I see you: insights into the neural and affective signatures of connectedness between parents and adolescents

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Chapter 5

Neural signatures of parental empathic responses to imagined suffering of their adolescent child

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ABSTRACT

Empathy is deemed indispensable for sensitive caregiving. Neuroimaging studies have identified canonical empathy networks consisting of regions supporting cognitive and affective aspects of empathy. However, not much is known about how these regions support empathy toward one's own offspring, and how this neural activity relates to parental caregiving. We introduce a novel task to assess affective and neural responses to the suffering of one's own adolescent child. While in the scanner, 60 parents ($n = 35$ mothers, $n = 25$ fathers) were confronted with unpleasant situations involving their own child, an unfamiliar child, and themselves. Parents were asked to vividly imagine these situations and indicate their levels of distress. Parents reported higher levels of distress when imagining suffering for their own child relative to an unfamiliar child or themselves. Neuroimaging results showed increased activation within the cognitive empathy network (i.e., temporoparietal junction, dorsomedial- and ventromedial prefrontal cortex), when contrasting suffering of one's own child versus an unfamiliar child or the self. The task also engaged regions of the affective empathy network (i.e., anterior insula and anterior mid-cingulate cortex), which was however not modulated by whether suffering was for the self, one's own child, or an unfamiliar child. Parental care did not co-vary with activity in the empathy networks, but parents who were perceived as less caring exhibited increased activity in anterior and lateral prefrontal regions when imagining their own child suffering. These results provide new insights into neural processes supporting parental empathy, highlighting the importance of regions in the cognitive empathy network when confronted with the imagined suffering of their own adolescent child, and suggest that additional (i.e., emotion regulation) networks may be relevant for parental caregiving behavior in daily life.

Keywords: Empathy; Parenting; Parent-child relationship; Affective responses; Pain; Perspective taking; Mentalizing.

INTRODUCTION

One of the most fundamental and evolutionary conserved functions of empathy is its role in parental care. Empathy can be defined as the capacity to share an emotional state with another individual, assess the reasons for the other's state, and identify with the other, adopting his or her perspective (De Waal & Preston, 2017). Empathy facilitates caregivers to perceive and appropriately respond to physiological and emotional cues from their offspring, such as hunger, pain or distress, and serves as an innate parental protection system (De Waal, 2008). As social lives became increasingly complex across human evolution, caregiving behavior also evolved and became more complex too. Moreover, throughout parenthood, human caregivers' role slowly transitions from mainly protecting offspring from potential physical threat into preparing them for successfully navigating their complex social worlds (Abraham et al., 2018; Swain et al., 2014). Empathetic parents provide more sensitive and attuned care for their children resulting in healthy parent-child relationships (Kochanska, 1997) and socio-emotional development of children (Abraham et al., 2018; Manczak et al., 2016; Richaud et al., 2013; Soenens et al., 2007). Although several studies focused on neural processes supporting parental sensitivity and attachment to the own child in parents of babies and young children (Abraham et al., 2018; Atzil et al., 2011; Barrett et al., 2012; Elmadih et al., 2016; Kuo et al., 2012; Leibenluft et al., 2004; Lenzi et al., 2009; Wan et al., 2014), only a hand full of neuroimaging studies on this topic have been performed in parents of adolescents (Kerr et al., 2020; Turpyn et al., 2020). Moreover, so far, no prior studies have investigated the neural processes of imagined suffering of one's own child and how these neural responses relate to sensitive caregiving behavior in parents of adolescents in daily life. Therefore, this study examined the affective and neural responses to one's own adolescent child when confronted with unpleasant situations and whether these responses are related to parental care as perceived by the adolescent child in daily life.

During adolescence, parent-child dyads find themselves in a complex emotional landscape, and although not in every family, increases in the frequency and intensity of conflicts are more likely in this period than in others (Arnett, 1999; De Goede et al., 2009; Restifo & Bögels, 2009; Shanahan et al., 2007). Adolescents start to behave more autonomously in their relationships with their parents, and show higher levels of affect lability and irritability (Steinberg & Silk, 2002). Parents, in turn, need to adapt to these changes and need to find a new balance between being sensitive and responsive to the changing needs and emotional states of the child, while also giving appropriate guidance and support their child's ability to make autonomous decisions (Kobak et al., 2017). However, achieving such a new balance might be easier to accomplish for some parents than for others (Allen et al., 1998), as adolescence entails many new challenges for the child which are not always easy for parents to imagine or understand, let alone to empathize with. In addition, as a consequence of increasing autonomy of the child during adolescence and the fact that they spend more time without adult supervision, parents often find themselves in situations in which they rather hear about instead of directly seeing their child suffering (Collins & Russell, 1991; Feldman & Elliott, 1990). Such situations are less common during infancy or childhood and might place higher demands on socio-cognitive capacities needed for empathic responses, such as the ability to imagine complex suffering of an adolescent (e.g., being excluded from a peer group). A better understanding of the neural circuitry supporting cognitive and affective empathy in parents of adolescents might help to elucidate which level of processing is most affected when parental empathy is sub-optimal, and hence should be addressed in particular when designing parenting interventions to facilitate parental empathy during adolescence. Furthermore, appropriate empathic responses of parents are important for the psychological and social adjustment of their child and for a healthy parent-child relationship (Abraham et al., 2018; Kochanska, 1997; Manczak et al., 2016; Richaud et al., 2013; Soenens et al., 2007). Therefore, we examined neural processes in parents supporting empathizing with a range of unpleasant situations an adolescent child may experience.

While parental empathy is deemed fundamental for sensitive caregiving (Abraham et al., 2018; Decety, 2011), studies about the neural underpinnings of parental empathic responses are sparse, particularly during adolescence. Elucidating neural correlates of parental empathy during adolescence might yield important insights in whether and how the brain of parents distinguishes between their own child and unfamiliar children in this particular period of transition, and may elucidate which regions are related to sensitive parenting behaviors, such as parental care. Therefore, we developed a novel, ecologically valid task to assess affective and neural parental responses to imagined suffering of their own adolescent child during both physically and socially unpleasant situations, such as their child enduring a physical injury (e.g., a fractured leg) or social adversity (e.g., being humiliated by others).

Although the involvement of brain regions in empathic responses in general have been extensively studied, not much is known about how these regions support empathy specifically toward one's own offspring. Broadly, two neural systems involved in empathy can be distinguished. At the core of empathetic responses in most mammalian species, including humans, there is the *affective empathy network*, including bilateral anterior insula (AI) and anterior mid-cingulate cortex (aMCC) (De Waal & Preston, 2017; Shamay-Tsoory, 2011). This network supports the vicarious experience of emotions and thereby facilitates emotion contagion and affect sharing. It may help parents to "feel" the emotions and needs of their children, which could then promote carrying out adequate caregiving responses needed for sensitive parenting (Abraham et al., 2018; Ainsworth et al., 1978; Fan et al., 2011; Feldman, 2015; Feldman, 2017; Turpyn, 2018). In addition, a more recently evolved *cognitive empathy network* has been identified that includes regions in temporal, parietal and prefrontal cortex (De Waal, 2008; De Waal & Preston, 2017; Decety, 2011; Decety & Jackson, 2004; Shamay-Tsoory et al., 2009; Zaki & Ochsner, 2012). More specifically, this network includes dorsomedial prefrontal cortex (dmPFC), ventromedial prefrontal cortex (vmPFC), temporoparietal junction (TPJ), temporal pole, superior temporal sulcus, and frontopolar cortex (Abraham et al., 2018; Feldman, 2017; Shamay-Tsoory, 2011), and facilitates understanding of another's point of view by making inferences of others' mental states (Shamay-Tsoory, 2011). In the context of parenting, this cognitive empathy network may promote a better understanding of the feelings, actions, motives and intentions of the child (Abraham et al., 2018).

Constructs that were found to modulate the neural responses underpinning empathy for others are interpersonal closeness and similarity to the person suffering (Bruneau et al., 2013; Cheng et al., 2010; Lee et al., 2017). For example, activity in anterior cingulate cortex and insula is higher when empathizing with the self and loved-ones compared to strangers (Cheng et al., 2010), and AI is more activated in both black and white participants when they observe someone of their own race in physical pain compared to someone of another race (Azevedo et al., 2013). With the parent-child bond being one of the most intimate and closest social relationships (Abraham et al., 2016; Abraham et al., 2018; Atzil et al., 2011; Laurita et al., 2019b; Leibenluft et al., 2004), it is not unreasonable to hypothesize that neural responses in empathy networks are more intense in parents when confronted with the suffering of their own child versus an unfamiliar child.

So far, several neuroimaging studies have examined neural networks involved in empathic responses in parents of babies and young children (Abraham et al., 2018; Atzil et al., 2011; Barrett et al., 2012; Elmadih et al., 2016; Kuo et al., 2012; Leibenluft et al., 2004; Lenzi et al., 2009; Wan et al., 2014), but no prior studies focused on how these neural networks support empathy in parents of adolescents. Moreover, prior work in parents of infants and young children examined neural responses to pictures and videos of their own versus another child, which makes sense given that parents of infants are most often present when their child is in distress. Given the increasing autonomy of adolescents and the fact that they spend more time without adult supervision, it is likely that parents of adolescents have to rely on more higher-order socio-cognitive functions in order to appropriately empathize with their child when they verbally share their distress about painful situations. In addition, it is relevant to examine whether such brain responses are related to sensitive parenting behavior during adolescence in daily life. Current evidence in this direction emphasizes the involvement of empathy and emotion regulation networks in parents (Barrett et al., 2012; Kuo et al., 2012; Turpyn et al., 2020; Wan et al., 2014). For example, Turpyn et al. (2020) reported that higher levels of observed structured parenting behavior (e.g., problem solving and guiding) were associated with decreased neural responses in "affective empathy" regions (i.e., AI and ACC) and increased neural responses in "cognitive control" regions (i.e., dorsolateral PFC) to negative adolescent stimuli. In addition, Kuo et al. (2012) showed that observed parental sensitivity in fathers was associated with decreased neural responses to video clips of their own child (versus an unfamiliar child) in right orbitofrontal gyrus. Also, Wan et al. (2014) found that self-reported positive mother-infant interactions were associated with greater neural responses in the medial frontal gyrus in response to video vignettes of their own versus another infant. However, these studies were mostly performed in parents of infants and none of the behavioral measures was reported from the perspective of the child.

The present study examined neural responses to both physically and socially unpleasant situations involving parents' own child versus an unfamiliar child and also involving themselves in 60 parents of adolescent children (11-17 years of age). Additionally, we aimed to determine whether individual differences in parental neural responses to their own child's suffering are associated with parental care in daily life as reported by the adolescent child. Based on prior neuroimaging work on affective empathy and interpersonal closeness (Cheng et al., 2010; Kogler et al., 2020; Singer et al., 2004), we expected that the affective empathy network (i.e., AI and aMCC) is sensitive to the imagined suffering of participants' own child or an unfamiliar child and also when it concerns themselves. Moreover, we expected that these regions would be more activated in response to their own child's imagined suffering compared to when parents imagine an unfamiliar child suffering. Additionally, based on prior work (Abraham et al., 2018; Cheng et al., 2010; Kogler et al., 2020), we expected that the cognitive empathy network (i.e., TPJ, dmPFC and vmPFC) is more sensitive to imagined suffering of others as compared to the suffering of themselves, and would also be more activated in response to imagined suffering of their own child versus an unfamiliar child. Moreover, parental care is expected to be associated with neural responses towards their own child (versus an unfamiliar child) in both the cognitive and affective empathic networks and other brain areas that may be relevant for parental responding, such as emotion regulation and cognitive control (Barrett et al., 2012; Kuo et al., 2012; Turpyn et al., 2020; Wan et al., 2014). Although we would like to emphasize that empathy can encompass both positive and negative emotions and situations (Lenzi et al., 2009; Perry et al., 2011), this task examines parental responses to negative situations first.

METHOD

Participants

Sixty-three parents participated in this study. Three parents were excluded due to brain abnormalities, scanner artefacts, or incomplete data, resulting in a final sample of 60 parents of healthy adolescents, including 35 mothers (M_{age} = 48, SD_{age} = 4.22) and 25 fathers (M_{age} = 51, SD_{age} = 4.40). Demographics are reported in Table 5.1. Mothers were somewhat younger, and reported significantly higher empathic concern than fathers, but they did not differ on perspective taking (subscales of the interpersonal reactivity index, IRI (De Corte et al. (2007))) and on parental care (subscale of the parental bonding instrument, PBI (Parker et al. (1979))).

Data were collected in the context of the RE-PAIR study: “Relations and Emotions in Parent-Adolescent Interaction Research”. The RE-PAIR study uses a multi-method and multi-informant approach and examines the relation between parent-child interactions and adolescent depression by comparing families with an adolescent with a current major depressive disorder or dysthymia to families with an adolescent without psychopathology. The present study focused on neuroimaging data collected from parents of healthy adolescents in this larger study. Families were included in this study if the adolescent and at least one of the parents/caregivers were willing to participate in the study and had a good command of the Dutch language. Further inclusion criteria for the adolescents included being aged between 11 and 17 years, living with at least one of their parents/caregivers, no diagnosis of a (neuro)psychiatric disorder in the two years leading up to the study, and no lifetime diagnoses of major depressive disorder or dysthymia. Additionally, exclusion criteria for the functional magnetic resonance imaging (MRI) part of the study were incompatibilities with the MRI scanner.

The study was approved by the medical ethical committee of the Leiden University Medical Centre (LUMC) (P17.241) and was performed in accordance with the declaration of Helsinki and the Dutch Medical Research Involving Human Subjects Act (WMO).

Table 5.1 Demographic characteristics

	All parents	**Mothers**	**Fathers**	**Mothers vs. fathers**[1]		
Mean (SD) or *n* (%)	**(*n* = 60)**	**(*n* = 35)**	**(*n* = 25)**	***t***	**df**	***p***
Age parent, y	49.07 (4.73)	47.48 (4.22)	51.31 (4.40)	3.35	58	.001
Gender parent, *n* male (%)	25 (41.7)	-	-			
Age adolescent, y	16.02 (1.23)	15.60 (0.93)	16.32 (1.53)	-2.30	58	.025
Gender adolescent, *n* male (%)	22 (36.7)	11 (31.4)	11 (44)			
Education						
Vocational training, *n* (%)	19 (31.7)	12 (34.3)	7 (28)			
Higher education, *n* (%)	41 (68.3)	23 (65.7)	18 (72)			
Empathic concern (IRI)	17.52 (5.15)	18.91 (4.81)	15.56 (4.86)	-2.61	58	.012
Perspective taking (IRI)	16.93 (4.36)	17.66 (4.54)	15.92 (3.79)	-1.54	58	.130
Parental care (PBI)[2]	30.76 (5.34)	31.54 (4.86)	29.63 (5.70)	-1.36	58	.178
Handedness						
Right-handed (EHI), *n* (%)	54 (90)	31 (88.6)	23 (92)			
Current psychopathology						
Internalizing, *n* (%)	5 (8.3)	4 (1.4)	1 (4.0)			
Externalizing, *n* (%)	1 (1.7)	-	1 (4.0)			

Note. EHI, Edinburgh Handedness Inventory; IRI, Interpersonal Reactivity Index; PBI, Parental Bonding Instrument; SD, standard deviation. [1] *p*-values were obtained using independent samples t-tests comparisons between mothers and fathers. [2] Adolescents' perceived parental cared ata of one father was missing resulting in *n* = 59 for this variable.

Procedure

Families were recruited via public places and (online) social media, including Facebook and advertisement in the monthly magazine of the Royal Dutch Touring Club (ANWB). All family members were briefed about the study and underwent a comprehensive telephone screening during which family circumstances and informed consent were discussed. Adolescents underwent a short screening for (a history of) psychiatric disorders. Families were invited for two appointments: An assessment day in the lab and an MRI session on a separate day. Prior to the first appointment participants were asked to fill out an online questionnaire battery that included questions about demographics and clinical and cognitive constructs, including trait empathy (assessed by the IRI) and parental care (as perceived by parents' adolescent child and assessed with the care subscale of the PBI). During the first appointment, families performed parent-adolescent interaction tasks and filled out additional questionnaires, and parents were screened on psychopathology with the Mini International Neuropsychiatric Interview. During the second appointment one of the parents underwent an MRI scan at the LUMC in Leiden, and performed, amongst other tasks, the parental empathy task in the scanner (described below). Before and after the MRI scan parents filled out a set of questionnaires. Upon completion of the MRI scans, participants were fully debriefed about the aims of the study and received monetary compensation. Participants provided informed consent for each individual testing day. The average number of days between the first and second appointment was 53 (SD = 46) and ranged between 13 and 265 days.

Measures and materials

Parental empathy task

The validated parental empathy task is a newly developed functional MRI paradigm. In the parental empathy task, parents were shown 16 sentences describing physically or socially unpleasant situations that involved either themselves, their own child, or an unfamiliar child. The paradigm allows for comparisons of empathic responding toward someone's own child and an unfamiliar child, as well as to isolate processes associated with other-oriented distress compared to self-oriented distress (i.e., imagined suffering for someone else versus imagined suffering for the self). The latter contrast provides insight into whether distinct brain regions were activated between the self and other perspective of parents (i.e., brain regions relevant for self-other distinction), which might strengthen the idea that our task elicits processes involved in empathy for others in parents. Moreover, by including both physically (i.e., having a fractured leg) and socially (i.e., being humiliated by others) unpleasant situations the task covered a wide range of adverse events, contributing to the ecological validity of the task. Participants were instructed to imagine the situations as vividly as possible for the particular person involved. Subsequently, they were shown a picture of an unfamiliar adolescent boy or girl accompanied by its age and school grade, which were matched to their own child's demographic information. Each trial started with a fixation cross (2000-4000 ms), after which participants were presented with a picture of a person (i.e., either themselves, their own child, or the unfamiliar child) and a sentence describing a physically or socially unpleasant situation (e.g. self condition: "*You* were bullied by others"; own child condition: "[*Name own child*] was bullied by others"; unfamiliar child condition: "*[Lotte/Lucas]* was bullied by others") for 5000 ms (see Figure 5.1 and Supplement S5.1-A). After a delay (5000 ms) a question was presented below the statement probing self-reported affective distress while imagining an unpleasant situation (i.e., "How do you feel about this?"). Participants could rate their distress on a 7-point Likert scale, ranging from 1 (*not negative at all*) to 7 (*very negative*). Participants were instructed to answer and confirm the question within 8000 ms. They could press any button to display a box around the middle option and then press the button corresponding to their right index (to go left) and right middle finger (to go right) to move the box to their preferred answer. They could confirm their answer by pressing a button corresponding to their left index finger. Two stimulus types (eight physically unpleasant and eight socially unpleasant situations, see also Supplement S5.1-A) with in total 16 sentences were shown for each perspective (i.e., self, own child and unfamiliar child) resulting in 48 trials in total, divided in two blocks of 24 trials. All trials were presented in random order with no more than two subsequent trials with the same perspective, and no consecutive trials with the same sentence.

Pictures of parents and their adolescent child were taken during the lab visit in front of a white wall. We asked adolescent to look into the camera with a friendly, but neutral facial expression. The pictures of the unfamiliar child condition (a white adolescent girl and a white adolescent boy) derived from the Radboud Faces Database (Langner et al., 2010), and were selected based on age (between 11 and 17 years) and gender. The sentences used in the task derived from a separate pilot experiment in an independent sample of young adults. The aim of the pilot study was to select a set of sentences (16 out of 30) in which we validated whether the physically and socially unpleasant sentences were comparable in negativity, self-reported negative affect for self and other, and the ability of people to vividly imagine and empathize with the situations (see Supplement S5.1-B). Physically and socially unpleasant sentences were matched on letter, word and syllable count. The task took about ± 11 minutes in total.

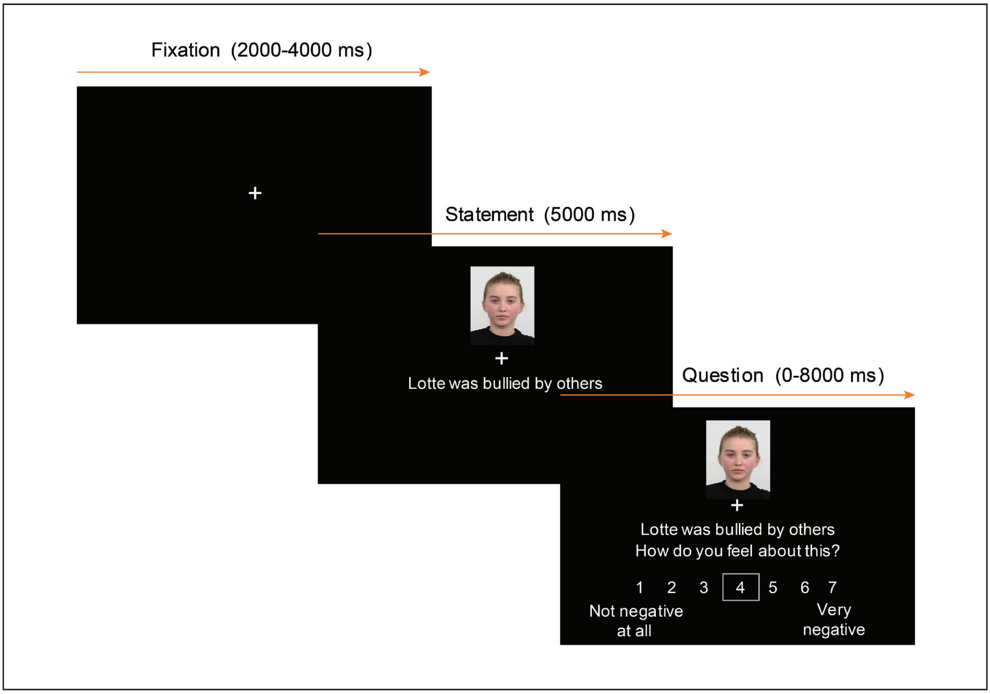


Figure 5.1 *Displays and timings of a socially unpleasant trial for the unfamiliar child perspective. Pictures of the unfamiliar boy and girl derived from the Radboud Faces Database (Langner et al., 2010).*

Parental care

To assess parental care from the perspective of the child, participants' adolescent children filled out the care subscale of the parental bonding instrument (PBI) prior to the first assessment day (Parker et al., 1979). Adolescents were asked to report on perceived parenting styles of their mother and father separately. The PBI care subscale consists of 12 items that were scored on a Likert scale from 0 (*very like*) to 3 (*very unlike*). Examples of items were "My mother/father speaks to me in a warm and friendly voice" and "My mother/father can make me feel better when I am upset". A total score was computed by the sum of all items (total range = 0-36; range in this sample = 13-36). The internal validity and reliability has been established (Arrindell et al., 1998; Enns et al., 2002), and the internal consistency of the PBI care subscale in the current sample was $\alpha = 0.89$.

Psychopathology

Parental current Axis-I psychopathology based on DSM-IV was assessed with the full version of the semi-structured Mini International Neuropsychiatric Interview (MINI; Dutch version 5.0.0), except for the optional module about antisocial personality disorders (Sheehan et al., 1998). The interview was taken by trained students who held the interview face-to-face during the first visit. Current psychopathology was coded as a binary variable (0 = no current psychopathology, 1 = current psychopathology), and was used to control for in the analyses.

Handedness

Handedness was assessed by a modified 10-item version of the Edinburgh Handedness Inventory (EHI) developed by Oldfield (1971). The self-report questionnaire consists of ten questions about which hand is used during specific actions and answer categories were always left (−100), most times left (-50), both (0), most times right (50), and always right (100). Sum scores were calculated by the following formula for the laterality quotient (LQ): $[R-L]/[R+L] \times 100$ and ranged from -100 (left-handedness in all tasks) to +100 (right-handedness in all tasks). To convert the continuous laterality quotient into a dichotomous variable of left- and right-handedness that was sued to control for in analyses we used the cut-off score of zero with quotients >0 indicating right-handedness and <0 indicating left-handedness.

Data acquisition

MR images were acquired at the LUMC using a Philips 3.0T Achieva MRI scanner equipped with a SENSE-32 channel head coil. For the parental empathy task, T2*-weighted echo planar imaging (EPI) was used with the following parameters: TR = 2200 ms, TE = 30 ms, flip angle = 80°, FOV 220 x 220 x 114.7 mm, matrix size = 80 x 80, voxel size = 2.75 mm^3, slice gap = 0.275 mm, 38 transverse slices in descending order. As the parental empathy task was self-paced, number of volumes varied between participants (run 1: M = 122.65, SD = 7.85, range = 108-147; run 2: M = 114.75, SD = 5.40, range = 103-129). A structural 3D T1 scan was acquired with the following parameters: TR = 7.9 ms, TE = 3.5 ms, TI = 820 ms, flip angle: 8°, voxel size = 1 mm^3, 155 transverse slices FOV 195.8 x 250 x 170.5 mm, matrix size = 228 x 177, duration: 4:11 min. The first five volumes were discarded to allow for equilibration of T1 saturation effects. A b0 field map was acquired with the following parameters: TR = 200 ms, TE = 3.2 and 4.2 ms, matrix size = 80 x 80, with 38 slices, voxel size = 2.75 mm^3. The task was programmed and presented electronically using E-prime 2.0 (Tools Psychology Software, 2012) and participants could see the task through a mirror attached to the head coil. Foam inserts were used to restrict head motion. Scans were examined by a radiologist in case of any suspicion of abnormalities.

Data preprocessing and analyses

Affective responses

Self-reported affective responses in the task were analyzed in *R* (version 3.6.1), with the following packages: Nlme for mixed model analysis, psych for descriptive statistics, and ggplot2 for creating figures (Bates, Maechler, Bolker, & Walker, 2015; R Core Team, 2013; Wickham, 2009). Trials that were not answered by the participants within a set time period of 8000 ms were reported as missing values and excluded from the analyses. To assess the influence of 'perspective' (3 levels: Self, own child, unfamiliar child) and 'stimulus type' (2 levels: Physical and social) on self-reported distress we used a generalized linear mixed regression model with 'perspective' and 'stimulus type' as predictors of participants' self-reported distress ratings. To examine how these affective responses towards the own child were associated with parental care as reported by the adolescent child, we ran correlation analyses where we correlated mean Δself-reported distress for the own child (i.e., distress for own child minus distress for unfamiliar child) against child-reported parental care. All analyses were controlled for gender and age of the parents and adolescents. Significance was set at $p < .05$ (two-tailed) and Cohen's *d* effect sizes were calculated for significant effects.

Neural data analyses

MRI data were preprocessed and analyzed using SPM12 (Wellcome Trust Centre for Neuroimaging, University College London). Functional MR images were slice-time corrected, corrected for field-strength inhomogeneity's using b0 field maps, unwarped and realigned, co-registered to subject-specific structural images, normalized to MNI space (using the DARTEL toolbox (Ashburner, 2007)), and smoothed using an 8-mm full width at half maximum isotropic Gaussian kernel. Raw and preprocessed data were checked for quality, registration and movement. Head movement did not exceed 1 voxel/3 mm for any of the participants. Furthermore, we corrected for serial autocorrelations using a first order autoregressive model (AR(1)). We removed low-frequency signals using a high-pass filter (cutoff = 128 s) and included nuisance covariates to remove effects of run.

To examine neural responses to imagined social and physical suffering for the self, own child and an unfamiliar child, we constructed a GLM with six regressors indicating cue onset for each condition separately and one regressor for subjective rating onsets. Cue onset regressors were defined from the onset of the statement period ("imagine the situation") and modeled for the duration of this period (5000 ms). The subjective rating regressor was defined from the onsets of the question and modeled for the duration each question was displayed on the screen (self-paced; max = 8000 ms; mean duration = 2321 ms; SD = 1079 ms; range = 640-7896 ms). We included six motion parameters (based on the realignment parameters) to correct for head motion. First, first-level SPM T-contrasts were specified for each condition (self-physical, self-social, own child-physical, own child-social, unfamiliar child-physical, unfamiliar child-social). Second, these T-contrast images were entered in a 3 x 2 full factorial ANOVA design with two within-subject factors: 'Perspective' (3 levels: Self, own child and unfamiliar child) and 'stimulus type' (2 levels: Physical and social). SPM F-maps were computed to assess main effects of 'perspective' and 'stimulus type', and their interaction, followed up by post-hoc analyses contrasting own child responses versus unfamiliar child responses, self versus own child, and self versus unfamiliar child.

To determine neural correlates of parental empathy in brain regions robustly implicated in cognitive and affective empathy, we carried out region of interest (ROI) analyses. We used independently defined functional ROIs (8-mm spheres MNI space) surrounding peak voxels of brain regions consistently found to support affective and cognitive empathy in the extensive meta-analysis of Bzdok et al. (2012), for specific coordinates see Supplement S5.2. We used the MarsBar toolbox (Brett et al., 2002) to extract activity from 8 ROIs, i.e., bilateral AI and aMCC (affective empathy network), and bilateral TPJ, bilateral dmPFC and vmPFC (cognitive empathy network). To assess the effects of 'perspective' and 'stimulus type' in these ROIs, we performed repeated-measures ANOVAs and post-hoc tests in *R*. All analyses were Bonferroni corrected for the number of tests ($p < .05/8$). To explore task-related blood oxygenation level-dependent (BOLD)-activation in brain regions outside the ROIs, we performed complementary whole-brain analyses. All whole-brain results were corrected for multiple comparisons with Family-Wise Error (FWE) cluster correction at $p < .05$ (with a cluster-forming threshold of $p < .001$).

To investigate whether parental care as experienced by the adolescent was associated with differential parental neural empathic responses towards their own child we calculated correlations between individual levels of parental care and the difference score in BOLD-responses between the own child and unfamiliar child perspectives within the priori selected ROIs (i.e., bilateral AI, aMCC, bilateral TPJ, bilateral dmPFC and vmPFC). ROI analyses were corrected for comparison across multiple ROIs using Bonferroni corrections ($p < .05/8$). Lastly, we explored whole-brain associations between parental care and BOLD-responses unique to empathizing with the own child (own child minus unfamiliar child contrast).

To check whether results were not driven by differences in handedness, gender of parents, current psychopathology and psychotropic medication status, we performed additional analyses to control for these variables.

RESULTS

Affective responses

Fifteen participants did not confirm their answer on one trial and two participants did not confirm their answer on two trials for the affective response question, resulting in 19 missing trials (out of 2880; 0.7%) that were excluded from further analyses in both the analyses of the affective and neural responses. In order to correctly handle these missing trials a generalized linear mixed regression model was performed to assess the influence of 'perspective' (3 levels: Self, own child, unfamiliar child) and 'stimulus type' (2 levels: Physical and social) on self-reported levels of distress. First, physically unpleasant sentences elicited higher levels of distress compared to socially unpleasant sentences independent of perspective (main effect 'stimulus type': $\chi^2(1) = 10.52$, $p = .001$, $B = -0.131$, SE = .040, t(2796) = -3.249, $p = .001$, $d = 0.12$). No interaction was found between 'perspective' and 'stimulus type' ($\chi^2(2) = 3.46$, $p = .177$).

With regard to the main focus of our study and in line with our hypothesis, the perspective parents empathized with significantly influenced their levels of distress (main effect 'perspective': $\chi^2(2) = 518.37$, $p < .001$, see Figure 5.2, Supplement S5.3). Post-hoc pairwise comparisons (using Bonferroni correction for multiple comparisons) indicated significantly higher levels of distress when confronted with unpleasant situations involving one's own child versus an unfamiliar child ($B = 1.103$, SE = .049, $t(2796) = 22.375$, $p < .001$, $d = 1.02$) and higher levels of distress for one's own child versus self ($B = -0.733$, SE = .049, t(2796) = -14.838, $p < .001$, $d = 0.68$). Furthermore, parents reported significantly higher levels of distress for the self versus an unfamiliar child ($B = 0.370$, SE = .049, $t(2796) = 7.509$, $p < .001$, $d = 0.34$).

In terms of covariates, mothers reported significantly higher levels of distress than fathers, independent of 'perspective' or 'stimulus type' (main effect parental gender: $\chi^2(1) = 6.32$, $p = .012$, $d = 0.47$). Parental age and adolescents' age and gender did not significantly affect self-reported distress (all p-values $> .304$) (see Figure 5.2 and Supplement S5.3).

Lastly, Spearman rank-order correlation analysis indicated that parental care, as reported by the adolescent child, was not associated with the mean Δself-reported parental distress towards their own child (i.e., own child minus unfamiliar child perspective), $r_s = -0.017$, $p = .905$.

All outcomes remained significant after controlling for gender of parents, current psychopathology, and psychotropic medication status in separate analyses (see Supplement S5.9).

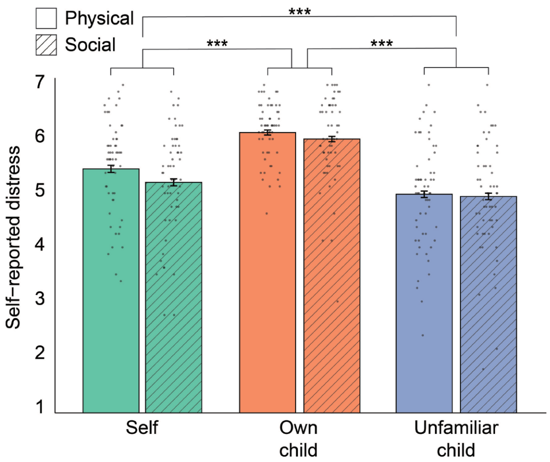


Figure 5.2 *Mean levels of subjective distress in parents after imagining socially and physically unpleasant situations involving the self, their own child, or an unfamiliar child. Dots represent mean levels of self-reported subjective distress per parent for each condition. Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

Neuroimaging findings: ROI analyses

For all ROIs we extracted BOLD-responses to physically and socially unpleasant situations for each of the three perspectives (i.e., self, own child and unfamiliar child). We examined the effects of ‘perspective’ and ‘stimulus type’, while controlling for multiple comparisons in eight separate repeated-measures ANOVAs.

Our analyses revealed a main effect of ‘perspective’ in ROIs involved in the cognitive, but not in the affective, empathy network. Parents exhibit significant differences in BOLD-responses in the cognitive empathy network in bilateral TPJ (right: $F(2,118) = 5.680$, $p = .004$; left: $F(2,118) = 6.182$, $p = .003$), bilateral dmPFC (right: $F(2,118) = 10.871$, $p < .001$; left: $F(2,118) = 7.781$, $p < .001$) and vmPFC ($F(2,118) = 21.101$, $p < .001$), dependent on perspective, see Figure 5.3 and Supplement S5.5. Post-hoc pairwise comparisons (using Bonferroni correction for multiple comparisons) indicated that parents exhibited significantly increased BOLD-responses for own child versus unfamiliar child perspective in left TPJ ($p = .005$), left dmPFC ($p < .001$) and right dmPFC ($p < .001$), and a significant decreased deactivation in BOLD-response in vmPFC ($p < .001$). No significant differences were found in bilateral AI, aMCC and right TPJ between own child and unfamiliar child.

For own child versus self, parents exhibited significantly increased BOLD-responses towards their own child in right TPJ ($p = .025$) and right dmPFC ($p < .001$), and a significant decreased deactivation in BOLD-response towards their own child in vmPFC ($p <.001$). Results indicated no significant differences between suffering for self versus own child in bilateral AI, aMCC, left TPJ and left dmPFC.

In addition, for an unfamiliar child versus self, parents exhibited significantly increased BOLD-responses in right TPJ ($p = .007$). We found no significant differences between the suffering for self versus an unfamiliar child in bilateral AI, aMCC, bilateral dmPFC, left TPJ and vmPFC.

Analyses revealed a main effect of ‘stimulus type’ in right AI ($F(1,59) = 9.268$, $p = .003$) and an interaction between ‘perspective’ and ‘stimulus type’ in aMCC ($F(2,118) = 6.105$, $p = .003$) and vmPFC ($F(2,118) = 7.410$, $p <.001$) at ROI level (see Supplement S5.6 and S5.7 for more details).

All outcomes at ROI level remained significant after controlling for handedness, gender of parents, current psychopathology, and psychotropic medication status in separate analyses (see Supplement S5.9).

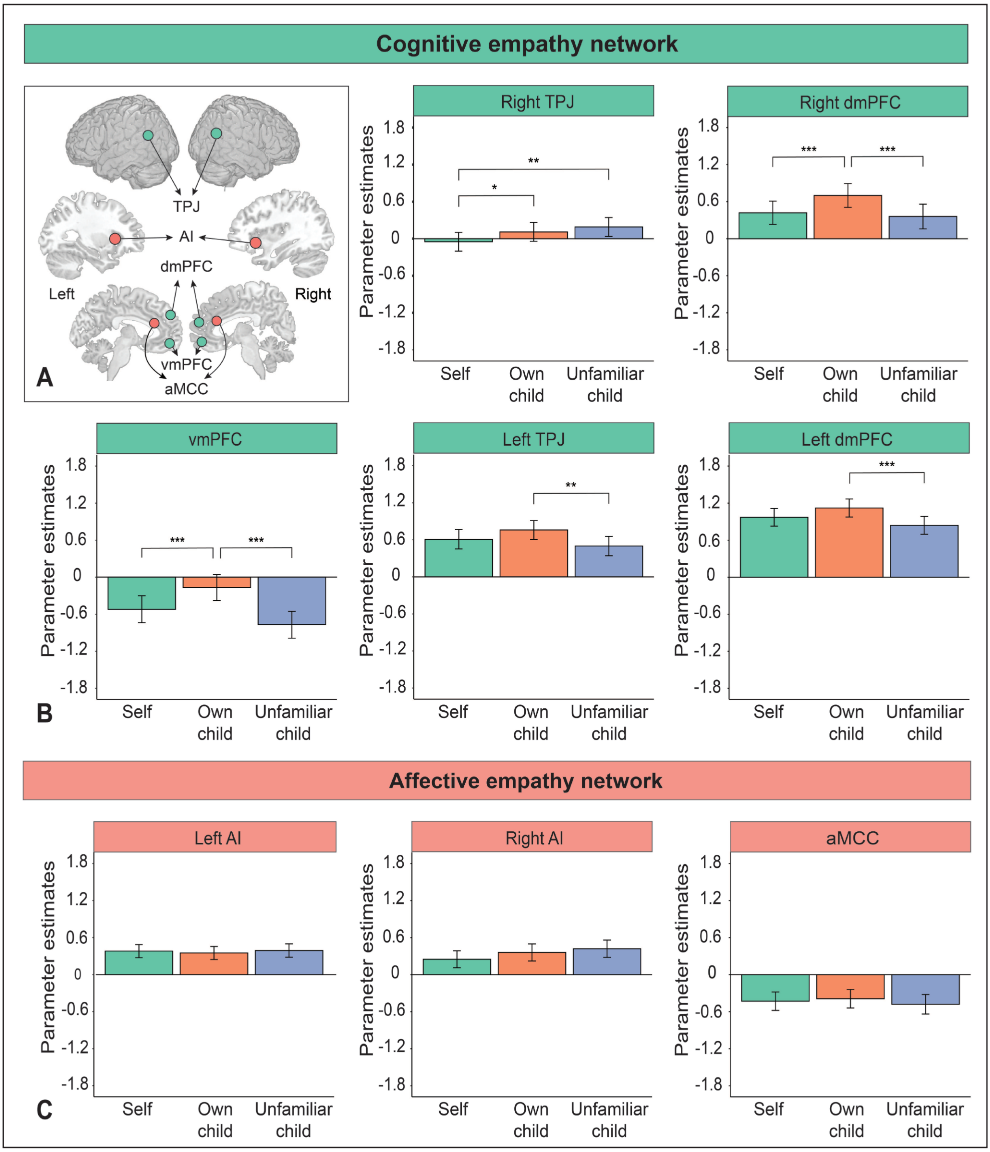


Figure 5.3 *Overview of regions of interest in cognitive and affective empathy networks and results showing how the perspective of imagined suffering modulated activity within the cognitive, but not the affective, empathy network. A) Schematic overview of ROI spheres in affective empathy network in red (bilateral AI and aMCC) en cognitive empathy network in green (bilateral TPJ, bilateral dmPFC and vmPFC). B) Parameter estimates of BOLD-responses in ROIs in the cogntive empathy network where the perspective of imagined suffering impacted on activity in the regions (i.e., main effect of 'perspective'). C) Parameter estimates of BOLD-responses in ROIs in the affective empathy network. No main effect of 'perspective' was found in bilateral AI and aMCC. All ROI results were Bonferroni corrected for the number of tests (p <.05/8). Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

Neuroimaging findings: Whole-brain results

To test whether task-related BOLD-activation in brain regions outside the ROIs was found in response to the unpleasant sentences, we performed a complementary whole-brain analysis. In line with the ROI analyses, we found a main effect of 'perspective' with similar directionalities in clusters including sub regions of vmPFC, bilateral dmPFC and right TPJ, with peak-coordinates in vmPFC, bilateral inferior frontal gyrus (IFG) and left precuneus, respectively.

Outside these regions we found a main effect of 'perspective' in the right inferior temporal gyrus (ITG), left inferior occipital gyrus (IOG), right superior frontal gyrus (SFG), and right middle frontal gyrus (MFG) (see Figure 5.4 and Supplement S5.4). Post-hoc pairwise comparisons (using Bonferroni correction for multiple comparisons) indicated that parents exhibited significantly decreased deactivation in BOLD-responses for own child versus unfamiliar child in vmPFC ($p < .001$) and increased BOLD-responses in right ITG ($p < .001$), and for unfamiliar child versus own child in right SFG ($p < .001$), right IFG ($p < .001$), and right MFG ($p < .001$).

For own child versus self, parents exhibited significantly increased BOLD-responses towards their own child in left precuneus ($p = .002$) and a significantly decreased deactivation towards their own child in vmPFC ($p < .001$), and for self versus own child in left IOG ($p < .001$), left IFG ($p < .001$) and right SFG ($p = .011$).

Furthermore, parents exhibited significantly increased BOLD-responses for an unfamiliar child versus the self in left precuneus ($p = .003$), right SFG ($p = .014$), right IFG ($p < .001$) and right MFG ($p = .001$), and for self versus unfamiliar child in left IOG ($p < .001$), left IFG ($p < .001$), and right ITG ($p < .001$), and a significantly decreased deactivation for self versus unfamiliar child in vmPFC ($p = .010$).

Analyses revealed a main effect of 'stimulus type' in left MFG, bilateral IFG, left ITG, middle cingulate gyrus (MCG), right middle temporal gyrus, left inferior parietal gyrus, left precentral gyrus, right supramarginal gyrus, dorsal anterior cingulate cortex (dACC) and right superior temporal gyrus and an interaction between 'perspective' and 'stimulus type' in left insula, right dmPFC and right posterior orbitofrontal gyrus at whole-brain level (see Supplement S5.6 and S5.7 for more details).

All outcomes at whole-brain level remained significant after controlling for handedness, gender of parents, current psychopathology, and psychotropic medication status in separate analyses, except for the interaction effect between 'perspective' and 'stimulus type' that was found in the right posterior orbitofrontal gyrus. Remarkably, we found no evidence for differences between mothers and fathers in terms of neural responses to imagined suffering on a whole-brain level, despite mean differences in empathic concern and empathic distress ratings (see Supplement S5.9).

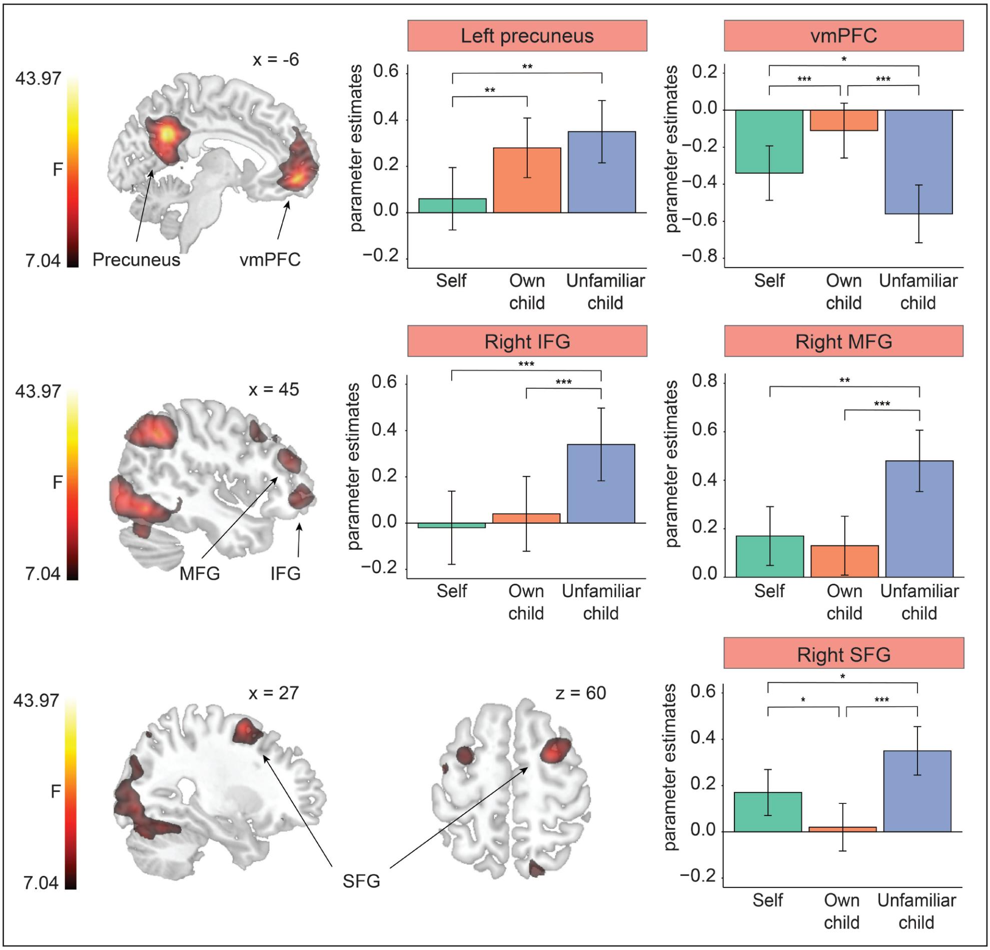


Figure 5.4 *Whole-brain results for the main effect of 'perspective'. Main effect of 'perspective' revealed significant clusters of activation in left precuneus, vmPFC, right IFG, right MFG, and right SFG. Whole-brain analyses were thresholded at p <.05 (FWE cluster-corrected using a cluster-forming threshold of p <.001). Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

Associations with perceived parental care

To examine whether parental care, as perceived by the adolescent child, was associated with individual differences in empathy-related neural responses, we correlated parental care with brain activation in the ROIs for the own child specifically (i.e., extracted BOLD-response of own child minus unfamiliar child perspective). Spearman rank-order correlation analyses revealed no significant correlations between parental care and neural activity towards the own child versus unfamiliar child in any of the ROIs (right AI: $p = .233$, left AI: $p = .933$, aMCC: $p = .668$, right TPJ: $p = .382$, left TPJ: $p = .877$, right dmPFC: $p = .356$, left dmPFC: $p = .155$, and vmPFC: $p = .119$).

Additionally, we performed an exploratory whole-brain regression analysis testing for the association between individual differences in parental care and neural responses to imagined suffering of the own child specifically (i.e., contrast own child minus unfamiliar child perspective). This analysis revealed negative associations between parental care and neural responses to imagined suffering of the own child in right SFG and left anterior orbitofrontal gyrus (OFG) (see Figure 5.5, Supplement S5.8), and showed overlap with whole-brain outcomes for the main effect of 'perspective' in right SFG and left IFG.

Confound analyses revealed that the negative correlation between parental care and neural activity in the left anterior OFG was no longer significant after controlling for gender of parents, current psychopathology, or psychotropic medication status (see Supplement S5.9).

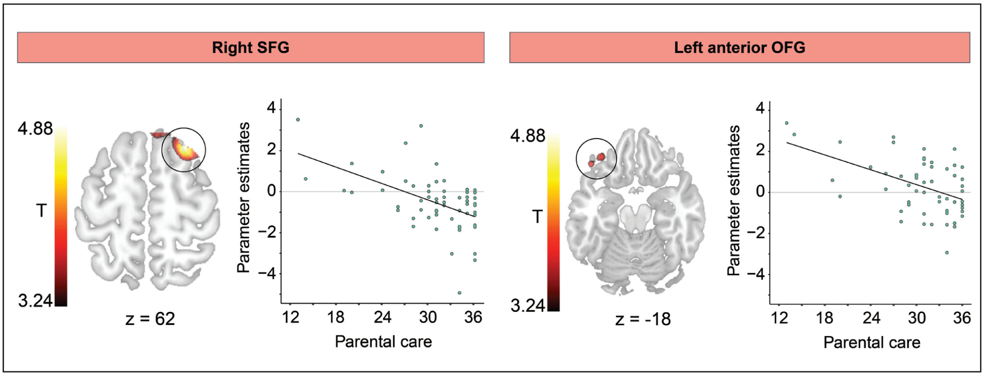


Figure 5.5 *Whole-brain regression analysis testing for individual differences in neural responses to imagined suffering of parents' own child explaining individual variation in parental care as perceived by the adolescent child. Results revealed significant negative correlations between parental care as perceived by the adolescent child and neural responses to imagined suffering of one's own child specifically (i.e., contrast own child minus unfamiliar child perspective) in right SFG and left anterior OFG. To visualize these associations, we plotted parameter estimates in these regions against adolescent-reported parental care. Regression lines are plotted for illustration purposes only. Whole-brain analyses were thresholded at p <.05 (FWE cluster-corrected using a cluster-forming threshold of p <.001).*

DISCUSSION

This study examined affective and neural responses in parents to the imagined suffering of their own adolescent child in physically and socially unpleasant situations. Our findings show that parents reported higher levels of distress when imagining their own child versus an unfamiliar child suffering. In addition, functional MRI analyses revealed increased activation within the cognitive empathy network (i.e., left TPJ, bilateral dmPFC and vmPFC), while no differential activation was found within the affective empathy network (i.e., bilateral AI and aMCC) when parents imagined their own versus an unfamiliar child suffering. Parental care did not co-vary with activity in the empathy networks, but parents who were perceived as less caring exhibited increased BOLD-responses in anterior and lateral prefrontal regions (i.e., right SFG and left OFG) when imagining their own child suffering.

In line with our hypotheses, parents reported higher levels of subjective distress and exhibited significantly increased neural activation in left TPJ and bilateral dmPFC and significantly decreased deactivation in vmPFC while imagining the suffering of their own child versus an unfamiliar child. Moreover, it is of note that the significant differences between these perspectives were medium to large in size (Cohen's *d* main effect 'perspective' = 1.02). These regions are part of the cognitive empathy network, involved in complex socio-emotional processes such as mentalizing and perspective taking (Kogler et al., 2020; Shamay-Tsoory, 2011). We speculate that this enhanced neural responding in this cognitive empathy network may be suggestive of recruitment of perspective-taking and theory of mind processes when imagining suffering for their own child (versus an unfamiliar child) (Mitchell, 2009), which is in line with prior research indicating that interpersonal closeness and similarity to the person suffering modulate the neural responses underpinning empathy for others (Bruneau et al., 2013; Cheng et al., 2010; Lee et al., 2017). However, it is of note that it is still a matter of debate whether specific regions in the "cognitive empathy" network are purely involved in cognitive empathy processes and not (also) in affective empathy processes (Schurz et al., 2020). The increased involvement of cognitive empathy regions for the imagined suffering of the own versus an unfamiliar child might relate to the fact that past experiences with the own child have created a vast array of social knowledge about how the own child responds to unpleasant situations. This might make it easier for parents to predict how the child respond in hypothetical situations, whereas this is not the case for the unfamiliar child (Krienen et al., 2010; Laurita et al., 2017; Laurita et al., 2019a; Spreng & Mar, 2012). This link with autobiographical memory is supported by the extensive overlap between neural patterns associated with autobiographical memory and brain regions involved in the cognitive empathy network as we found in the present study (i.e., TPJ, dmPFC and vmPFC), as indicated by Spreng and Mar (2012). It is of note that the observed deactivation in vmPFC might reflect a task-induced deactivation relative to the activation in this region in response to our implicit baseline (i.e., display of fixation crosses during inter-trial intervals). This pattern is consistent with prior studies (Binder et al., 1999; Mckiernan et al., 2003) and might suggest a decrease in socio-emotional processing in the vmPFC during imagined suffering of the own child. This is in line with a prior study by Krienen et al. (2010) that found a similar deactivation pattern in the vmPFC in relation to social closeness towards friends versus strangers.

For the own child and unfamiliar child versus self, parents, indeed, exhibited significantly increased neural activation in the cognitive empathy network in right TPJ, right dmPFC, vmPFC, left precuneus, right IFG and right MFG. These brain regions have been found to be involved in cognitive processes important for self-other distinction, such as distinguishing between own pain and that of another person (TPJ and precuneus) and taking the perspective of another person (dmPFC and vmPFC) (Lamm et al., 2011). Also, despite the finding that the sentences in general elicited significant activity in bilateral AI and aMCC, we found no evidence of differential levels of activity within these regions for self compared to “other” perspectives. This is partially in agreement with prior studies that reported neural activation in these brain regions in response to imagined pain in both self and others (Cheng et al., 2010; Christian et al., 2015; Decety et al., 2013; Jackson et al., 2006), although in most studies there was increased activation in imagining self versus others in pain. A possible explanation for this difference is that the stimuli in the present study consisted of both physical and social suffering, while in the other studies only physically painful stimuli were included.

A remarkable finding is that parents showed differences in neural activation towards their own child versus an unfamiliar child, in predominantly the cognitive rather than the affective empathy network. Although the sentences with adverse situations did elicit neural activation in bilateral AI and aMCC in both own and unfamiliar child condition, no differences in activation were found in these regions within the affective empathy network between these perspectives. This lack of differential activation, despite heightened subjective responses to sentences of their own (versus an unfamiliar) child, is not in line with our expectation and in contrast with prior research about empathic responses to pictures and video vignettes of parents’ own versus unfamiliar babies and children (Abraham et al., 2018; Atzil et al., 2011; Barrett et al., 2012; Elmadih et al., 2016; Kuo et al., 2012; Leibenluft et al., 2004; Lenzi et al., 2009; Wan et al., 2014). In general, these studies did not find enhanced neural activation in the cognitive empathy network, but reported greater activation in insular and cingulate regions in response to one’s own child versus another child. One explanation for this difference is that the imagined suffering of one’s own child in the current task might have elicited more cognitive rather than affective empathy processes in parents, compared to the more direct, and passive observation of pictures or video vignettes of the own child in the other studies. This could indicate that in situations in which parents need to imagine their child in an unpleasant situation rather than directly observe their child, parents need to engage brain regions important for cognitive rather than affective aspects of empathy. Given that situations of imagined suffering are more applicable to parents of adolescents than parents of younger children, one might speculate that recruitment of the cognitive empathy network becomes more important in parenting during adolescence compared to infancy. An alternative factor that might have contributed to the more pronounced involvement of the cognitive empathy network is that the task we used required more verbal and cognitive processing compared to tasks in which parents are presented with photos or videos of their own child. As a consequence, this might have contributed to a greater involvement of cognitive rather than affective empathy network, although the fact that the cognitive load was the same for all perspectives makes this less likely. Nevertheless, it is of interest for further research to examine parental empathy to imagined suffering using visual stimuli rather than verbal descriptions in order to gain a more detailed insight into the specific processes involved in these parental responses.

Although the neural responses of parents to the suffering of their own child involved for the greater part brain regions in “empathy networks”, we also found enhanced activity associated with neural responses to suffering of one’s own child in a set of brain regions (i.e., IFG, MFG and SFG) that we had no hypotheses about. Prior work has implicated these brain regions (e.g., IFG, MFG and SFG) in emotion regulation (Long et al., 2020) and the IFG is a key brain region in the mirror neuron system. In the context of the mirror neuron theory of empathy the IFG has been implicated in automated interoception and internal representation of mental states of others via perceptual-motor coupling, which is directly linked to empathy (Feldman, 2017). Interestingly, these regions have also been found to relate to individual differences in attachment and general sensitivity of parents when they view pictures or video vignettes of their own child (versus an unfamiliar child) (Atzil et al., 2011; Kuo et al., 2012; Riem et al., 2011), suggesting that associations between parenting and neural activity in our task may also be explained by more domain-general neural responses to one’s own child.

Regarding individual differences in adolescent-reported parental care and parents’ neural empathic responses to their own child’s suffering we found negative associations between parental care and neural activation in right SFG and left anterior OFG, indicating that lower levels of parental care are related to greater differential neural activation between parents’ own child and the unfamiliar child perspective in these brain regions. These brain regions are part of a prefrontal network consistently found to be important for emotion regulation (Long et al., 2020; Wager et al., 2008). Moreover, these regions overlap with our neural findings at whole-brain level in the present study and show that activation in these brain regions was in general higher in parents while imagining the perspective of the other child versus the own child. These findings were unexpected, particularly because in prior studies a higher emotion regulation activation in, particularly, the prefrontal brain regions are generally related to more adaptive and sensitive parenting behavior (Kuo et al., 2012; Laurent & Ablow, 2012; Michalska et al., 2014; Musser et al., 2012). What is remarkable and what might have contributed to different outcomes is that the majority of these studies presented parents with positive stimuli rather than more negative stimuli that were used in the present study. Although the underlying reason for the enhanced emotion regulation processing is not entirely clear, the results suggest that parental caregiving behavior in daily life might not be (directly) related to neural activation in parental empathy networks, but that additional (e.g., emotion regulation) networks may be relevant for parental empathic *behavior* in daily life. It is of note, however, that the negative correlation between parental care and neural activation in left anterior OFG did not remain significant after controlling for confounding variables (i.e., gender of parents, current psychopathology or psychotropic medication status), which implies that these effects need to be interpreted with caution and need to be replicated in larger samples. Also, parental care was based on the perspective of the child. Obviously, this is only one perspective and the inclusion of parents' own view or the discrepancy between both perspectives on parental care might give more insight into the nature of these emotion regulation processes.

To increase the ecological validity of our empathy task, both social and physical situations were presented to parents in order to cover a wide range of adverse events that people are exposed to in daily life. Although this was not the main aim of the study, several interesting differences became apparent when comparing brain activation in response to the adverse physical versus social situations. Parents showed higher levels of self-reported distress towards physical versus social suffering of both self and others, including their own child, and increased neural activation in right AI, dACC, MCG and various frontal and temporal brain regions. This is in accordance with prior studies that focused on differences in neural activation between physical and social pain (Bruneau et al., 2013; Eisenberger, 2012). A possible explanation for this finding is that the brain prioritizes physical pain over social pain because physical threats might be more impeding for immediate survival (Bruneau et al., 2013). Noticing someone else in pain might indicate that one is surrounded by a physical threat itself. As such, a quick response to physical threat might be biologically adaptive and evolutionary beneficial. The need to quickly detect social pain in others, however, is less strong as the sources of such responses were thought of being more internally driven and indirect (Timmers et al., 2018). However, it should be noted that the differences between the social and physical situations should not be exaggerated. With respect to self-reported distress the differences in response to physical and social suffering were rather small ($d = 0.12$). Moreover, several regions of the brain showed largely similar activation patterns, indicating also large resemblance in the responses to imagined social and physical adverse events.

In sum, although some previous studies focused on the effect of familiarity and interpersonal closeness on empathic responses to others, this study uniquely determined neural empathic responses to the suffering of others in the context of parent-adolescent relationships. The involvement of parent-adolescent dyads in the present study contributes to the field of neuroimaging of sensitive parenting behavior during adolescence, as prior studies were predominantly limited to parents of babies or very young children. Moreover, the newly developed parental empathy task used in this study benefits from a personalized task design, allowing for a proper comparison between behavioral and neural parental empathic responses towards their own versus an unfamiliar child. In addition, the inclusion of both mothers and fathers in the study is a major contribution to the current literature and increased the generalizability of the results.

Furthermore, the inclusion of both physically and socially unpleasant stimuli of various negative intensities covers a wide variety of real-life situations, contributing to the task's ecological validity.

Nevertheless, this study is not without limitations. Neural responses could be explained by empathic processes towards the own child (versus an unfamiliar child), but also by additional cognitive processes engaged when imagining one's own child, such as emotion regulation processes or a more general sensitivity of parents in response to the own child. Due to the lack of a neutral (versus negative) event condition, we cannot disentangle exactly whether the enhanced neural responses to the own child (versus the unfamiliar child) are the result of enhanced empathic responding or also reflect the engagement of such other processes. Future studies might benefit from the inclusion of a neutral condition to the task in order to gain more insight into the general neural responses to the own child versus responses to one's own child's suffering. Furthermore, including a specific measure of parental empathy towards their own child, such as the Parental Affective and Cognitive Empathy Scale (PACES) or the reflective functioning scale (Luyten et al., 2017; Stern et al., 2015), could further help to examine how neural activity during the task relates to self-reported parental empathy. Another limitation is that by asking parents how they felt themselves after imagining the suffering of their own child, we may have tapped more into a self-oriented than an other-oriented response. It is plausible, however, that imagining an unpleasant situation involving one's own child may elicit feelings of distress similar to the distress the child may experience. Moreover, for a prosocial response to the own child it is important to regulate one's own distress before focusing on how the child is feeling. Nevertheless, including an additional question assessing other-oriented feelings (e.g. "how does your child feel?") may provide important insight into which brain regions are involved in feelings of empathic distress and which regions are more involved in feelings of sympathy. However, asking such a question may also have increased the difficulty of the task due to a constant shifting in perspectives. Additionally, not incorporating a question about the feelings of the child allowed for similarity and consistency between sentences about the self and other perspectives. Also, a potential limitation of our study is that by asking participants to report on their affect during the task this may have elicited 'affect identification' as an emotion regulation strategy, which might have impacted neural responses to imagined suffering for self and others. However, as this was similar in all conditions, these effects may have been averaged out. Furthermore, we did not control for the fact that some parents might have experienced some of the unpleasant situations themselves or with their child. Prior research proposed that our representations of others are based on prior (self-referential) experiences, and thus this might have influenced the empathic responses of parents towards themselves or their child (Mitchell, 2009; Waytz & Mitchell, 2011). Future studies could ask parents about personal experiences with situations presented in the task and whether they or their child suffers from (a history of) chronic pain to be able to examine how such personal experiences may modulate neural responses. Lastly, although the present study focusses on parental responses to negative events of their child, empathy can encompass empathic concern and perspective taking with respect to both positive and negative emotions (Lenzi et al., 2009; Perry et al., 2011). As this was a new task that needed to be validated, and negative events are expected to be more salient (see Perry et al. (2011)), we focused on negative events in the present study. Future studies would benefit, however, from considering both the positive and negative components of empathy.

CONCLUSION

The present study demonstrates the engagement of unique brain responses to the imagined suffering of parents' own child versus an unfamiliar child in the cognitive empathy network, but not in the affective empathy network. It suggests that parents more strongly engage in perspective taking when imagining their own child suffering, as compared to the suffering of an unfamiliar child. In contrast, the lack of activation in the affective empathy network between their own child and an unfamiliar child suggests that at the level of the brain parents seem not to vicariously experience or "feel" the emotions of the own child to a greater extent than the emotions of an unfamiliar child when imagining their suffering, although they did subjectively report higher levels of affective distress towards their own child versus an unfamiliar child. In addition, parental care did not co-vary with activity in the empathy networks, but parents who were perceived as less caring exhibited increased activity in anterior and lateral prefrontal brain regions when imagining their own child suffering. These results provide new insights into neural processes supporting parental empathy, highlighting the importance of regions in the cognitive empathy network when being confronted with the suffering of their own child, and suggest that additional (e.g., emotion regulation) networks may be relevant for parental empathic behavior in daily life. Moreover, the present study provides a foundation for studying parental neural responses to imagined suffering of parents' own child in parents of children with (a history of) prolonged physical (e.g., chronic pain) or mental (e.g., adolescent anxiety or depression) suffering.

SUPPLEMENTARY MATERIALS

SUPPLEMENT S5.1-A

Overview unpleasant situations empathy task

The sentences were categorized per stimulus type (i.e., physical and social).

Physically unpleasant sentences (*n* = 8)	**Socially unpleasant sentences (*n* = 8)**
[perspective] broke his/her leg	*[perspective]* is alone on his/her birthday
[perspective] had a traffic accident	*[perspective]* is feeling very lonely
[perspective] suffers from an infection	*[perspective]* was bullied by others
[perspective] suffers from a concussion	*[perspective]* has nobody to talk to
[perspective] was beaten down	*[perspective]* was upset
[perspective] has a very high fever	*[perspective]* was humiliated by others
[perspective] broke his/her tooth	*[perspective]* is feeling excluded
[perspective] was pushed from the stairs	*[perspective]* came home crying

Note. The perspective either included the self ("you"), parents' own child ("*[name of own child]*") or an unfamiliar child ("Lotte/Lucas"). Sentences described above were English translations based on the original Dutch sentences.

SUPPLEMENT S5.1-B

Overview results pilot study empathy task

The sentences were categorized and matched per stimulus type ($n = 35$).

Mean (SD)	Physically unpleasant ($n = 8$)	Socially unpleasant ($n = 8$)	Physically vs. socially unpleasant [1] t	df	p
Negativity of events	6.81 (2.01)	7.05 (1.59)	-1.56	558	.119
How negative do you feel?	6.19 (2.35)	6.67 (1.86)	-2.68	558	.007
How does the other feel?	7.26 (1.69)	7.35 (1.46)	-0.67	558	.505
Empathizablity [2]	6.60 (1.85)	6.58 (1.89)	0.14	558	.892
Letter count	26.75 (2.96)	27.50 (2.67)	-0.53	14	.603
Word count	5.00 (.54)	5.13 (.99)	-0.31	14	.758
Syllable count	7.88 (1.13)	7.88 (1.25)	0	14	1.000

Note. Thirty-five adult participants ($n = 7$ males and $n = 28$ females; mean age = 24.52; SD = 3.18) participated in the pilot study. They reported how negative they experienced the events described by the sentences in general, how they would feel in case they would experience the situations themselves, how they think their loved-one would feel when experiencing the situations (9-point Likert scale, 1 = not negative at all, 9 = very negative), and how vividly they could imagine and empathize with the situation each sentence described (empathizability, 1 = not at all, 9 = very much). Final composition and matching of physically and socially unpleasant sentences used in the task was based on the original Dutch sentences. [1] p-values obtained using independent samples t-tests comparisons between physically and socially unpleasant sentences. [2] Empathizability is the extent to which participants were able to vividly imagine and empathize with the situation each sentence described.

SUPPLEMENT S5.2

MNI-coordinates of centers of mass of regions of interest in the affective and cognitive empathy network

Brain region	MNI-coordinates		
	x	y	z
Affective empathy network			
Right anterior insula (right AI)	36	22	-8
Left anterior insula (left AI)	-30	20	4
Anterior mid-cingulate cortex (aMCC)	-2	28	20
Cognitive empathy network			
Right temporoparietal junction (right TPJ)	52	-58	22
Left temporoparietal junction (left TPJ)	-56	-58	22
Right dorsomedial prefrontal cortex (right dmPFC)	2	56	18
Left dorsomedial prefrontal cortex (left dmPFC)	-8	54	34
Ventromedial prefrontal cortex (vmPFC)	0	52	-12

Note. The MNI-coordinates used in this study were consistently found to support affective and cognitive empathy in meta-analyses and reviews of empathy (Bzdok et al., 2012).

SUPPLEMENT S5.3

Parental empathic distress responses

Generalized linear mixed regression model for the main effects and interaction of ‘perspective’ (self, own child and unfamiliar child) and ‘stimulus type’ (physical and social) on levels of parental empathic distress responses. [1]

	B	**SE**	**df**	***t***	***p***
Intercept [2]	4.432	1.440	2796	3.079	.002
Perspective - own child	0.682	0.070	2796	9.785	<.001
Perspective - unfamiliar child	-0.462	0.070	2796	-6.626	<.001
Stimulus type - social	-0.226	0.070	2796	-3.228	.001
Gender parent - female	0.504	0.201	55	2.514	.015
Age parent	0.013	0.020	55	0.633	.529
Gender adolescent - girl	-0.188	0.183	55	-1.029	.308
Age adolescent	0.013	0.076	55	0.176	.861
Own child × Social	0.101	0.099	2796	1.022	.307
Unfamiliar child × Social	0.183	0.099	2796	1.857	.064

[1] Gender and age of parents and adolescents were added as covariates in the model.

[2] The intercept includes the self – physical condition.

SUPPLEMENT S5.4

Peak activation coordinates at whole-brain level for main effects of ‘perspective’ and ‘stimulus type’ and their interaction

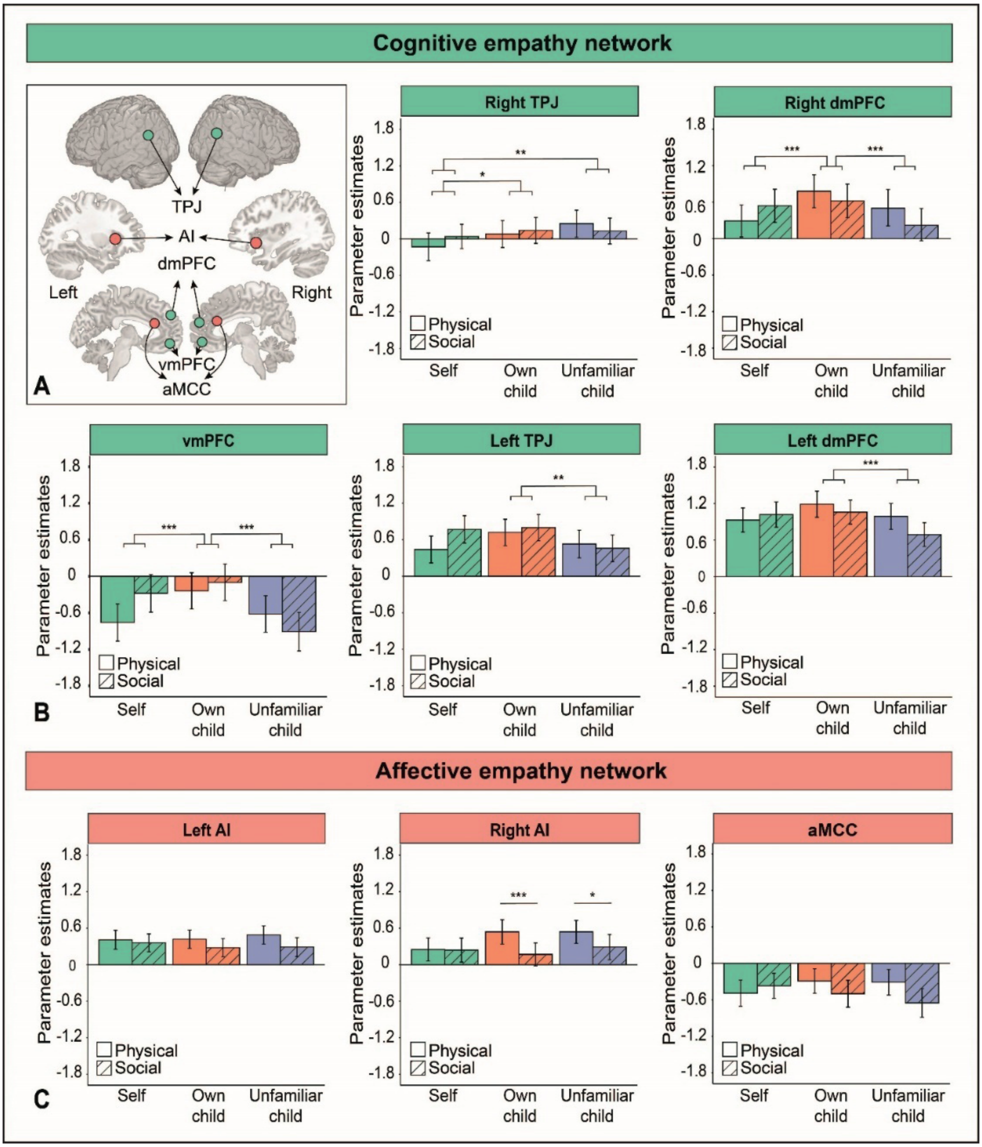
Brain regions	**MNI-coordinates**			**Voxel test value**	**Cluster *p*-value**	**Cluster size**
	x	**y**	**z**	**Z**		
Main effect ‘perspective’						
L Precuneus	-3	-56	30	≥8	<.001	13395
R Inferior parietal gyrus	47	-54	41	6.51		
R Precuneus	5	-68	41	6.22		
L Superior frontal gyrus, ventromedial	-6	54	-8	7.24	<.001	5209
L Superior frontal gyrus, medial	-5	54	20	4.78		
L Superior frontal gyrus, dorsolateral	-11	51	35	4.16		
R Inferior temporal gyrus	45	-63	-12	6.45	<.001	12268
R Inferior occipital gyrus	41	-71	-11	6.07		
R Middle occipital gyrus	41	-84	0	6.01		
L Inferior occipital gyrus	-44	-83	-9	6.10	<.001	5575
L Middle occipital gyrus	-39	-89	-6	5.83		
L Middle occipital gyrus	-38	-90	5	5.22		
R Superior frontal gyrus, dorsolateral	27	3	60	5.70	<.001	2139
R Middle frontal gyrus	35	9	54	5.24		
R Middle frontal gyrus	44	15	45	4.13		
R Middle frontal gyrus	47	39	21	4.84	.003	861
R Middle frontal gyrus	33	50	35	3.48		
R Middle frontal gyrus	36	50	26	3.32		
R Inferior frontal gyrus, orbital part	44	45	-6	4.59	.012	662
L Inferior frontal gyrus, triangular part	-60	18	29	4.40	<.001	1624
L Precentral gyrus	-42	5	39	4.19		
L Precentral gyrus	-45	-6	60	3.91		
Main effect ‘stimulus type’						
L Inferior frontal gyrus, triangular part	-48	39	11	< 8	<.001	5755
L Middle frontal gyrus	-26	27	53	3.98		
L Middle frontal gyrus	-45	53	-9	3.92		
L Middle frontal gyrus	-32	39	-12	< 8	.002	1039
L Inferior temporal gyrus	-59	-54	-9	6.78	<.001	3861
L Inferior temporal gyrus	-57	-47	-15	6.70		
L Inferior temporal gyrus	-50	-54	-20	5.78		

Brain regions	**MNI-coordinates**			**Voxel test value**	**Cluster *p*-value**	**Cluster size**
	x	**y**	**z**	**Z**		
R Inferior frontal gyrus, triangular part	51	41	8	6.15	<.001	5420
R Inferior frontal gyrus, orbital part	57	41	-5	4.51		
R Inferior frontal gyrus, triangular part	53	27	29	4.39		
L Middle cingulate gyrus	-2	-30	44	5.83	<.001	3930
L Middle cingulate gyrus	0	-35	36	5.77		
L Middle cingulate gyrus	0	-17	44	4.50		
R Middle temporal gyrus	62	-45	-8	5.58	<.001	2314
R Middle temporal gyrus	62	-54	-5	5.14		
R Middle temporal gyrus	69	-35	-9	4.60		
L Inferior parietal gyrus	-56	-44	39	5.29	<.001	5109
L Supramarginal gyrus	-60	-36	36	5.07		
L Inferior parietal gyrus	-51	-47	45	4.94		
R Supramarginal gyrus	51	-45	44	5.08	<.001	3428
R Superior parietal gyrus	35	-62	50	4.85		
R Angular gyrus	41	-56	51	4.81		
L Precentral gyrus	-44	11	30	5.01	.006	857
L Anterior cingulate cortex, pregenual	-3	41	23	4.62	<.001	1839
R Superior frontal gyrus, medial	5	35	38	3.97		
L Superior frontal gyrus, medial	3	26	50	3.93		
R Superior temporal gyrus	65	5	-6	3.93	.009	786
R Insula	42	18	-9	3.66		
R Inferior frontal gyrus, opercular part	63	12	6	3.64		
Interaction 'perspective' × 'stimulus type'						
L Insula	-27	18	-15	5.20	.003	861
L Inferior frontal gyrus, triangular part	-45	38	0	4.17		
L Superior temporal gyrus	-42	24	-23	3.61		
R Superior frontal gyrus, medial	11	50	27	4.48	.001	1075
L Superior frontal gyrus, medial	-11	35	30	4.16		
L Superior frontal gyrus, medial	-5	39	27	3.92		
R Posterior orbitofrontal gyrus [1]	41	24	-17	3.77	.048	468
R Superior temporal gyrus	50	18	-18	3.48		
R Posterior orbitofrontal gyrus	42	30	-24	3.43		

Note. The Automated Anatomical Labeling atlas (AAL3) by Rolls et al. (2019) was used to label the peak-coordinates. [1] Adding handedness, gender of parents, current psychopathology or psychotropic medication status to the model led to the loss of significance in the right posterior orbitofrontal gyrus.

SUPPLEMENT S5.5

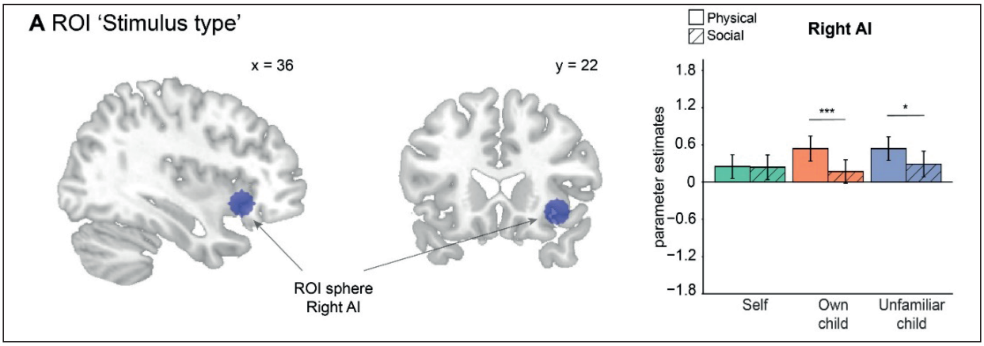
Brain results at region of interest level for the main effect of 'perspective' and 'stimulus type'

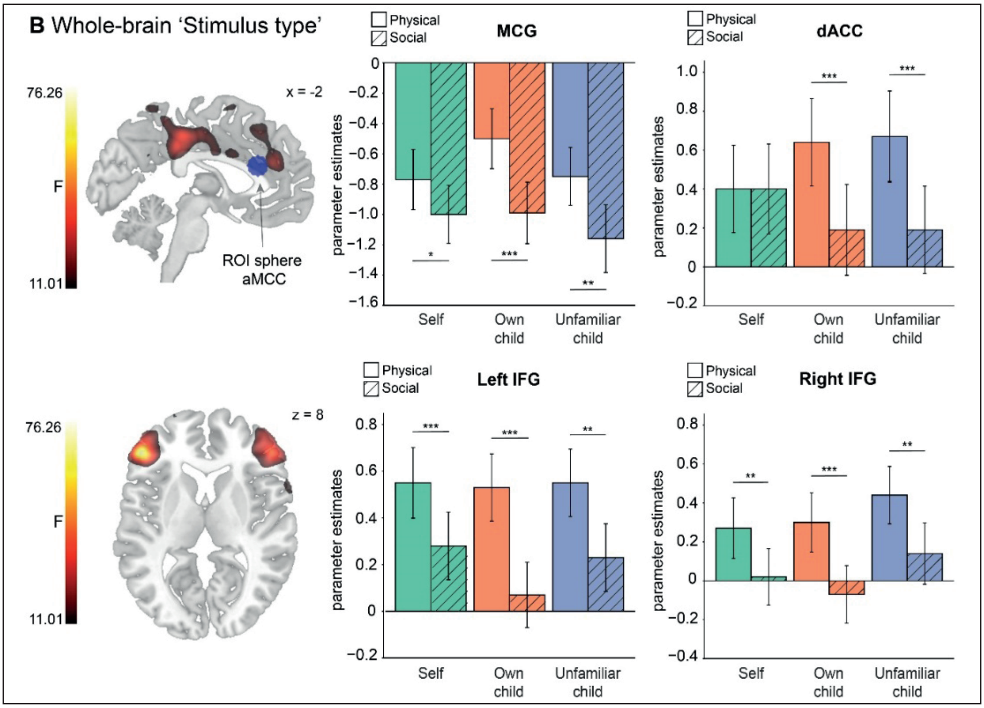


*A) Schematic overview of ROI spheres in the affective empathy network in red and the cognitive empathy network in green. B) Parameter estimates of BOLD-responses in ROIs in the cogntive empathy network where the perspective of imagined suffering impacted on activity in the regions (i.e., main effect of 'perspective' in bilateral TPJ, bilateral dmPFC and vmPFC). C) Parameter estimates of BOLD-responses in ROIs in the affective empathy network (i.e., main effect of 'sitmulus type' in right AI). All ROI results were Bonferroni corrected and post-hoc results were corrected for the number of tests (p <.05/8). Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

SUPPLEMENT S5.6

Brain results at region of interest and whole-brain level for the main effect of ‘stimulus type’

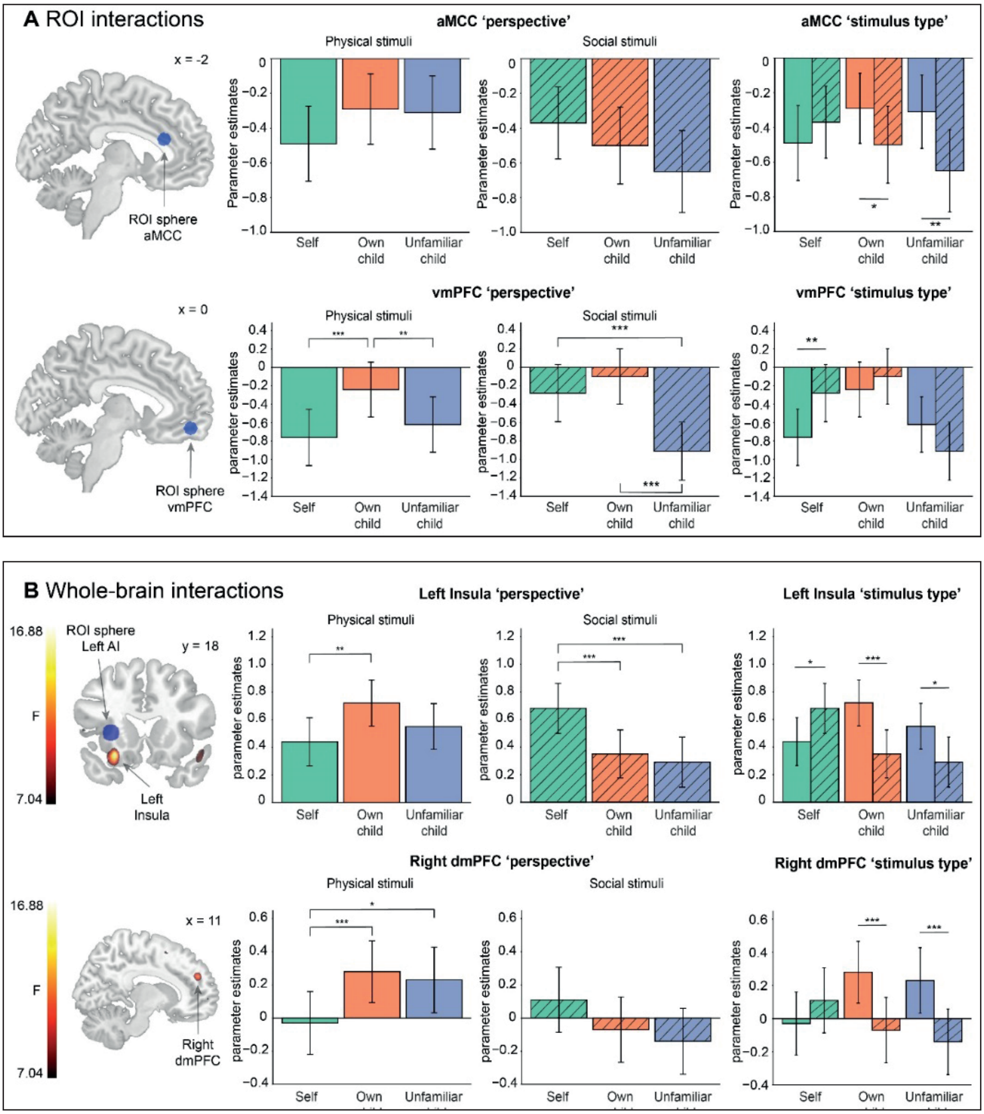




*A) Main effect of ‘stimulus type’ at ROI level was found in right AI. Physically unpleasant situations elicited significantly higher BOLD-responses compared to socially unpleasant situations in the right AI (p = .003). B) Main effect of ‘stimulus type’ at whole-brain level revealed significant clusters for physically versus socially unpleasant situations in MCG, dACC and bilateral IFG. The blue sphere represents the 8 mm MNI space spherical ROI of aMCC. The lack in overlap with the whole-brain activity confirms the lack of a main effect of ‘stimulus type’ in the ROI analyses for this region. Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

SUPPLEMENT S5.7

Brain results at region of interest and whole-brain level for the interaction between ‘perspective’ and ‘stimulus type’



*A) Significant interactions between ‘perspective’ and ‘stimulus type’ at ROI level were found in aMCC (p = .003) and vmPFC (p <.001). B) Significant interactions between ‘perspective’ and ‘stimulus type’ at whole-brain level revealed significant clusters of activity in left insula (p = .013), and right dmPFC (p <.001). Although we did not find a significant BOLD-response in the ROI of the left AI (blue sphere) for the interaction between ‘perspective’ and ‘stimulus type’, we did find a significant cluster at whole-brain level in the left insula, which is clarified in the figure by the lack of overlap between the whole-brain activation cluster and the ROI sphere of the left AI. Error bars represent standard error of the mean. Significant p-values <.05 were indicated by *, p <.01 by **, and p <.001 by ***.*

SUPPLEMENT S5.8

Peak activation coordinates of negative correlations between parental care and hemodynamic signal change at whole-brain level (own child minus unfamiliar child)[1]

Brain regions	**MNI-coordinates**			**Voxel test value**	**Cluster *p*-value**	**Cluster size**
	x	**y**	**z**	**Z**		
R Superior frontal gyrus, dorsolateral	26	24	62	4.45	.007	941
R Middle frontal gyrus	44	21	54	3.90		
R Middle frontal gyrus	48	24	44	3.35		
L Anterior orbitofrontal gyrus [2]	-35	39	-18	3.69	.049	591
L Inferior frontal gyrus, orbital part	-57	27	-6	3.66		
L Lateral orbitofrontal gyrus	-45	33	-18	3.64		

Note. The Automated Anatomical Labeling atlas (AAL3) by Rolls et al. (2019) was used to label the peak-coordinates. [1] Parental care data of one father was missing resulting in n=59 for this variable. [2] Adding gender of parents, current psychopathology or psychotropic medication status to the model led to the loss of significance in the left anterior orbitofrontal gyrus cluster.

SUPPLEMENT S5.9

Confound analyses

To exclude whether results may have been driven by differences in gender of parents (mother/father), handedness (left-handed/right-handed), current psychopathology (yes/no), and psychotropic medication status (on/off), we performed additional analyses with these potential confounding variables as covariates.

The present sample consisted of 35 mothers and 25 fathers of which 54 were right-handed and six were left-handed. Based on a structured interview to screen for current psychiatric disorders (MINI, Sheehan et al. (1998)) the majority of the parents had no current psychiatric disorders. Five parents fulfilled criteria for a current psychiatric disorder, i.e., obsessive-compulsive disorder ($n = 1$), dysthymia ($n = 1$), alcohol dependency ($n = 1$), panic disorder ($n = 1$), and agoraphobia ($n = 1$). One parent fulfilled criteria for multiple current mental disorders, including mania, generalized anxiety disorder, and alcohol- and drugs abuse. Five parents used psychotropic medication, i.e., Citalopram (SSRI, $n = 3$), Venlafaxine (SNRI, $n = 1$), Concerta (Methylphenidate, $n = 1$).

No effects of covariates were found at ROI level on neural activation related to main effects of ‘perspective’ and ‘stimulus type’ or their interaction. At whole-brain level, however, adding handedness, gender of parents, current psychopathology, or psychotropic medication status led to a loss of significance of the interaction between ‘perspective’ and ‘stimulus type’ in the right posterior orbitofrontal gyrus.

Regarding the correlation analyses between parental care and BOLD-activation at whole-brain level, adding gender of parents, current psychopathology, and psychotropic medication status led to a loss of significance in left anterior orbitofrontal gyrus. Handedness did not affect the correlational analyses at whole-brain level.