Exploring the self in adolescent depression: neural mechanisms underlying social evaluations and self-views from a parent-adolescent perspective

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GENERAL DISCUSSION

This dissertation examined affective and neural responses to social evaluations and self-views from a parent-adolescent perspective in healthy control adolescents and adolescents with depression, as well as their parents. The goal of this effort is to increase our knowledge about alterations within underlying (neural) mechanisms related to self-processing in adolescent depression, and bi-directional influences of parent-adolescent interactions. This chapter summarizes the main findings of this dissertation, and it includes a discussion about how these findings extend the literature, both within the parent-adolescent context, and within the context of adolescent depression. Finally, I will discuss clinical implications and future directions.

SUMMARY OF MAIN FINDINGS

A crucial first step in understanding social evaluation processing within the parent-adolescent context was to identify how *parents* process feedback about their adolescent child, which might be important for targeting awareness of parents' own perceptions and reactions to feedback about their child. In **Chapter 2**, we investigated how parents react on an affective and neural level to *vicarious* praise and criticism about their adolescent child. Results demonstrated that parents' mood increased after receiving vicarious praise, and decreased when receiving vicarious criticism – especially when this criticism was *inconsistent* with their views of the child. Vicarious social feedback engaged brain regions related to social saliency (i.e., ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), anterior insula (AI)) and mentalizing (i.e., dorsomedial PFC (dmPFC), inferior frontal gyrus (IFG), posterior cingulate cortex (PCC), precuneus). These areas are also commonly activated in response to feedback about the *self*. Finally, parents who *generally* viewed their child more positively showed amplified mood responses to both vicarious praise and criticism, and this criticism elicited increased activity in left IFG, insula, and thalamus.

Next, in **Chapter 3,** we examined how *parental* praise and criticism is processed – in terms of affective and neural responses – by adolescents *without* psychopathology, and whether and how self-views are incorporated in this processing. We found that parental praise improved mood and increased activity in a set of brain regions supporting social cognition, including temporoparietal junction (TPJ), posterior superior temporal sulcus (pSTS), and PCC/precuneus. Parental criticism worsened adolescents' mood, especially when this criticism did not match adolescents' own self-views. Furthermore, parental criticism was related to increased activity in areas related to salience processing (i.e., AI, ACC), and social cognition (i.e., dmPFC, IFG, temporal poles). In terms of individual differences, having a more positive self-view *in general* and perceiving higher levels of parental warmth in daily life were associated with elevated mood throughout the task, but we found no evidence of a significant impact on neural responses to feedback.

As a next step, we aimed to gain important insights into key features of depression, i.e., (neural) sensitivity to both positive and negative contexts and negative self-views, and their impact on feedback processing. To do so, in **Chapter 4**, we investigated affective and neural responses to parental praise and criticism in adolescents with depression and compared them to adolescents without psychopathology. Even though adolescents with depression were responsive to parental feedback, they had blunted mood responses after parental praise compared to adolescents without psychopathology. We did not find differences in mood after parental criticism. Parental praise consistent (vs. inconsistent) with adolescents' own self-views improved mood independent of depression status, while criticism consistent with self-views resulted in *smaller* mood increases in adolescents with depression. Adolescents with depression exhibited increased activity in response to parental criticism in areas related to saliency (i.e., subgenual ACC), mentalizing (i.e., left temporal pole), and memory (i.e., left hippocampus and parahippocampal gyrus). Parental praise was associated with *decreased* activity in right visual cortex in adolescents with depression. Parents of adolescents with depression generally viewed their child less positively, but this did not differentially impact adolescents' affective or neural responses to parental feedback. Exploratory analyses revealed that outside the scanner, adolescents with depression recalled words indicative of criticism more often than words indicative of praise, while adolescents without psychopathology recalled a similar amount of praise and criticism.

Finally, understanding how adolescents with depression engage in *positive* autobiographical memory imagery may be important for targeting other core features of depression related to negative self-perceptions and low mood. Therefore, in **Chapter 5**, we explored whether adolescents with depression reported lower memory pleasantness and vividness during positive (and neutral) autobiographical memory reliving. Second, we investigated whether spatial and temporal characteristics of neural (sub)networks during reliving are related to i) memory valence and vividness, and ii) adolescent depression. Adolescents with depression reported reduced pleasantness when reliving positive autobiographical memories, while we found no differences in memory vividness. Using event-related independent component analysis (eICA), we identified a broad autobiographical memory network, and subnetworks specifically related to reliving positive vs. neutral autobiographical memories. These subnetworks included a 'self-referential processing network' including PCC, precuneus, mPFC, and TPJ, anti-correlating with parts of the central executive network and salience network. Finally, adolescents with depression showed aberrant activation patterns in this 'self-referential processing network' during memory reliving when reliving *less* pleasant memories, being dependent on memory vividness. However, activation was *not* affected when reliving highly pleasant memories. These findings underline the potential of targeting positive memory reliving in therapeutic interventions to treat adolescent depression.

NEURAL RESPONSES TO PRAISE

In both adolescents and their parents, we found that receiving praise (about the adolescent) was related to increased activity in areas of the mentalizing network, i.e., PCC and precuneus, and additionally in the TPJ and pSTS in adolescents, and in the vmPFC in parents (**Chapter 2, 3**), see Figure 1. It seems plausible that receiving praise elicits cognitive processes that relate to the interpretation why this praise has been given by the messenger, to further decide whether it is personally relevant and should be integrated with one's own views or not (Silk et al., 2017). Interestingly, as outlined in **Chapter 1**, these areas overlap with both the default mode network, and the autobiographical memory network. Furthermore, in response to positive (vs. neutral) autobiographical memories, increased activity was found in adolescents in a network with similar central nodes, i.e., mPFC, TPJ, PCC, and precuneus (**Chapter 5**). Activation in these areas may support a representation of the 'narrative self', through self-referential evaluations of the significance, value, and meaning of (positive) stimuli (Davey & Harrison, 2022). These findings might suggest that for typically developing adolescents, and their (overall healthy) parents, processing praise about the adolescent – a relatively common experience –, as well as (for adolescents) reliving positive autobiographical memories, may rely on default state activity of the brain, which in principle reflects the representation of the positive self (Yang et al., 2016). Furthermore, prior studies proposed that subnetworks within the default mode network may particularly contribute to affective social processes, such as empathy, where vmPFC and PCC are primarily involved, as well as to more cognitive social processes, such as mentalizing, where dmPFC and TPJ are mainly involved (Bzdok et al., 2013; Feng et al., 2021; Li et al., 2014; Lieberman et al., 2019). This specific involvement of the vmPFC in affective *social* processes corroborates with our finding that increased activity in vmPFC was only found in parents receiving praise (about their child), and not in adolescents (about themselves).

Interestingly, both parents and adolescents felt more positive after receiving praise, but we did not find increased activity in ventral striatum in response to praise (**Chapter 2, 3, 4**), contradicting prior social interaction research (Feng et al., 2021). Given that we preprogrammed the feedback in such way that two consecutive words were never of similar valence, in combination with a neutral condition with personality traits that in fact can be quite ambiguous, the feedback was rather unpredictable for participants. In essential, participants could be criticized at any moment during the task. Additionally, the absence of any learning component (i.e., linking a certain stimulus to a certain outcome) may also explain the absence of VS activity in response to praise. That is, we optimized our design to specifically model neural responses when *receiving* feedback, and not during the *anticipation* of feedback, which may be another valuable perspective. For instance, prior studies suggest that adolescents with depression show reduced striatal responses, particularly to anticipation of reward (Keren et al., 2018). Remarkably, we found that adolescents (but not parents), exhibited increased VS activity in response to *criticism* (vs. praise) (**Chapter 3**), see Figure

2. Increased VS activity is also frequently observed in adolescents in response to social *exclusion*, but not in young adults (Vijayakumar et al., 2017). Speculatively, the striatum may respond to negative social stimuli more often in adolescence than in adulthood, consistent with increased salience of social evaluation during adolescence (Lamblin et al., 2017). This suggestion dovetails with our finding that adolescents, with and without depression, felt more negatively after performing the parental social feedback task, despite receiving an equal amount of positive and negative feedback (**Chapter 3, 4**), and with the idea that adolescence is a period marked by heightened sensitivity to social evaluation (Schriber & Guyer, 2016).

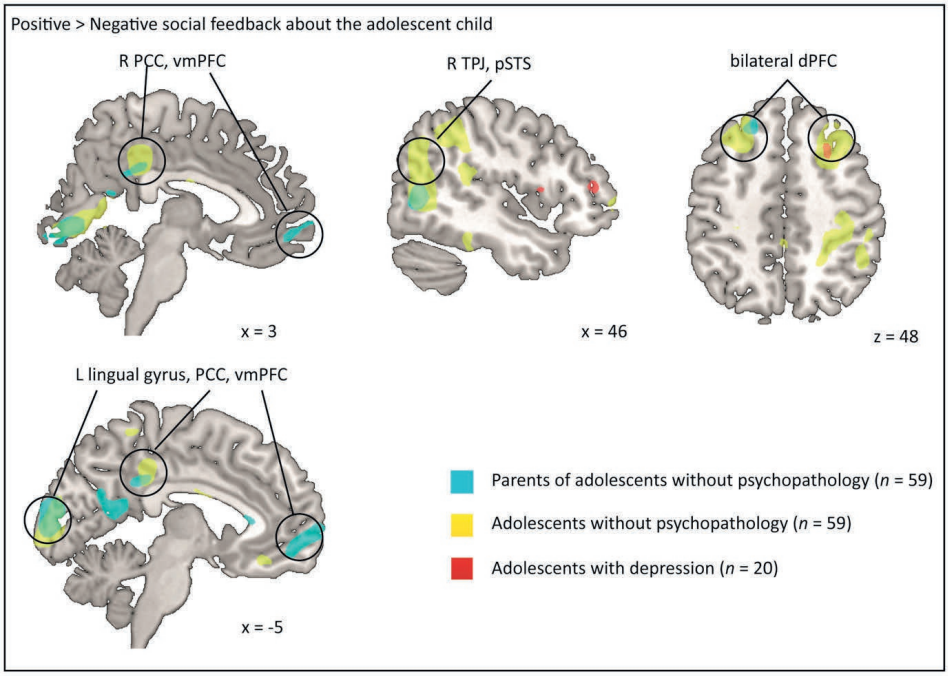

Figure 1. Neural responses to praise about the adolescent child in parents of adolescents without psychopathology (blue), adolescents without psychopathology (yellow), and adolescents with depression (red). Abbreviations: dPFC = dorsal prefrontal cortex; PCC = posterior cingulate cortex; pSTS = posterior superior temporal sulcus; TPJ = temporoparietal junction; vmPFC = ventromedial prefrontal cortex.

NEURAL RESPONSES TO CRITICISM

Receiving criticism about the adolescent negatively impacted mood and resulted in similar activation patterns in both adolescents and their parents, i.e., increased activity in areas related to social saliency: AI and ACC (**Chapter 2, 3**), see Figure 2. These findings dovetail with prior research about negative social evaluation from *unfamiliar* others (Cacioppo et al., 2013; Feng et al., 2021; Rotge et al., 2015), and suggest that (vicarious) criticism about the adolescent child is highly salient for both parents and adolescents. Furthermore, increased activity was found in both groups in areas important for mentalizing, i.e., dmPFC and IFG (Molenberghs et al., 2016). These findings further attest that receiving criticism about one's child can be very impactful for parents, which in turn may have consequences for parental reactions toward both the criticizer and the child itself. That is, depending on the strength of their emotions – which in turn depends on their own views of the child (**Chapter 2**) – as well as their emotion regulation skills, parents might minimize the critique, blame the criticizer, criticize the child themselves, (over)praise the child, or they just let it happen (Brummelman et al., 2017; Brummelman & Thomaes, 2017; Vogels & Perunovic, 2020). These different reactions each can have different outcomes, and ultimately can impact on adolescents' views of themselves (Harter, 2015). In a similar vein, receiving parental criticism can be very impactful for adolescents, with similar reactive consequences. Within the family context, adolescents are therefore especially vulnerable: both direct feedback, and feedback received via the parent, may impact their self-views and emotional well-being. Moreover, perceiving one's parent as critical may over time result in reactive or defensive responses, which further encourages negative parental responses, inducing a vicious cycle of negative parent-child interactions (Peris & Miklowitz, 2015). An interesting question for further research is whether criticism from parents would result in increased activation compared to criticism from peers, or non-significant others, and whether self-views are differentially impacted.

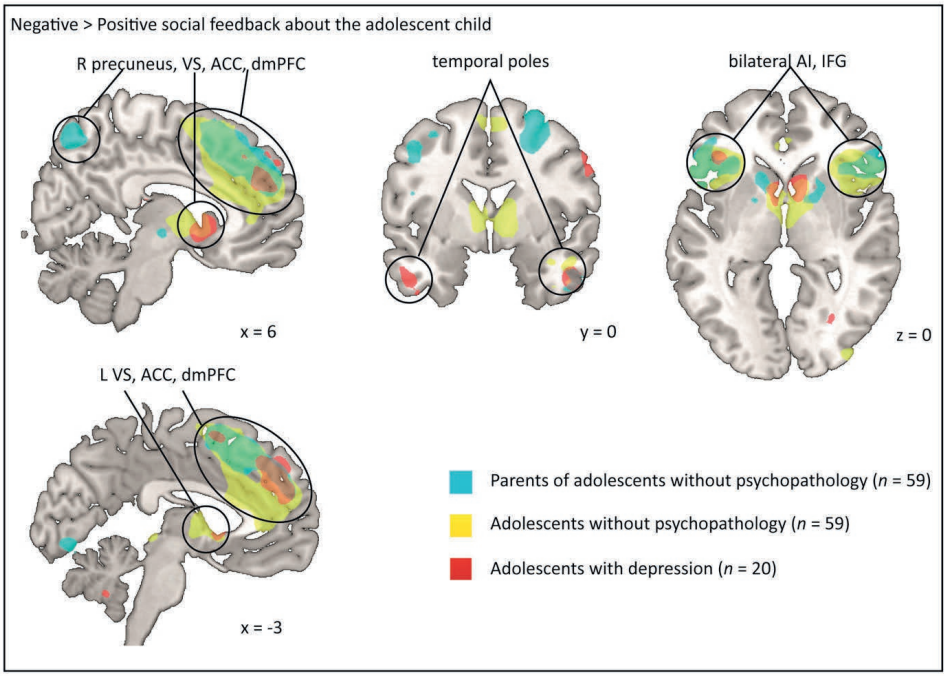

Figure 2. Neural responses to criticism about the adolescent child in parents of adolescents without psychopathology (blue), adolescents without psychopathology (yellow), and adolescents with depression (red). Abbreviations: ACC = anterior cingulate cortex; AI = anterior insula; dmPFC = dorsomedial prefrontal cortex; IFG = inferior frontal gyrus; VS = ventral striatum.

SELF-VIEWS AND PARENTAL VIEWS

Interestingly, in both parents and adolescents, we found that feedback *inconsistent* with self-views or views of the child, resulted in a more negative mood. Especially criticism inconsistent with own views resulted in elevated negative mood (**Chapter 2, 3**), in line with prior work (Sedikides & Gregg, 2008; Stinson et al., 2010; van Schie et al., 2018). Feedback that confirms existing beliefs can give a sense of predictability, even when negative, resulting in a higher mood, compared to feedback mismatching own beliefs (Vandellen et al., 2011). Despite these robust findings on the level of affect, we did not find any evidence of consistency of one's own views with the provided feedback impacting *neural* responses to praise and criticism. Prior work on self-evaluations demonstrated a crucial role for the mPFC, both in adults (Denny et al., 2012), and adolescents (Pfeifer & Peake, 2012), with the ventral part of the mPFC being more sensitive to affective and motivational aspects, and the dorsal part to cognitive aspects. Increased mPFC activity to self-relevant stimuli has been linked to signaling personal relevance and value (D'Argembeau, 2013). In adolescents, it has been shown that evaluating personality traits resulted in valence-dependent recruitment of the vmPFC: evaluating negative traits considered as applicable (vs. inapplicable) was related

to more vmPFC and pregenual ACC activity, while the opposite was found for positive traits (Barendse et al., 2020; Cosme et al., 2019). Although we did not find such effect, larger sample sizes might be needed to capture more fine-grained effects on a neural level. Moreover, in self-evaluation paradigms, participants are directly asked to evaluate to what extent certain personality characteristics fit with the self, which might result in differential processing compared to neural responses to *being* socially evaluated.

Another interesting observation was that both parents and adolescents generally saw the adolescent child in a positive light, rating many positive personality characteristics as applicable, and many negative characteristics as inapplicable to the adolescent child (**Chapter 2, 3**). Viewing oneself or one's child positively is a robust finding in healthy individuals (Cohen & Fowers, 2004; Murray et al., 1996; Sedikides & Gregg, 2008; Taylor & Brown, 1988; Wenger & Fowers, 2008). In general, people are highly motivated to maintain one's positive view, which promotes emotional well-being (Alicke et al., 2020). Interestingly, in parents, having more 'rosy' glasses when viewing the child resulted in amplified mood responses to both praise and criticism about the child, whereas in adolescents, viewing oneself more positively related to an overall higher mood, independent op feedback valence. Possibly, for adolescents, a more positive self might be a proxy for a better self-image and higher self-esteem (Harter, 2015), as feedback generally has less impact on their mood. For parents, however, viewing one's child more positively might index a certain level of empathy for their child, as they literally feel more positive after praise and negative after criticism about their child. This idea corroborates with our neural findings in these parents, where they exhibited increased activity in areas related to empathy (left IFG) and pain processing (insula, thalamus) in response to vicarious critique. Indeed, a recent large meta-analysis revealed that particularly left IFG appears to be a core node of the affective empathy network, and recruitment may reflect the level of subjective emotional distress or involvement in empathetic responding. Furthermore, insula and thalamus are particularly involved in processing of pain (Kogler et al., 2020). It seems thus sensible that viewing oneself vs. one's child positively are separate constructs, meaning that how one views the adolescent child, goes much further than an extension of one's self-image. As direct comparisons are lacking, future research should tap into this, and further validate and replicate our findings.

DAMPENED AFFECTIVE RESPONSES IN ADOLESCENT DEPRESSION

While adolescents with depression were responsive to praise, they showed blunted positive mood to parental praise as well as intermediate parental feedback (**Chapter 4**), and blunted pleasantness responses to positive autobiographical memories (**Chapter 5**), compared to adolescents without psychopathology. These findings align with prior studies (Rappaport & Barch, 2020; Werner-Seidler et al., 2017), as well as with the emotion context insensitivity (ECI) hypothesis (Bylsma et al., 2008; Rottenberg et al., 2005) discussed in **Chapter 1**. This dampened positive affect may be indicative of anhedonia, a core feature

of depression (Pizzagalli, 2014), and could reflect a more negative experiential self (Davey & Harrison, 2022). However, we did not find evidence for adolescents with (vs. without) depression being either more or less responsive to parental criticism, contradicting ECI. Thus, although parental criticism generally was more in line with their self-views, and therefore maybe also more expected, criticism did not result in blunted negative mood responses. Adolescents with depression even seemed to be more sensitive to parental criticism, as indexed by increased neural activity in subgenual ACC and hippocampus, even though they did not show heightened sensitivity in terms of affective responses. However, criticism in line with self-views resulted in smaller mood increases compared to adolescents without psychopathology (**Chapter 4**). For adolescents with depression, even though identifying with multiple negative personality characteristics, it might feel more threatening to hear this criticism from their parent, resulting in lower mood responses. Possibly, they take their self-views less into account when reacting to parental criticism, further fueling their negative feelings and in turn, negative self-views. It could also be that when receiving criticism matching with self-views, which is not per se something to feel bad about (**Chapter 2, 3**), these adolescents show smaller mood increases, as their mood to more neutral stimuli (e.g., intermediate parental feedback) might also be blunted (**Chapter 4**). Investigating emotional reactivity to more neutral stimuli in adolescent depression might be an important direction for future research, as differences in this type of reactivity might also have broader implications for interpretation of prior positive and negative emotional reactivity findings (Bylsma, 2021). For instance, dampened affective responses to more neutral stimuli could result from an interpretation bias in which adolescents with depression prefer more negative explanations for rather ambiguous situations (Everaert et al., 2017).

NEGATIVITY BIASES IN ADOLESCENT DEPRESSION

In line with prior work (Orchard et al., 2019), adolescents with depression had more negative self-views, i.e., rating positive personality characteristics as less applicable to the self, and negative characteristics as more applicable compared to adolescents without psychopathology. Moreover, adolescents with depression showed dampened affective responses to parental praise (**Chapter 4**), as well as dampened pleasantness responses when reliving their positive self (**Chapter 5**), further underlining their more negative narrative self, in the present and possibly also across time. Furthermore, these adolescents recalled more negative compared to positive feedback words about themselves, while adolescents without psychopathology recalled a similar amount of positive and negative feedback words. Together with increased hippocampal activity in response to parental criticism (**Chapter 4**), these findings point towards a negative memory bias, but also a selective attention toward negative stimuli (Everaert & Koster, 2020). These findings thus suggest that multiple negativity biases play a role in adolescent depression, and relate to other key features of depression, such as low mood, emphasizing the complexity of the disorder (Everaert & Koster, 2020).

NEURAL NETWORKS AFFECTED IN ADOLESCENT DEPRESSION

Adolescents with depression exhibited neural sensitivity to social threat contexts, as indexed by increased activity in subgenual ACC and memory-related areas (left hippocampus, parahippocampal gyrus, fusiform gyrus) in response to parental criticism, compared to adolescents without psychopathology (**Chapter 4**). Furthermore, aberrant activity in a self-referential processing subnetwork of the default mode network was found, encompassing major nodes in mPFC, TPJ, PCC, and precuneus, in adolescents with depression, particularly when reliving less pleasant autobiographical memories (**Chapter 5**). With the key coordinating role of the mPFC, this network also integrates interoceptive information, which forms the core part of the *experiential* self, and in turn can influence the content of the *narrative* self, and vice versa (Davey & Harrison, 2022). Interestingly, subgenual ACC and the hippocampal formation, i.e., hippocampus and parahippocampal gyrus, have important functional relations to (parts of) the default mode network, involved in self-related processing (Andrews-Hanna et al., 2010; Buckner et al., 2008; Mulders et al., 2015), that may underlie the overall aberrant self-processing in adolescent depression. A hyperactive subgenual ACC is a quite robust finding in depression (Disner et al., 2011; Mayberg et al., 2005; Silk et al., 2022; Silk et al., 2014). The subgenual ACC, having dense connections with limbic structures, such as the amygdala, constitutes an affective network important for emotional processing (Benschop et al., 2022; Li et al., 2018). In turn, the subgenual ACC projects information from this affective network to the central executive network, which results in top-down emotion regulation (Disner et al., 2011; Scharnowski et al., 2020). A hyperactive subgenual ACC in adolescents with depression may therefore suggest either inability to inhibit the limbic system, or requirement of increased effort to regulate emotions when confronted with parental criticism. Although our amygdala finding did not survive correction for multiple comparisons, and therefore replications of our findings are crucial, a hyperactive limbic system, as has been reported in meta-analyses in depression (Fitzgerald et al., 2008; Hamilton et al., 2012; Li & Wang, 2021), seems plausible within this context.

Furthermore, we found decreased activity in visual cortex (i.e., right lingual gyrus, calcarine fissure, and fusiform gyrus) when adolescents with depression (vs. adolescents without psychopathology) received parental praise (**Chapter 4**). Interestingly, similar activation was found in the visual cluster when parents received praise vs. criticism about their own child (**Chapter 2**), and when female adults received positive vs. negative social feedback from a stranger (van Schie et al., 2018). These findings are in line with prior work showing that visual cortex is sensitive to emotional and/or arousing stimuli (Phan et al., 2002). Recently, a neuro-feedback study found that youth with depression who exhibited increased activity in self-referential and visual areas during recall of positive autobiographical memories while seeing one's own happy face, showed reduced depressive symptoms after neuro-feedback (Ahrweiler et al., 2022). These findings point towards an important role of responsiveness to positive self-related stimuli, as indexed by increased activity in visual areas, which might

be affected in adolescent depression. Possibly, parental praise evoked diminished sensory-emotional/arousing responses in adolescents with depression, which was also reflected in blunted affective responses, but more research is needed to further investigate this.

STRENGTHS AND LIMITATIONS

The studies presented in this dissertation yield valuable new insights in social- and self-related processing within the parent-adolescent context, and within the context of adolescent depression. With the use of ecologically valid and realistic functional magnetic resonance imaging (fMRI) paradigms, we were able to identify key neural networks involved in both positive and negative social feedback processing and positive autobiographical memory reliving. Currently, the field is predominated by paradigms involving *negative* affective stimuli (Rappaport & Barch, 2020), utilized for instance by the 'Cyberball' task (Vijayakumar et al., 2017). Our findings contribute to the understanding of the impact of *positive* emotional stimuli on affective and neural responses, in general, and specifically related to adolescent depression. Furthermore, our multi-method approach with extensive study procedures yielded rich data about individual characteristics from the perspective of both adolescents *and* their parent(s), as well as about brain-behavioral relationships from different methodological perspectives, for instance by utilizing both daily life ecological momentary assessments (EMA) and fMRI measurements. Combining multiple approaches and perspectives can be important for hands-on recommendations for clinical practice. Lastly, the inclusion of both mothers *and* fathers provided relevant insights and allowed for more generalizable conclusions, as most fMRI studies focusing on the parent-child relationship only included mothers. While we found some first indications for differential activation patterns in mothers and fathers in response to vicarious feedback, more research with larger sample sizes is needed to draw valid conclusions.

The studies included in this dissertation should also be considered in light of some limitations. First, the sample size of the RE-PAIR study, particularly involving families with an adolescent with depression, was relatively small. It was especially difficult to get these families to participate in an extensive study, which became even more challenging during the COVID-19 pandemic. Although of the 35 families with an adolescent with depression participating in RE-PAIR, still 27 families (77%) participated in the fMRI part (participation families with an adolescent without psychopathology: 65/80 = 81%), five adolescents could not participate due to braces, resulting in a final sample of 22 adolescents with depression. Depression severity did, however, not differ between adolescents with depression who did vs. did not participate in the fMRI part of RE-PAIR. Nevertheless, larger sample sizes are needed to further test reliability of our findings. Moreover, adolescents with depression had quite some comorbid disorders, particularly anxiety disorders. Although comorbidities are frequently observed in adolescent depression (Avenevoli et al., 2015), these should be taken into account when interpreting our findings. For instance, receiving social feedback

or reliving positive autobiographical memories while having a social anxiety disorder can greatly impact the affective and neural responses (Krans et al., 2014; Rappaport & Barch, 2020). Third, as findings from the vicarious and the parental social feedback task are not one-to-one comparable, we were not able to disentangle social feedback processes particularly related to adolescence vs. adulthood. Related to this, we only incorporated feedback from parents in our design, and not from other relevant others, such as peers. Since adolescence is a period of heightened social sensitivity, particularly toward peers (Schriber & Guyer, 2016), it remains an open question whether parental feedback would be more impactful during adolescence compared to adulthood, and whether feedback from peers compared to parents would result in differential responses.

CLINICAL IMPLICATIONS

The findings reported in this dissertation support the imperative that several aspects of the parent-child relationship can be targeted in clinical practice to effectively improve the adolescent mood and potentially also reduce symptoms in adolescent depression. First, although adolescents with depression seem to benefit less from parental praise, by showing blunted mood after receiving a compliment from one's parent, parental praise in line with their self-views still boosted their mood. Relatively, this mood-boosting effect after applicable praise was not different from adolescents without psychopathology (**Chapter 4**). These findings may convey an important clinical implication: for parents and adolescents, it may be important to identify characteristics that they both value in the adolescent. In the context of an intervention, parents could learn to focus more on actively mentioning these valued characteristics of the child, in order to boost adolescents' mood, and subsequently, adolescents' self-views. Furthermore, teaching parents to mix criticism with praise, and to deliver criticism in a specific and constructive way, may reduce negative affective feelings and positively impact the family environment (Peris & Miklowitz, 2015). Actively involving parents in treatment may therefore have a large added value, which is consistent with findings showing that involvement of parents in adolescents' cognitive behavioral therapy improves therapy outcomes in adolescents with depression (Oud et al., 2019).

Furthermore, our findings show that assessing not only adolescents' own views of themselves, their behaviors, and their emotions, but also their *parents'* view of them, might be important for clinical practice. Assessing multiple views gives a unique insight in more shared views of parent and child, next to self-negativity biases in adolescent depression. For instance, we found that not only adolescents with depression themselves showed negativity biases in self-views, also their parents viewed them more negatively as compared to parents of adolescents without psychopathology. That is, both adolescents with depression *and* their parents regarded positive feedback words as less applicable, whereas negative and intermediate feedback words were regarded as more applicable to the adolescent child. When taking a closer look, particularly feedback words that are

relevant to adolescent depression, such as gloomy, lazy, insecure, and emotional were relatively much more applicable to adolescents with depression compared to adolescents without psychopathology according to their parents (**Chapter 4** and additional analyses). These appraisals about what their adolescent child is experiencing may be true to a certain extent, given their adolescent's depressed state, but may also reflect some incorrect attributions and stigma. Furthermore, these appraisals may impact parental attitudes and responses toward the child (Johnco & Rapee, 2018). In turn, depressive symptoms in adolescents may color perceptions of parenting in a negative way, which may further impact the emotional climate within the family. Therefore, providing tools for parents to better understand their child emotionally and where behavior may stem from, may be a promising clinical intervention strategy to diminish symptoms in adolescent depression, and at the same time foster a healthier family climate. Recently, meta-analyses showed that attachment- and emotion-focused parenting interventions can reduce internalizing and externalizing symptoms in adolescents (Jugovac et al., 2022). Adolescents could in turn learn more adaptive ways to communicate their own thoughts and feelings towards their parents, making it easier for parents to interpret their child's emotional experiences and behavior.

Next to targeting parent-adolescent relationships, our findings underscore the relevance of clinical interventions that seek to strengthen adolescents' ability to recollect positive autographical memories. Mental imagery techniques may help adolescents in strengthening their *positive* self (Korrelboom et al., 2022; Pile et al., 2021). During positive memory recall, we did not find any differences between adolescents with and without depression in memory characteristics, suggesting that adolescents with depression are able to generate pleasant, vivid, and specific positive memories when specifically instructing them. Furthermore, although adolescents with depression reported reduced pleasantness of positive memories compared to adolescents without psychopathology, reliving positive vs. neutral memories still induced pleasant feelings, and vividness was not affected. Additionally, when memories were highly pleasant, adolescents did not differ in level of recruitment of a self-referential subnetwork (**Chapter 5**). Our findings therefore suggest that mental imagery might buffer positive feelings in adolescents with depression, making it a promising approach to reduce depression symptoms. However, in daily life, adolescents with depression may only occasionally think about their (past) positive self. In clinical practice, promoting positive memory recollection, not only to repair mood (positively impacting one's experiential self), but also for everyday use, may positively enrich one's narrative self in adolescents with depression. Furthermore, prior work in adults with depression demonstrated that positive autobiographical memories improves mood, only when in line with their current sense of self, whereas for healthy controls mood improvements occur regardless of whether this positive memory is concordant or discordant with their current self-views (Werner-Seidler et al., 2017). Interestingly, this finding fits well with our finding that parental praise in line with

self-views improves mood in adolescents with depression (**Chapter 4**). Another implication for clinical practice that might be valuable to further evaluate is to specifically target positive autobiographical memories that are in line with the current narrative self, to create the largest mood-boosting effects.

Lastly, although some interesting conclusions could be derived from this dissertation, heterogeneity in findings were also observed. For instance, adolescents with depression showed large individual differences in affective response patterns after receiving parental feedback. While some adolescents reported a stable low mood in response to parental feedback, independent of whether this feedback was praise or criticism, others were more blunted, or showed extreme reactivity to praise and/or criticism. Remarkably, reporting stable low mood regardless of valence seemed to be strongly related to having a comorbid social anxiety disorder (**Chapter 4** and additional analyses). Similarly, substantial individual differences were observed in activity in a self-referential network, depending on memory pleasantness and vividness, when adolescents with depression relived autobiographical memories (**Chapter 5** and additional analyses). These heterogeneities substantiate the complexity of the disorder and advocate to move beyond a one-size-fits-all-approach in depression. Recognizing subtleties of individual experiences and variable patterns might be essential to enhance our understanding of (adolescent) depression (Herrman et al., 2022).

FUTURE DIRECTIONS

The findings reported in this dissertation inspire future directions in (neuroimaging) research from a parent-adolescent point of view, and particularly related to adolescent depression. First, future studies should utilize longitudinal data collection to ascertain directionality of effects between neural sensitivities, the family environment and emergence of adolescent depression. In **Chapter 4**, we have shown that adolescents with depression might have a vigilant profile, indexed by: increased subgenual ACC and hippocampus activity when confronted with parental criticism, enhanced memory for this criticism, together with less mood improvement through parental praise, and negative self-views. To what extent this vigilant profile reflects a latent vulnerability that is the expression of an at-risk environment present (long) before depression-onset (McCrory & Viding, 2015), or whether this vigilant profile is a consequence of suffering from a depression, or both, are important questions that need further investigation. Furthermore, it would be interesting to examine whether negative parental appraisals about the child already exist (far) before actual depression-onset, and whether these appraisals play a role in the maintenance of adolescent depression. Longitudinal designs starting from infancy, or even prenatally, as well as intervention studies using a randomization approach, are necessary to unravel the possible emergence of more negative self-views, other negativity biases, and neural sensitivities, particularly related to the parent-child relationship, and relations with psychopathology, such as depression.

Furthermore, given the relevancy of fostering a positive self for mental well-being across the lifespan (Harter, 2015), and evidence that the self seems more fluid and malleable in early-adolescence (Rapee et al., 2019), future directions should strive for a better understanding of how the positive self develops, and where it could be strengthened during childhood and adolescence. For instance, prior work demonstrated that adolescents, compared to adults, not only felt more negative, but also updated their self-views more negatively in response to negative peer feedback, which might indicate that self-protective biases are still in development (Rodman et al., 2017). Given the important role parents play in identity development, being fostered by high levels of closeness and relatedness to parents (Branje et al., 2021), important questions are if and how self-views change in response to *parental* feedback, and whether there are critical time windows for the development of a positive self. More insights in updating processes of one's self-views after receiving parental praise and criticism could for instance be gained by asking to re-evaluate the applicability of personality characteristics. Although one's self-concept becomes relatively stable over time, a certain malleability is also important, to adapt to changing situations in life (Sedikides et al., 2021). In that sense, turning more negative self-views into positive ones is not an impossible mission, and unravelling the features of this malleability may be of particular importance.

Another direction for future research concerns combining fMRI and EMA methods to investigate relevant, ecologically-valid brain-behavioral relationships. Ecological validity and real-world relevance are often questioned in imaging research (Sequeira et al., 2021). By capturing day-to-day emotions and (perceived) behaviors over time, and relating these to neuroimaging measures, one may identify how certain neural activity contributes to real-life emotions and behaviors (Hasson & Honey, 2012; Powers et al., 2016). Although we did not find robust evidence for relationships between neural responses to parental praise and criticism and daily parental warmth and criticism using EMA (**Chapter 4**), linking neural correlates of sensitivity to social evaluation (in our case: parental feedback) to real-life perceptions of social evaluation, could inform bio-behavioral targets for clinical interventions (Sequeira et al., 2021). Therefore, such data might advance our understanding of associations between neural activity and adolescent depression.

Another interesting line of research not investigated in RE-PAIR, is how *reflected* self-views, i.e., adolescents' perceptions of how their parents view them, impact mood and neural responses to parental feedback in adolescents with and without depression (Pfeifer et al., 2009). As outlined in **Chapter 1**, the self is informed by our perceptions of how others –particularly parents and peers –view us (Cooley, 1902; Leary et al., 1995). This might imply that *actual* views of parents may not be important per se (since these views remain unknown to us), but even more so how we *think* that our parents view us. Rather, next to direct self-views, reflected self-views might play a crucial role in responses to feedback, whereas

actual views of parents may only be a proxy for these reflected views. This idea aligns with prior work suggesting that adolescents' own perception of the family environment, but not their parents' perception, is a powerful predictor of adolescents' emotional functioning and well-being (Berla et al., 2022; Janssen et al., 2021). This has important implications for clinical practice, as making parents aware that perceptions of parent and child can greatly differ, and encouraging parents to communicate with their child about self-views of the child, may help the child with depression in strengthening the positive self. It should be noted, however, that assessing reflected views, by asking: '*To what extent do you think that your mother/father thinks this personality characteristic applies to you?*' requires a certain cognitive capacity, that might be challenging for younger adolescents.

Finally, future work should address the role of parents in positive autobiographical memory recollection, and thus a positive narrative self, of their adolescent children. Prior research suggests that parents play a vital role in fostering autobiographical memorizing during early childhood (Fivush et al., 2011; McLean et al., 2007). In particular, the extent to which parents (in this case, mothers) elaborately discuss past shared memories and experiences with their child, i.e., elaborative reminiscing, shape autobiographical memory recollection skills of their children, with enduring effects, even into adulthood (Fivush et al., 2011). Intriguingly, using an intervention where mothers learned these elaborative reminiscing skills when their children were 1.5–2.5 years old, researchers found that at age 21, these emerging adult children had more connections between past and present self when telling narrative life stories, reported higher self-esteem, as well as lower depressive symptoms, compared to children in a control condition (Marshall & Reese, 2022). These findings indicate that parental reminiscing may have a long-lasting impact on the narrative self and well-being of offspring, having clinical potential. Parental reminiscing skill-training within the context of adolescent depression, might therefore be promising.

CONCLUSIONS

Taken together, this dissertation shows that parents, as well as adolescents with and without depression, are affected by social feedback about the adolescent child in terms of mood and neural responses. Particularly criticism about the child seems to be highly salient to parents and adolescents, both in terms of affective and neural responses. Both praise and reliving positive autobiographical memories activates areas important for self-referential processing in adolescents, which might reflect the representation of a 'positive self'. Aberrant self-related processing when reliving autobiographical memories and increased sensitivity to parental criticism might be key underlying neural mechanisms in adolescent depression. By feeling more negatively, viewing the self as more negatively, interpreting the environment as more negatively, memorizing past experiences in a more negative way, and focusing on negative events more often, adolescents with depression seem to have multiple negativity biases. These negativity biases are likely to negatively impact social relationships, and in particular the parent-child relationship, potentially further reinforcing negative feelings, a negative self, and associated biases. Interventions exploring and strengthening the *positive* self, in particular the positive self that still aligns with the current self, might be useful for treating, or even preventing adolescent depression.