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

Wever, M.C.M.

Chapter 7

Summary and general discussion

The goal of this thesis was to generate insights into the neural and affective signatures of the socio-emotional connection between parents and adolescents. This was operationalized by the assessment of two key processes in parent-child interactions: Eye contact and empathy. In addition to parents' and adolescents' responses to these processes in well-functioning families, two inter-individual characteristics were examined that may interfere with parents' and adolescents' ability to engage in meaningful interactions with each other, which were a history of childhood emotional maltreatment in parents and adolescent depression. Studying this provides insight into mechanisms involved in the maintenance of the parent-child bond during adolescence and contributes to potential ways to modify and repair this relationship in situations in which it got disrupted.

In this chapter, the findings of the studies are summarized and discussed within the framework of the socio-emotional connection between parents and adolescents in well-functioning families and families with a parent with a history of childhood emotional maltreatment or a depressed adolescent. First, the main findings of each chapter are summarized and this summary is accompanied by a schematic overview of the neural signatures of connectedness between parents and adolescents (see Figure 7.1). Thereafter, parents' and adolescents' responses to eye contact, parental empathic responses to the imagined suffering of their child, and eye contact as an index of empathy are discussed in more detail, including overlap and differences in neural responses between parents and adolescents and in parents' responses to their own child between the two fMRI tasks. The final sections of this chapter are dedicated to general strengths and limitations of the studies and clinical implications followed by directions for future research, and concluding remarks.

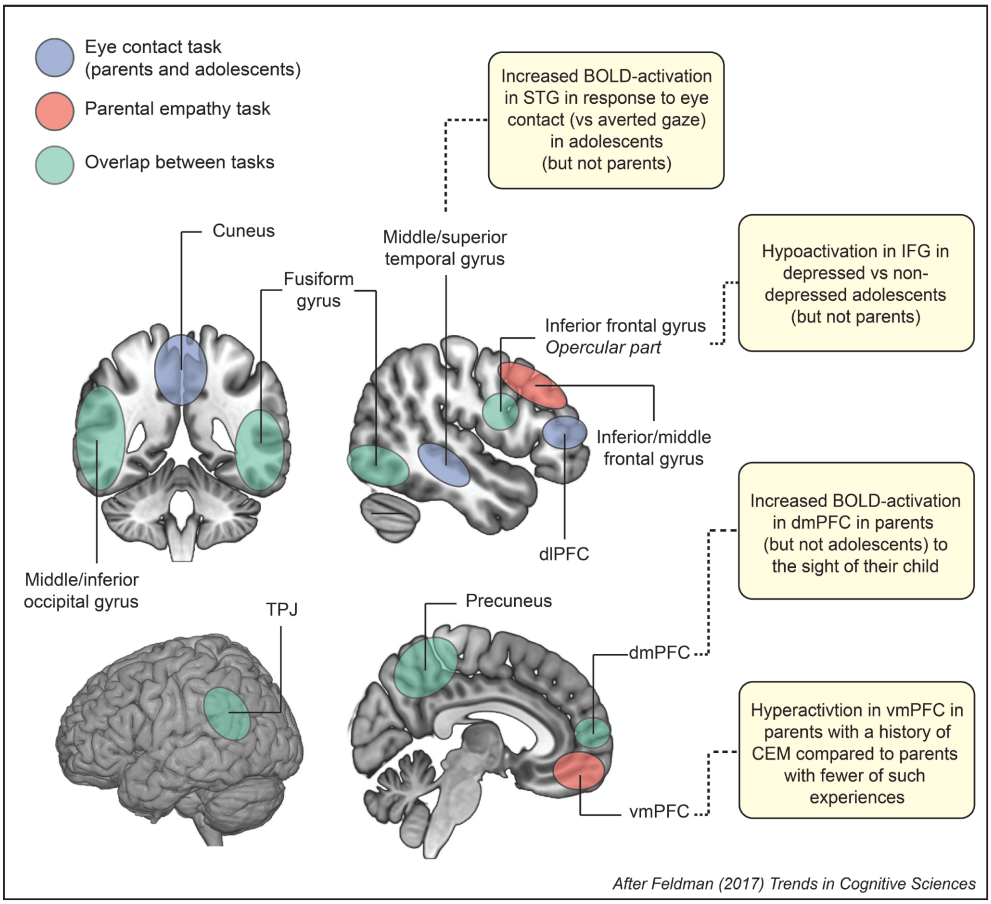

Figure 7.1 *Schematic summary of the activations in response to the parent-child bond from the perspective of parents and adolescents in the eye contact task and parents in the parental empathy task. CEM = Childhood emotional maltreatment, dlPFC = Dorsolateral prefrontal cortex, dmPFC = Dorsomedial prefrontal cortex, IFG = Inferior frontal gyrus, STG = Superior temporal gyrus, TPJ = Temporoparietal junction, vmPFC = Ventromedial prefrontal cortex.*

SUMMARY OF MAIN FINDINGS

Chapter 2 investigated parents' neural and affective (i.e., mood and feelings of connectedness) responses when making prolonged eye contact with their own child versus unknown others. The first key finding was that engaging in prolonged eye contact boosted parents' feelings of connectedness with others more compared to the short presentation of a picture. In addition, they reported a better mood and felt more connected after a direct versus an averted gaze of others. Effects were amplified for unknown targets, which is probably due to the already high mood and connectedness ratings at baseline when seeing their own child. While no evidence was

found for neural correlates of prolonged eye contact (i.e., direct versus averted gaze) in parents, neuroimaging results showed that the sight of one's own child versus an unfamiliar child was associated with decreased deactivations of blood-oxygen-level-dependent (BOLD)-responses in middle/inferior occipital gyrus, fusiform gyrus, and inferior frontal gyrus (IFG). Lastly, activity in dorsomedial prefrontal cortex (dmPFC) increased with the duration of eye contact, which was positively associated with parents' self-reported feelings of connectedness. Together, the results provide first insights into the neural and affective signatures of prolonged eye contact between parents and adolescents and show that prolonged duration is key to eliciting positive affect and affiliation within the parent-child context and to others in general.

Chapter 3 examined the impact of a history of childhood emotional maltreatment (CEM) in parents on their neural and affective responses to gazing into their own and others' eyes. Participants who reported more CEM exhibited increased activity in ventromedial prefrontal cortex (vmPFC) to one's own, but not others', direct gaze. This brain region has been robustly implicated in self-referential processing. Despite equivalent amounts of time spent looking into other people's eyes, participants with more experienced CEM did not benefit as much from the mood-boosting effects of eye contact with others compared to people who reported fewer of such experiences. In sum, participants who reported more severe CEM seem to show altered neural and affective responses to gazing into their own eyes and those of others, which may be a mechanism underlying negative evaluations about self and others that is common in individuals with a history of CEM.

Chapter 4 investigated adolescents' neural and affective responses when making prolonged eye contact with their parent and unknown others. In addition, differences in these responses between depressed and non-depressed adolescents were examined. Similar to their parents, prolonged eye contact boosted adolescents' feelings of connectedness compared to the presentation of a static picture. Furthermore, adolescents reported to feel better and more connected with others after a direct versus an averted gaze. In contrast to their parents, adolescents showed specific neural correlates related to gaze direction, in the inferior frontal gyrus, temporal pole, and superior frontal gyrus. Unlike non-depressed adolescents, depressed adolescents did not report a better mood in response to direct versus averted gaze of others and they did not report a better mood and enhanced feelings of connectedness when seeing their parent relative to others. This suggests blunted affective responses to eye contact in depressed versus non-depressed adolescents, particularly with their own parent. Regarding their neural responses, depressed adolescents exhibited blunted activity in IFG and secondary visual cortex. Since these brain regions have been implicated in inferring other's feelings and social exclusion, this might reflect a lack of social engagement characteristic of adolescent depression, and even a feeling of being excluded.

Chapter 5 examined parents' empathic responses to the imagined suffering of their adolescent child. Parents' self-reported empathic distress and neural responses were examined to a variety of unpleasant situations that included either their own or an unknown child. TheyParents reported more empathic distress and exhibited enhanced BOLD-responses within the cognitive empathy network (i.e., temporoparietal junction (TPJ), dmPFC, vmPFC) when imagining their own versus an unknown child suffering. The task also engaged the affective empathy network (i.e., anterior insula, anterior mid-cingulate cortex), but activity in these regions was not modulated by the person parents empathized with (i.e., whether parents imagined the suffering of one's own or an unknown child). Together, this suggests that parents more strongly engage the cognitive empathy network (i.e., perspective taking) rather than the affective empathy network (i.e., vicarious experience of emotions) when imagining their own child suffering. Furthermore, adolescent-reported parental care was not associated with parents' self-reported distress or with neural empathic responses to imagining their own child's suffering. The results provide new insights into neural processes supporting parental empathy, highlighting the importance of regions in the cognitive empathy network when imagining the suffering of their own adolescent child.

In addition to focusing on parents' empathic reactions to their child, the final aim was to examine whether parents were also able to accurately infer the feelings of (unknown) others and whether making eye contact contributes to this process. ***Chapter 6*** examined the association between this so-called empathic accuracy and the extent to which parents were making eye contact with (unknown) targets during videos of positive and negative emotional target stories, assessed with eye tracking. The results demonstrate that gazing into the eyes of others did not contribute to one's level of empathic accuracy. However, parents who made more eye contact during the emotional target stories reported higher levels of state and trait empathy. Together this suggests that, rather than (only) collecting information about the other's internal state, eye gazing might play a role in affiliative bonding by signaling empathy and social engagement to others.

PARENTS' AND ADOLESCENTS' RESPONSES TO EYE CONTACT

Chapters 2-4 examined parents' and adolescents' neural and affective responses to prolonged eye contact with each other versus with unknown others as an approximation of socio-emotional connectedness. First, parents' and adolescents' general responses to eye contact (direct versus averted gaze) are discussed (i.e., gaze direction), independent of the identity of the person with whom they make eye contact. Thereafter, parents' and adolescents' responses when making eye contact with each other versus unknown others (i.e., target identity) are addressed. In

addition to the differences between parents' and adolescents' responses to eye contact with each other and unknown others, the overlap in their responses is highlighted.

Parents' and adolescents' responses to gaze direction (i.e., direct versus averted gaze)

Chapters 2 and 4 examined parents' and adolescents' neural and affective responses to eye contact with each other and unknown others using the same eye contact task. In line with our expectations, parents and adolescents reported a better mood and enhanced feelings of connectedness in response to a direct versus an averted gaze of others. Moreover, both adolescents and adults (parents) made more eye contact with others during direct versus averted gaze videos (assessed with eye tracking), indicating that a direct gaze attracts and maintains one's attention more than an averted gaze.

In contrast to the overlapping subjective and gaze responses between adults and adolescents, our findings identified differences in the neural responses to direct versus averted gaze of others. While adolescents exhibited enhanced neural responses to prolonged direct versus averted gaze in several brain regions previously linked to gaze direction, including the superior and inferior frontal gyri (Hietanen, 2018; Senju & Johnson, 2009), parents' neural responses to prolonged eye contact with others were not moderated by the gaze direction of the targets. Despite the fact that parents' and adolescents' responses were not directly compared, this finding seems to suggest that adolescents attend more to whether or not another person is making eye contact compared to adults. Although further research is necessary to support this, this would corroborate previous research postulating enhanced sensitivity to social cues during adolescence (Davey et al., 2008; Morris et al., 2018; Nelson et al., 2016; Nelson et al., 2005; Somerville, 2013).

In order to investigate to what extent these findings were specifically attributable to the *prolonged* duration of eye contact, parents' and adolescents' affective responses to prolonged eye contact in the task were compared with their similar responses to the short presentation of static pictures of the same targets, prior to the task. This comparison specifically yielded enhanced feelings of connectedness to prolonged eye contact videos versus the short presentation of pictures in both parents and adolescents and validates the prolonged eye contact stimuli used in the eye contact task. It is of note, however, that prolonged eye contact did not further enhance feelings of connectedness in response to eye contact between parents and adolescents compared to unknown others, most likely because these ratings were already high at baseline.

Together, these findings indicate that eye contact is generally experienced as positive and socially rewarding, both in adults and adolescents, and that particularly prolonged eye contact contributes to building a connection with others. Moreover, feeling connected with others seem

to not only arise when making eye contact with one's parent or child, but also when making eye contact with unknown others. This emphasizes the strong affective component of eye contact, which might find its origin in our intrinsic need to belong to others and to literally be *seen*.

Parents' and adolescents' responses to making eye contact with each other

In line with our expectations, parents (***Chapter 2***) and adolescents (***Chapter 4***) both reported a better mood and enhanced feelings of connectedness in response to the sight of each other compared to unknown others, which is thought to reflect the closeness of their affiliative bond. This is supported by the finding that parents and adolescents did not make more eye contact to the sight of each other compared to unknown others, suggesting that the mood-boosting and connectedness-enhancing impact of prolonged eye contact is rather based on prior social knowledge and prior experiences with one's parent or child than the direct effects of making eye contact in the task.

At the neural level, parents and adolescents showed overlapping patterns of neural activation in response to the sight of each other and unknown others in general. They both activated a set of brain regions including the fusiform gyrus, middle/inferior occipital gyrus, dorsolateral prefrontal cortex (dlPFC), TPJ, IFG, middle temporal gyrus (MTG) and cuneus (visualized in Figure 7.2). However, there were also some remarkable differences. Parents exhibited enhanced activation in dmPFC when making eye contact with others (versus themselves), a brain region robustly involved in the mental representation of others (Frith & Frith, 2010), while activity in this region was not found in adolescents in the same contrast. Although this findings was unexpected, it aligns with a recent study showing that the dmPFC undergoes major changes during adolescence related to the development of a consistent representation of self and others and that the specialization of this region continues to refine into young adulthood (van Buuren et al., 2022). Since the adolescents in our sample were aged between 11-17 years, it is possible that the lack of differentiation in the dmPFC when making eye contact with others versus gazing into their own eyes is associated with ongoing maturation processes in this brain region in these adolescents.

Another remarkable difference is that whereas parents show profound differences in their neural responses to their own child versus unknown others, adolescents did not show differences in their neural responses to their parent and an unfamiliar peer in the same task. Interestingly, adolescents start to become more autonomous and independent of their parents during adolescence and focus more on peers (Crone & Dahl, 2012). Speculatively, the lack of differences in neural responses in adolescents between the sight of one's parent and an unfamiliar peer might reflect their interest to engage in social contact with (unknown) peers. Moreover, this dovetails with prior work (Lee et al., 2017) showing an 'unconditional' neural response pattern of parents to the imagined suffering of their child that was independent of relationship quality, while

in the same task the neural responses of their adolescent child did dependent on the quality of the bond they experienced with their parent (Lee et al., 2017). This indicates that parents' and adolescents' neural responses to the sight of each other are not identical and emphasize the fact that the perspectives of parents towards their adolescent child and adolescents towards their parent are intrinsically different.

Lastly, adolescents showed enhanced neural activity in the right superior temporal gyrus (STG) during eye contact with their parent, while this region was not activated in parents while making eye contact with their child. The STG has been linked to social cognition and seems to be an important hub for the integration of multisensory information regarding social situations, including the representation of eye gaze direction (Adolphs, 2003; Hoffman & Haxby, 2000). This finding corroborates with a study on the neural representations of eye gaze and identity of targets, in which Hoffman and Haxby (2000) showed that the STG was specifically linked to selective attention to gaze direction, while other regions were related to attending to the targets' identity. As such, this suggests that adolescents may be more sensitive to the direction of others' gaze as compared to adults.

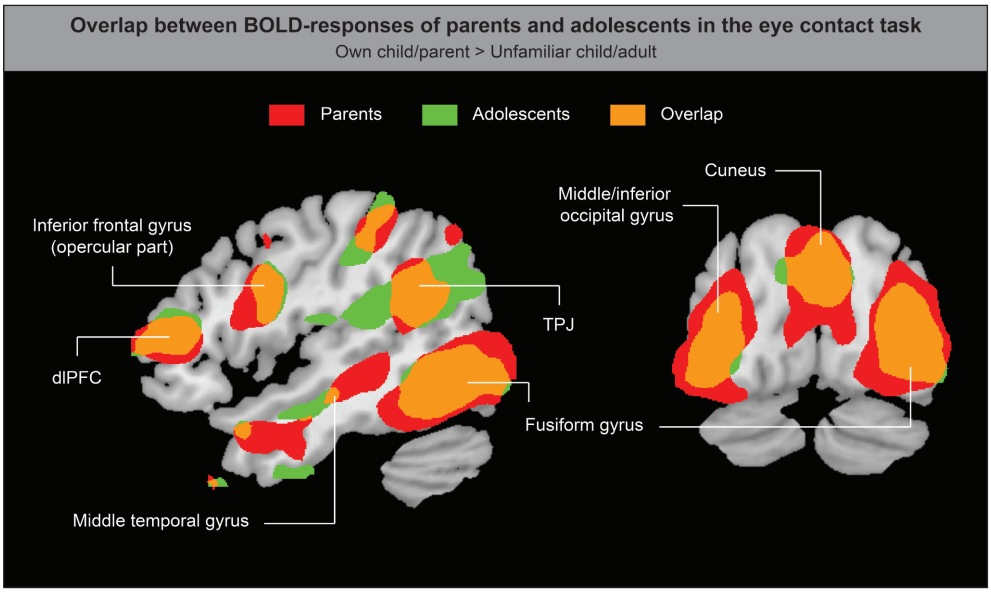

Figure 7.2 *Overview of overlap (orange) between parents (red) and adolescents (green) for the main effect of target (i.e., own child/parent versus an unfamiliar child/adult) in various brain regions. The figure includes F-maps of the 4 × 2 ANOVA in SPM of parents (n = 79) and non-depressed adolescents (n = 59). dlPFC = Dorsolateral prefrontal cortex, TPJ = Temporoparietal junction.*

INTER-INDIVIDUAL DIFFERENCES IN CONNECTEDNESS

Chapters 3 and 4 demonstrated that both parents with a history of childhood emotional maltreatment (CEM) and depressed adolescents reported a consistently lower mood throughout the eye contact task. This is in line with prior evidence showing that depressed adolescents were found to have a tendency to perceive neutral facial stimuli as negative (Ahmed et al., 2015; Gilbert, 2012), and might therefore interpret eye contact as more negative compared to non-depressed adolescents. Furthermore, the profound overlap in responses to eye contact with others in parents with a history of CEM and depressed adolescents is no surprise given the fact that CEM is a key risk factor for depression (Spinhoven et al., 2016). Nevertheless, the lower mood in parents with a history of CEM survived a correction for the severity of depressive symptoms, indicating that this result was at least not entirely driven by symptoms of depression.

Remarkably, parents with a history of CEM and depressed adolescents not only reported a lower mood in response to eye contact with unknown others, but also after making eye contact with their own child or parent. This is in contrast to parents with no CEM and non-depressed adolescents who experienced a better mood after making eye contact with their child or parent, respectively. Although not directly investigated, it is conceivable that these blunted mood responses to their own child or parent contribute to dysfunctional interaction patterns between parents and adolescents, potentially threatening the parent-child relationship. Moreover, given the overlap between parents with a history of CEM and adolescent depression it is likely that such blunted response patterns might generalize to parent-child dyads of whom a caregiver suffers from depression or situations in which a child has been emotionally abused and/or neglected by their parent. Elucidating such factors potentially contributes to the early identification of families that are at high risk for dysfunctional family dynamics and might contribute to the development of targeted interventions focus on strengthening of the parent-child bond, which may be a fruitful direction for future research.

In line with the blunted mood responses in depressed adolescents towards their own parents, we found a comparable effect in this sample in another task within the RE-PAIR study. Unlike their non-depressed counterparts, depressed adolescents showed difficulties to benefit from parental praise, aligning with the thought that they are struggling with the acceptance of social support of others, including of their parents (van Houtum, wever, et al., 2023). Although these findings seem to point into the direction of an altered perception of their parents' caregiving behavior, evidence has shown that a more negative parenting style (i.e., less warmth, more overprotection, less autonomy granting) has also been linked to the development of depression in adolescents, also in studies with a prospective design (Schwartz et al., 2014). Moreover, both processes may also reinforce each other. The current studies cannot disentangle these two pathways. However, future analyses on behaviorally coded observed parent-child interactions,

that were also part of the RE-PAIR study, may potentially disentangle differences in objective assessments versus subjective experiences of parenting behavior between depressed and non-depressed adolescents (Wentholt et al., *In prep.*). Disentangling whether parenting behavior itself or only the *perception* of the parenting behavior in the eyes of the adolescent is non-optimal is important for interventions for adolescents with depression and whether and how their parents need to be involved.

Parents with a history of CEM and depressed adolescents did not differ in their neural responses to making eye contact with familiar versus unfamiliar others, nor did they show altered neural responses to the different gaze directions. This suggests that their perceived lower mood in response to the videos of direct and averted gaze was not reflected in their neural responses. Instead, depressed adolescents exhibited overall blunted BOLD-responses in the secondary visual cortex and IFG throughout the task (i.e., in response to all task conditions). This part of the secondary visual cortex has been consistently found in relation to experiences of social exclusion in 7-10 year old children in a meta-analysis of three distinct samples (van der Meulen et al., 2017). The IFG, in addition, has been linked to emotion-regulation and resonating with another's mental state and emotions (Feldman, 2017). Given the involvement of these brain regions in the processing of social information, the blunted neural responses might reflect a lack of social engagement characteristic of adolescent depression, and even a feeling of being excluded whilst making eye contact (Arce et al., 2009; Jankowski et al., 2018; Joiner et al., 2002). This finding corroborates with the difficulties in the social domain of adolescents with depression, although the precise psychological processes remain to be investigated.

In contrast to altered responses to making eye contact with others, parents with a history of CEM and depressed adolescents also reported a lower mood in response to gazing into their own eyes when compared to parents with no CEM and non-depressed adolescents. Moreover, parents with more experienced CEM showed enhanced BOLD-activation in vmPFC, a brain consistently found in self-referential processing, in response to gazing into one's own, but not others', eyes. These findings suggest that both parents with a history of CEM and depressed adolescents might experience a certain discomfort when looking at themselves. This converges with studies showing, in addition to negative views about others, increased negative self-views, which is common in both people with experienced CEM and depression (Hammond & Romney, 1995).

Lastly, parents with a history of CEM and depressed adolescents did not make less eye contact with the each other, unfamiliar others or with themselves in the task, which was assessed by measuring their gaze responses during the eye contact task. This suggests that they did not avoid eye contact more and that the differences that were found are not attributable to differences in how well they adhered to the task instruction to make eye contact with the targets throughout

the videos. Future studies should examine whether this holds true for real life interactions as this could potentially result in different outcomes, including more discomfort in response to eye contact leading to a greater avoidance.

PARENTAL RESPONSES TO THE IMAGINED SUFFERING OF THEIR CHILD

Another way of connecting with one's child is by empathizing with their feelings, especially when adversity crosses their path, which often occurs during adolescence. ***Chapter 5*** therefore examined neural and affective signatures of parental empathic responses to the imagined suffering of their own adolescent child versus an unfamiliar child.

In line with the hypotheses, parents reported higher levels of self-reported distress when imagining the suffering of their own child relative to an unknown child. Accordingly, they showed enhanced BOLD-activation within the cognitive empathy network (i.e., TPJ, dmPFC, vmPFC) in favor of their own child that is linked to perspective taking. This increased engagement of the cognitive empathy network might be related to the fact that parents are better able to imagine how their own versus another child would feel in a certain situation as they collected a vast amount of social knowledge about the child's responses in equivalent situations in the past. Interestingly, the brain regions involved in the cognitive empathy network show extensive overlap with neural signatures of such autobiographical memory processes.

Although the task elicited enhanced BOLD-responses in the affective empathy network (i.e., anterior insula, AI; anterior mid-cingulate cortex, aMCC), parents' neural responses in these brain regions did not differ between the imagined suffering of their own child versus an unfamiliar child. This was not in line with our hypothesis and diverges from what was found in other studies on parents' empathic responses, who did report enhanced activation in the AI and aMCC to the sight of one's own versus an unfamiliar child (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). Although this finding was unexpected, there are several methodological differences with other studies that might explain the diverging outcomes. First, the parental empathy task that was used outlined a more negative context compared to most of neuroimaging studies that assessed parents' neural responses to pictures of their own child versus an unknown child instead of being confronted with their suffering. As such, parents might have felt empathically concerned for both perspectives, but were better able to take the perspective of their own child versus an unknown child. In line with this, parents were asked to *imagine*, instead of directly experiencing, their child's suffering, which might have placed higher demands on cognitive rather than affective empathic abilities of parents. Lastly, most studies on parental empathy

examined parents' responses to infants or young children instead of to children in the adolescent age range. Although there are currently no studies that directly examined whether parents of young children and adolescents show distinct neural responses to parental empathy, this might have given rise to diverging outcomes.

In addition to the cognitive empathy network, enhanced neural activity in bilateral IFG, left precuneus, right inferior temporal gyrus, right fusiform gyrus, left middle/inferior occipital gyrus, right superior frontal gyrus and middle frontal gyrus was found to the imagined suffering of their own child versus an unfamiliar child. Part of these brain regions (precuneus, fusiform gyrus, and middle/inferior occipital gyrus) overlap with brain regions that were found in the eye contact task in response to the sight of parents' own child compared to unknown others (see Figure 7.3). Amongst other processes, these regions are involved in emotion regulation and might be specifically involved when parents are presented with faces of their own child, which was the case in both tasks.

Opposed to the expectation that parents' self-reported distress or neural responses in the cognitive and affective empathy networks would be linked to the child's perception of parental care, no evidence was found for such relationships. Although this seems to suggest that parents' empathic responses do not act as a marker of the parent-child bond, the lack of covariation between these measures may have other (methodological) explanations. One explanation is that the lack of association may be due to differences in time frames about which perceived parental care (i.e., first 16 years of adolescents' lives) and parental empathic responses in the task (i.e., snapshot of current situation) are assessed. Another explanation is that parents' responses to the suffering of their child are independent of the quality of the parent-child bond, similar to the study of Lee et al. (2017), and instead have a more "unconditional" character.

Our findings have broadened our knowledge about parental empathic responses to imagining, instead of directly experiencing, the suffering of one's adolescent child. Parents more strongly engage in thecognitive empathy network when imagining their own child suffering compared to an unfamiliar child, while they did not differ in their neural responses in the affective empathy network towards their own child versus an unknown child. It is of note that this study focused on the average levels of parental empathic responses, overlooking individual differences between parents. In addition, the vast majority of studies on empathy are dedicated to the positive effects of parental empathy, e.g., more attuned parenting and better socio-emotional development of the child, however, providing parental empathy can also come with psychological and physiological costs for parents (e.g., empathic distress and inflammation) (Manczak et al., 2016), which has been less extensively studied. A situation in which this might be particularly relevant is when a child has chronic mental or physical problems. Being confronted with the suffering of one's child might chronically induce empathic distress in these parents. As a consequence, parents

might suppress their own emotional and physiological needs to be (emotionally) available for their child, which might eventually lead to psychological and physiological ailments. Therefore, we will focus on these inter-individual differences between parents in a follow-up study as well as on how they relate to the well-being of their child in the context of depressed adolescents.

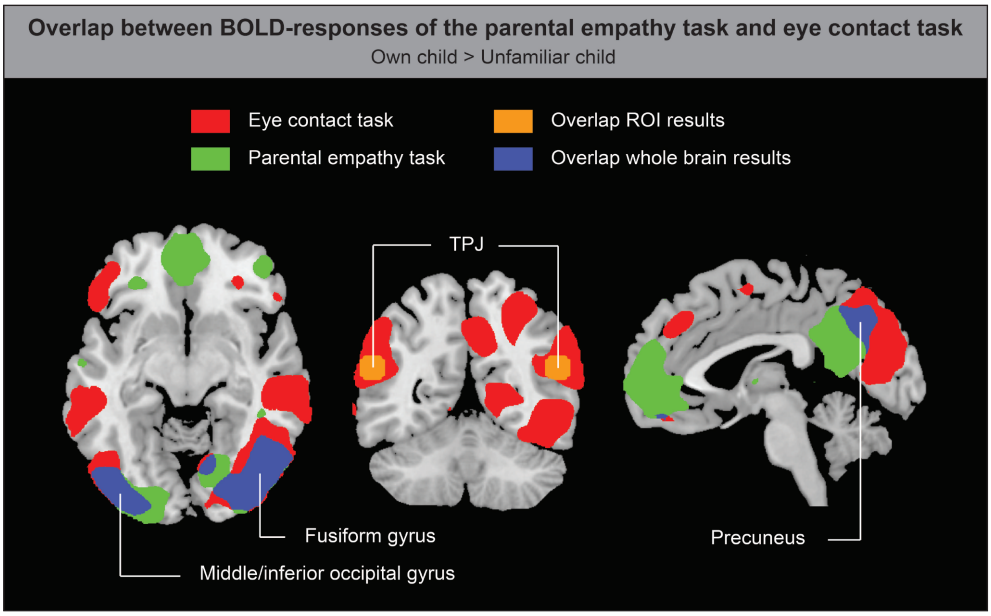

Figure 7.3 *Overview of overlap between region of interest (ROI) and whole-brain results of the parental empathy task and the whole-brain results of the eye contact task in parents for the own child > unfamiliar child contrast. TPJ = Temporoparietal junction.*

EYE CONTACT AS AN INDEX OF EMPATHY

Besides the role of eye contact in connecting with others on a socio-emotional level it might also be a way to infer others' feelings. ***Chapter 6*** therefore examined to what extend the eyes of others are used to collect social information that contributes to infer others' feelings, also referred to as empathic accuracy. It is of note that, in contrast to the other studies, this chapter was not focused on the parent-child bond, but on the assessment of empathic accuracy in adults in general.

In contrast to the hypotheses, there was no evidence that gazing into the eyes of others helped parents to be more empathically accurate about others' feelings. This suggests that, at least in the empathic accuracy task that was used, parents did not significantly rely on social cues

conveyed by the eyes. It might be possible that the content-rich stimuli used in the task, including verbal speech, were clear enough to extract the feelings of the target person, making additional social cues from the eye region redundant. Moreover, it might be possible that parents were not fully motivated to accurately infer the feelings of the targets as there was no direct benefit of knowing, especially because the targets were unknown to the parents.

Interestingly, there was a positive association between parents' self-reported levels of empathy and the amount of eye contact they made with others. More specifically, participants who reported to be more empathic (i.e., empathic concern) and find it easier to take others' perspective (i.e., perspective taking), both on a state (self-report after each trial) or trait (interpersonal reactivity index questionnaire) level, gazed more into the eyes of others when listening to their (positive or negative) emotional story. This is in line with prior studies (Cowan et al., 2014; Martínez-Velázquez et al., 2020), and suggests that eye contact might be a way to convey to others that we empathize with their (emotional) circumstances. The idea that eye contact might be a way to signal rather than only receive social cues to others has been previously described by Kobayashi and Hashiya (2011) and was referred to as the gaze grooming hypotheses. This theory is rooted in the notion that humans use eye contact as a contact-free way to groom other humans in order to maintain social bonds. It has been thought to be an evolutionary adaptation that replaced direct grooming behavior that is known from primate species and is useful in maintaining a large number of social bonds, even from a certain distance. As such, our findings support the idea that eye contact might be a way to connect with others and signal: "I see you".

GENERAL STRENGTHS AND LIMITATIONS

The studies in this thesis contribute to our understanding of the neural and affective signatures of connectedness between parents and adolescents and with unknown others. By using several tasks, including developing and validating two novel functional magnetic resonance imaging (MRI) paradigms, we captured how parents and adolescents connected with each other via eye contact and parental empathy. Our tasks used a personalized design, including videos and photos of participants' child or parent and of themselves. These stimuli were contrasted with those of unknown others, allowing for the extraction of responses unique to the parent-child context. In addition, contrasting the 'self'-condition with all 'other' conditions enabled us to identify which neural responses were social in nature. Within the tasks, we used a multi-method approach, including subjective reports and functional MRI responses, which not only informed us on how parents and adolescents felt when connecting with each other and unknown others, but gave additional insight on how they respond to each other at the level of the brain. Moreover, the tracking of participants' gaze during the eye contact task in the MRI scanner informed us on the actual amounts of eye contact participants made and how well they adhered to the

task instruction to make eye contact with the targets throughout the videos. We were able to conduct the eye contact task in adolescents with a clinically diagnosed depressive disorder, which yields new knowledge on how this may affect one's responses to eye contact with others and potentially undermine the parent-child bond. Lastly, almost all study measures, hypotheses, and analyses were preregistered prior to data analysis, which contributes to the credibility of the results and to the transparency of science in general.

Although our studies yield novel results that contribute to the field, several limitations need to be kept in mind when interpreting the findings. First, we tried to present the participants with video clips of social settings closely mimicking daily life situations, while at the same time being able to control the targets' gaze direction and facial expressions (eye contact task), and autobiographical stories (empathic accuracy task). However, the ecological validity of these social situations remains a matter of debate. It is well possible that the pre-recorded target videos of eye contact used in this study did not elicit a comparable level of physiological arousal in the participants as might have happened during eye contact encounters and interactions in real life. In addition, participants did not receive any reciprocal feedback from the targets during the sight of the pre-recorded videos in the eye contact task and empathic accuracy task and did not have the opportunity to adjust their responses accordingly as they probably would have during face-to-face eye contact in real life. Using real interaction partners to assess eye contact, however, would have introduced several other, even more serious, methodological challenges. We could not have controlled targets' gaze direction, which is an important factor in our design, and people might have made behavioral responses interfering with the experiment, e.g., bursting into laughter when gazing into each other's eyes. As such, this would have limited experimental control within the paradigms and potentially introduced considerable experimental noise. Nevertheless, future studies including the assessment of eye contact during real life or virtual reality interactions are necessary to examine whether these study set-ups give rise to different outcomes and would inform us on which kind of stimuli are needed in future studies on eye contact.

In the context of the replicability crisis in the field of psychology and neuroscience, especially for task-based functional MRI research (Collaboration;, 2015; Poldrack et al., 2017), it is of note that our findings from the novel functional MRI paradigms need to be interpreted with caution. Future studies should aim for replicating the findings to prevent false positive results. It is worth to say, however, that the neuroimaging results of the eye contact task conducted in the parents and adolescents showed considerable overlap (Figure 7.2), supporting the robustness of the findings using this task. Another challenge that is closely linked the reproducibility crisis is the use of small sample sizes. Although the larger part of our studies includes accountable sample sizes ($n \geq 60$), the study on depressed adolescents (***Chapter 6***) might be underpowered ($n =$ 19 depressed adolescents). As such, replication with larger sample sizes is recommended to

confirm the reliability of these findings, especially at the level of the brain. In order to mitigate the replicability crisis, it remains important to join our forces to publicly share data and study designs with other labs. This would generate accountable knowledge at a faster pace and accelerates scientific breakthroughs.

Lastly, despite the fact that participation to the study was open for all depressed adolescents and their parents seeking treatment in one of the participating mental health facilities, the inclusion of participating families may have suffered from selection bias. Parents and adolescents that are not on speaking terms with each other were most likely not willing to participate in our study. In addition, practitioners might not have introduced the study to depressed adolescents and their parents for whom, in their opinion, the study would be too demanding or would potentially interfere with the psychotherapy that was offered. As such, one must keep in mind that our findings in the context of adolescent depression might at least apply to families that were at the same page with each other and were open for treatment and scientific research. Moreover, this might have rather led to an underestimation than an overestimation of the effects for this sample, as parent-child dyads with a worse relationship quality are expected to have more difficulties connecting with each other.

CLINICAL IMPLICATIONS

Depressed adolescents seem to experience eye contact as less positive and less socially satisfying, and do not benefit from its mood-boosting effect (***Chapter 4***). This corroborates with the feeling of parents not being able to get through to their depressed adolescent, which makes it difficult for parents to offer (emotional) support. In addition to addressing interpersonal difficulties in depressed adolescents, e.g., with interpersonal psychotherapy, it can be helpful to focus also on parents. Psychoeducation for parents focusing on the depressed adolescent's difficulties in the interpersonal domain may foster a better understanding of the challenges depressed adolescents are facing and provide them with tools to break the negative spiral of getting alienated from each other. Recently, such a program has been developed for parents of depressed adolescents in the Netherlands: Samen Sterk, where parents are provided with tools to help (re-)establish or strengthen the bond with the child (Elzinga et al., 2022).

Another result that might have the potential to be implemented in the clinical field is the use of eye gazing into one's own eyes in a therapeutic session (e.g., via a mirror) to elicit negative self-cognitions in people with negative self-views. Although this was studied in parents with a history of childhood emotional maltreatment in ***Chapter 3***, this way of directly addressing one's self-view can potentially be used in a broader context as negative cognitions about the self can be considered a transdiagnostic symptom of various psychiatric disorders, including adolescent

depression (Thew et al., 2017). If these negative cognitions can be addressed by letting those who suffer from negative self-views gaze into their own eyes, and create a state of mind that facilitates modification of these self-views, this potentially alleviates the negative feelings and fosters more positive feelings.

Lastly, the results of the study in ***Chapter 6*** suggest a possible link between eye contact and signaling one's empathetic feelings to others. Given that eye contact is important in signaling parents' emotional availability and engagement with their child, but also of (mental) health practitioners with their patients, being distracted by e.g., smartphone or computer use might hamper this way of connecting with each other. In parents, it might diminish their opportunity to show emotional availability to their adolescent child. In adolescents, it might hamper letting their parents comfort them and give emotional support when needed. Both examples show that it would be helpful to inform parents and adolescents about the importance of literally keeping an eye on each other or checking in on each other's emotional state via eye contact. In addition, (mental) health professionals might also benefit from expressing their empathy to their patients via eye contact, especially when a patient is sharing sensitive content that demands an empathetic response. Making eye contact might help them to express that they understand where their patient is going through,. Patients, in turn, feel better understood and supported, which might positively affect the patient-practitioner relationship, potentially benefitting treatment response.

FUTURE DIRECTIONS

An empirical question that is raised is whether the neural networks that were found in response to the sight of one's own child or parent are unique to the parent-child bond or generalize to other affiliative connections, e.g., romantic couples, close friends, siblings. It is possible, for example, that how people respond to seeing another person might not be driven by the type of affiliative relationship, but rather by the quality of this bond. To answer this question, it is necessary to perform functional MRI studies involving these distinct types of affiliative bonds, preferably with a within-subject design, using stimuli including one's own child, one's sibling, one's best friend, and one's partner. This would allow for a direct comparison between these affiliative bonds and whether such accompanied neural response patterns generalize on an inter- and intra-individual level. Additional self-reported assessments of the bonds could give insight into individual differences in how subjectively close people feel with these persons in their daily life.

Another, more applied, clinical avenue of further research and the next step in our line of research, is to examine how parenting a depressed adolescent (or other mental illness) and

being confronted with their mental suffering on a daily basis might affect parents' own well-being. These parents experience probably even more empathic distress when they see their child suffering compared to parents of non-depressed adolescents, which might negatively affect their capacity to engage in their role as a parent, and in turn, negatively affects the child. Moreover, depressed adolescents, especially those who are sensitive to the distress of their parent, might be more inclined to keep their (depressed) feelings to themselves, because they do not want to hurt or (further) upset their parents. Interestingly, this has indeed been mentioned by depressed adolescents in qualitative interviews within the RE-PAIR study. As a consequence, adolescents might shield themselves against the negative feelings of their parent, but also for their support. Parents, in turn, might feel hopeless as they cannot get through to their child anymore. This might bring the parent-child bond in a downward spiral and negatively affects the child's well-being and interfere with clinical treatment of the child's depression. Actively involving parents in the treatment of their child, boosting their parental self-efficacy, and support parents to appropriately cope with their empathic distress might help to break this downward spiral (Elzinga et al., 2022).

In addition to the fact that sharing negative feelings with others may foster strong social bonds, sharing one's joyful experiences with another person may just as well contribute to a stronger socio-emotional connection. While ***Chapter 5*** investigated the neural and affective signatures of parents' empathic responses to the suffering of their adolescent child, an interesting follow-up study could be to examine parents' ability to share in the positive emotional state or joy of their child. In addition, it is of interest to investigate whether sharing in the happiness of their child would positively affect parents' own mood and feelings of connectedness with the child as well as that of the child when they notice the vicarious joy of their parent. The idea that vicariously sharing in happy feelings might enhance feelings of socio-emotional connectedness between parents and children is consistent with the finding that parental warmth, which is also referred to as emotional closeness (Gladstone & Parker, 2005), is a crucial factor in the development of a strong sense of self and identity during adolescence and positive self-views (Erikson, 1968; McCranie & Bass, 1984).

Another direction for future research and an extension of our findings on eye contact as an index of signaling empathy to others is whether receiving eye contact also contributes to feeling seen and understood by the sender. This is of particular interest in a patient-therapist setting, as this might be a feasible way to foster the quality of a therapeutic relationship. In addition, the emotionally laden and sensitive conversations in this setting showcase ideal circumstances to study the sending and receiving of empathy via eye contact. A useful method to study patients' *and* therapists' gaze responses during such conversations would be a virtual reality setup combined with eye tracking and the assessment of their accompanied feelings. Moreover, the flexible nature of virtual reality makes it possible to present patients and therapist with a wide

variety of simulated situations in order to examine under which circumstances eye contact is appropriate or not, and for how long. Lastly, examining how trainee therapists make eye contact can potentially be used as a selection tool to select future therapists or for training therapists how to optimize their responses.

CONCLUDING REMARKS

This thesis generated insights into the neural and affective signatures of connectedness between parents and adolescents and between people in general, which is operationalized by responses to eye contact and empathy. Overall, our findings show that during adolescence, parents are still highly attuned to their child at the neural and affective level. In addition, adolescents report to feel more connected with their parents than with unknown others, although this was not directly reflected in stronger neural responses. Another interesting finding is that making eye contact for a prolonged period generally enhanced the socio-emotional connection between people, both between parents and adolescents and with unknown others. For individuals with a history of CEM and depressed adolescents eye contact is less socially rewarding, however, and does not seem to foster a stronger connectedness with others. Studying the psychobiological underpinnings of affiliative bonding, including the parent-adolescent bond, brings us a step closer to unraveling how such bonds are established and maintained during adolescence. And even more important: Once we know how these bonds are established, we might be better able to modify and *repair* these bonds in situations in which they for some reason got disrupted.