

## Pass it on? The neural responses to rejection in the context of a family study on maltreatment

Lisa J. M. van den Berg,<sup>1,2</sup> Marieke S. Tollenaar,<sup>1,2</sup> Katharina Pittner,<sup>2,3</sup>  
Laura H. G. G. Compier-de Block,<sup>3</sup> Renate S. M. Buisman,<sup>3</sup>  
Marinus H. van IJzendoorn,<sup>4</sup> and Bernet M. Elzinga<sup>1,2</sup>

<sup>1</sup>Department of Clinical Psychology, Leiden University, <sup>2</sup>Leiden Institute for Brain and Cognition (LIBC), Leiden University Medical Center, <sup>3</sup>Department of Child and Family Studies, Leiden University, and <sup>4</sup>Faculty of Social and Behavioural Sciences, Leiden University, 2333 AK Leiden, The Netherlands

Correspondence should be addressed to: Lisa J. M. van den Berg, Department of Clinical Psychology, Leiden University, Wassenaarseweg 52, 2333 AK Leiden, The Netherlands. E-mail: l.j.m.van.den.berg@fsw.leidenuniv.nl

### Abstract

Rejection by parents is an important aspect of child maltreatment. Altered neural responses to social rejection have been observed in maltreated individuals. The current study is the first to examine the impact of experienced and perpetrated abuse and neglect on neural responses to social exclusion by strangers versus family using a multigenerational family design, including 144 participants. The role of neural reactivity to social exclusion in the intergenerational transmission of maltreatment was also examined. Exclusion by strangers was especially associated with increased activation in the left insula, while exclusion by a family member was mainly associated with increased activation in the ACC. Neural reactivity to social exclusion by strangers in the insula, ACC and dmPFC, was associated with experienced maltreatment but not with perpetrated maltreatment. In abusive parents, altered neural reactivity during exclusion was found in other brain areas, indicating different neural correlates of experienced and perpetrated maltreatment. Hence, no mechanisms could be identified that are involved in the transmission of maltreatment. Hypersensitivity to social rejection by strangers in neglected individuals underscores the importance to distinguish between effects of abuse and neglect and suggests that the impact of experiencing rejection and maltreatment by your own parents extends beyond the family context.

**Key words:** social rejection; child maltreatment; insula; ACC; dmPFC

### Introduction

Child physical and emotional abuse and neglect are associated with increased risk for long-lasting behavioral, physical and mental health problems (e.g. Heim *et al.*, 2010; Spinhoven *et al.*, 2010; Twardosz and Lutzker, 2010; McCrory *et al.*, 2011a; Norman *et al.*, 2012; Spinhoven *et al.*, 2014). Among the adverse consequences is the increased risk for maltreated individuals to maltreat their own children (e.g. Kaufman and Zigler, 1987; Egeland *et al.*, 1988; Pears and Capaldi, 2001; Dixon *et al.*, 2005; Berlin *et al.*, 2011). To

better identify risk factors for perpetrating abuse and neglect, it is crucial to examine factors that might play a role in the transmission of maltreatment. In this multigenerational family study, we aim to investigate the impact of experienced and perpetrated abuse and neglect on neural reactivity to social exclusion in 144 family members (90 parents and 54 offspring). The possible role of sensitivity to social rejection in the intergenerational transmission of maltreatment is also examined.

One of the core aspects of both child abuse and neglect is parental rejection of needs for attention and nurturance (Bolger

Received: 30 August 2017; Revised: 12 April 2018; Accepted: 21 May 2018

© The Author(s) (2018). Published by Oxford University Press.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

and Patterson, 2001; Glaser, 2002), which can occur through parental aggression and hostility or via parental neglect and indifference (Loue, 2005). Chronic exposure to rejection during childhood is associated with emotional, cognitive, behavioral and social deficits, for instance, decreased self-esteem and hypersensitivity to signs of threat and rejection (Van Beest and Williams, 2006; DeWall and Bushman, 2011; Eisenberger, 2012; Sreekrishnan et al., 2014). Rejection sensitivity is associated with increased feelings of aggression and aggressive behavior (Downey and Feldman, 1996; Downey et al., 1998; Jacobs and Harper, 2013). Being rejected by your own parents can enhance sensitivity for social rejection in all sorts of situations, including next-generation parent–child interactions.

Multiple studies show that the network of brain areas associated with social rejection and exclusion includes the insula, anterior cingulate cortex (ACC) and medial prefrontal cortex (mPFC; e.g. Eisenberger et al., 2003; DeWall et al., 2010; Bolling et al., 2011; Sebastian et al., 2011; Cacioppo et al., 2013; Eisenberger, 2015; Rotge et al., 2015). The insula and ACC are key brain regions involved in social functioning (Wager and Barrett, 2004; Shackman et al., 2011; Cacioppo et al., 2012, 2013), including empathic abilities (Carr et al., 2003; Lamm et al., 2007; Shirtcliff et al., 2009; Rameson et al., 2012). The mPFC is implicated in self-processing, cognitive control, social evaluation and regulation of stress and negative emotions (Ochsner and Gross, 2005; Güroğlu et al., 2010; Etkin et al., 2011; Sebastian et al., 2011; Van den Bos et al., 2011; Denny et al., 2012).

Altered neural responses to social exclusion (compared to social inclusion) have been observed in maltreated individuals. For instance, children with early separation experiences showed reduced activation in the dorsal ACC (dACC) and dorso-lateral PFC (dlPFC) and reduced dlPFC–dACC connectivity (Puetz et al., 2014). Maltreated children also showed a hypoactivation to rejection-related words, including the left anterior insula and ventrolateral PFC (vlPFC; Puetz et al., 2016). In young adults, in contrast, childhood emotional maltreatment (CEM) severity was found to be associated with increased dorsal mPFC (dmPFC) responsivity to social exclusion, suggesting they show increased levels of self- and other referential processing after social exclusion (Van Harmelen et al., 2014).

A history of maltreatment appears to affect neural networks (i.e. insula, ACC and mPFC) that are also implicated in parenting behavior (Swain and Ho, 2017). These networks enable parents to respond to infant pain and emotions, understand non-verbal signals and infer intentions through empathy and mentalizing (Feldman, 2015; Rilling and Mascaró, 2017). Neural alterations in these areas implicated in social exclusion might mediate the association between experienced and perpetrated abuse and neglect. The current study is the first to examine the role of the neural correlates of social exclusion in the transmission of maltreatment.

Individual differences in response to social exclusion may depend on the relationship with the person who is excluding (Krill and Platek, 2009; Bernstein et al., 2010; Sacco et al., 2014; Scanlon, 2015). Since child maltreatment takes place within the family context, an important question is whether maltreated individuals display a general rejection sensitivity or a more specific hypervigilance for exclusion in their own parent–child context. No functional magnetic resonance imaging (fMRI) studies have been conducted comparing responsivity to exclusion by family members versus strangers. An electroencephalogram (EEG) study suggested however increased sensitivity to exclusion by family members as reflected by increased frontal P2 peaks and left frontal positive slow waves in mothers and children when excluded by one another versus by a stranger

(Sreekrishnan et al., 2014). The current study is the first that aims to unravel the neural activity following exclusion by one's own mother or child versus strangers and how this is specifically affected in maltreated and maltreating individuals.

In sum, this study examined the impact of experienced and perpetrated abuse and neglect on neural reactivity to social exclusion by strangers and family members. We used a multi-generational family design, including 144 participants from 8 to 69 years. We differentiated between effects of (experienced and perpetrated) abuse and neglect, as abuse and neglect may be differentially related to the affective and neural correlates of social rejection (e.g. Compier-de Block et al., 2016; Nemeroff, 2016; Van den Berg et al., 2017). We predicted that experienced and perpetrated child abuse and neglect are associated with altered sensitivity to social signals and rejection as reflected by decreased ACC, insular and/or increased dmPFC responsivity to social exclusion. As a second aim, we examined whether the effects represent a general sensitivity to exclusion or a specific sensitivity to one's own family members.

## Materials and methods

### Participants

The current sample was part of a larger sample from the 3G parenting study, a three-generation family study on the intergenerational transmission of parenting styles, stress and emotion regulation (see also Compier-de Block, 2017; Van den Berg et al., 2017). Participants were recruited via three other studies that included the assessment of caregiving experiences (Penninx et al., 2008; Scherpenzeel, 2011; Joosen et al., 2013). We oversampled participants with an increased risk of maltreatment and included participants who had at least one child of 8 years or older. After consent for participation in the 3G study, their family members (parents, partners, offspring, adult siblings, nephews, nieces and in-laws) were invited to participate. For the current study, all participants from the 3G study who participated in the fMRI part of the study were included. In total, we included 144 participants from two generations (parents and their offspring) of 54 families.

Participants played one round of the Cyberball task with strangers and one with family. We included only the first round of Cyberball in our analyses (using a between-subject design) because affective and neural effects of exclusion were only observed in the first round of the task, irrespective of the familiarity of the other players. This was possibly due to habituation to the task. Participants played their first round of Cyberball with strangers (unfamiliar condition; 28 men and 44 women) or with family (familiar condition;  $n = 72$ ; see Figure 1). In the familiar condition, 41 participants played with their child (18 men and 23 women) and 31 with their mother (11 men and 20 women). Separate analyses were run to link experienced maltreatment (all participants;  $n = 144$ ) and perpetrated maltreatment (parents only;  $n = 90$ ) to neural responses. See [Supplementary data](#) for more information.

### Procedure

Informed consent was obtained after describing the study to the participants. If eligible, offspring and their parents were asked to participate in the fMRI session, performing three tasks in the scanner, with the Cyberball task always second. Results on the other tasks are reported elsewhere (Van den Berg et al., 2017). All participants younger than 18 years old were first familiarized with the scanner environment using a mock scanner. The full protocol was conducted according to the principles expressed in

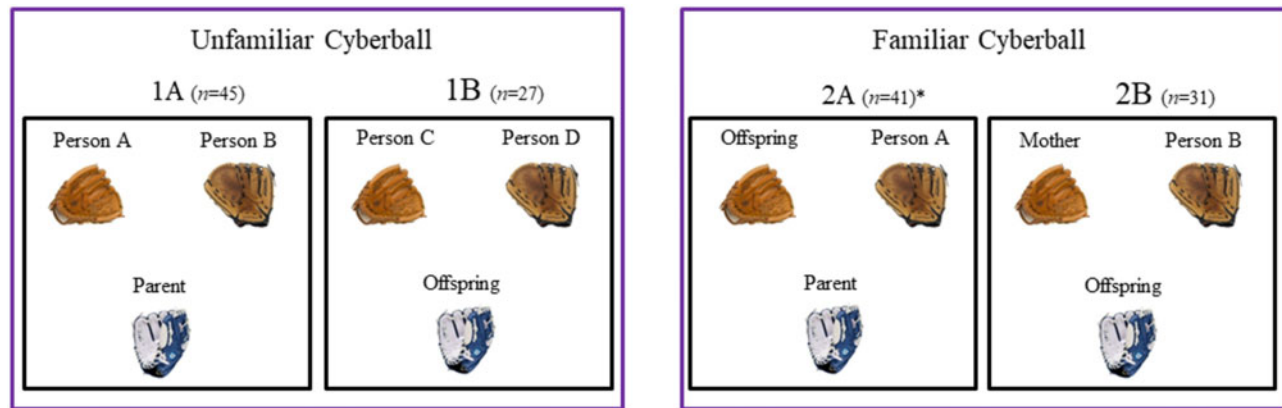


Fig. 1. Unfamiliar (1A and 1B) and familiar (2A and 2B) Cyberball for parents (1A and 2A) and offspring (1B and 2B). \*Four parents played with their mother because their offspring were too young to participate.

the Declaration of Helsinki and approved by the Medical Ethics Committee of the Leiden University Medical Center (LUMC).

## Measures

**Childhood maltreatment.** 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) to measure experienced childhood abuse and neglect by mother and/or father. Parents also completed a CTS version to assess their own abusive or neglectful behaviors towards 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 [Supplementary data](#)), resulting in a total of 237 informants on experienced childhood maltreatment and 163 informants on perpetrated maltreatment. Because the distributions of CTS scores were skewed, scores were logarithmically transformed ( $\log_{10}$ ). Outliers, meaning values more extreme than a standardized value of  $\pm 3.29$ , were winsorized to the most extreme value within the normal range  $\pm$  the difference between the two most extreme values within the normal range ( $n = 1$  for experienced abuse and  $n = 1$  for neglect).

**Cyberball task.** The Cyberball task is a commonly used paradigm to study the neural correlates of social exclusion (Williams *et al.*, 2000). For the current study, an adapted version of the task was used in which participants played two rounds of this virtual ball-tossing game with two other players (computer controlled confederates; see [Supplementary data](#)). All participants played one round with two strangers (unfamiliar round) and another round with a family member and a stranger (familiar round). For offspring, this family member was their own mother, and parents played with their oldest child (participating in the 3G study). The order of the rounds was counterbalanced across participants within the two generations. As described above, only the first round of Cyberball was included in our analyses. During the game, each player was represented by a picture of a different baseball glove (see Figure 1).

Each round consisted of an inclusion and exclusion block of 36 trials each. During the inclusion block, the ball was thrown to the participant in 33% of the total number of tosses (hence, achieving fair play in which the participant got an equal

**Table 1.** Mood (SD) before the Cyberball, after round 1 for parents and offspring

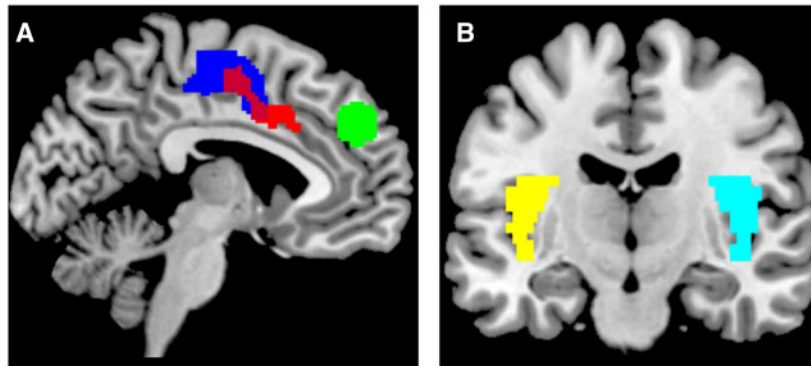
	Parents	Offspring
Baseline	8.39 (1.04)	8.80 (0.86)
After round 1 of Cyberball	8.16 (1.23)**	8.55 (1.15)*

\*P < 0.05; \*\*P < 0.01 compared to baseline.

number of tosses as compared to the other players). After receiving the ball, participants could throw back the ball to one of the other players using a button press. The inclusion block was followed by a social exclusion block with the same players, during which participants received the ball only once at the start of the game (the unfair play in which participants were excluded from the game). Participants' tosses were self-paced, and ball tosses of the other players were preceded by a random jitter interval (100–4000 ms). It took 2 s before each toss reached the designated player, and ball tosses varied in trajectory. The task was projected on a screen at the end of the scanner and was visible via a mirror positioned on the head coil.

**Mood and need satisfaction.** Right before the Cyberball game (inside the scanner) and immediately after each round of the game, participants completed four items from a mood questionnaire (Sebastian *et al.*, 2010). The items measured feeling sad, happy, angry and insecure. After each Cyberball round, additional items from the Need Threat Scale (Van Beest and Williams, 2006) were completed to measure levels of need satisfaction. The five items from the Need Threat Scale measured belonging, control, self-esteem and meaningful existence. All questions were presented on the screen. Each item was rated on a scale from 1 ('not at all') to 10 ('very much'). Items were recoded and averaged to create an overall index of mood and need satisfaction at each time point with higher scores reflecting a better mood (see Table 1) and higher levels of need satisfaction.

**Covariates.** Questionnaires were used to assess demographic information (age, gender, handedness and household social economic status [SES]). Three versions of Achenbach's behavior problems assessment were used to control for psychopathology symptoms. Parents completed the Child Behavioral Checklist (CBCL; Achenbach, 1991a) when their child was younger than 12 years old. For 12- to 17-year-old participants, the Youth Self Report (YSR; Achenbach, 1991b; Achenbach and Rescorla, 2001)



**Fig. 2.** Region of interest (ROI) masks. **A** = Red: functional ACC ROI mask for the unfamiliar condition based on whole brain activation for the contrast no-ball exclusion > no-ball inclusion at  $P < 0.005$  (uncorrected); Dark blue: functional ACC ROI mask for the familiar condition based on whole brain activation for the contrast no-ball exclusion > no-ball inclusion at  $P < 0.005$  (uncorrected); Green: dmPFC ROI mask based on the peak activation described by Van Harmelen et al. (2014; centered on MNI-coordinates  $x = -3, y = 48, z = 33$ ). **B** = Yellow: anatomical left insula ROI mask; Cyan: anatomical right insula ROI mask.

was used, and older participants completed the Adult Self Report (ASR; Achenbach and Rescorla, 2003). A total psychopathology symptom score was calculated for all three questionnaires. Cronbach's  $\alpha$ s were good to excellent (.76–.93).

### fMRI acquisition

Imaging data were acquired using a whole-head coil on a 3.0-Tesla Philips Achieva scanner (Philips Medical Systems, Best, the Netherlands) located at the LUMC. To restrict head motion, foam cushions were used around the head. T2\*-weighted echo-planar images (EPI) were obtained for all participants [repetition time (TR) = 2200 ms, echo time (TE) = 30 ms, matrix size:  $80 \times 79$ , 38 transverse slices of 2.75 mm, slice gap = 0.28 mm, field of view (FOV) = 220]. In accordance with the LUMC policy, all anatomical MRI scans were reviewed and cleared by a radiologist from the radiology department. No anomalous findings were reported.

### fMRI data analysis

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). Preprocessing, after extensive quality control of the data, included 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  $3 \times 3 \times 3$  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 ( $n = 16$ ).

MRI data were analyzed with the General Linear Model in SPM8. The fMRI time series were modeled as a series of events convolved with the hemodynamic response function (HRF). BOLD responses were distinguished for events on which participants received or did not receive the ball by a stranger or a family member (see [Supplementary data](#)). The first trials of the exclusion blocks during which participants received and played the ball once were not analyzed. The onset of the ball movement 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.

To examine the effect of social exclusion, the following contrasts were computed for all participants for the familiar and unfamiliar round: no-ball exclusion block > no-ball inclusion block. To test neural correlates of social exclusion, key region of interests (ROIs) were identified using the MARSBAR toolbox (Brett et al., 2002) in SPM: namely, the insula, dACC and dmPFC (see Figure 2). We defined anatomical ROIs of the insula using the TD label atlas within the Wakeforest-pickatlas toolbox (Maldjian et al., 2003). Because the boundaries of ACC subdivisions are to date not well defined (Lieberman and Eisenberger, 2015; Rotge et al., 2015), and the whole brain peak voxels of the ACC were located in different areas of the ACC dependent on whether participants were playing with strangers or family members (see Figure 2), we extracted two distinct areas of the dACC as functional ROIs (Poldrack, 2007) using the MARSBAR toolbox (Brett et al., 2002). We generated the dACC functional ROIs using whole-brain activation of the unfamiliar round to analyze the no-ball exclusion block versus no-ball inclusion block contrast for the unfamiliar condition and whole brain activation of the familiar round for the familiar condition (see Figure 2, Tables 2 and 3). Additionally, because CEM was found to be specifically associated with enhanced dmPFC activity to social exclusion (Van Harmelen et al., 2014), this area was defined by a 10-mm sphere around the peak activation described by Van Harmelen et al. (2014; centered on MNI-coordinates  $x = -3, y = 48, z = 33$ ). All results are reported in MNI space.

### SPSS data analysis

Activity in the ROIs was examined using three-level multilevel regression analyses in SPSS 23, in which participants were nested within households and households were nested within families, to take the family structure of the data into account. This way, level 1 models variation at the participant level, level 2 captures variation among participants within the same households and level 3 estimates variation among families. Random intercept models were built sequentially, starting with an empty (null) model without explanatory variables in which the total variance in brain reactivity in response to social exclusion was divided into a component at each level. This empty model was used to test for random variation in the outcome variables at the different levels (see [Supplementary data](#)). We consistently used multilevel analyses for all ROIs to control for the nested structure of data.

**Table 2.** Significant clusters for the contrast no-ball exclusion block > no-ball inclusion block for the unfamiliar Cyberball round

Clusters	Cluster level		Peak level		Coordinates		
	Number of voxels	T	P value	x	y	z	
Left insula	832	5.74	<0.001	-33	8	7	
		5.44	<0.001	-24	-4	1	
		5.35	<0.001	-45	-7	13	
Precentral gyrus		3.69	<0.001	-57	5	10	
Postcentral gyrus	169	4.99	<0.001	48	-22	25	
ACC	269	4.90	<0.001	-6	11	37	
Right insula	450	3.85	<0.001	0	-7	55	
		3.51	<0.001	9	5	43	
		4.21	<0.001	45	2	4	
		4.04	<0.001	36	-1	13	
		3.91	<0.001	54	5	4	

Note.  $P < 0.005$  uncorrected,  $> 25$  voxels.

As a next step, age, gender, handedness, SES and psychopathology were added to the model as possible covariates. Variables were only kept in the final covariates model when they were significant ( $P < 0.05$ ). To explore fixed effects of abuse and neglect, main effects of abuse and neglect were added to Model 1.

Multilevel regression analyses were run for each ROI for the familiar and the unfamiliar contrast separately. Separate models were run for experienced and perpetrated maltreatment. For multilevel analyses in the context of the familiar Cyberball, participants playing with their own child (41 parents) or mother (31 offspring) were analyzed separately (see Figure 1). All (continuous) predictor variables and covariates were centered. All independent and dependent variables were measured at the individual level (except SES; see [Supplementary data](#)) and considered in the fixed part of the model. Unstandardized regression coefficients are reported. If similar significant ROIs were found for experienced and perpetrated abuse and/or neglect, mediation analyses were planned to assess their role in the intergenerational transmission of maltreatment. However, this was not relevant for the current findings.

## Results

### Transmission of maltreatment

Demographics and mean (SD) maltreatment scores are presented in Table 4. The correlation between experienced abuse and neglect was  $r = .51$  ( $P < 0.001$ ) and between perpetrated abuse and neglect  $r = .34$  ( $P = 0.001$ ). To examine intergenerational transmission of maltreatment in our sample, regression analyses were conducted with experienced childhood abuse and neglect as predictors and with perpetrated abuse and neglect as outcome measures separately for participants with offspring ( $n = 88$  parents). Results indicated that, controlling for age, gender, household SES and psychopathology in the first block, experienced abuse ( $\beta = .53$ ,  $t(81) = 4.66$ ,  $P < 0.001$ ) was the only significant predictor of perpetrated abuse. Experienced neglect did not predict perpetrated abuse ( $P = 0.113$ ). None of the covariates were significant. Perpetrated neglect was not predicted by experienced neglect ( $P = 0.306$ ) nor by experienced abuse ( $P = 0.945$ ). Age ( $\beta = 0.29$ ,  $t = 2.54$ ,  $P = .013$ ) and psychopathology ( $\beta = 0.30$ ,  $t = 2.68$ ,  $p = .009$ ) were significant covariates for perpetrated neglect.

### Mood and need satisfaction

A time (mood before versus after the first round of Cyberball)  $\times$  type (playing with family or strangers) repeated measures

**Table 3.** Significant clusters for the contrast no-ball exclusion block > no-ball inclusion block for the familiar Cyberball round for parents (A) and offspring (B)

Clusters	Cluster level		Peak level		Coordinates		
	Number of voxels	T	P value	x	y	z	
<b>A. Parents (n = 90)</b>							
Postcentral gyrus	62	4.68	<0.001	-54	-25	43	
		4.47	<0.001	-45	-28	49	
Precentral gyrus	152	4.16	<0.001	-33	-25	55	
		4.57	<0.001	6	-7	52	
ACC	152	3.91	<0.001	-9	-7	52	
		3.77	<0.001	-12	-31	49	
Precentral gyrus	34	3.68	<0.001	33	-25	52	
<b>B. Offspring (n = 54)</b>							
ACC	567	6.34	<0.001	-6	-4	55	
		6.00	<0.001	6	2	52	
Left insula	165	5.44	<0.001	-6	5	43	
		5.35	<0.001	-42	-4	10	
Precentral gyrus	185	5.00	<0.001	36	-22	55	
		4.11	<0.001	42	-19	67	
		3.71	<0.001	42	-28	67	
Postcentral gyrus	230	4.93	<0.001	-54	-19	49	
		4.46	<0.001	-45	-22	55	
		3.86	<0.001	-36	-28	52	
Right insula	65	3.85	<0.001	42	-25	22	
		3.46	0.001	54	-19	22	
Postcentral gyrus	65	3.43	0.001	60	-25	25	
		3.77	<0.001	-45	-22	19	
Left insula	72	3.77	<0.001	-63	-22	31	
		3.29	0.001	-57	-22	22	

Note.  $P < 0.005$  uncorrected,  $> 25$  voxels.

ANOVA with mood as a dependent variable showed a significant main effect of time on mood for parents ( $F(1, 80) = 8.76$ ,  $P = 0.004$ ) and offspring ( $F(1, 60) = 6.10$ ,  $P = 0.016$ ), with mood scores significantly decreasing after the first Cyberball round compared to baseline for both parents and offspring. There were no significant interaction effects between time and type for parents ( $P = 0.097$ ) or offspring ( $P = 0.260$ ).

Correlation analyses revealed that levels of experienced or perpetrated abuse or neglect were not related to mood after exclusion during the Cyberball task for parents ( $P > 0.05$ ). However, a lower mood after exclusion was significantly related with higher levels of experienced abuse ( $r = -.37$ ,  $P = 0.003$ ) and neglect ( $r = -.38$ ,  $p = 0.003$ ) for children. No relationships were found between experienced or perpetrated abuse or neglect and need satisfaction after the Cyberball task for parents or children ( $P > 0.05$ ).

### Unfamiliar cyberball

**Whole brain analyses.** For the unfamiliar Cyberball ( $n = 72$ ; see Figure 1), whole brain analyses for the contrast no-ball exclusion block versus no-ball inclusion block revealed a significant cluster of activation in the left insula at  $P < 0.01$  family-wise error (FWE) corrected for multiple comparisons. For exploratory purposes, brain activation was also examined at the whole brain level with a threshold of  $P < 0.005$  (uncorrected). To reduce the risk of false positives, only clusters larger than 25 significantly activated voxels were considered (Lieberman and Cunningham, 2009). At this threshold, the contrast no-ball exclusion block versus no-ball inclusion block showed activation in clusters including the insula and ACC (see Table 2).

**Table 4.** Demographics, psychopathology, and maltreatment scores

Variables	Mean (SD)	Range
Age	36.85 (16.38)	8.75 - 69.67
Gender (n: men/women)	57/87	–
Handedness (n: left/right)	18/126	–
CBCL	14.00 (7.64)	3.20 - 28.80
YSR	9.68 (8.27)	0.00 - 30.00
ASR	24.22 (15.69)	1.00 - 83.00
Abused <sup>a</sup>	1.65 (0.50)	1.02 - 4.50
Neglected <sup>a</sup>	1.89 (0.61)	1.00 - 5.00
Maltreated <sup>a</sup> (total)	1.77 (0.49)	1.02 - 4.75
Abusive <sup>b</sup> (n = 90)	1.49 (0.31)	1.00 - 2.53
Neglectful <sup>b</sup> (n = 90)	1.55 (0.32)	1.00 - 2.48
Maltreating <sup>b</sup> (total; n = 90)	1.52 (0.25)	1.00 - 2.11

Note. Values of all included participants are presented (n = 144) unless otherwise specified. Raw scores are presented.

<sup>a</sup>Combined experienced maltreatment scores by averaging parent and child reports as measured with the CTS.

<sup>b</sup>Combined perpetrated maltreatment scores by averaging parent and child reports as measured with the CTS.

CBCL = Child Behavioral Checklist; YSR = Youth Self Report; ASR = Adult Self Report.

**Multilevel ROI analyses: experienced abuse and neglect.** Multilevel analyses were first performed for the contrast no-ball exclusion by strangers versus no-ball inclusion by strangers for all participants in the unfamiliar Cyberball condition (n = 72; see Figure 1). Analyses were run with experienced abuse and neglect as predictors and BOLD responses in the ROIs as outcome measures (see Tables 5A–8A and [Supplementary data](#)). In none of these multilevel analyses age, gender, handedness, SES nor psychopathology were significant covariates.

Adding abuse and neglect experience as predictors significantly improved the models for activation in the left ( $\chi^2(2) = 8.75, P = 0.013$ ) and right insula ( $\chi^2(2) = 6.07, P = 0.048$ ), dACC ( $\chi^2(2) = 8.70, P = 0.013$ ) and dmPFC ( $\chi^2(2) = 11.09, P = 0.004$ ). Higher levels of experienced maltreatment were associated with higher BOLD responses in the left and right insula and the dmPFC, and with lower BOLD responses in the dACC during social exclusion by strangers. Analyses on experienced abuse versus neglect revealed that the increased reactivity in the left insula ( $\beta = 2.49, t = 2.03, P = 0.046$ ) and dmPFC ( $\beta = 3.27, t = 2.07, P = 0.042$ ) were mainly due to neglect.

**Multilevel ROI analyses: perpetrated abuse and neglect.** Similar multilevel analyses were run for parents in the unfamiliar Cyberball condition (n = 45; see Figure 1) with perpetrated abuse and neglect as predictors for the contrast no-ball exclusion by strangers versus no-ball inclusion by strangers (see Tables 5A–8A and [Supplementary data](#)). Age, gender, handedness, SES and psychopathology were not significant as covariates in any of those analyses.

Adding perpetrated abuse and neglect as predictors did not significantly improve the models for activation in the left ( $\chi^2(2) = 2.34, P = 0.311$ ) or right insula ( $\chi^2(2) = 4.27, P = 0.119$ ), dACC ( $\chi^2(2) = 2.80, P = 0.247$ ) or dmPFC ( $\chi^2(2) = 2.39, P = 0.302$ ) regarding exclusion by strangers.

### Familiar cyberball

**Whole brain analyses.** For the familiar Cyberball (n = 72; see Figure 1), whole brain analyses for the contrast no-ball

exclusion block versus no-ball inclusion block showed a significant cluster of activation in the ACC at  $p < 0.01$  FWE corrected for multiple comparisons. At  $p < 0.005$  (uncorrected, 25 voxels) both parents and offspring showed activation in clusters including the ACC during exclusion (see Table 3 for an overview of all activated clusters). Moreover, offspring also showed activation in the left and right insula during exclusion by their parents, whereas this was not found for parents playing with their offspring.

**Multilevel ROI analyses: experienced abuse and neglect.** Multilevel analyses were repeated for the contrast no-ball exclusion by family versus no-ball inclusion by family for participants in the familiar Cyberball condition for parents (n = 41) and offspring (n = 31) separately (see Figure 1, Tables 5B–8B and [Supplementary data](#)).

**Parents.** For parents, a higher SES was associated with higher activity in the left ( $\beta = 0.37, t = 2.09, P = 0.043$ ) and right insula ( $\beta = 0.43, t = 2.41, P = 0.021$ ). Higher levels of psychopathology were associated with higher right insula activation ( $\beta = 1.71, t = 3.41, P = 0.006$ ). Age, gender and handedness were not significant covariates in those analyses.

Adding experiences of abuse and neglect as predictors did not significantly improve the models for activation in the left ( $\chi^2(2) = 0.40, P = 0.817$ ) or right insula ( $\chi^2(2) = 0.59, P = 0.746$ ), dACC ( $\chi^2(2) = 0.47, P = 0.792$ ) or dmPFC ( $\chi^2(2) = 3.91, P = 0.142$ ) regarding exclusion by offspring.

**Offspring.** For offspring, higher levels of psychopathology were associated with higher activity in the right insula ( $\beta = 3.10, t = 2.60, P = 0.013$ ). Right-handed participants exhibited higher dACC activation ( $\beta = -1.68, t = -2.61, P = 0.014$ ). Age, gender and SES were not significant covariates in any of those analyses.

Adding experiences of abuse and neglect as predictors did not significantly improve the models for activation in the left ( $\chi^2(2) = 1.65, P = 0.437$ ) or right insula ( $\chi^2(2) = 1.68, P = 0.432$ ), dACC ( $\chi^2(2) = 0.32, P = 0.851$ ) or dmPFC ( $\chi^2(2) = 0.69, P = 0.707$ ) regarding exclusion by parents for offspring.

**Multilevel ROI analyses: perpetrated abuse and neglect.** Multilevel analyses were repeated for the contrast no-ball exclusion by family versus no-ball inclusion by family for all parents in the familiar Cyberball condition (n = 41; see Figure 1, Tables 5B–8B and [Supplementary data](#)). Younger participants ( $\beta = -0.03, t = -3.54, P = 0.003$ ) and participants with higher levels of psychopathology ( $\beta = 1.50, t = 3.42, P = 0.004$ ) exhibited higher activity in the right insula. Gender was a significant covariate for the dACC ( $\beta = 0.64, t = 2.09, P = 0.044$ ; higher activation in men). Handedness and SES were not significant.

Adding perpetrated abuse and neglect as predictors did not significantly improve the models for activation in the left ( $\chi^2(2) = 0.12, P = 0.941$ ) or right insula ( $\chi^2(2) = 0.20, P = 0.904$ ), dACC ( $\chi^2(2) = 0.20, P = 0.903$ ) or dmPFC ( $\chi^2(2) = 0.997, P = 0.607$ ) in the context of exclusion by family.

## Discussion

This is the first multigenerational family study that examined the impact of experienced and perpetrated abuse and neglect on neural reactivity to social exclusion. Moreover, we examined whether the effects represented a general sensitivity to exclusion or a sensitivity in the family context. Previous neuroimaging studies showed that being excluded during the Cyberball

**Table 5.** Multilevel model of brain reactivity in the left insula in response to social exclusion as related to experienced and perpetrated abuse and neglect: unfamiliar Cyberball and familiar Cyberball

## (A) Unfamiliar Cyberball

Left insula: Unfamiliar round

	Experienced maltreatment				Maltreating behavior		
	Parents and offspring (n = 72)				Parents (n = 45)		
	b	SE	P		b	SE	P
Abused	0.28	1.68	0.869	Abusive	3.01	2.12	0.162
Neglected	2.31	1.65	0.167	Neglectful	-2.86	2.38	0.236
	$\chi^2(2) = 8.75^*$				$\chi^2(2) = 2.34$		
			0.013				0.311

## (B) Familiar Cyberball

Left insula: Familiar round

	Experienced maltreatment							Maltreating behavior		
	Parents (n = 41)			Offspring (n = 31)				Parents (n = 41)		
	b	SE	P	b	SE	P		b	SE	P
abused	0.70	1.12	0.538	3.42	2.65	0.207	abusive	0.62	1.75	0.724
neglected	-0.34	1.02	0.740	-0.56	2.67	0.836	neglectful	-0.22	1.27	0.861
	$\chi^2(2) = 0.40$			$\chi^2(2) = 1.65$				$\chi^2(2) = 0.12$		
			0.817			0.437				0.941

Note. Significant covariates are included in the model (see [Supplementary data](#)).

\*P &lt; 0.05; \*\*P &lt; 0.01.

SE = standard deviation.

**Table 6.** Multilevel model of brain reactivity in the right insula in response to social exclusion as related to experienced and perpetrated abuse and neglect: unfamiliar Cyberball and familiar Cyberball

## (A) Unfamiliar Cyberball

Right insula: Unfamiliar round

	Experienced maltreatment				Maltreating behavior		
	Parents and offspring (n = 72)				Parents (n = 45)		
	b	SE	P		b	SE	p
Abused	-0.17	1.77	0.922	Abusive	0.78	2.20	0.725
Neglected	1.13	1.73	0.516	Neglectful	-5.17*	2.46	0.041
	$\chi^2(2) = 6.07^*$				$\chi^2(2) = 4.27$		
			0.048				0.119

## (B) Familiar Cyberball

Right insula: Familiar round

	Experienced maltreatment							Maltreating behavior		
	Parents (n = 41)			Offspring (n = 31)				Parents (n = 41)		
	b	SE	P	b	SE	P		b	SE	P
Abused	0.58	.74	0.454	3.51	2.91	0.237	Abusive	0.71	1.57	0.656
Neglected	-0.16	1.02	0.877	0.87	2.96	0.770	Neglectful	-0.41	1.03	0.699
	$\chi^2(2) = 0.59$			$\chi^2(2) = 1.68$				$\chi^2(2) = 0.20$		
			0.746			0.432				0.904

Note. Significant covariates are included in the model (see [Supplementary data](#)).

\*P &lt; 0.05; \*\*P &lt; 0.01.

task in the general population is typically associated with activation in the insula, ACC and mPFC (e.g. Eisenberger et al., 2003; DeWall et al., 2010; Sebastian et al., 2011; Bolling et al., 2011; Cacioppo et al., 2013; Eisenberger, 2015; Rotge et al., 2015). We also found that social exclusion was associated with insular and ACC activation. However, our whole brain analyses revealed differential reactivity to social exclusion by strangers

versus family (one's own mother or child). That is, exclusion by strangers was significantly associated with increased BOLD responses in the left insula, while exclusion by a family member was mainly associated with increased activation in the ACC, especially in offspring.

There are no previous fMRI studies comparing neural responsiveness to exclusion by family members versus strangers.

**Table 7.** Multilevel model of brain reactivity in the dACC in response to social exclusion as related to experienced and perpetrated abuse and neglect: unfamiliar Cyberball and familiar Cyberball(A) Unfamiliar Cyberball  
dACC: Unfamiliar round

	Experienced maltreatment			Maltreating behavior			
	Parents and offspring (n = 72)			Parents (n = 45)			
	b	SE	P	b	SE	p	
Abused	-2.72	2.12	0.206	Abusive	-4.59	2.70	0.096
Neglected	2.61	2.05	0.207	Neglectful	1.34	3.03	0.660
	$\chi^2(2) = 8.70^*$			$\chi^2(2) = 2.80$			
			0.013				0.247

(B) Familiar Cyberball  
dACC: Familiar round

	Experienced maltreatment						Maltreating behavior			
	Parents (n = 41)			Offspring (n = 31)			Parents (n = 41)			
	b	SE	P	b	SE	P	b	SE	P	
Abused	1.04	1.52	0.497	1.36	2.47	0.586	Abusive	-0.84	2.03	0.683
Neglected	-0.28	1.34	0.836	-0.80	2.43	0.745	Neglectful	0.73	2.05	0.725
	$\chi^2(2) = 0.47$			$\chi^2(2) = 0.32$			$\chi^2(2) = 0.20$			
			0.792			0.851				0.903

Note. Significant covariates are included in the model (see [Supplementary data](#)).  
\*P < 0.05; \*\*P < 0.01.

**Table 8.** Multilevel model of brain reactivity in the dmPFC in response to social exclusion as related to experienced and perpetrated abuse and neglect: unfamiliar Cyberball and familiar Cyberball(A) Unfamiliar Cyberball  
dmPFC: Unfamiliar round

	Experienced maltreatment			Maltreating behavior			
	Parents and offspring (n = 72)			Parents (n = 45)			
	b	SE	P	b	SE	P	
Abused	1.17	2.16	.591	Abusive	4.12	2.82	.151
Neglected	2.50	2.12	.242	Neglectful	-3.03	3.16	.343
	$\chi^2(2) = 11.09^{**}$			$\chi^2(2) = 2.39$			
			.004				.302

(B) Familiar Cyberball  
dmPFC: Familiar round

	Experienced maltreatment						Maltreating behavior			
	Parents (n = 41)			Offspring (n = 31)			Parents (n = 41)			
	b	SE	P	b	SE	P	b	SE	P	
Abused	0.82	1.75	0.640	-2.19	2.71	0.426	Abusive	-2.08	2.43	0.396
Neglected	-3.26*	1.52	0.038	1.36	2.68	0.616	Neglectful	1.83	2.13	0.396
	$\chi^2(2) = 3.91$			$\chi^2(2) = 0.69$			$\chi^2(2) = 0.997$			
			0.142			0.707				0.607

Note. Significant covariates are included in the model (see [Supplementary data](#)).  
\*P < 0.05; \*\*P < 0.01.

However, an EEG study found increased responses in mothers and their offspring while they were excluded by one another compared to a stranger (Sreekrishnan et al., 2014). The insula and ACC are both involved in social functioning (Wager and Barrett, 2004; Shackman et al., 2011; Cacioppo et al., 2012, 2013), including empathic abilities (Carr et al., 2003; Lamm et al., 2007; Shirtcliff et al., 2009; Rameson et al., 2012). However, the insula

is found to be involved in automatic affective-empathetic processing, whereas the ACC is associated with more general cognitive functions, for instance, task control and response selection (Gu et al., 2010) but also with the motivational component of emotions (Craig, 2009). ACC activity is also found in response to viewing a loved one, for example a child (Bartels and Zeki, 2004).



## Experienced abuse and neglect

**Exclusion by strangers.** As expected, maltreated individuals showed altered neural responses to social exclusion by strangers. Maltreated offspring and parents showed higher activity in the left and right insula and the dmPFC and lower reactivity in the dACC during social exclusion by strangers. Higher activity in the left insula and dmPFC during social exclusion by strangers was especially associated with experienced neglect. Increased dmPFC responsivity to social exclusion by strangers in neglected individuals is in line with previous findings for individuals who experienced CEM (Van Harmelen et al., 2014), strengthening the hypothesis that neglected individuals show increased levels of self- and other-referential processing after social exclusion (e.g., Gusnard et al., 2001; Kelley et al., 2002; Mitchell et al., 2005). Lower dACC reactivity in maltreated individuals is also in line with reduced dACC activation during social exclusion in children with early separation experiences (Puetz et al., 2014) and might reflect avoidant or dissociative responses (Krause-Utz et al., 2012; Heringa et al., 2013; Puetz et al., 2016).

Higher insula activity during social exclusion by strangers in maltreated individuals is consistent with increased insular activity in response to angry faces and trauma-related words in maltreated children (McCrorry et al., 2011b; Thomaes et al., 2012) but is not in line with a blunted insula response to rejection-related words in maltreated children (Puetz et al., 2016). Since the insula is associated with various functions including self-awareness and emotion processing (Phan et al., 2002), altered insula activation seems to be linked to functional deficits in emotion processing in maltreated subjects (Hart and Rubia, 2012). Hypersensitivity to social rejection by strangers might help explain why maltreated (and especially neglected) individuals may exhibit specific difficulties with social relationships, including the parent-child relationships (DeGregorio, 2013).

**Exclusion by family.** Whole brain analyses showed differential reactivity to social exclusion by strangers versus family. In contrast to our expectations, higher levels of experienced abuse or neglect were not associated with altered BOLD responses in the insula, dACC or dmPFC during exclusion by family for both offspring and parents. It has been reported that mentalizing about strangers activates more dorsal parts of the MPFC, whereas more ventral regions of the MPFC may be activated during mentalization related to close significant others (for example family members) with whom individuals experience self-other overlap (Mitchell et al., 2005; Krienen et al., 2010). We might have missed important brain areas with our selected ROIs, and future research might also include other regions, for instance ventral parts of the PFC.

Generally, rejection by a member of an established in-group is associated with enhanced pain of rejection (Bernstein et al., 2010). Little is known about the neural correlates of family-related entitativity (Rüsch et al., 2014), but lower levels of perceived family-related entitativity in maltreated individuals might explain why they do not show altered neural activity after social exclusion by a family member compared to non-maltreated individuals. Maltreated individuals may have become relatively insensitive for exclusion by their own family, while showing increased sensitivity for rejection in other situations (e.g., rejection by strangers). Another explanation might be that the presentation of the first name of a family member during the Cyberball game was not strong enough to elicit a clear (attachment) representation. For future research, it is

therefore recommended to also use (neutral) pictures of family members to examine this in more detail.

## Perpetrated abuse and neglect

Perpetrated abuse and neglect were not associated with activation in the insula, dACC or dmPFC during exclusion by strangers or family, even though it is suggested that these areas might play a role in parenting behavior (Feldman, 2015). Exploratory analyses (see [Supplementary data](#)) did suggest that abusive parents show lower reactivity in the precentral and postcentral gyrus during exclusion by strangers. While the precentral gyrus is mainly thought to control motor function, the postcentral gyrus is mostly known for processing sensory information. However, postcentral gyrus reactivity has also been identified in imaging studies of emotion and has been associated with the recognition of both positive and negative emotions and perspective taking (George et al., 1996; Canli et al., 2002; Hooker et al., 2012; Meyer et al., 2015). The precentral gyrus has also been associated with emotional memory, empathic concern and processing rewarding and aversive stimuli (Canli et al., 2002; Montoya et al., 2012; Meyer et al., 2015). Moreover, the precentral gyrus is thought to be involved in the social monitoring system (SMS), an outer monitoring system enhancing perceptual and cognitive responses to social cues and information including social exclusion (Kawamoto et al., 2015). Altered functioning of the SMS might induce antisocial behavior, including rejection and maltreating behavior. Although specific roles of the pre- and postcentral gyrus in affective processes remain to be examined, reduced activation in these areas might implicate that abusive parents are less sensitive to negative emotional and social stimuli.

## Intergenerational transmission of maltreatment

While in our sample intergenerational transmission of abuse was observed, neglect did not appear to be transmitted from one generation to the next. This is likely due to the smaller sample size of this fMRI subsample, since transmission of neglect was found in the complete sample of the 3G study.

Altered neural reactivity to social exclusion by strangers in the insula, ACC and dmPFC was associated with experienced maltreatment, whereas abusive parents showed decreased reactivity in the precentral and postcentral gyrus during exclusion by strangers. Hence, we found different neural correlates of experienced and perpetrated maltreatment and therefore no neural mechanisms playing a role in the transmission of maltreatment were found.

## Strengths and limitations

This is the first multigenerational family study in which differential neural effects of (experienced and perpetrated) abuse and neglect are examined, and the role of neural reactivity to social exclusion by strangers versus family is investigated. Research about the neural correlates of child maltreatment and maltreating parenting behavior in particular is scarce, and our family study design enabled the investigation of intergenerational transmission of maltreatment directly. Another strength is that parent (both fathers and mothers) and child reports of maltreatment were combined to minimize the influence of individual reporter bias. Moreover, our study allowed to differentiate between a general sensitivity for exclusion versus rejection sensitivity in the family context.

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. Moreover, in our paradigm names of family members were used. For future research, pictures of own offspring and parents might be used, although this would decrease standardization of the task. 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.

## Conclusion

In sum, we found that exclusion by strangers was especially associated with increased activity in the left insula, while exclusion by a family member was mainly associated with higher activation in the ACC. Furthermore, altered neural reactivity to social exclusion by strangers in the insula, ACC and dmPFC was associated with experienced maltreatment but not with parents' own maltreating behavior, indicating different neural correlates of experienced and perpetrated maltreatment. More specifically, hypersensitivity to social rejection in maltreated individuals was mainly driven by experienced neglect. Furthermore, exploratory analyses showed that abusive parents exhibited lower activation in the pre- and post-central gyrus during exclusion by strangers, possibly reflecting lower levels of perspective taking and empathic abilities. Our study underscores the importance to distinguish between effects of abuse and neglect and suggests that the impact of experiencing rejection and maltreatment by your own parents goes beyond the family context.

## Supplementary data

Supplementary data are available at SCAN online.

## Acknowledgements

We thank all Family Lab team members for their help with the data collection and all participants for their willingness to participate in the study. Furthermore, we thank Sandy Overgaauw for her help with the analyses.

## Funding

This work was supported by NWO VIDI and VICI-grants awarded to Dr. Bernet M. Elzinga [grant number 016.085.353 and 016.160.067] and an NWO VICI-grant awarded to Dr. Marian J. Bakermans-Kranenburg [grant number 453.09.003].

*Conflict of interest.* None declared.

## References

Achenbach, T.M. (1991a). *Manual for Child Behavior Checklist/4-18 and 1991 Profile*. Burlington, VT: Department of Psychiatry, University of Vermont.

Achenbach, T.M. (1991b). *Manual for the Youth Self-Report and 1991 Profile*. Burlington, VT: Department of Psychiatry, University of Vermont.

Achenbach, T.M., Rescorla, L.A. (2001). *Manual for the ASEBA School-Age Forms & Profiles*. Burlington, VT: Research Center for Children, Youth, & Families, University of Vermont.

Achenbach, T.M., Rescorla, L.A. (2003). *Manual for the ASEBA Adult Forms & Profiles*. Burlington, VT: Research Center for Children, Youth, & Families, University of Vermont.

Bartels, A., Zeki, S. (2004). The neural correlates of maternal and romantic love. *NeuroImage*, *21*(3), 1155–66.

Berlin, L.J., Appleyard, K., Dodge, K.A. (2011). Intergenerational continuity in child maltreatment: mediating mechanisms and implications for prevention. *Child Development*, *82*(1), 162–76.

Bernstein, D.P., Stein, J.A., Newcomb, M.D., et al. (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse and Neglect*, *27*(2), 169–90.

Bernstein, M.J., Sacco, D.F., Young, S.G., Hugenberg, K., Cook, E. (2010). Being “in” with the in-crowd: the effects of social exclusion and inclusion are enhanced by the perceived essentialism of ingroups and outgroups. *Personality and Social Psychology Bulletin*, *36*(8), 999–1009.

Bolger, K.E., Patterson, C.J. (2001). Developmental pathways from child maltreatment to peer rejection. *Child Development*, *72*(2), 549–68.

Bolling, D.Z., Pitskel, N.B., Deen, B., Crowley, M.J., Mayes, L.C., Pelphrey, K.A. (2011). Development of neural systems for processing social exclusion from childhood to adolescence. *Developmental Science*, *14*(6), 1431–44.

Brett, M., Anton, J.L., Valabregue, R., Poline, J.B. (2002). Region of interest analysis using an SPM toolbox. *NeuroImage*, *16*(2), 497.

Cacioppo, S., Bianchi-Demicheli, F., Frum, C., Pfaus, J.G., Lewis, J.W. (2012). The common neural bases between sexual desire and love: a multilevel kernel density fMRI analysis. *Journal of Sexual Medicine*, *9*(4), 1048–54.

Cacioppo, S., Frum, C., Asp, E., Weiss, R.M., Lewis, J.W., Cacioppo, J.T. (2013). A quantitative meta-analysis of functional imaging studies of social rejection. *Scientific Reports*, *3*(1), 2027.

Canli, T., Desmond, J.E., Zhao, Z., Gabrieli, J.D.E. (2002). Sex differences in the neural basis of emotional memories. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(16), 10789–94.

Carr, L., Iacoboni, M., Dubeau, M.C., Mazziotta, J.C., Lenzi, G.L. (2003). Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Sciences of the United States of America*, *100*(9), 5497–502.

Compier-de Block, L.H.C.G. (2017). Child maltreatment: underlying risk factors and perspectives of parents and children. Unpublished doctoral dissertation, Leiden University.

Compier-de Block, L.H.C.G., Linting, M., Van den Berg, L.J.M., et al. (2016). The role of maltreatment history and emotion recognition in parent-to-child maltreatment. *Manuscript submitted for publication*.

Craig, A.D. (2009). How do you feel - now? The anterior insula and human awareness. *Nature Reviews Neuroscience*, *10*(1), 59–70.

DeGregorio, L.J. (2013). Intergenerational transmission of abuse: implications for parenting interventions from a neuropsychological perspective. *Traumatology*, *19*(2), 158–66.

Denny, B.T., Kober, H., Wager, T.D., Ochsner, K.N. (2012). A meta-analysis of functional neuroimaging studies of self- and other judgments reveals a spatial gradient for mentalizing in medial prefrontal cortex. *Journal of Cognitive Neuroscience*, *24*(8), 1742–52.

DeWall, C.N., Bushman, B.J. (2011). Social acceptance and rejection: the sweet and the bitter. *Current Directions in Psychological Science*, *20*(4), 256–60.

DeWall, C.N., MacDonald, G., Webster, G.D., et al. (2010). Acetaminophen reduces social pain. *Psychological Science*, *21*(7), 931–7.

- Dixon, L., Browne, K., Hamilton-Giachritsis, C. (2005). Risk factors of parents abused as children: a mediational analysis of the intergenerational continuity of child maltreatment (Part I). *Journal of Child Psychology and Psychiatry*, *46*(1), 47–57.
- Downey, G., Feldman, S.I. (1996). Implications of rejection sensitivity for intimate relationships. *Journal of Personality and Social Psychology*, *70*(6), 1327–43.
- Downey, G., Freitas, A.L., Michaelis, B., Khouri, H. (1998). The self-fulfilling prophecy in close relationships: rejection sensitivity and rejection by romantic partners. *Journal of Personality and Social Psychology*, *75*(2), 545–60.
- Egeland, B., Jacobvitz, D., Sroufe, A.L. (1988). Breaking the cycle of abuse. *Child Development*, *59*(4), 1080–8.
- Eisenberger, N.I. (2012). The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. *Nature Reviews Neuroscience*, *13*(6), 421–34.
- Eisenberger, N.I. (2015). Social pain and the brain: controversies, questions, and where to go from here. *Annual Review of Psychology*, *66*, 601–29.
- Eisenberger, N.I., Lieberman, M.D., Williams, K.D. (2003). Does rejection hurt? An fMRI study of social exclusion. *Science*, *302*(5643), 290–2.
- Etkin, A., Egner, T., Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93.
- Feldman, R. (2015). The adaptive human parental brain: implications for children's social development. *Trends in Neurosciences*, *38*(6), 387–99.
- George, M.S., Ketter, T.A., Parekh, P.I., Herscovitch, P., Post, R.M. (1996). Gender differences in regional cerebral blood flow during transient self-induced sadness or happiness. *Biological Psychiatry*, *40*(9), 859–71.
- Glaser, D. (2002). Emotional abuse and neglect (psychological maltreatment): a conceptual framework. *Child Abuse & Neglect*, *26*(6–7), 697–714.
- Gu, X., Liu, X., Guise, K.G., Naidich, T.P., Hof, P.R., Fan, J. (2010). Functional dissociation of the fronto-insular and anterior cingulate cortices in empathy for pain. *Journal of Neuroscience*, *30*(10), 3739–44.
- Güroğlu, B., van den Bos, W., Rombouts, S.A.R.B., Crone, E.A. (2010). Unfair? It depends: neural correlates of fairness in social context. *Social Cognitive and Affective Neuroscience*, *5*(4), 414–23.
- Gusnard, D.A., Akbudak, E., Shulman, G.L., Raichle, M.E. (2001). Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America*, *98*(7), 4259–64.
- Hart, H., Rubia, K. (2012). Neuroimaging of child abuse: a critical review. *Frontiers in Human Neuroscience*, *6*, 52.
- Heim, C., Shugart, M., Craighead, W.E., Nemeroff, C.B. (2010). Neurobiological and psychiatric consequences of child abuse and neglect. *Developmental Psychobiology*, *52*(7), 671–90.
- Herringa, R.J., Phillips, M.L., Fournier, J.C., Kronhaus, D.M., Germain, A. (2013). Childhood and adult trauma both correlate with dorsal anterior cingulate activation to threat in combat veterans. *Psychological Medicine*, *43*(7), 1533–42.
- Hooker, C.I., Bruce, L., Fisher, M., Verosky, S.C., Miyakawa, A., Vinogradov, S. (2012). Neural activity during emotion recognition after combined cognitive plus social-cognitive training in schizophrenia. *Schizophrenia Research*, *139*(1–3), 53–9.
- Jacobs, N., Harper, B. (2013). The effects of rejection sensitivity on reactive and proactive aggression. *Aggressive Behavior*, *39*(1), 3–12.
- Joosen, K.J., Mesman, J., Bakermans-Kranenburg, M.J., Van IJzendoorn, M.H. (2013). Maternal overreactive sympathetic nervous system responses to repeated infant crying predicts risk for impulsive harsh discipline of infants. *Child Maltreatment*, *18*(4), 252–63.
- Kaufman, J., Zigler, E. (1987). Do abused children become abusive parents? *American Journal of Orthopsychiatry*, *57*(2), 186–92.
- Kawamoto, T., Ura, M., Nittono, H. (2015). Intrapersonal and interpersonal processes of social exclusion. *Frontiers in Neuroscience*, *9*, 62–111.
- Kelley, W.M., Macrae, C.N., Wyland, C.L., Caglar, S., Inati, S., Heatherton, T.F. (2002). Finding the self? An event-related fMRI study. *Journal of Cognitive Neuroscience*, *14*(5), 785–94.
- Krause-Utz, A., Oei, N.Y.L., Niedtfield, I., et al. (2012). Influence of emotional distraction on working memory performance in borderline personality disorder. *Psychological Medicine*, *42*(10), 2181–92.
- Krienen, F.M., Tu, P.C., Buckner, R.L. (2010). Clan mentality: evidence that the medial prefrontal cortex responds to close others. *Journal of Neuroscience*, *30*(41), 13906–15.
- Krill, A., Platek, S.M. (2009). In-group and out-group membership mediates anterior cingulate activation to social exclusion. *Frontiers in Evolutionary Neuroscience*, *1*(1), 1–7.
- Lamm, C., Batson, C.D., Decety, J. (2007). The neural substrate of human empathy: effects of perspective-taking and cognitive appraisal. *Journal of Cognitive Neuroscience*, *19*(1), 42–58.
- Lieberman, M.D., Cunningham, W.A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience*, *4*(4), 423–8.
- Lieberman, M.D., Eisenberger, N.I. (2015). The dorsal anterior cingulate cortex is selective for pain: results from large-scale reverse inference. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(49), 15250–5.
- Loue, S. (2005). Redefining the emotional and psychological abuse and maltreatment of children: legal implications. *The Journal of Legal Medicine*, *26*(3), 311–37.
- Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage*, *19*(3), 1233–9.
- McCrorry, E., De Brito, S.A., Viding, E. (2011). The impact of childhood maltreatment: a review of neurobiological and genetic factors. *Frontiers in Psychiatry*, *2*, 48.
- McCrorry, E.J., De Brito, S.A., Sebastian, C.L., et al. (2011). Heightened neural reactivity to threat in child victims of family violence. *Current Biology*, *21*(23), R947–8.
- Meyer, M.L., Masten, C.L., Ma, Y., et al. (2015). Differential neural activation to friends and strangers links interdependence to empathy. *Culture and Brain*, *3*(1), 21–38.
- Mitchell, J.P., Macrae, C.N., Banaji, M.R. (2005). Forming impressions of people versus inanimate objects: social-cognitive processing in the medial prefrontal cortex. *NeuroImage*, *26*(1), 251–7.
- Montoya, J.L., Landi, N., Kober, H., et al. (2012). Regional brain responses in nulliparous women to emotional infant stimuli. *PLoS One*, *7*(5), e36270.
- Nemeroff, C.B. (2016). Paradise lost: the neurobiological and clinical consequences of child abuse and neglect. *Neuron*, *89*(5), 892–909.
- Norman, R.E., Byambaa, M., De, R., Butchart, A., Scott, J., Vos, T. (2012). The long-term health consequences of child physical abuse, emotional abuse, and neglect: a systematic review and meta-analysis. *PLoS Medicine*, *9*(11), e1001349.
- Ochsner, K.N., Gross, J.J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences*, *9*(5), 242–9.

- Pears, K.C., Capaldi, D.M. (2001). Intergenerational transmission of abuse: a two-generational prospective study of an at-risk sample. *Child Abuse & Neglect*, *25*(11), 1439–61.
- Penninx, B.W.J.H., Beekman, A.T.F., Smit, J.H., et al. (2008). The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *International Journal of Methods in Psychiatric Research*, *17*(3), 121–40.
- Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage*, *16*(2), 331–48.
- Poldrack, R.A. (2007). Region of interest analysis for fMRI. *Social Cognitive and Affective Neuroscience*, *2*(1), 67–70.
- Puetz, V.B., Kohn, N., Dahmen, B., et al. (2014). Neural response to social rejection in children with early separation experiences. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(12), 1328–37.
- Puetz, V.B., Viding, E., Palmer, A., et al. (2016). Altered neural response to rejection-related words in children exposed to maltreatment. *Journal of Child Psychology and Psychiatry*, *57*(10), 1165–73.
- Rameson, L.T., Morelli, S.A., Lieberman, M.D. (2012). The neural correlates of empathy: experience, automaticity, and prosocial behavior. *Journal of Cognitive Neuroscience*, *24*(1), 235–45.
- Rilling, J.K., Mascaró, J.S. (2017). The neurobiology of fatherhood. *Current Opinion in Psychology*, *15*, 26–32.
- Rotge, J.Y., Lemogne, C., Hinfray, S., et al. (2015). A meta-analysis of the anterior cingulate contribution to social pain. *Social Cognitive and Affective Neuroscience*, *10*(1), 19–27.
- Rüsch, N., Bado, P., Zahn, R., Bramati, I.E., de Oliveira-Souza, R., Moll, J. (2014). You and your kin: neural signatures of family-based group perception in the subgenual cortex. *Social Neuroscience*, *9*(4), 326–31.
- Sacco, D.F., Bernstein, M.J., Young, S.G., Hugenberg, K. (2014). Reactions to social inclusion and ostracism as a function of perceived in-group similarity. *Group Dynamics: Theory, Research, and Practice*, *18*(2), 129–37.
- Scanlon, B.E. (2015). *The moderating effect of in-group ostracism on needs threat: a gendered social identity increases effects of Cyberball-ostracism*. Unpublished doctoral dissertation, University of West London.
- Scherpenzeel, A. (2011). Data collection in a probability-based internet panel: how the LISS panel was built and how it can be used. *Bulletin of Sociological Methodology/Bulletin De Méthodologie Sociologique*, *109*(1), 56–61.
- Sebastian, C.L., Tan, G.C.Y., Roiser, J.P., Viding, E., Dumontheil, I., Blakemore, S.J. (2011). Developmental influences on the neural bases of responses to social rejection: implications of social neuroscience for education. *NeuroImage*, *57*(3), 686–94.
- Sebastian, C., Viding, E., Williams, K.D., Blakemore, S.J. (2010). Social brain development and the affective consequences of ostracism in adolescence. *Brain and Cognition*, *72*(1), 134–45.
- Shackman, A.J., Salomons, T.V., Slagter, H.A., Fox, A.S., Winter, J.J., Davidson, R.J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience*, *12*(3), 154–67.
- Shirtcliff, E.A., Vitacco, M.J., Graf, A.R., Gostisha, A.J., Merz, J.L., Zahn-Waxler, C. (2009). Neurobiology of empathy and callousness: implications for the development of antisocial behavior. *Behavioral Sciences & the Law*, *27*(2), 137–71.
- Spinhoven, P., Elzinga, B.M., Hovens, J.G.F.M., et al. (2010). The specificity of childhood adversities and negative life events across the life span to anxiety and depressive disorders. *Journal of Affective Disorders*, *126*(1–2), 103–12.
- Spinhoven, P., Penninx, B.W., Van Hemert, A.M., De Rooij, M., Elzinga, B.M. (2014). Comorbidity of PTSD in anxiety and depressive disorders: prevalence and shared risk factors. *Child Abuse & Neglect*, *38*(8), 1320–30.
- Sreekrishnan, A., Herrera, T.A., Wu, J., et al. (2014). Kin rejection: social signals, neural response and perceived distress during social exclusion. *Developmental Science*, *17*(6), 1029–41.
- Straus, M.A., Hamby, S.L., Finkelhor, D., Moore, D.W., Runyan, D. (1998). Identification of child maltreatment with the parent-child Conflict Tactics Scales: development and psychometric data for a national sample of American parents. *Child Abuse and Neglect*, *22*(4), 249–70.
- Swain, J.E., Ho, S.H.S. (2017). Neuroendocrine mechanisms for parental sensitivity: overview, recent advances and future directions. *Current Opinion in Psychology*, *15*, 105–10.
- Thomaes, K., Dorrepaal, E., Draijer, N., et al. (2012). Treatment effects on insular and anterior cingulate cortex activation during classic and emotional Stroop interference in child abuse-related complex post-traumatic stress disorder. *Psychological Medicine*, *42*(11), 2337–49.
- Twardosz, S., Lutzker, J.R. (2010). Child maltreatment and the developing brain: a review of neuroscience perspectives. *Aggression and Violent Behavior*, *15*(1), 59–68.
- Van Beest, I., Williams, K.D. (2006). When inclusion costs and ostracism pays, ostracism still hurts. *Journal of Personality and Social Psychology*, *91*(5), 918–28.
- Van den Berg, L.J.M., Tollenaar, M.S., Compier-de Block, H.C.G., Bakermans-Kranenburg, M.J., Elzinga, B.M. (2018). An intergenerational family study on the impact of experienced and perpetrated child maltreatment on neural face processing. Manuscript submitted for publication.
- Van den Bos, W., van Dijk, E., Westenberg, M., Rombouts, S.A.R.B., Crone, E.A. (2011). Changing brains, changing perspectives: the neurocognitive development of reciprocity. *Psychological Science*, *22*(1), 60–70.
- Van Harmelen, A.L., Hauber, K., Gunther Moor, B., et al. (2014). Childhood emotional maltreatment severity is associated with dorsal medial prefrontal cortex reactivity to social exclusion in young adults. *PLoS One*, *9*(1), e85107.
- Wager, T.D., Barrett, L.F. (2004). From affect to control: functional specialization of the insula in motivation and regulation. Available: PsycExtra. Retrieved from [www.apa.org/psycextra/](http://www.apa.org/psycextra/) (February 6, 2017).
- Williams, K.D., Cheung, C.K.T., Choi, W. (2000). Cyberostracism: effects of being ignored over the internet. *Journal of Personality and Social Psychology*, *79*(5), 748–62.