 years) and the mean age of the offspring (n = 71; 28 male and 43 female) was 19.0 (SD = 7.32, age range: 8.3–37.0 years). See supplement for more information on the relatedness, ethnicity and educational level of our participant sample.

2.2. Procedure

After description of the study to the participants, written informed consent was obtained. If eligible, participants performed three tasks in the fMRI scanner, with the emotional faces task always first. Results on the other tasks are reported elsewhere (Van den Berg et al., 2018). Prior to scanning, children < 18 years were familiarized with the scanner environment using a mock scanner. The full protocol was conducted according to the principles expressed in the Declaration of Helsinki, and approved by the Medical Ethics Committee of the Leiden University Medical Center (LUMC).

2.3. Measures

2.3.1. Childhood maltreatment

To assess experienced childhood abuse and neglect by mother and/or father, adapted versions of the Conflict Tactics Scales (CTS; Straus et al., 1998) were administered in combination with the emotional neglect scale from the Childhood Trauma Questionnaire (CTQ-SF; Bernstein et al., 2003; see also Compier-de Block, 2017). Parents also completed a CTS version to assess their own abusive or neglectful behaviors towards (each of) their child(ren). An overall *Neglect*-score was calculated by averaging Emotional and Physical Neglect, and an overall *Abuse*-score by averaging Emotional and Physical Abuse. For our analyses we combined information from two informants (parents and offspring) whenever possible (see Supplement for more information), resulting in a total of 285 informants on experienced childhood maltreatment of 171 participants and 184 informants on perpetrated maltreatment of 100 participants. Internal consistencies of the scales were as follows: α-mother = .93 and α-father = .93 for physical abuse, α-mother = .80 and α-father = .77 for emotional abuse, α-mother = .76 and α-father = .65 for physical neglect, and α-mother = .92 and α-father = .91 for emotional neglect. Because the distributions of CTS scores were skewed, scores were logarithmically transformed. Outliers (i.e., values with a standardized value of +/- 3.29), were winsorized to the most extreme value within the normal range plus or minus the difference between the two most extreme values within the normal range (for abuse ($n = 1$) and neglect history ($n = 1$)).

2.3.2. Emotional faces task

The emotional faces task was based on a paradigm used in previous work (Van Harmelen et al., 2013) that has been found to activate a number of brain regions that are involved in emotion processing, including the amygdala, hippocampus, insula and IFG (e.g., Fusar-Poli et al., 2009; Sabatinelli et al., 2011). E-prime software (Psychological Software Tools, Pittsburgh, PA, USA) was used to present this task using an event-related design. Photographs of 10 women and 10 men were selected from the Radboud Faces Database (Langner et al., 2010) for angry, fearful, surprised, happy and neutral faces. 66 scrambled faces with an arrow in the middle pointing left (50%) or right (50%) were presented as a baseline measure. In total, 166 stimuli were presented against a black background. Each photograph was shown on the screen for 2.5 s, with an inter-stimulus (black screen) interval varying between 0.5 and 1.5 s. Each particular face was presented only once. Stimuli were projected on a screen at the end of the scanner and were visible via a mirror positioned on the head coil. Participants were instructed to indicate whether they saw a man or woman in the photographs by pressing one of two buttons, and when presented with a scrambled face, whether the arrow was pointing left or right.

2.3.3. Covariates

Demographic information (age, gender, handedness and household social economic status (SES)) was assessed using questionnaires. To control for level of psychopathology, three widely used versions of Achenbach's screening tools were used. For participants younger than 12 years old their parents filled out the Child Behavioral Checklist (CBCL; Achenbach, 1991a). The Youth Self Report (YSR; Achenbach, 1991b) was completed by participants from 12 to 17 years. The Adult Self Report (ASR; Achenbach and Rescorla, 2003) was used from 17 years up. For all three instruments a total psychopathology symptom score was calculated. Cronbach's alphas were good to excellent (.76–.93; see Supplement). Of all participants from 17 years and up 7–14% reported symptoms in the subclinical or clinical range on the anxious/depressed, withdrawn, somatic complaints, aggressive behavior, rule-breaking behavior and/or the intrusive subscale of the ASR (Achenbach and Rescorla, 2003; see Supplement Table S1). In the group of younger participants (< 17 years) 3–16% reported symptoms in the subclinical or clinical range on the following subscales of the CBCL (Achenbach, 1991a) or YSR (Achenbach, 1991b): anxious/depressed, withdrawn, aggressive behavior, rule-breaking behavior, somatic complaints, thought problems, attention problems, social problems and other problems (see Supplement Table S2).

2.4. fMRI data acquisition

Scanning was performed using a whole-head coil on a 3.0-Tesla Philips Achieva scanner (Philips Medical Systems, Best, The Netherlands) located at the LUMC. Head motion was restricted using foam inserts that surrounded the head. For all participants, T2*-weighted echo-planar images (EPI) were obtained [repetition time (TR) = 2200 ms, echo time (TE) = 30 ms, matrix size: 80 × 79, 38 transverse slices of 2.75 mm, slice gap = 0.28 mm, field of view (FOV) = 220]. In accordance with the LUMC policy, a radiologist from the Radiology department examined all anatomical scans. No incidental findings were reported.

2.5. fMRI data preprocessing

Functional imaging data were preprocessed and analyzed using Statistical Parametric Mapping version 8 (SPM8; Wellcome Department of Cognitive Neurology, London) software implemented in Matlab 5.0.7 (Mathworks, Sherborn, MA). After extensive quality control of the data, preprocessing consisted of the following steps: manually reorienting the functional images to the anterior commissure, slice time correction, image realignment, registration of the T1-scan to the mean echo-planar image, warping to Montreal Neurological Institute (MNI)-space as defined by the SPM8 T1-template, reslicing to 3 × 3 × 3 mm voxels and spatial smoothing with a Gaussian kernel (8 mm, full width at half-maximum). Subject movement (> 3 mm) resulted in exclusion of the data from further analysis ($n = 9$).

2.6. fMRI data analysis

Data were analyzed using the General Linear Model in SPM8. The fMRI time series data were modeled by a series of events convolved with a canonical hemodynamic response function (HRF). The picture presentation of each emotional face was modeled as a zero duration event. Low-frequency noise was removed by applying a high-pass filter (cut-off 120 s) to the fMRI time series at each voxel. Statistical parametric maps for each comparison of interest were calculated on a voxel-by-voxel basis. For each subject, the following contrasts were computed: angry > scrambled, fearful > scrambled, happy > scrambled, neutral > scrambled and all expressions > scrambled. Surprised faces were not of interest for the current study and therefore not included in separate analyses. To investigate the neural correlates of emotional face processing, four anatomical key regions of interest (ROIs) were defined using the automatic anatomical labeling (AAL) toolbox within the Wakeforest-pickatlas toolbox (Maldjian et al., 2003): the amygdala, hippocampus, IFG and insula. See below for more details. All results are reported in MNI space.

2.7. SPSS data analysis

Brain activity was examined with three-level multilevel regression analyses in which participants were nested within households and households were nested within families, using SPSS 23, to take the family structure of the data into account. In this approach, level 1 models variation at the participant (individual) level, level 2 estimates variation among participants within the same household, and level 3 captures variation among families. Random intercept models were built sequentially, starting with an empty (null) model without explanatory variables in which the total variance of brain reactivity in response to faces was partitioned into a component at each level. This empty model was used to test for random variation of the outcome variables at the different levels. Most, but not all, of the reported intraclass correlations (ICCs) were low (see Supplement). To control for the nested structure of data we decided to consistently use multilevel analyses for all ROIs. In the next model, age, gender, handedness, SES and psychopathology were added as covariates to the model to control for these factors. Only significant covariates ($p < .05$) were kept in the final model. Because of the large age range and our focus on age, age was always included as a covariate. To explore fixed effects of abuse and neglect, main effects of abuse and neglect were added to Model 1, and interaction effects of age × abuse and age × neglect in Model 2. In case of significant interaction effects between experienced maltreatment and age we split up the sample in participants up to 18 years old (children and adolescents who are generally still living at home with their parents) and participants older than 18 years old (generally living on their own) for illustrative purposes only. Multilevel regression analyses were run for each of our four ROIs (the amygdala, hippocampus, IFG and insula) for fearful, angry, happy and neutral faces separately. Separate analyses were run for severity of maltreatment history (all participants: $n = 171$) and for

Table 1
Demographics, psychopathology, and maltreatment scores (n = 171).

Variables	Mean (SD)	Range
Age	35.14 (16.60)	8.25 - 69.67
Gender (*n:* men/women)	73/98	–
Handedness (*n:* left/right)	22/149	–
CBCL	12.79 (7.02)	3.00-28.50
YSR	20.00 (14.70)	0.00 - 46.00
ASR	24.56 (15.51)	1.00 - 83.00
Abused[a]	1.62 (0.48)	1.00 - 4.50
Neglected[a]	1.86 (0.58)	1.00 - 5.00
Maltreated[a] (total)	1.74 (0.47)	1.00 - 4.75
Abusive[b] (n = 100)	1.48 (0.32)	1.00 - 2.53
Neglectful[b] (n = 100)	1.58 (0.32)	1.00 - 2.48
Maltreating[b] (total; n = 100)	1.53 (0.26)	1.00 - 2.22

CBCL = Child Behavioral Checklist; YSR = Youth Self Report; ASR = Adult Self Report [a]Combined experienced maltreatment scores by averaging parent and child reports as measured with the CTS. [b]Combined maltreating behavior scores by averaging parent and child reports as measured with the CTS. Values of all included participants are presented (n = 171) unless otherwise specified. Raw scores are presented.

severity of maltreating parenting behavior (participants with offspring: n = 100). All (continuous) predictor variables and covariates were centered. All independent and dependent variables were measured at the individual level (except SES) and considered in the fixed part of the model. Unstandardized regression coefficients are reported.

3. Results

Table 1 shows demographics and mean (SD) maltreatment scores. Pearson correlations were calculated between all variables (see Supplement). The correlation between experienced abuse and neglect was $r = .57$ ($p < .001$), whereas abusive and neglectful behavior were also moderately associated ($r = .32$, $p < .001$). To examine intergenerational transmission of maltreatment in our sample, regression analyses were conducted with experienced childhood abuse and neglect as predictors and with abusive and neglectful behavior as outcome measures for participants with offspring (n = 100 parents). Results indicated that, controlling for age, gender, household SES and psychopathology in the first block, experienced abuse ($\beta = .55$, $t(93) = 5.35$, $p < .001$) was the only significant predictor of perpetrated abuse. Experienced neglect did not predict perpetrated abuse ($p = .122$). None of the covariates were significant. Perpetrated neglect was not predicted by experienced neglect ($p = .709$) nor by experienced abuse ($p = .884$). Age ($\beta = .21$, $p = .049$) and psychopathology ($\beta = .33$, $p = .003$) were significant covariates for perpetrated neglect.

3.1. Face processing

The whole brain analysis for the contrast all expressions versus scrambled faces (baseline) showed significant clusters of activation in brain areas involved in face processing (namely the amygdala, hippocampus, insula and IFG; e.g., Fusar-Poli et al., 2009) at $p < 0.01$ family-wise error (FWE) corrected for multiple comparisons on cluster level with a threshold of 10 or more contiguous voxels (see Supplement for an overview of all activated clusters). We extracted the left and right amygdalae, hippocampi, IFG and insulae as anatomical ROIs using the automatic anatomical labeling (AAL) toolbox within the Wakeforest-pickatlas toolbox (Maldjian et al., 2003) and the MARSBAR toolbox (Brett et al., 2002; see Fig. 1). Left and right clusters were combined for all ROIs as there were no effects of laterality.

3.2. Multilevel analyses

In the following section results of our multilevel regression analyses

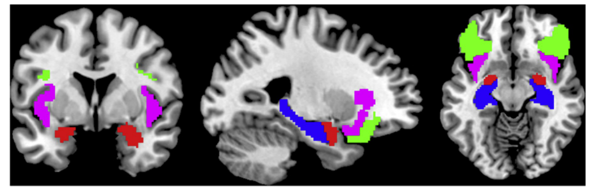

Fig. 1. Anatomical ROI masks. Red: left and right amygdalae; Blue: left and right hippocampi; Green: IFG; Violet: left and right insulae (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

will be described per ROI for severity of maltreatment history (all participants: n = 171) and for severity of maltreating parenting behavior (participants with offspring: n = 100) separately. All multilevel regression analyses were run controlling for age, gender, handedness, SES and psychopathology (see Tables 2a–5b).

3.2.1. Amygdala: experienced abuse and neglect

Multilevel analyses were performed with experienced abuse and neglect as predictors and BOLD responses in the amygdala as outcome measure (see Table 2a, and see Supplement for an overview of all significant multilevel analyses results). Analyses were run for fearful, angry, happy and neutral versus scrambled faces separately. No significant main effects were found for abuse or neglect regarding activation in the amygdala for angry, fearful, happy or neutral faces. However, results revealed a significant improvement of the model when the interactions with age were added for fearful faces (χ^2 (2) = 8.56, p = .014). Younger participants (up to 18 years old) who experienced more neglect showed lower activation in the amygdala while viewing fearful faces than younger participants who experienced less neglect ($\beta = 0.08$, $t = 2.91$, $p = .004$). For older participants an opposite effect for fearful faces was found, with higher amygdala activation for older participants who experienced more neglect (see Supplement Figure S1 and S2 for a visual representation of the significant interaction effects between experienced maltreatment and age).

3.2.2. Amygdala: abusive and neglectful behavior

Similar multilevel analyses were run for participants with offspring with abusive and neglectful behavior as predictors (see Table 2b). Results showed no significant main effects for abusive or neglectful behavior nor interaction effects with age for brain reactivity in the amygdala in response to neutral or emotional faces.

3.2.3. Hippocampus: experienced abuse and neglect

Multilevel regression analyses were conducted for fearful, angry, happy and neutral faces separately, with BOLD responses in the hippocampus as outcome measure and experienced abuse and neglect as predictors (see Table 3a). Results showed no significant main effects for experienced abuse or neglect nor interaction effects with age for brain reactivity in the hippocampus in response to neutral or emotional faces.

3.2.4. Hippocampus: abusive and neglectful behavior

Similar multilevel analyses were run for participants with offspring with abusive and neglectful behavior as predictors (see Table 3b). Results showed no significant main effects for abusive and neglectful behavior nor interaction effects with age for brain reactivity in the hippocampus in response to neutral or emotional faces.

3.2.5. IFG: experienced abuse and neglect

Multilevel regression analyses were done for fearful, angry, happy and neutral faces separately, with BOLD responses in the IFG as outcome measure and experienced abuse and neglect as predictors (see Table 4a). No significant main effects were found for abuse or neglect regarding activation in the IFG. However, results revealed a significant

Table 2a
Multilevel models of brain reactivity in the left and right amygdalae in response to neutral and emotional faces as related to experienced childhood abuse and neglect (n = 171).

Amygdala ROI	Anger			Fear			Happy			Neutral		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model												
age	−0.01	.00	.078	−0.00	.00	.540	−0.00	.00	.269	0.00	.00	.616
gender	0.03	.10	.745	−0.03	.09	.740	0.03	.10	.725	0.04	.11	.689
handedness	−0.20	.15	.177	−0.00	.13	.975	−0.07	.15	.619	0.04	.16	.788
SES	−0.01	.07	.847	0.06	.06	.375	0.10	.07	.159	0.08	.08	.309
PP	−0.00	.24	.984	−0.11	.22	.617	0.01	.24	.970	−0.11	.26	.687
Model 1												
abused	−0.73	.51	.151	−0.61	.46	.182	0.18	.51	.722	0.10	.56	.860
neglected	1.00	.50	.050	0.73	.45	.112	0.07	.51	.883	0.17	.56	.767
	χ^2 (2) = 4.21		.122	χ^2 (2) = 3.00		.223	χ^2 (2) = 0.25		.884	χ^2 (2) = 0.21		.900
Model 2												
abused*age	−0.01	.03	.791	−0.02	.03	.523	−0.01	.03	.723	−0.03	.03	.354
neglected*age	0.05	.03	.098	0.08	.03	.004**	0.02	.03	.416	0.08	.03	.017*
	χ^2 (2) = 2.99		.224	χ^2 (2) = 8.56		.014*	χ^2 (2) = 0.66		.717	χ^2 (2) = 5.75		.057

* $p < .05$; ** $p < .01$.

Table 2b
Multilevel models of brain reactivity in the left and right amygdalae in response to neutral and emotional faces as related to abusive and neglectful behavior (n = 100 parents).

Amygdala ROI	Anger			Fear			Happy			Neutral		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model												
age	0.00	.01	.459	0.00	.01	.644	0.01	.01	.359	0.00	.01	.496
gender	0.01	.14	.948	−0.10	.11	.359	−0.04	.13	.753	−0.12	.14	.405
handedness	−0.21	.23	.364	0.02	.19	.920	0.01	.21	.962	0.27	.24	.263
SES	−0.04	.09	.630	0.07	.08	.377	0.11	.09	.208	0.06	.10	.585
PP	−0.06	.34	.856	−0.17	.28	.545	−0.18	.32	.562	−0.16	.36	.660
Model 1												
abusive	0.35	.79	.664	−0.08	.66	.900	0.42	.74	.572	0.53	.84	.526
neglectful	0.54	.84	.524	−0.09	.70	.896	−0.36	.78	.642	−0.23	.89	.800
	χ^2 (2) = 0.84		.658	χ^2 (2) = 0.05		.976	χ^2 (2) = 0.41		.815	χ^2 (2) = 0.40		.819
Model 2												
abusive*age	−0.03	.10	.793	−0.04	.08	.606	−0.07	.09	.429	−0.06	.10	.544
neglectful*age	0.03	.08	.729	0.03	.07	.646	0.05	.07	.480	0.07	.09	.418
	χ^2 (2) = 0.13		.937	χ^2 (2) = 0.32		.851	χ^2 (2) = 0.76		.685	χ^2 (2) = 0.70		.703

* $p < .05$; ** $p < .01$.

improvement of the model when the interactions with age were added for fearful (χ^2 (2) = 8.25, p = .016), happy (χ^2 (2) = 9.46, p = .009) and neutral faces (χ^2 (2) = 8.92, p = .012). All three interaction effects revealed the same interaction pattern. Younger participants who experienced more abuse showed lower activation in the IFG while viewing fearful ($\beta = 0.05$, $t = 2.23$, p = .027), happy ($\beta = 0.05$, $t = 2.26$, p = .025) and neutral faces ($\beta = 0.06$, $t = 2.41$, p = .017) than younger participants who experienced less abuse. For older participants there was no effect of experienced abuse on activation in the IFG.

For neglect we found an opposite effect in younger individuals. Younger participants who experienced more neglect showed higher activation in the IFG while viewing fearful ($\beta = -0.06$, $t = -2.68$, p = .008), happy ($\beta = -0.06$, $t = -2.91$, p = .004) and neutral faces ($\beta = -0.06$, $t = -2.71$, p = .007) than younger participants who experienced less neglect. For older participants there was no effect of experienced neglect on activation in the IFG for fearful, happy or neutral faces.

3.2.6. IFG: abusive and neglectful behavior

Similar multilevel analyses were performed for all participants with offspring with abusive and neglectful behavior as predictors (see Table 4b). Results showed no significant main effects for abusive or neglectful behavior nor interaction effects with age for brain reactivity in the IFG in response to neutral or emotional faces.

3.2.7. Insula: experienced abuse and neglect

Multilevel regression analyses were run for fearful, angry, happy and neutral faces separately, with BOLD responses in the insula as outcome measure and experienced abuse and neglect as predictors (see Table 5a). Results showed no significant main effects for experienced abuse or neglect nor interaction effects with age for brain reactivity in the insula in response to neutral or emotional faces.

3.2.8. Insula: abusive and neglectful behavior

Multilevel analyses were repeated for all participants with offspring with abusive and neglectful behavior as predictors (see Table 5b). Results showed no significant main effects for abusive or neglectful behavior nor interaction effects with age for brain reactivity in the insula in response to neutral or emotional faces.

Table 3a
Multilevel models of brain reactivity in the left and right hippocampi in response to neutral and emotional faces as related to experienced childhood abuse and neglect (n = 171).

Hippocampus ROI	Anger			Fear			Happy			Neutral		
	b	SE	p	b	SE	p	b	SE	p	b	SE	p
Null model												
age	−0.00	.00	.263	−0.00	.00	.548	−0.00	.00	.710	0.00	.00	.836
gender	−0.02	.07	.804	−0.05	.06	.351	0.03	.07	.701	0.06	.07	.428
handedness	0.01	.10	.941	0.13	.09	.141	−0.01	.11	.950	0.08	.11	.495
SES	−0.03	.05	.502	0.03	.04	.433	0.07	.05	.195	0.10	.05	.065
PP	0.25	.17	.133	0.01	.14	.940	−0.00	.18	.981	0.02	.18	.898
Model 1												
abused	−0.21	.36	.567	−0.41	.31	.188	−0.15	.38	.694	0.30	.38	.433
neglected	0.61	.35	.085	0.50	.31	.104	0.24	.38	.532	−0.06	.38	.868
	χ^2 (2) = 2.99		.224	χ^2 (2) = 3.01		.222	χ^2 (2) = 0.39		.825	χ^2 (2) = 0.66		.718
Model 2												
abused*age	0.01	.02	.763	−0.01	.02	.606	−0.01	.02	.630	−0.03	.02	.232
neglected*age	−0.00	.02	.892	0.02	.02	.235	0.00	.02	.878	0.04	.02	.097
	χ^2 (2) = 0.09		.956	χ^2 (2) = 1.40		.496	χ^2 (2) = 0.23		.890	χ^2 (2) = 3.04		.219

* $p < .05$; ** $p < .01$.

Table 3b
Multilevel models of brain reactivity in the left and right hippocampi in response to neutral and emotional faces as related to abusive and neglectful behavior (n = 100 parents).

Hippocampus ROI	Anger			Fear			Happy			Neutral		
	b	SE	p	b	SE	p	b	SE	p	b	SE	p
Null model												
age	0.00	.00	.726	0.00	.00	.716	0.00	.00	.305	0.00	.00	.395
gender	−0.05	.09	.594	−0.08	.07	.259	−0.01	.09	.888	−0.05	.09	.624
handedness	−0.00	.15	.979	0.28	.12	.020*	0.11	.15	.497	0.27	.16	.095
SES	−0.07	.06	.286	0.01	.05	.794	0.03	.06	.613	0.02	.06	.771
PP	0.30	.23	.180	−0.11	.18	.527	−0.25	.23	.290	−0.11	.23	.651
Model 1												
abusive	0.58	.52	.270	0.04	.42	.931	−0.17	.54	.759	−0.05	.55	.925
neglectful	0.76	.55	.174	−0.09	.44	.846	−0.07	.57	.901	−0.16	.59	.786
	χ^2 (2) = 4.28		.117	χ^2 (2) = 0.04		.981	χ^2 (2) = 0.15		.927	χ^2 (2) = .11		.946
Model 2												
abusive*age	0.02	.06	.801	−0.01	.05	.782	0.04	.06	.531	−0.05	.07	.411
neglectful*age	0.06	.05	.261	0.01	.04	.887	0.05	.05	.371	0.10	.06	.085
	χ^2 (2) = 2.11		.349	χ^2 (2) = 0.08		.962	χ^2 (2) = 2.34		.310	χ^2 (2) = 2.99		.225

* $p < .05$; ** $p < .01$.

Table 4a
Multilevel models of brain reactivity in the IFG in response to neutral and emotional faces as related to experienced childhood abuse and neglect (n = 171).

IFG ROI	Anger			Fear			Happy			Neutral		
	b	SE	p	b	SE	p	b	SE	p	b	SE	p
Null model												
age	−0.00	.00	.555	−0.00	.00	.491	0.00	.00	.802	−0.00	.00	.203
gender	0.00	.08	.972	0.01	.07	.910	0.11	.07	.122	0.13	.07	.078
handedness	0.10	.12	.421	0.06	.11	.595	−0.04	.11	.698	0.05	.11	.643
SES	0.00	.06	.982	−0.00	.06	.996	0.09	.05	.073	0.09	.06	.090
PP	−0.04	.20	.843	−0.13	.19	.483	−0.18	.18	.302	0.09	.18	.631
Model 1												
abused	−0.54	.43	.207	−0.77	.40	.057	−0.28	.38	.473	−0.33	.40	.406
neglected	0.40	.42	.340	0.07	.39	.856	0.06	.38	.873	0.55	.40	.168
	χ^2 (2) = 1.79		.409	χ^2 (2) = 3.91		.142	χ^2 (2) = 0.55		.761	χ^2 (2) = 1.92		.383
Model 2												
abused*age	0.04	.02	.116	0.05	.02	.027*	0.05	.02	.025*	0.06	.02	.017*
neglected*age	−0.04	.02	.126	−0.06	.02	.008**	−0.06	.02	.004**	−0.06	.02	.007**
	χ^2 (2) = 3.32		.191	χ^2 (2) = 8.25		.016*	χ^2 (2) = 9.46		.009**	χ^2 (2) = 8.92		.012*

* $p < .05$; ** $p < .01$.

Table 4b
Multilevel models of brain reactivity in the IFG in response to neutral and emotional faces as related to abusive and neglectful behavior (n = 100 parents).

IFG ROI	Anger			Fear			Happy			Neutral		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model												
age	0.00	.01	.384	0.00	.00	.858	0.01	.00	.060	−0.00	.00	.878
gender	−0.03	.11	.791	0.06	.08	.450	−0.02	.08	.829	0.05	.10	.629
handedness	0.05	.19	.777	−0.32	.13	.014*	−0.13	.14	.370	0.04	.17	.822
SES	0.01	.08	.891	0.03	.05	.550	0.03	.06	.574	0.06	.07	.413
PP	−0.27	.28	.332	−0.52	.19	.008**	−0.52	.21	.015*	0.00	.26	.996
Model 1												
abusive	1.10	.64	.087	0.24	.46	.608	0.38	.50	.447	0.57	.61	.352
neglectful	0.37	.68	.587	0.40	.48	.413	0.38	.52	.468	0.29	.64	.658
	χ^2 (2) = 4.27		.118	χ^2 (2) = 1.28		.528	χ^2 (2) = 1.51		.471	χ^2 (2) = 1.49		.474
Model 2												
abusive*age	0.02	.08	.748	−0.02	.05	.659	0.03	.06	.664	0.05	.07	.505
neglectful*age	0.06	.06	.333	0.01	.04	.792	0.05	.05	.273	−0.05	.06	.460
	χ^2 (2) = 1.81		.405	χ^2 (2) = 0.20		.906	χ^2 (2) = 2.49		.289	χ^2 (2) = 0.61		.738

* $p < .05$; ** $p < .01$.

Table 5a
Multilevel models of brain reactivity in the left and right insulae in response to neutral and emotional faces as related to experienced childhood abuse and neglect (n = 171).

Insula ROI	Anger			Fear			Happy			Neutral		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model												
age	−0.00	.00	.064	−0.00	.00	.043*	−0.00	.00	.241	−0.00	.00	.150
gender	0.02	.06	.807	0.00	.06	.934	0.07	.06	.252	0.13	.06	.038*
handedness	0.05	.10	.579	0.17	.09	.057	0.04	.09	.675	0.19	.09	.044*
SES	−0.01	.05	.778	−0.01	.04	.745	0.04	.04	.312	0.09	.04	.043*
PP	0.07	.16	.650	−0.07	.15	.649	−0.14	.15	.367	0.10	.15	.494
Model 1												
abused	−0.12	.33	.719	−0.51	.31	.106	−0.30	.33	.366	0.04	.33	.896
neglected	0.37	.33	.266	0.36	.31	.243	0.36	.32	.260	0.24	.33	.462
	χ^2 (2) = 1.27		.531	χ^2 (2) = 2.72		.257	χ^2 (2) = 1.46		.483	χ^2 (2) = 0.80		.671
Model 2												
abused*age	0.02	.02	.393	0.02	.02	.232	0.03	.02	.097	0.02	.02	.315
neglected*age	−0.01	.02	.461	−0.03	.02	.067	−0.04	.02	.022*	−0.02	.02	.403
	χ^2 (2) = 0.90		.638	χ^2 (2) = 3.56		.169	χ^2 (2) = 5.81		.055	χ^2 (2) = 1.21		.545

* $p < .05$; ** $p < .01$.

Table 5b
Multilevel models of brain reactivity in the left and right insulae in response to neutral and emotional faces as related to abusive and neglectful behavior (n = 100 parents).

Insula ROI	Anger			Fear			Happy			Neutral		
	b	SE	*p*	*b*	SE	*p*	*b*	SE	*p*	*b*	SE	*p*
Null model												
age	0.00	.00	.787	−0.00	.00	.224	0.00	.00	.763	−0.01	.00	.117
gender	−0.07	.08	.408	−0.09	.06	.170	−0.08	.07	.218	0.05	.08	.567
handedness	0.07	.14	.599	0.08	.11	.435	−0.01	.11	.929	0.20	.13	.130
SES	−0.01	.06	.917	0.02	.04	.648	0.01	.05	.869	0.04	.05	.422
PP	−0.01	.21	.969	−0.07	.16	.667	−0.38	.17	.028*	0.05	.20	.798
Model 1												
abusive	0.44	.48	.355	0.29	.37	.444	−0.17	.40	.680	0.26	.47	.584
neglectful	0.26	.51	.606	−0.33	.39	.401	0.12	.43	.775	−0.19	.50	.699
	χ^2 (2) = 1.61		.448	χ^2 (2) = 0.98		.613	χ^2 (2) = 0.21		.903	χ^2 (2) = 0.35		.839
Model 2												
abusive*age	0.04	.06	.536	0.00	.04	.983	0.06	.05	.236	0.00	.06	.948
neglectful*age	0.05	.05	.328	0.02	.04	.526	0.04	.04	.358	0.01	.05	.819
	χ^2 (2) = 2.60		.273	χ^2 (2) = 0.56		.756	χ^2 (2) = 4.41		.110	χ^2 (2) = 0.09		.956

* $p < .05$; ** $p < .01$.

4. Discussion

The current study is the first to examine the role of neural reactivity to emotional faces in the intergenerational transmission of childhood maltreatment using a large multi-generational family study design. Our findings indicate that neural activation in the amygdala and IFG are associated with experienced childhood maltreatment, but not with maltreating behavior. Moreover, our results point to somewhat differential effects for experienced abuse and neglect, depending on current age.

4.1. Experienced abuse and neglect

As expected and in line with previous studies (e.g., Maheu et al., 2010; Van Harmelen et al., 2013), our results showed that adults who experienced childhood neglect exhibited enhanced bilateral amygdala activation in response to fearful faces, indicating hypervigilance to negatively valenced faces in neglected adults. However, this hypervigilance was only observed in older neglected individuals, and in contrast, younger neglected individuals showed lower amygdala activation when fearful faces were presented compared to young, non-neglected individuals. Increased amygdala reactivity in neglected adults is in line with other imaging studies in adults (Van Harmelen et al., 2013). Decreased amygdala activation in younger neglected individuals is in line with offspring from risky families showing little amygdala activation during the observation of emotional faces (Taylor et al., 2006). This might suggest that younger individuals, still living at home with their (possibly neglectful) parents, experience a form of disengagement or even emotional avoidance of emotional, or in our study, fearful faces. Against our expectations, amygdala and hippocampus activation was not associated with experienced abuse. This is not in line with other studies, where associations have been reported between, for example, experienced physical abuse and heightened right amygdala reactivity (e.g., Grant et al., 2011). These discrepant findings might be due to the fact that most previous studies did not disentangle abuse and neglect (e.g., Hart and Rubia, 2012). Although a recent meta-analysis showed that neglect is the most prevalent type of maltreatment and long-term effects of neglect seem to be at least as important as those of abuse, it is striking that neglect still is an understudied form of maltreatment (e.g., Stoltenborgh et al., 2013). Altered neural reactivity to emotional faces associated with neglect emphasizes the importance to specifically focus on the neural correlates of neglect in future research.

Our results further showed that activity in the IFG for fearful, happy and neutral faces was associated with experienced abuse and neglect, dependent on the age of participants. In younger maltreated individuals, we found that younger abused individuals showed lower activation in the IFG while viewing fearful, happy and neutral faces, whereas younger neglected individuals showed higher activation in the IFG while viewing these faces. These effects disappeared with increasing age, since no associations between experienced abuse or neglect were found with activation in the IFG while viewing emotional or neutral faces for older participants.

The finding that experiences of abuse and neglect were associated with altered IFG reactivity was found irrespective of valence, is consistent with studies reporting that neglected children have poor valence discriminatory abilities for emotional faces (e.g., Pollak et al., 2000; Vorria et al., 2006; Van Harmelen et al., 2013). Additionally, altered processing of positive emotions (happy faces) in maltreated individuals is in line with results of previous research (Koizumi and Takagishi, 2014). The IFG is considered as one of the core regions of emotional face processing and is associated with attentional control (e.g., Hampshire et al., 2010; Sabatinelli et al., 2011). Our findings may suggest that neglected children have to work harder to process emotional faces since neglectful parents offer fewer opportunities to their children in learning to interpret emotional signals. On the contrary, abused children are more often exposed to behavior that may induce fear and hypervigilance which might explain our opposite findings regarding experienced abuse and neglect (Crittenden, 1981; Bousha and Twentyman, 1984; Pollak et al., 2000).

4.2. Age effects

Independent of abuse and neglect experiences, older participants exhibited lower activation in the insula while viewing fearful faces than younger participants. This is consistent with previous findings, although these studies included smaller samples with a more restricted age range (e.g., Gunning-Dixo et al., 2003). Interestingly, all effects of experienced abuse and neglect on neural reactivity to emotional and neutral faces were moderated by age. Taken together, this seems to indicate age-dependent sensitivity of the amygdala and IFG during face perception in maltreated individuals. While amygdala reactivity in response to fearful and neutral faces showed an opposite effect in younger (decreased activation) versus older (increased activation) neglected individuals, in older abused and neglected individuals the neural effects in the IFG seemed to disappear with increasing age. A possible explanation for these age effects could be that children or adolescents up to 18 years old are generally still living at home with their (possibly maltreating) parents, which is not the case for older individuals. Altered brain reactivity to emotional faces in these younger individuals might reflect temporary adaptation to or coping with current threat which disappears with time, when one leaves the threatening situation at home. Also, depending on age, experienced maltreatment may be perceived in different ways, as there may be cohort effects, alteration of memories with time in older individuals, or other buffering factors in older people who are not currently experiencing maltreatment (e.g. having been in therapy). There may have also been effects of timing of the experienced maltreatment on developmental windows for some brain regions, which might have contributed to our findings, particularly in the IFG. So far, a clear developmental perspective across the life span on the neural basis of emotion processing in maltreated individuals is missing, and our findings emphasize that future research using samples with a large age range might reveal important new insights on this topic.

4.3. Abusive and neglectful behavior

Parental abusive or neglectful behavior was not associated with bilateral amygdala, hippocampus, IFG or insula activation in response to emotional or neutral faces, even though some functional imaging studies have suggested these brain areas might play a role in (dysfunctional) parenting behavior (e.g., Atzil et al., 2011; Barrett and Fleming, 2011). Previous research showed that intrusive mothers exhibited higher activation to their own infant's cry sounds in the insula (Musser et al., 2012) – however, cry sounds of their own child were used as a stimulus, which may explain the different results. Other studies also made use of idiosyncratic stimuli of one's own infants that might specifically activate attachment representations (Barrett and Fleming, 2011) instead of the unfamiliar and non-infant pictures of adult faces as presented in the current study. To further explore whether parental maltreatment is predominantly associated with altered processing of emotions in the family context, future research that investigates neural reactivity to both familiar and unfamiliar faces is recommended. In addition, the age effects in abused and neglected individuals in the IFG and insula indicate that altered neural responses to emotional and neutral faces fade during adolescence and adulthood, which might explain the absence of associations between maltreating behavior and neural reactivity to emotional faces in our results. Another possible explanation for our results could be that the levels of abusive and neglectful behavior in our sample were not high enough to observe significant differences in neural reactivity. Future research should focus on also including participants who show higher levels of maltreating behavior to investigate this hypothesis.

4.4. Intergenerational transmission of maltreatment

In the sample of the current study we found intergenerational transmission of abuse in our behavioral results, whereas transmission of neglect was not observed. However, this is likely due to the smaller sample size of the imaging study, since we did find evidence for intergenerational transmission of neglect in the total sample of the 3 G study ($n = 202$). On a neural level, altered neural reactivity to emotional and neutral faces in the amygdala and IFG was associated with experienced abuse and neglect, but not with abusive or neglectful behavior. Hence, no neural mechanisms playing a role in the transmission of maltreatment were found in these brain areas.

4.5. Strengths and limitations

Our study is the first multi-informant, multi-generation family study on child maltreatment in which potentially differential neural effects of abuse and neglect on emotional face processing are examined. Research on the neural correlates of child maltreatment, and maltreating parenting behavior in particular, is scarce, and our family design enables the examination of intergenerational transmission within families directly. A further strength of the current study is that we combined parent (both fathers and mothers) and child reports in the maltreatment scores, which may diminish the influence of individual reporter bias. A limitation of the current study is the use of retrospective reports to measure maltreatment, which can be subject to recall bias. However, we combined parent and child reports in the maltreatment scores and research shows that maltreatment history is more likely to be under- than over-reported (e.g., Hardt and Rutter, 2004). Furthermore, our sample to examine the effects of perpetrated maltreatment was smaller than our sample to assess the effects of experienced maltreatment since only part of the sample were parents. Hence, the stronger effects that were found in association with experienced abuse and neglect rather than with abusive and neglectful behavior may also be due to differences in sample size. Another limitation of the current study is the high number of analyses. We have chosen for these exploratory analyses without strict correction of the alpha level since this is the first study to examine the role of neural reactivity to emotional and neutral faces in the transmission of maltreatment, using a multi-generational family design with an age range this large. However, we are aware that the current findings require replication before strong conclusions can be drawn.

Conclusion

In sum, neural reactivity to emotional and neutral faces in the amygdala and IFG was associated with experienced maltreatment (abuse and neglect) but not with maltreating (abusive and neglectful) behavior. Hence, we found no indications for a role of neural reactivity to emotional faces in the intergenerational transmission of abuse and neglect. Moreover, we found differential effects of experienced abuse and neglect on neural reactivity to emotional faces. This might be related to the fact that neglectful parents offer fewer opportunities to their children in learning to interpret emotional signals, whereas abusive parents interact with their children more often, but also expose them to behavior that may induce fear and hypervigilance (Crittenden, 1981; Bousha and Twentyman, 1984; Pollak et al., 2000). Our study highlights the importance to distinguish between maltreatment subtypes in research and clinical practice. A further strength of our study was the large age range of our sample (8–69 years) and the significant age effects that could be observed as a result. Further identification of the age-dependent alterations in emotion processing in individuals with experienced and perpetrated abuse and neglect is important to ultimately unravel the mechanisms involved in abuse and neglect and design and implement effective preventive interventions.

Conflict of interest

None declared.

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Author contributions

Conceived and designed the experiments: LJMvdB MST MJBK BME. Performed the experiments: LJMvdB LHCGCdB. Analyzed the data: LJMvdB MST MJBK BME. Wrote the paper: LJMvdB MST LHCGCdB MJBK BME.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.psyneuen.2019.01.030.

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