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Major Depressive Disorder in Adolescents: Quality of Life, Concordance of Self- and Parental-Ratings, and Negative Attentional Bias

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Introduction

Prevalence of Depressive Disorders in Children and Adolescents

Depressive disorders are amongst the most prevalent mental disorders in children and adolescents. Shorey and colleagues (2022) conducted a meta-analysis on the international prevalence of depressive disorders in adolescents aged 10 to 19 years. A total of $N = 72$ studies, published between the years 2001 to 2020 and covering $N = 324{,}859$ participants from Asia, Europe, Africa, North America, Middle East, Oceania and South America, was included. Point prevalences of 34 % for elevated depressive symptoms, 8 % for major depressive disorder (MDD) and 4 % for dysthymia were found. Pooled one-year prevalence was found to be 8 % and lifetime prevalence was 19 %. The overall prevalence of depressive symptoms was found to have increased by 13 % between the time spans of 2001 to 2010 (24 %) and 2011 to 2020 (37 %) (Shorey et al., 2022). Mental health inflictions of COVID-19 measures indicate an increase in symptoms of depressive, and anxiety disorders in children and adolescents (Racine et al., 2020). During and after the COVID-19 pandemic, overall psychiatric disorder symptom severities of - especially female - adolescents, have increased significantly (Hawes et al., 2022; Zolopa et al., 2022). The age of onset for a large section of mental disorders is in childhood (Thapar et al., 2022), which highlights the vulnerability of children and adolescents regarding mental disorders. An early onset of interventions is crucial for the avoidance of severe symptom developments. Youth mental health is a predictor for physical and mental health later in life (Bernaras et al., 2019; Caspi et al., 2006; Hemmingsson et al., 2008; Kessler et al., 2007; Shorey et al., 2022), therefore, worsening of mental health in adolescents must be prevented. The most fatal direct consequence of depressive disorders is suicide, which is the second most common cause of death in 15- to 29-year-olds (Bernaras et al., 2019). Rates of adolescent suicide have been rising over the last decade (Curtin, 2020). As stated in the 2022 WHO world mental health report (World Health Organization, 2022), there is a need to enlarge the variety of therapeutic options and their accessibility to meet the increasing demand of therapy for depressive disorders. Understanding symptoms, manifestation and assessment of depressive disorders is crucial for designing and establishing new therapeutic approaches.

Clinical Symptoms of MDD

As defined by the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) of the American Psychiatric Association (2013), diagnosis of MDD must be indicated by the presence of at least two primary, and four additional symptoms. The primary symptoms include depressed mood and loss of pleasure or interest. Additional symptoms are insomnia or hypersomnia, changes in appetite or weight, indecision or poor concentration, low energy or fatigue, agitation or slowing of psychomotor functions, feelings of guilt or worthlessness, and recurrent thoughts of death or suicide (American Psychiatric Association, 2013). Rice and colleagues (2019) investigated differences in depressive symptomatology between N = 109 adults (mean age = 41.5 years) and N = 37 adolescents (mean age = 14.2 years), diagnosed with MDD. Mean total symptom number in adults was 7.1 and 7.5 in adolescents. The most common primary symptom in both subgroups was depressed mood, while loss of interest was more common in adults. In adults, predominant symptoms were depressed mood (98.2 %), loss of interest or pleasure (88.1 %) and feelings of worthlessness or guilt (85.2 %). Low energy (97.2 %), depressed mood (94.6 %), insomnia (86.5 %), and feelings of worthlessness or guilt (86.5 %) were highly prevalent in adolescents. Symptoms more common in adolescents than adults, that remained stable after sensitivity analysis, were weight gain (adolescents: 40.5 %, adults: 3.7 %; $OR_{\text{adolescent}}$ = 4.33), weight loss (adolescents: 31.4 %, adults: 7.4 %; $OR_{\text{adolescent}}$ = 4.33), insomnia (adolescents 86.5 %, adults: 63.3 % $OR_{\text{adolescent}}$ = 1.74) and low energy (adolescents: 97.2 %, adults: 70.6 %; $OR_{\text{adolescent}}$ = 3.33). These findings indicate that adolescents exhibit vegetative symptoms to a higher extent than adults. Furthermore, MDD is associated with symptoms interfering with social interactions. These symptoms include diminished desire for communication, difficulties in emotion identification und interpretation in others, higher sensitivity to rejection by peers, reduced cooperativeness, changes in social decision-making, competition avoidance and difficulties in social role fulfilment (Cho et al., 2019; Katschnig, 2006; Kupferberg et al., 2016).

Comorbid Symptoms and MDD-Related Impairments: Quality of Life

In addition to clinical symptoms as mentioned above, MDD has been linked to deteriorated quality of life (Cho et al., 2019; Katschnig, 2006). To operationalise the concept of quality of life, the term *Health-Related Quality of Life (HRQoL)* has been established. It refers to physical, social, and psychological aspects of health. (Hirschfeld et al., 2000; Testa

&Simonson, 1996). The three areas are considered as separate in the context of HRQoL. They can be influenced by multiple environmental and intraindividual factors (Testa &Simonson, 1996; Patrick et al., 1973). Simplifying, HRQoL can be seen as the individual perception of health status (Cho et al., 2019). Different domains of quality of life could be measured separately, employing multiple subscales or instruments (Testa &Simonson, 1996), but mostly including: physical, mental, and psychological health, social and global functioning, and well-being. If relevant in the context of a given condition, other domains assessing specific symptoms such as pain, energy, sleep, and appetite, can be included in the assessment of HRQoL (Berzon et al., 1993).

Supporting the association between MDD and HRQoL, a meta-analysis by Hofmann and colleagues (2017) found large increases in HRQoL, along with improvements of MDD symptoms, after MDD treatment in adults. Addressing effects of MDD on specific dimensions of HRQoL, overall mental health has been found to be severely impaired in MDD, compared to the general population, as well as to other affective disorders, such as anxiety disorder (Zayfert et al., 2002). Additionally, social functioning and subjective well-being can be affected by MDD (Cho et al., 2019; Katschnig, 2006). Impairments in social functioning and general HRQoL are often important motivational factors for affected individuals to seek professional help, since the inflicted burdens are perceived as severe (Hirschfeld et al., 2000).

Addressing physical dimensions of HRQoL, physical functioning, pain, and general health perception were found to be significantly inferior in MDD as compared to healthy individuals (Zayfert et al., 2002), and other mental health disorders (Schonfeld et al., 1997). In line with these findings, diverse links between depressive disorders and physical impairments, such as arthritis, diabetes mellitus, respiratory illnesses, cardiovascular diseases, and different kinds of chronic pain were reported by Scott and colleagues (2016). The reported associations were stronger if patients were young at the onset of the depressive disorder. Attempting avoidance of bias, exact age at onset was not assessed by the authors, since the data-assessment was performed cross-sectional and retrospective. These findings were supported by the results of Stubbs and colleagues (2017), who found that 17.7 % of a clinical sample had at least one physical illness in addition to MDD. In a never-depressed control sample, only 7.4 % of individuals had physical illnesses. In the same vein, Cho and colleagues (2019) identified older age, low income, low education level, unemployment, deficient subjective perception of health, obesity, and mental health problems to be specific factors contributing to low HRQoL in adult depression.

Psychological Assessment: Self- and Parental-Ratings of Depressive Disorders & HRQoL

For the assessment of depressive symptoms in children and adolescents, commonly self-reports as well as parental reports are considered. Kim and colleagues (2020) investigated the consistency of ratings in questionnaire responses between $N = 289$ parents and their adolescent children. Overall emotional distress, including depressive symptoms, was assessed cross-sectionally. Adolescents' age ranged from 12 to 17, and parents' age from 35 to 64 years. Levels of concordance within parent-adolescent dyads were low with a polychoric *r* score of 0.27. They identified a tendency of parents judging adolescents' depressive symptoms to be in the normal, non-depressive range. Meanwhile adolescents reported their symptom severity to be in the clinically conspicuous range. Concordances were particularly low for high school students, male adolescents, and father-child dyads. There was tendency for parents to underestimate symptom severity, especially of hardly observable, internalized symptoms. Lewis and colleagues (2014) similarly found underestimation of suicidal thoughts and behaviour in parent-reports, but overestimation for overall depressive symptoms, compared to the childrens' responses. They found self-reports of depressive symptoms to be better predictors for clinical depression than parental reports. In line with these findings, Ko and Choi (2015) found only 32.5 % of parental participants to be able to recognize MDD in their adolescent children.

Concerning HRQoL, Eiser and Morse (2001) conducted a systematic review and found observable behavioural, physical, and somatic aspects of quality of life to have higher concordance between self and parental- ratings ($r > 0.50$) than non-observable emotional and social aspects ($r < 0.30$). Rating concordances were found to be higher for chronically ill than healthy children, with no significant differences for age or gender. Northfield and colleagues (2023) conducted a meta-analysis on variables moderating reliable proxy ratings of adolescents' well-being. Overall concordance of parent- adolescent ratings was moderate. They found some evidence of the concordance declining with the age of adolescents, as sense of independence increases. Also, some evidence for parent-daughter dyads to have greater concordance was found, but gender effects remained inconclusive. Concerning the impact of the gender of the parents on the questionnaire response consistency, they found some evidence for maternal ratings to be more accurate in emotional domains than paternal. But overall, no difference was found between ratings of mothers and fathers. As predictors of concordance, they found characteristics of relationships such as communication, closeness, and warmth to be more valid than age or gender (Eiser & Morse, 2001). Concerning differences in concordance between internalized and externalized symptoms, Vierhaus and colleagues (2018) investigated the source of this variation and found no indication for these differences in concordance and could not identify internalizing behaviour to be less observable than its externalizing counterpart. They identified perceived observability of behaviour to influence concordance between self- and maternal reports. Internalized behaviour was only perceived as less observable by mothers, and not the adolescents.

Neurophysiology of MDD

Depressive symptoms are associated with structural, as well as functional cortical changes (Brakwoski et al., 2017). The frontoparietal network is associated with cognitive control of attention and emotion regulation and has been found to be affected by MDD (Kaiser et al., 2015; Palm et al., 2016; Razza et al., 2021; Zhang et al., 2021). MDD has been found to manifest as hypoconnectivity between frontoparietal and parietal systems, responsible for controlling externalised attention. Additionally, hyperconnectivity in the medial frontoparietal network, associated with internalized attention and self-referential processes, was found (Kaiser et al., 2015). In line with these findings, Grimm and colleagues (2008) found the left dorsolateral prefrontal cortex (DLPFC) to be hypoactive, whilst for the right DLPFC the opposite was shown, resulting in imbalances. These imbalances were linked to cognitions and behavioural characteristics of MDD, such as a cognitive bias, rumination and self-referential processing (Grimm et al., 2008; Kaiser et al., 2015), as well as to depressed mood (Kaiser et al., 2015). Another brain area associated with anhedonia, cognitive rumination and disrupted sleep patterns, is the lateral habenula, an epithalamic structure responsive to stress and bidirectionally connected to the hypothalamic-pituitary-adrenal axis (Gold & Kadriu, 2019). Kupferberg and colleagues (2016) found reduced reward system activation in response to social stimuli to be caused by serotonin deficiency and opioid receptor deactivation. This was further linked to social withdrawal in depressed individuals. Furthermore, they linked negatively biased perception of social information to hypoactivity of dorsal neocortical structures and to hyperactivity of the ventral system in response to social stimuli. Additionally, they associated increased sensitivity to rejection with reduced endogenous opioid release in the amygdala.

Neuropsychology of MDD: Attentional Bias

As stated above, neurophysiological investigations found imbalances in the frontoparietal network to be associated with depressive symptomatology (Grimm et al., 2008; Kaiser et al., 2015). A meta-analysis by Stuhrmann and colleagues (2011) identified several brain areas of face processing networks to show altered processing of facial stimuli in MDD. These alterations could further be linked to mood-congruent attentional bias as hyperactivation to negative, and hypoactivation to positive facial stimuli. In adolescents, overall attentional bias has been found to be a significant predictor of higher self-report MDD scores, but only explaining 10.1 % of the overall symptom variance (Klein et al., 2018). This finding was confirmed by the results of a randomized controlled trial (RCT) of Yang and colleagues (2016): the successful, experimental modification of attentional bias (i.e. reduction) was demonstrated to be linked to reduced depressive symptomatology in the adolescent treatment group, compared to a placebo control group. The term *negative attentional bias* refers to preferential processing of mood-congruent stimuli (LeMoult & Gotlib, 2019; Leppänen, 2006; Shane & Peterson, 2007; Stuhrmann et al., 2011; Suslow et al., 2020). Positive attentional bias refers to attentional bias away from positive stimuli which has been found employing between-, rather than within subject measures (Huang et al., 2022; Klawohn et al. 2020; LeMoult & Gotlib, 2019; Stuhrmann et al., 2011 Suslow et al., 2020). The origin of negative attentional bias in depressive disorders has been associated with cognitive rumination, as well as impaired disengagement from dysphoric stimuli. Hence, the phenomenon might be top-down as well as bottom-up controlled (Armstrong & Olatunji, 2012; Koster et al., 2011). Moderate to large effect sizes of negative attentional bias towards dysphoric pictures of scenes, as well as faces, were previously found (Sears et al., 2019; Suslow et al., 2020). Huang and colleagues (2022) also reported moderate to large effect sizes of negative attentional bias in eye-tracking paradigms employing angry and sad faces, but not for threatening or dysphoric pictures of scenes. Faces are popular stimuli for assessing attentional bias in depressive disorders (Leppänen, 2006; Stuhrmann et al., 2011). Processing of emotional faces is fundamental for social interactions, and social interacting as well as emotion processing is often impaired in depressive disorders (Stuhrmann et al., 2011).

Assessment of Attentional Bias

In studies investigating attentional bias, either reaction-time-based or eye-tracking measures are usually used to assess the degree of bias.

Reaction-Time-Based Measures. A task frequently employed for measuring attentional bias is the dot-probe task, which is a psychological task designed to measure latencies of responses. Typically, participants are presented with neutral-emotional stimuli pairs, followed by a dot in the location of either. They are instructed to react to the dot by pressing a button assigned to each of the two specific locations. With this setup, attentional bias is measured as response time (Macleod et al., 1986). Faster reaction times in congruent trials (dot appears in location of negative stimulus) and slower reaction in incongruent trials (dot appears in location of neutral stimulus) are interpreted as negative attentional bias (Macleod et al., 1986; Platt et al., 2015). Cognitive deficits caused by MDD include potentially decreased processing speed, which must be considered when evaluating reaction time, and consequently dot-probe tasks. Furthermore, dot-probe tasks have been found to sub-optimally differentiate between early and maintained attention (LeMoult & Gotlib, 2019). Sears and colleagues (2019) synthesized investigations of reliability of reaction time-based measures (mainly dot-probe tasks) and found overall reliability to be unacceptably low.

Eye-Tracking Measures. Eye-tracking has been found to be a more reliable method of measuring attentional bias than reaction time-based measures (Armstrong & Olatunji, 2012; Klawohn et al., 2020; Sears et al., 2019; Suslow et al., 2020). Although, whether reaction-time-based, or eye-tracking measures were employed for bias assessment, was not found to significantly moderate results of attentional bias assessments (Shamai-Leshem et al., 2022). Still, eye-tracking measures and subsequent gaze behaviour analysis allow for direct and continuous measuring of visual attention (Armstrong & Olatunji, 2012; LeMoult & Gotlib, 2019). Eye-tracking techniques can measure attention without motor components of processing speed, as active during button-pressing, causing temporal delay in reactions (Armstrong & Olatunji, 2012; Lange et al., 2018). Therefore, they further allow for differentiation between early and late stages of attention, as they overcome restrictions of portraying a single time point (Armstrong & Olatunji, 2012). Attentional bias in depressive disorders has been found if stimulus presentation exceeded 1000 ms. If presentation duration was below 500 ms, findings of attentional bias were mixed (Shane & Peterson, 2007).

Therefore, conclusions on attentional bias based on reaction-time should be complemented by analysis of gaze behaviour, to paint a bigger picture of attentional processes. Sears and colleagues (2019) even recommend presentation durations above 4 s to ensure reliable measures of attentional bias in eye-tracking tasks.

Calculation of Attentional Bias

For the analyses of attentional bias in gaze behaviour, generally mean fixation durations in areas of interest (AOIs) (instead of absolute values of fixation durations) are considered. In experimental setups with face pairs of one emotional and one neutral face, commonly mean fixation durations of neutral AOIs are subtracted from emotional AOIs, resulting in a relative bias score towards emotional categories. This relative bias score reveals the direction of individual attentional bias (Bodenschatz et al., 2019; Klawohn et al., 2020; Sears et al., 2019; Vazquez et al., 2018). In reaction time-based measures, calculation of relative bias is performed similarly: reaction times for congruent trials are subtracted from those of incongruent trials. Positive scores are interpreted as bias towards emotional, whereas negative scores indicate bias towards neutral stimuli (Klein et al., 2018). If group comparisons are performed, relative bias scores can be considered for comparisons or further, bias differentials can be calculated and considered for comparisons. Bias differentials have been found to benefit sensitivity for small effect sizes. They are estimated by subtracting relative bias towards negative from relative bias towards positive stimuli (Shane & Peterson, 2007).

Manifestation of Attentional Bias

Early Attentional Orientation (> 500 ms presentation duration). According to the vigilance hypothesis, early orientation towards stimuli reflects vigilance. Previous research focussed on vigilance in attentional bias mainly in anxiety disorders, rather than MDD (Armstrong & Olatunji, 2012). In anxiety disorders, attentional bias has been found to surface in early non-conscious orientation towards threatening stimuli, such as angry faces (Armstrong & Olatunji, 2012; Mathews & Macleod, 2005). This initial attention evolves into maintained avoidance of threatening stimuli resulting in decreased dwell time (Mathews & Macleod, 2005). Investigations on vigilance in MDD are sparse. As the first 500 ms (of reaction time-based or eye-tracking measures) portray important early attentional processes of orientation (Armstrong et al., 2010), an overview over recent studies targeting this time frame is given in the following section.

Results of a meta-analysis by Suslow and colleagues (2020) on the effect of MDD on first fixation duration were mixed. Studies found significantly longer or shorter first fixation durations on sad facial stimuli compared to control groups or found no significant effect at all. In a meta-analysis by Armstrong and Olatunji (2012), comparing MDD and control groups, no bias was found for early orientation towards negative stimuli. Similar findings of no bias in early orientation towards negative stimuli resulted from analyses of Huang and colleagues (2022). In contrast, Klein and colleagues (2018), and Yang and colleagues (2016) found adolescents diagnosed with MDD to show attentional bias towards sad stimuli in a visual search, and a dot-probe task. De Voogd and colleagues (2016) detected attentional bias towards negative stimuli in depressed and anxious adolescents only in a visual search, and not a dot-probe task. In a study by Duque and Vázquez (2015), attentional bias in depressed adults towards sad faces was significant in first fixation duration.

Concerning attentional bias towards threatening stimuli, some publications discovered negative attention bias in depressed adolescents performing a visual search task, but not in a dot-probe task (de Voogd et al., 2016; Klein et al., 2018; Platt et al., 2015) and this attentional bias to be correlated with depressive symptoms (r = .20) (Platt et al., 2015). Armstrong and Olatunji (2012) could not find bias in early orientation towards threatening stimuli during the first 500 ms of stimulus presentation, compared to healthy controls. This is in line with Duque and Vázquez (2015) finding no group differences in first fixation duration of angry faces.

Maintained attention (> 1000 ms presentation duration). According to the maintenance hypothesis, attentional bias can surface in prolonged attention to stimuli. In depressive disorders, attentional bias has previously been found to emerge mainly in maintained attention, as top-down cognitively controlled bias (Armstrong & Olatunji, 2012). Results of three meta-analyses are in line with this hypothesis: In an evidence synthesis of reviews and meta-analyses by Armstrong and Olatunji (2012), individuals with depressive disorders were maintaining gaze on dysphoric stimuli longer than healthy controls. Suslow and colleagues (2020) retrieved evidence of individuals with depressive symptoms exhibiting longer maintained gaze on dysphoric images and sad faces than healthy controls. Stimulus presentation durations ranged from 3 to 30 s. A meta-analysis by Shamai-Leshem and colleagues (2022) reported dysphoric attentional bias in formerly depressed individuals to be significantly larger than in healthy individuals without any episode of depressive disorders.

Additional publications support findings of negative attentional bias in prolonged attention in individuals with depressive symptomatology: An eye-tracking study performed by Duque and Vázquez (2015) demonstrated attentional bias towards sad faces in maintained attention, operationalised as total fixation duration. Previous findings of a dot-probe task indicated attentional biases to emerge in selective attention to sad faces in sad-neutral face pairs, if stimuli presentation exceeded 1000 ms (Gotlib et al, 2004). In a free-viewing eye-tracking paradigm, Klawohn and colleagues (2020) compared average dwell times of individuals with MDD and healthy individuals on sad-neutral face pairs. Healthy participants showed bias away from sad, resulting in increased dwell time on neutral faces, whilst the MDD group was found to dwell longer on sad than neutral faces (Depressed: M_{sad}=76.63 s ± 10.01, $M_{neutral}$ = 75.09 ± 11.52). Vazquez and colleagues (2018) investigated changes in attentional bias after 10 weekly CBT and Positive Psychology interventions. Before intervention, mean total fixation time on sad faces was longer than on neutral (M_{Sad} = 1.41 ± 0.36 s, M_{Neutral} = 1.33 ± 0.35 s), which significantly decreased after interventions (M_{Sad}: 1.25 ± 0.38 s; M_{Neutral}: 1.42 ± 0.47 s). Improvements in depressive symptoms assessed with Beck’s Depression Inventory II (BDI-II, Beck et al., 1996) were correlated with changes in attentional bias, measured as total fixation time (r = .26).

Concerning attentional bias of positive stimuli in patients diagnosed with depressive disorders, findings of meta-analyses by Huang and colleagues (2022), and Suslow and colleagues (2020) indicated adults to show significantly lower fixation durations of positive emotional stimuli than healthy participants. Individuals who recovered from MDD (Shamai-Leshem et al., 2022) and individuals with active MDD exhibited reduced attention towards positive stimuli, compared to healthy individuals (Armstrong & Olatunji, 2012; Shamai-Leshem et al., 2022; Suslow et al., 2020). In the same vein, considering stimuli type, healthy individuals were found to dwell longer on happy faces than on sad, neutral, or on threatening faces and longer on neutral faces than on sad faces. This is in line with findings of Vazquez and colleagues (2018), showing total fixation duration on happy faces to be increased after therapeutical interventions in patients with MDD. BDI-II scores of MDD were significantly associated with attentionally biased avoidance of happy faces. Contrary to those findings, analysing attentional bias in depressed individuals with a dot-probe task and presentation duration > 1000 ms, Gotlib and colleagues (2004) found no bias investigating happy-neutral stimuli pairs. Results from Klawohn and colleagues (2020) indicated dwell times on happy faces to be longer than on neutral faces, for individuals with depressive disorders and healthy groups. Similarly, bias of reduced attention towards happy faces surfaced in between-group comparisons, rather than within subject analyses of fixation durations in AOIs (Klawohn et al., 2020).

Publications covering attentional bias manifestation in maintained attention towards angry faces in individuals with depressive disorders are sparse. Leyman and colleagues (2007) detected attentional bias, operationalised as increased maintained attention towards angry faces, in a dot-probe task with angry-neutral face pairs (presentation duration > 1000 ms). Healthy controls showed an opposite bias towards neutral faces. In line with those findings, Vazquez et al. (2018) observed an altered pattern of mean total fixation durations of angry-neutral face pairs after therapeutic interventions (M_{Angry}: 1,213 ± 404 ms; M_{Neutral}: 1,448 ± 547 ms), while mean total fixation durations of angry and neutral faces hardly differed before interventions (M_{Angry}: 1,368 ± 378 ms; M_{Neutral}: 1,370 ± 409 ms). After interventions, total fixation time spent on angry faces decreased significantly. Contrary, Gotlib and colleagues (2004) found no bias analysing fixation durations of angry faces.

Summary. Taking overall findings of negative attentional bias manifestation into consideration, increased maintained attention (as measured with total fixation duration) to sad faces has been found to be a suitable indicator of MDD within- and between-subjects (Duque & Vázquez, 2015; Huang et al., 2022; Klawohn et al., 2020; Mathews & Macleod, 2005; Suslow et al., 2020). Manifestation in first fixation duration and angry faces remain inconclusive (Armstrong & Olatunji, 2012; Huang et al., 2022; LeMoult & Gotlib, 2019; Suslow et al., 2020). Performing between-group comparisons, dwell times on happy faces might as well be a suitable indicator, but since both depressed and healthy have been found to dwell longer on happy than neutral faces, this parameter does not seem to be suitable for within-subject operationalisation of attentional bias (Klawohn et al., 2020). Total fixation durations allow for assessment of overall maintained attentional capture of a stimulus. Gaze duration within the first 500 ms has been shown to be highly correlated with initial attentional orientation (Armstrong et al., 2010; Armstrong & Olatunji, 2012) and first fixation duration to capture initial attentional orientation (Suslow et al., 2020).

Summary: Attentional Bias in Adolescence. Concerning age effects on attentional bias in MDD, Huang and colleagues (2022) found younger age to significantly predict larger effect sizes. Noteworthy, their study sample consisted of adults aged ≥ 18 years. Previous findings indicate negative attentional bias to be inherent in adolescents diagnosed with MDD (de Voogd et al., 2016; Klein et al., 2018; Platt et al., 2015; Yang et al., 2016). Negative bias towards sad faces (de Voogd et al., 2016; Klein et al., 2018), angry faces (de Voogd et al., 2016; Klein et al., 2018, Platt et al., 2015) and sad word pairs (Yang et al., 2016) was reported. All mentioned publications employed reaction time-based measures, assessing early, rather than maintained attentional processes. No eye-tracking studies investigating attentional bias of adolescents diagnosed with MDD were found.

Considering the different levels of manifestation of depressive symptoms, this study aims to shed light on the subjective, psychological level (via the analysis of self and parental reports), but also on the objective behavioural level (via the analysis of the attentional bias using an eye tracking measure) of MDD in adolescents.

Hypotheses

Primary

1. MDD and HRQoL are expected to be of a negative correlative relationship in adolescents.
2. Low concordance of adolescent self- and parental-ratings of MDD is expected (Pearson's r = .20 to .39).
3. Moderate concordance of adolescent self- and parental-ratings of externalized HRQoL dimensions is expected (Pearson's r = .40 to .59).
4. Low concordance of adolescent self- and parental-ratings of internalized HRQoL dimensions is expected (Pearson's r = .20 to .39).
5. Total fixation durations of sad and neutral faces are expected to differ in adolescents diagnosed with MDD in a free-viewing eye-tracking task.

Exploratory

1. Is attentional bias towards sad stimuli manifested in first fixation duration in adolescents diagnosed with MDD, in a free-viewing eye-tracking task?
2. Is attentional bias towards angry stimuli manifested in total fixation duration in adolescents diagnosed with MDD, in a free-viewing eye-tracking task?
3. Is attentional bias towards angry stimuli manifested in first fixation duration in adolescents diagnosed with MDD, in a free-viewing eye-tracking task?

4. Do adolescents diagnosed with MDD exhibit relative bias towards angry or sad faces?
5. Is MDD symptom severity congruent between BDI-II and DISYPS-III-SBB-DES assessments?

Methods and Materials

Study Design

Data was collected as part of a larger, at time of thesis submission still ongoing, preregistered triple-blind RCT investigating changes in emotion regulation in adolescents with psychiatric disorders after a transcranial direct current stimulation intervention (DRKS-ID: DRKS00025601X). For the scope of this thesis, cross-sectional baseline data of adolescent participants diagnosed with MDD was analysed. Subsequent intervention and measures are described in Konicar and colleagues (2022) and are not part of the present thesis.

Participants

The total sample consisted of N = 17 adolescents of which n = 14 were female. Age at study participation ranged from 13 to 18 years (M = 15.59, SD = 1.54 years). Diagnoses of MDD were conducted by trained professionals / licenced clinical psychologists, according to ICD-10 (F32, F33) (World Health Organization, 2019), and performing the diagnostic interview for MDD in children and adolescents ("Diagnostisches Interview bei Psychischen Störungen im Kindes- und Jugendalter", Margraf et al., 2017). For study inclusion, an IQ score ≥ 70 was required. Cognitive performance assessments were either pre-existent from prior psychological assessments or performed in house, using Wechsler Adult Intelligence Scale–Fourth Edition (WAIS-IV, Wechsler, 2012) or Wechsler Intelligence Scale for Children–Fifth Edition (WISC-V, Wechsler, 2017). Participants had to have sufficient understanding of the German language to follow instructions. Informed consent was obtained prior to study participation. Exclusion criteria were acute suicidality, epilepsy and related seizure disorders, severe neurologic and psychiatric disorders, any metallic devices, and continuous benzodiazepine medication. Other psychopharmacological medication had to be held stable in dosage for 1 to 4 weeks prior to intervention start, depending on respective agent. Participants were recruited from the Department of Child and Adolescent Psychiatry of the Medical University of Vienna via informative flyers and booklets. Information material was distributed in-house, in hospitals, doctor’s, psychologist’s and psychiatrist’s offices, universities, and sheltered facilities for children and adolescents. The parental sample consisted of n = 15 mothers, n = 1 stepmother, and n = 1 father.

Instruments

A total of four instruments was used for data assessment. Behavioural, as well as psychological measures were employed.

Behavioural Assessment: Attentional Bias Task with Eye Tracking

Behavioural eye tracking data was collected during an Attentional Bias Task (ABT). The ABT was designed to capture attentional focus. Shifts in attention as found in MDD (Klawohn et al., 2020; LeMoult & Gotlib, 2019; Suslow et al., 2020) and described above, can be operationalised performing the ABT. During the ABT, participants viewed face pairs on a screen while gaze behaviour was monitored with an eye-tracking device. Similarly to the task design of Vazquez and colleagues (2018), neutral faces were presented simultaneously with happy, sad, or angry emotion-expressing faces. While the task also included happy faces, data analysis of this thesis focused exclusively on sad and angry facial expressions. The inclusion of happy faces was based on the broader experimental design of Konicar and colleagues (2022). Faces used in the paradigm stem from the FACES database of Max Planck Institute for Human Development (Ebner et al., 2010). The pictures are comprised of equal ratios of young (19-31 years), middle aged (39-55 years) and older (69-80 years) natural faces expressing emotions, with 50 % being female and all models being Caucasian. All faces are without distinct facial features such as piercings, beards, and tattoos to ensure average appearance over all faces (Ebner et al., 2010). Facial expressions were cut out oval and portrayed in black and white, to ensure gaze focus on the face and diminish distractions by hair, neck, and skin features, as shown in in Figure 1. During the task, each emotional category was represented by 28 faces paired with a neutral face of the same person. Pairs were presented with one face on the left, and one on the right side of the screen. Presentation side of emotional and neutral faces varied randomly. Stimuli pairs were presented for 4.5 s parallel to Sears and colleagues (2019). The task started with the depiction of a black screen for 0.5 s, followed by a white fixation cross. After presentation of the fixation cross for 0.5 s, a random number from one to nine appeared on the same location for 1 s. Participants were instructed to read the number aloud to ensure attention focus on the screen centre. Next, presentation of a face pair followed, with order of emotional stimuli type varying randomly. The procedure was repeated for all 84 pairs and the total duration of the task ranged from approximately 10 to 15 min. The whole task was performed while eye gaze behaviour was monitored. AOIs consisted of emotional facial expressions of the stimulus pairs. Outcome variables of interest were first and total fixation duration in seconds on angry and sad faces compared to neutral faces for assessment of bottom-up and top-down controlled attention.

Eye tracking during ABT was performed on a Tobii TX300 23"screen-based device with the Tobii Pro Lab operating software, version 1.171.34906 (x64). The sampling rate provided by the device was 300 Hz with a variability < 0.3 % under non-optimal conditions. Resolution of stimuli was 1929x1080. Tolerance for head movement was given with the TX300 and tracking mechanisms were robust to individual variations in facial constitution and skin colour. Ideal distance of participants to screen is 65 cm. The eye tracking technique applied with the TX300 is dark pupil tracking. Working mechanisms behind eye tracking as used here are eye position estimation via pupil centre identification and corneal reflection interpretation. Eye gaze behaviour was assessed during the ABT via Velocity-Threshold-Identification fixation filters which operated with fixation classifiers of 30 degrees/second thresholds. Data points below the threshold were classified as parts of fixations. Minimum duration of an observation to be classified as fixation was 60 ms (Tobii Pro AB, 2021).

Figure 1

Emotional Face Pair

Note. Sad-Neutral face pair as shown of the ABT.

Psychological Assessment: Self- and Parental-Ratings

Regarding self-report questionnaires, three instruments, namely the BDI-II (Beck et al., 1996), DISYPS-III-DES ("Diagnostik-System für Psychische Störungen nach ICD-10 und DSM-5 für Kinder und Jugendliche-III", Döpfner & Görtz-Dorten, 2017), and KIDSCREEN- 52 (Ravens-Sieberer et al., 2005) were used. For the third-party assessments, parental versions of the DISYPS-III-DES and KIDSCREEN-52 were performed. All questionnaires were designed and performed on the digital platform SoSci Survey (Leiner, 2019).

BDI-II. BDI-II is a self-report questionnaire with 21 items (Beck et al., 1996). It is used for the assessment of depressive symptom severity in adolescents and adults (≥ 13 years). The symptom scale according to Diagnostic Manual 4 (DSM-4, American Psychiatric Association, 1994) is covered, considering a time frame of the last two weeks, up to the date of questionnaire assessment. Items are answered in a scale format, where statements are corresponding to ascending severity. One of four statements must be chosen per item. Each answer is valued with 0 to 3 points. As outcome measure, a total score is calculated, with higher scores indicating higher symptom severity. Five categories of total scores and corresponding symptom severity have been identified (Beck et al., 1996). Table 1 gives an overview of total score categories. For the German version of BDI-II, Besier and colleagues (2006) conducted investigations of psychometric properties for adolescents. They found discriminant validity to be sufficient for most items ($> .5\ r_{it}$). Internal consistency was high (Cronbach's $\alpha = .92$-$.94$) and content validity was found to be good. Item-analyses revealed BDI-II to reliably measure symptom severity and discriminative validity was good. In the same vein, correlations with instruments/subscales assessing similar constructs were found to be moderate to good.

Table 1

Categories of BDI-II

Score Range	Interpretation
0-8	No Clinical Depression
9-13	Minimal Clinical Depression
14-19	Mild Clinical Depression
20-28	Moderate Clinical Depression
29-63	Severe Clinical Depression

DISYPS-III-DES. DISYPS-III is a diagnostical instrument for mental disorders in children and adolescents (age = 4.00-17.11 years) (Döpfner & Görtz-Dorten, 2017). The DISYPS-III survey battery includes instruments for multiple mental disorders. For the scope of this thesis, the instrument for clinical depression (DISYPS-III-DES) was considered. Parental- as well as self-rating instruments were used. For standardization and cutoff-calculation of the instrument, representative population and clinical samples were considered. For this thesis, clinical sample references were used. Representative clinical samples were based on the data of n = 461 (Mean age = 15.35 ± 1.70 years) patients diagnosed with clinical depression and n = 475 parents (mean age of children and adolescents = 14.87 ± 2.35 years) of the University Clinic for Adolescent Psychiatry in Cologne. Additionally, indicative reviews of subscale-scores were provided for estimating symptom severity. Factor analysis was performed and all items covering affective and behavioural symptoms were grouped in the subscale “Total Score Depression” (29 items). Additionally, a subscale assessing Competencies, Confidence, and Enjoyment was found to be valid (8 items). As another additional subscale, Impairment and Psychological Strain was included, which assesses impairments caused by the experienced depressive symptoms, but no indicative categories for score interpretations were provided by the authors. Concerning reliability, internal consistency was high. Response-style is scale-based, with every item providing four response categories displaying participants’ concordance with the statement. Item scores range from 0 to 3, with some items having to be reverse coded for score calculation. Scores are calculated as subscale-sums, divided by the number of items of the scale (Döpfner & Görtz-Dorten, 2017). Subscale score categories of the total score can be seen in Table 2 and in Table 3, corresponding categories of the Competencies, Confidence and Enjoyment subscale are depicted. Scores of participants were calculated for all three subscales of DISYPS-III-DES to get a more nuanced representation of the facets of MDD.

Table 2

Interpretation of Subscale Scores of Symptom Scales (Total Score)

Score Range	**Interpretation**
0.00-0.49	Inconspicuous
0.50-0.99	Mildly Conspicuous
1.00-1.49	Conspicuous
> 1.49	Very Conspicuous

Table 3

Interpretation of Subscale Scores of Competency Scales (Competency, Confidence and Enjoyment)

Score Range	**Interpretation**
> 2.49	High Competency
1.50-2.49	Average Competency
0.50-1.49	Low Competency
0.00-0.49	Very Low Competency

KIDSCREEN-52. KIDSCREEN-52 is a health-related quality of life questionnaire for children and adolescents aged 8 to 18 years (Ravens-Sieberer et al. 2005). The questionnaire is available in a self-report, and a caregiver version. The instrument includes

10 Rasch-scaled dimensions which are covered by 52 items. Development of the instrument included data from *N*=22.296 individuals from twelve countries. Internal consistency measured by Cronbach's α ranges from .77 to .89. The questionnaire is comprised of 10 subscales: Physical Well-Being, Psychologic Well-Being, Moods and Emotions, Self-Perception, Autonomy, Parent Relation and Home Life, Social Support and Peers, School Environment, Social Acceptance (Bullying) and Financial Resources (Table 4). Items are answered on a scale with five response options, and answers are valued with 1 to 5 points. There is no total score, but subscale scores are calculated. Before summing up the respective scores of a subscale, some items must be reverse coded. The resulting scores can be translated to T-values since subscales are Rasch-scaled. Ranges of subscale scores and T-values are depicted in Table 4. Mean scores of T-values are 50, with standard deviations of 10. Values above or below this range indicate very high, respectively very low HRQoL. In the current dataset, items for the Social Acceptance (Bullying) subscale are missing due to a shortcoming during the digitalisation process.

Table 4

Subscales of KIDSCREEN-52 Self- and Parental-Ratings with Corresponding Score- and T-Value-Ranges

Subscale	**Number of Items**	**Score Range**	**T-Value Range Self-Report**	**T-Value Range Parental-Report**
Physical Well-Being	5	5-23	12.13-73.20	9.35-71.23
Psychologic Well-Being	6	6-30	9.86-68.49	9.42-69.88
Moods and Emotions	7	7-35	7.92-70.91	-2.01-70.82
Self-Perception	5	5-25	12.10-69.78	6.93-70.98
Autonomy	5	5-25	10.19-68.75	4.74-67.95
Parent Relation and Home Life	6	6-30	9.93-65.87	5.70-69.22
Social Support and Peers	3	6-30	9.40-71.46	8.28-73.08
School Environment	6	6-30	14.02-73.80	9.55-72.50
Financial Resources	3	3-15	23.24-62.86	23.96-65.02

Experimental Procedure

Initial clinical study interviews took place at the Medical University Vienna in the Department of Child and Adolescent Psychiatry. Potential participants and caregivers were informed about the study procedures, intervention, and measures. Inclusion criteria were checked by trained professionals and written informed consent was obtained from caregivers and participants before study inclusion. Data was collected in two steps: After study inclusion, participants and their caregivers received E-mails containing links to the questionnaires (DISYPS-III-DES, BDI-II, KIDSCREEN-52 amongst others). Questionnaires were performed digitally, timely close to their next in-house appointment (approximately 1–3 days prior to behavioural measures). Total expenditure of time for all surveys was < 1.5 h. The in-house appointment started with a verbal introduction to procedures and general standardized information assessment through the experimenter. Measurements started with three paradigms on a PC (total duration < 30 min), which are not the focus of the current thesis. After completion, participants were asked to take a seat in front of the Tobii TX300 eye-tracking screen to perform the ABT. The experimenter explained the upcoming task starting with an introduction about eye-tracking, calibration, and the procedure of ABT. For performance of ABT, participants were asked to look at a fixation cross appearing centrally on the screen, followed by reading a presented number out loud and finally viewing faces with different emotional expressions. If participants had no further questions, calibration was started. Participants' seating position was adjusted to be of approximately 65 cm distance to the screen. Eye position was monitored in a frame on the screen with seating position and screen angle being further adjusted if needed. Participants were asked to remain in the adjusted position for the calibration and the consecutive ABT. Calibration started and participants were instructed to follow a dot on the screen with their eyes. Duration of calibration procedures was < 1 min. Quality of the calibration was shown on the experimenter screen as data loss. If data loss was < 5 %, the ABT was started, otherwise calibration was repeated. At ABT onset, instructions were written on the screen again. Total task duration including calibration was approximately 9 to 12 minutes. After completion, ABT ended automatically.

Data Preprocessing and Statistical Analysis

Eye-Tracking Data of ABT

To assess attentional bias in adolescents diagnosed with MDD, viewing behaviour of sad-neutral and angry-neutral face pairs during ABT was assessed with a screen-based eye tracking device. Recording quality was assessed as percentage of correctly identified gaze samples. Blinking can account for 5 to 10 % of data loss (Tobii AB, 2021). Recordings with > 25 % data loss were excluded from analysis for the present thesis (Sears et al., 2019). Accordingly, four recordings had to be excluded due to bad quality and therefore high percentage of data loss, leaving $n = 13$ recordings eligible for further analysis. As outcome measures, mean total fixation duration and mean first fixation duration (s) on sad, angry, and neutral faces were assessed. For analysis, neutral AOIs were grouped as neutral faces presented with sad faces, or neutral faces presented with angry faces.

To compare mean total and first fixation durations in emotional AOIs, paired samples *t*-tests were performed. No outliers were identified (1.5*IQR method). Independence of paired observations was given due to the standardized study design. Assumptions of normality, linearity, and homoscedasticity were assessed using Shapiro-Wilk Tests, Q-Q-plots, and scatter plots of standardized residuals vs. standardized predicted values. One of the *t*-tests performed served investigation of Hypothesis 5, whilst all others were performed for exploratory purposes. Therefore, no correction for multiple comparisons was applied (Field, 2018, p. 447). Relative bias scores were assessed on an individual level subtracting mean total or first fixation duration of neutral faces from corresponding mean fixation durations of emotional faces.

Questionnaire Data of BDI-II, DISYPS-III-DES and KIDSCREEN-52

Assessing the relationship of MDD and HRQoL, the HRQoL dimensions mental health/subjective well-being, social health and physical health were chosen for analysis. Relationships of BDI-II and DISYPS-III-SBB-DES total scores and the KIDSCREEN-52 self-report subscales Psychologic Well-Being, Moods and Emotion, and Self Perception were analysed for the assessment of the relationship between MDD and mental health/subjective well-being, performing simple linear regression. To assess the relationship of MDD and social health, relationships of BDI-II and DISYPS-III-DES total scores of self-reports with the KIDSCREEN-52 self-report subscale Social Support and Peers were analysed. For MDD and physical health, relationships of BDI-II and DISYPS-III-DES total scores of self-reports with the KIDSCREEN-52 self-report subscale Physical Well-Being were analysed. Intercepts are not reported since they are of little relevance for the given hypothesis, as relationships of different instruments were assessed.

Analyses were performed employing simple linear regression of the General Linear Model. Assumptions of simple linear regression were checked. Shapiro-Wilk-Tests and Q-Q Plots were conducted to check for normality of residuals. Linearity and homoscedasticity were assessed by plotting predicted values against residuals and examining the patterns in the scatterplots. Homoscedasticity was further inspected performing Breusch-Pagan tests. Independence of observations was assumed due to study design as RCT and checked using Durbin-Watson Test. Multicollinearity was not assessed since only one measure was implemented as predictor. Outliers were inspected but not removed since they seemed to reflect genuine variability in symptoms. In cases of violation of the assumption of normally distributed residuals, Spearman's rank-order correlation was performed as non-parametric alternative to simple linear regression. *P*-values were adjusted using the Method of False Discovery Rate (FDR) according to the Benjamini-Hochberg-Procedure, since multiple tests were performed.

Results

Hypothesis 1: MDD and HRQoL are Expected to be of a Negative Correlative Relationship in Adolescents.

BDI-II and Psychologic Well-Being.

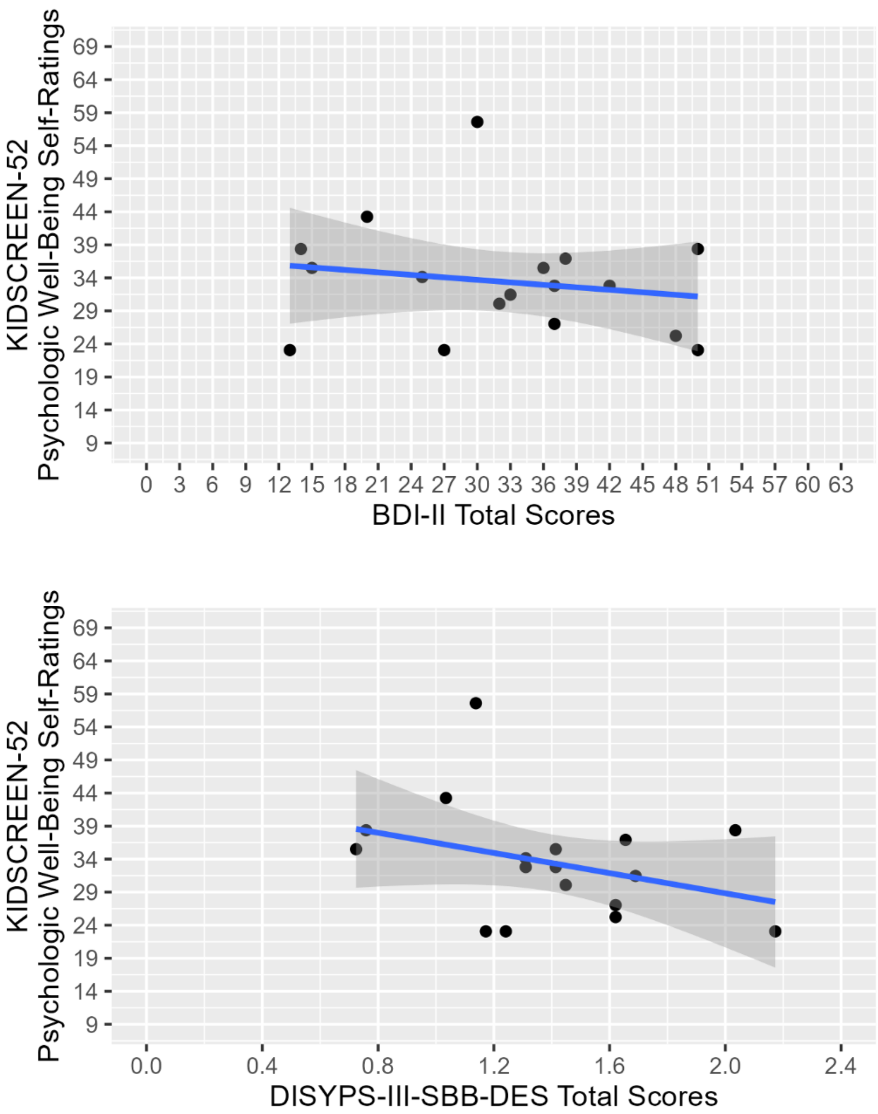
The linear regression model with BDI-II as a predictor of the KIDSCREEN-52 subscale Psychologic Well-Being was not significant with F (1,15) = 0.47, residual SE = 8.80, multiple R^2 = 0.03, $p_{\text{uncorrected}}$ = 0.50, p_{adjusted} = 0.75. The non-significant slope estimate was -0.13 (SE = 0.18, 95% CI [-0.51, 0.25], t = -0.69). Residuals ranged from -12.77 to 23.90 with a median of -0.09. Interquartile Range was 36.67 (Figure 2).

DISYPS-III-SBB-DES and Psychologic Well-Being

The linear regression model with DISYPS-III total score as a predictor of the KIDSCREEN-52 subscale Psychologic Well-Being was not significant with F (1,15) = 2.0, residual *SE* = 8.39, multiple $R^2 = 0.12$, , $p_{uncorrected} = 0.18$, $p_{adjusted} = 0.26$). The non-significant slope estimate was -7.63 (*SE* = 5.40, 95% *CI* [-19.13, 3.87], $t = -1.41$). Residuals ranged from -12.08 to 22.19 with a median of -0.50. Interquartile Range was 34.27 (Figure 2).

Figure 2

Scatterplots with Regression Line of MDD Scores and KIDSCREEN-52 Psychologic Well-Being Self-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent possible ranges of instrument scores.

BDI-II and Moods and Emotion

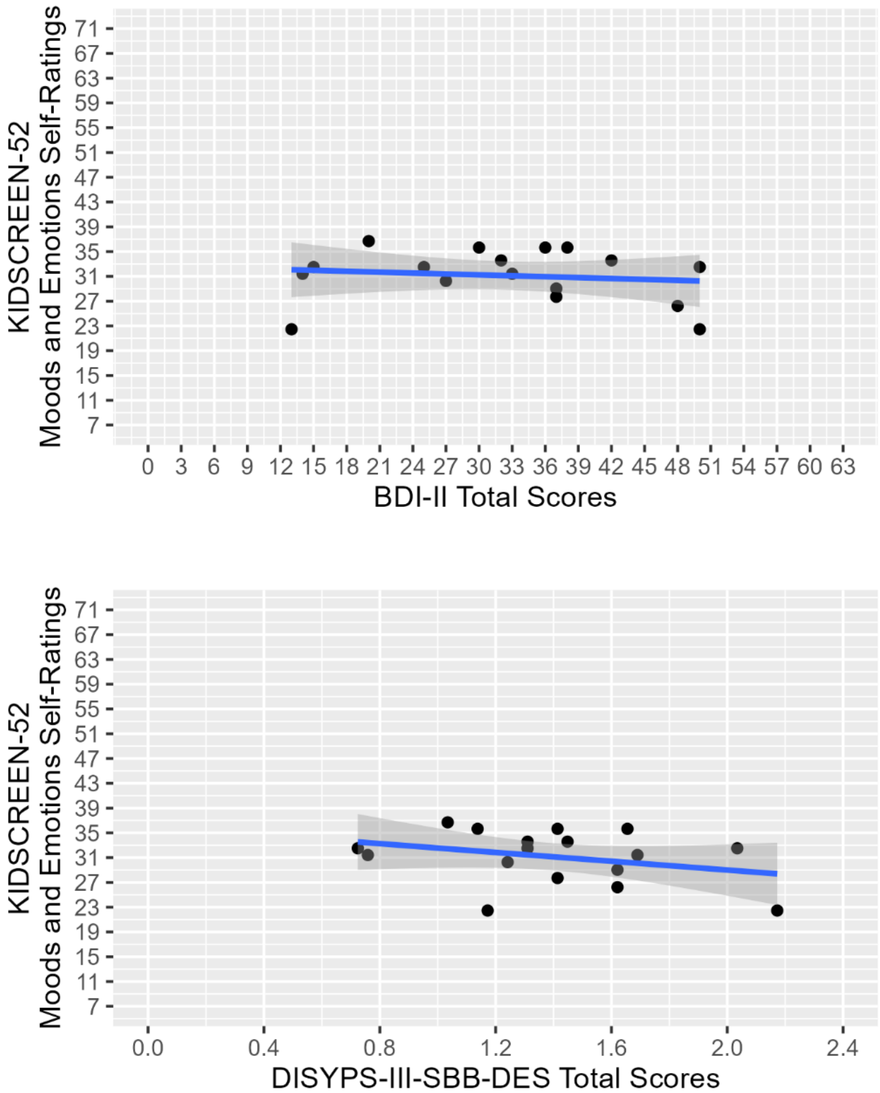
The linear regression model with BDI-II as a predictor of the KIDSCREEN-52 subscale Moods and Emotion was not significant with *F* (1,15) = 0.28, residual *SE* = 4.44, multiple R^2 = 0.02, $p_{uncorrected}$ = 0.60, $p_{adjusted}$ = 0.75). The non-significant slope estimate was -0.05 (*SE* = 0.09, 95% *CI* [-0.24, 0.14], *t* = -0.53). Residuals ranged from -9.61 to 4.97 with a median of 0.53. Interquartile Range was 14.58 (Figure 3).

DISPYS-III-SBB-DES and Moods and Emotion

The linear regression model was not significant with *F* (1,15) = 1.68, residual *SE* = 4.25, Multiple R^2 = 0.10, $p_{uncorrected}$ = 0.21, $p_{adjusted}$ = 0.26). The non-significant slope estimate was -3.55 (*SE* = 2.74, 95% *CI* [-9.39, 2.29], *t* = -1.30). Residuals ranged from -9.48 to 5.43 with a median of 1.06. Interquartile Range was 14.91 (Figure 3).

Figure 3

Scatterplots with Regression Line of MDD Scores and KIDSCREEN-52 Moods and Emotions Self-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent possible ranges of instrument scores.

BDI-II and Self-Perception

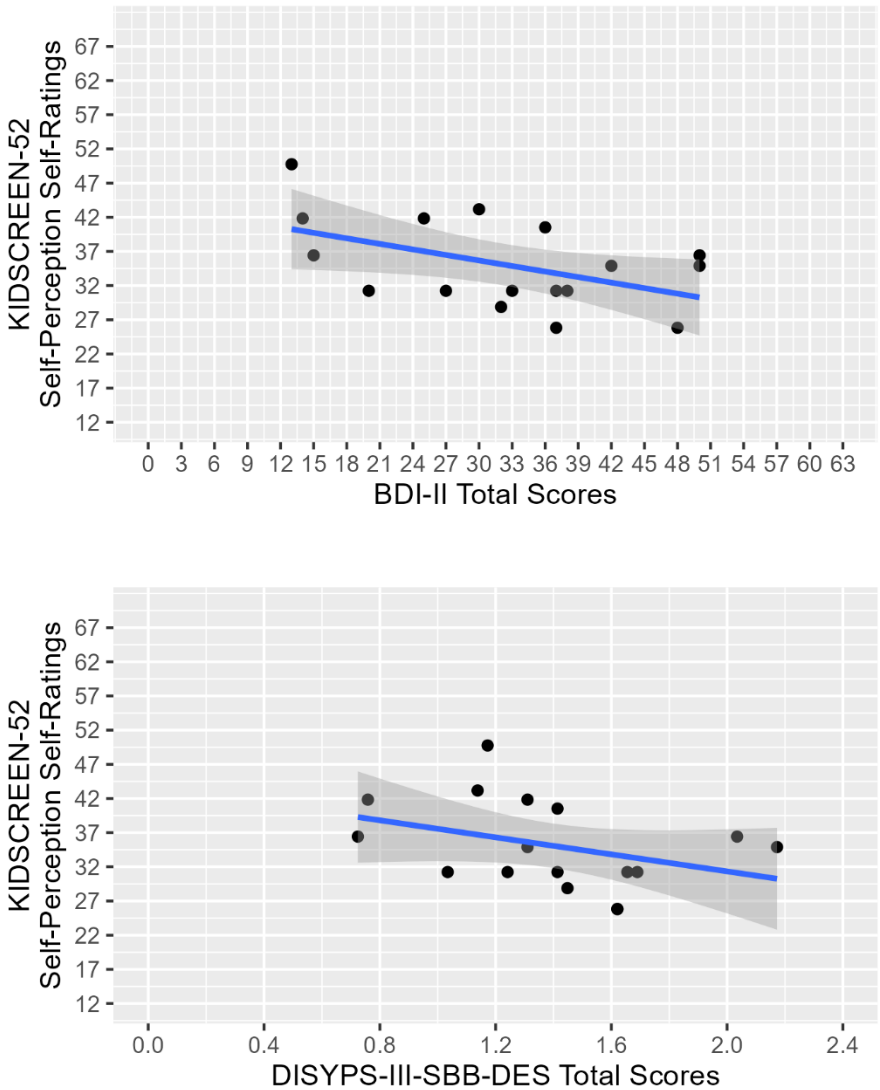
The linear regression model was not significant after FDR correction (F (1,15) = 4.82, residual SE = 5.89, Multiple $R^2 = 0.24$, $p_{uncorrected} = 0.04$, $p_{adjusted} = 0.10$). The slope coefficient was -0.27 (SE = 0.12, 95% CI [-0.53, -0.01], t = -2.20). Residuals ranged from -7.96 to 9.5 with a Median of -2.28. Interquartile Range was 17.46 (Figure 4).

DISPYS-III-SBB-DES and Self-Perception

The linear regression was not found to be significant (F (1,15) = 2.36, residual SE = 6.30, Multiple R^2 = 0.14, $p_{uncorrected}$ = 0.15, $p_{adjusted}$ = 0.26). The slope coefficient was -6.23 (SE = 4.06, 95% CI [-14.88, 2.42], t = -1.54). Residuals ranged from -7.87 to 13.27 with a Median of -2.03. Interquartile Range was 21.14 (Figure 4).

Figure 4

Scatterplots with Regression Line of MDD Scores and KIDSCREEN-52 Self-Perception Self-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent possible ranges of instrument scores.

BDI-II and Social Support and Peers

The linear regression model (Figure 8) was significant with F (1,15) = 23.05 (residual SE= 7.80, Multiple $R^2 = 0.61$, $p_{uncorrected} < 0.001$, $p_{adjusted} = 0.001$), with BDI-II total scores implemented as predictor accounting for 60.60 % of variance in the KIDSCREEN-52 Social Support and Peers subscale. The significant slope estimate was -0.78 (SE = 0.16, 95 % CI [-1.12, -0.44], t = -4.80). Residuals ranged from -11.69 to 12.79 with a median of -1.27. Interquartile Range was 24.01 (Figure 5).

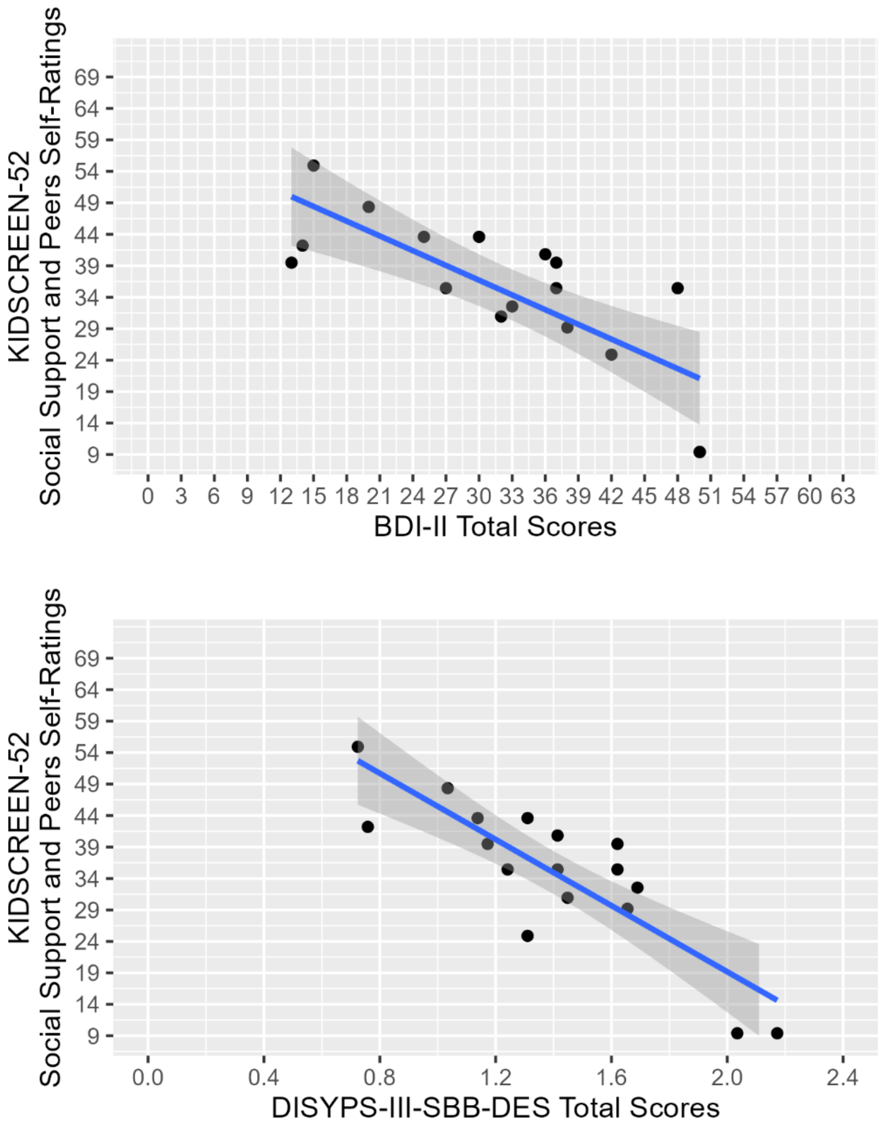
DISYPS-III-SBB-DES and Social Support and Peers

The linear regression model was significant (F (1,15) = 38.34, residual SE= 6.59, Multiple $R^2 = 0.72$, $p_{uncorrected} < 0.001$, $p_{adjusted}$ = < 0.001), with DISYPS-III total scores implemented as predictor accounting for 72 % of variance in the KIDSCREEN-52 Social Support and Peers subscale. The significant slope estimate was -26.29 (SE = 4.25, 95 % CI [-35.34, -17.24], t = -6.19). Residuals ranged from -12.42 to 10.35 with a median of 0.95 (Figure 5).

Both models reaching significance, indicates a significant negative association between MDD and social functioning.

Figure 5

Scatterplots with Regression Line of MDD Scores and KIDSCREEN-52 Social Support and Peers Self-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores.

BDI-II and Physical Well-Being

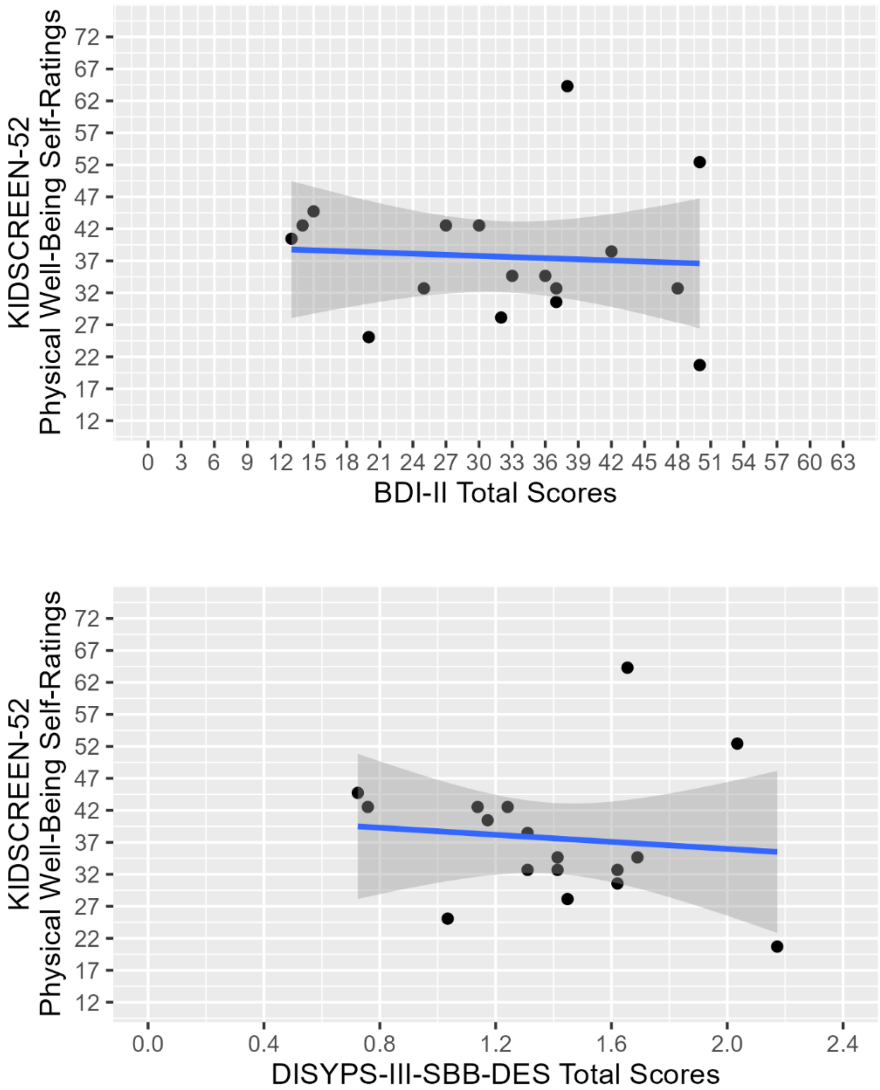
The linear regression model with BDI-II as a predictor and the KIDSCREEN-52 subscale Physical Well-Being was not significant (F (1,15) = 0.07, residual SE = 10.74, Multiple $R^2 = 0.004$, $p_{uncorrected} = 0.80$, $p_{adjusted} = 0.80$). The non-significant slope estimate was -0.06 (*SE* = 0.22, 95 % *CI* [-0.53, 0.41], *t* = -0.26). Residuals ranged from -15.89 to 27.01 with a median of -2.76 (Figure 6).

DISYPS-III-SBB-DES and Physical Well-Being

The linear regression was not significant (F (1,15) = 0.16, residual *SE* = 10.7, Multiple $R^2 = 0.01$, $p_{uncorrected} = 0.70$, $p_{adjusted} = 0.70$). The non-significant slope estimate was -2.76 (*SE* = 6.9, 95 % *CI* [-17.46, 11.94], *t* = -0.4). Residuals ranged from -14.8 to 27.37 with a median of -2.18 (Figure 6).

Figure 6

Scatterplots with Regression Line of MDD Scores and KIDSCREEN-52 Physical Well-Being Self-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores.

Hypothesis 2: Low Concordance of Adolescent Self- and Parental-Ratings of MDD is Expected

Concordance was assessed analysing congruence of self- and parental ratings of adolescents' MDD assessed with DISYPS-III-DES total scores and subscales. Means and standard deviations are depicted in Table 5.

Table 5

Mean Scores and Standard Deviations of Self- and Parental-Ratings of DISYPS-III-DES Subscales

Subscale	Self-Ratings	Parental-Ratings
Total Score	M = 1.40 SD = 0.39	M = 1.91 SD = 0.55
Competencies, Confidence and Enjoyment	M = 1.83 SD = 0.49	M = 2.21 SD = 0.71
Impairment and Psychological Strain	M = 1.62 SD = 0.64	M = 2.44 SD = 0.79

DISYPS-III-DES Total Scores

Mean scores for self-ratings were 1.40 ± 0.39 and 1.91 ± 0.55 for parental-ratings. Therefore, on average, parental-reports judged depressive symptom severity to be very conspicuous, whilst adolescents judged their symptom severity to be conspicuous.

Checking assumptions of simple linear regression, Durbin-Watson-Test for assessment of autocorrelation of errors was significant (p = 0.03), therefore, data was visually inspected and robust standard errors were used to further proceed with regression analysis, since no other assumptions were violated. Linear regression analysis was conducted to examine the concordance between parental and self-ratings of DISYPS-III total scores. The regression model (Figure 7) with DISYPS-III-DES self-ratings as predictor of parental ratings was not statistically significant (F (1, 15) = 0.03, $p_{adjusted.}$ = 0.89, $p_{\text{uncorrected}}$ = 0.83, Multiple R^2 = 0.002). The non-significant slope coefficient for self-reports was 0.07 (SE= 0.29, 95% *CI* [-0.55, 0.69], t = 0.22). Residuals ranged from -0.99 to 0.95, with a median value of -0.12. The intercept was significant and estimated to be 1.82 with *SE* = 0.38 (t = 4.75, p = < 0.001).

DISYPS-III-DES Competencies, Confidence and Enjoyment

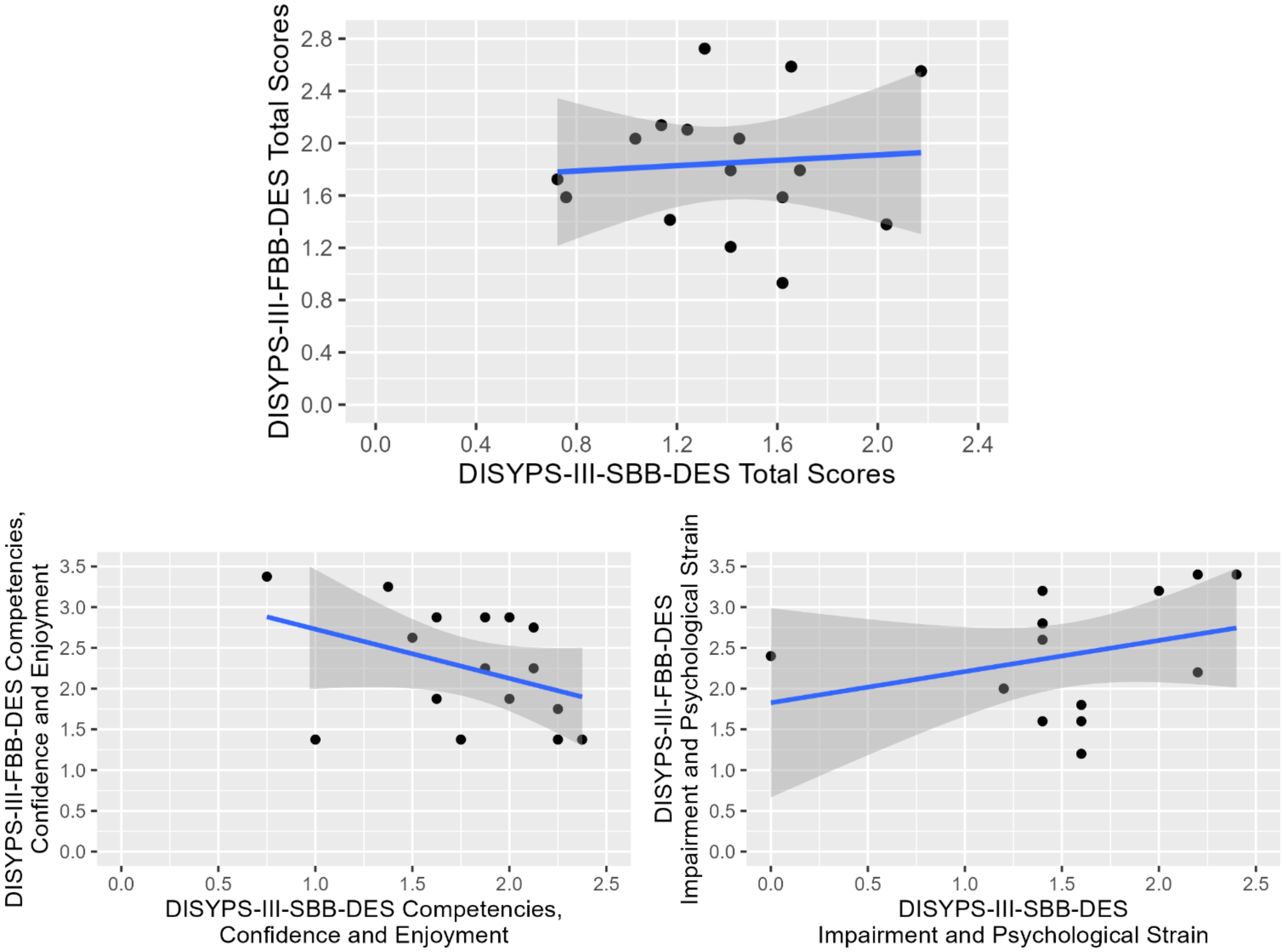
Mean scores of self-ratings were 1.83 ± 0.49 and 2.21 ± 0.71 of parental-ratings, with both parental- and self-reports judging adolescents' competencies as average. A linear regression analysis was performed to assess concordance (Figure 7). The intercept of 3.42 (t = 5.4, $p < 0.001$) reached significance and represents the estimated mean value of parental-ratings when self-ratings are zero. The F (1,15)-value of 3.86 and therefore the model did not reach significance ($p_{adjusted.}$ = 0.21, $p_{uncorrected.}$ = 0.07, multiple R^2 = 0.21, residual *SE* = 0.65) The slope coefficient was -0.66 (*SE* = 0.33, 95% *CI* [-1.36, 0.04], t = -1.96). Median of residuals was 0.07 with residuals ranging from -1.38 to 0.77.

DISYPS-III-DES Impairment and Psychological Strain

Mean scores for self- ratings were 1.62 ± 0.64 and 2.44 ± 0.79 for parental-ratings. Simple linear regression was conducted to explore the relationship between self- and parental-ratings (Figure 7). The model did not reach statistical significance (F (1,15) = 0.02, residual *SE*= 0.82, multiple R^2 = 0.0014, $p_{adjusted}$ = 0.89, $p_{uncorrected}$ = 0.89). The non-significant slope estimate was 0.05 (*SE* = 0.32, 95% *CI* [-0.63, 0.73], t = 0.15). The intercept of the model was estimated to be 2.55 (*SE* = 0.56, t = 4.25, $p < 0.001$). Residuals ranged from -1.23 to 1.37. The median residual was found to be 0.04.

Figure 7

Scatterplots with Regression Line of Subscales of DISYPS-III-SBB-DES and DISYPS-III-FBB-DES Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores. Parental-ratings are depicted on the y-axis (DISYPS-III-FBB-DES) and self-ratings are on the x-axis (DISYPS-III-FBB-DES).

Hypothesis 3: Moderate Concordance of Adolescent Self- and Parental-Ratings is Expected in Externalized HRQoL Dimensions

For assessment of concordance of parental- and self-ratings of externalized HRQoL dimensions, the subscales Physical Well-Being, School Environment and Financial

Resources of KIDSCREEN-52 were selected after item and subscale inspection. Means and standard deviations of the samples' *T*-values in the corresponding subscales are depicted in Table 6.

Table 6

Mean T-Values and Standard Deviations of Self- and Parental-Ratings of KIDSCREEN-52 Subscales of Externalized Symptoms

Subscale	Self-Ratings	Parental-Ratings
School Environment	M = 38.47 SD = 7.47	M = 37.98 SD = 9.17
Physical Well- Being	M = 37.64 SD = 10.42	M = 36.66 SD = 6.15
Financial Resources	M = 52.15 SD = 10.68	M = 55.83 SD = 7.63

Physical Well-Being

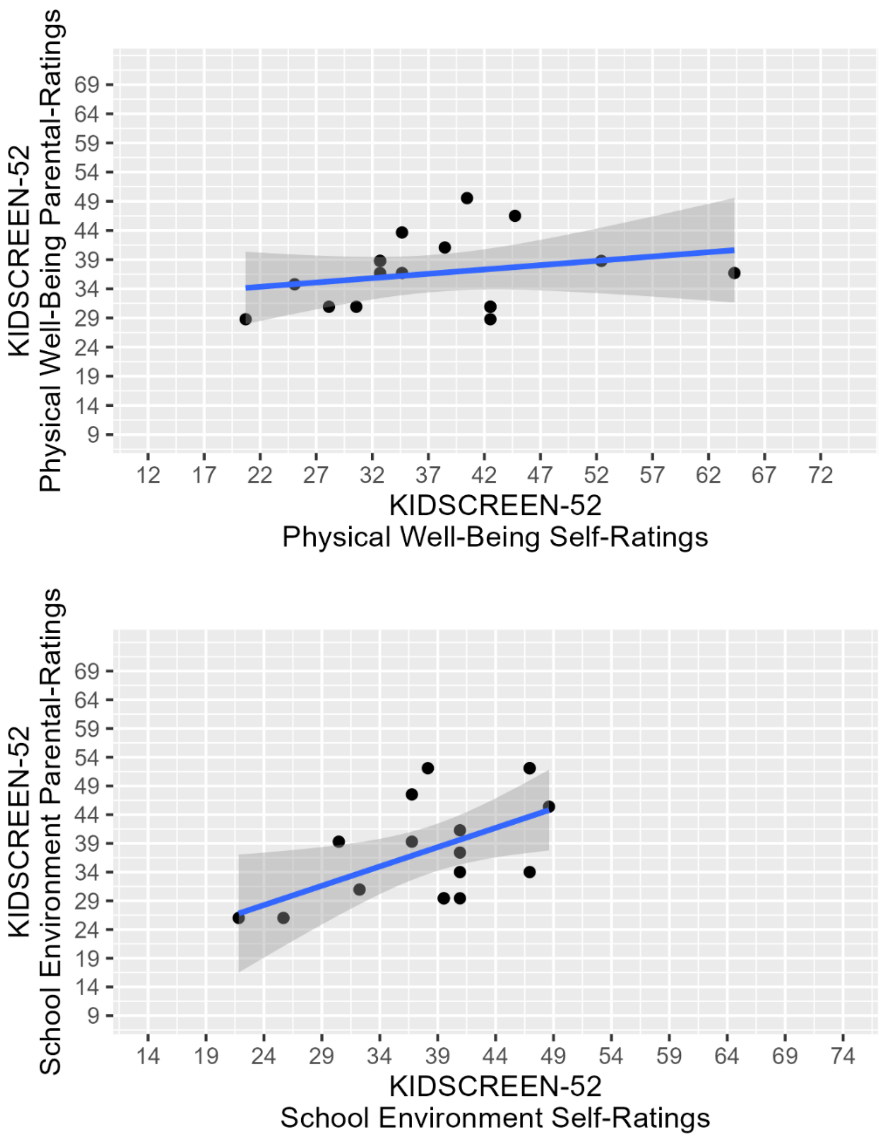
The linear regression model was not found to be significant (F (1,15) = 1.01, residual SE= 6.14, Multiple R^2 = 0.06, $p_{\text{uncorrected}}$ = 0.33, p_{adjusted} = 0.40). The intercept was significant (estimate = 31.08, SE = 5.74, t = 5.41, p < 0.001). The non-significant slope coefficient was 0.15 (SE = 0.15, 95% CI [-0.17, 0.46] t = 1.00). Residuals ranged from -8.61 to 12.46 with a median of -0.03 (Figure 8).

School Environment

The linear regression model was significant before, and marginally significant after correction of multiple testing with F (1,15) = 6.44, residual SE= 7.92, multiple R^2 = 0.30, $p_{\text{uncorrected}}$ = 0.02, p_{adjusted} = 0.06. Self-reports implemented as predictors accounted for 30.04 % of variance in parental-reports (Pearson's r = .55). The intercept was not significant (estimate = 12.11, SE = 10.37, t = 1.17, p = 0.26). The slope estimate was 0.67 (SE = 0.27, 95% CI [0.10, 1.24], t = 2.54). Residuals ranged from -10.20 to 14.33 with a median of -0.78 (Figure 8).

Figure 8

Scatterplot with Regression Line of KIDSCREEN-52 Subscales Physical Well-Being and School Environment Self- and Parental-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores.

Financial Resources

Spearman's rank-order correlation was performed to assess concordance between self-and parental-ratings instead of simple linear regression due to violation of normality assumptions. Results indicated no significant correlation ($p_{uncorrected} = 0.43$, $p_{adjusted} = 0.63$) and a correlation coefficient of $\rho = 0.20$ indicating a weak association between the two variables.

Hypothesis 4: Low Concordance of Adolescent Self- and Parental-Ratings is Expected in Internalized HRQoL Dimensions

As measures of internalized symptoms, the subscales Psychologic Well-Being, Moods and Emotions, Self-Perception, Autonomy, Parent Relation and Home Life, and Social Support and Peers have been selected after inspection of all items and subscales. Means and standard deviations of the samples' *T*-values in the corresponding subscales are depicted in Table 7.

Table 7

Mean T-Values and Standard Deviations of Self- and Parental-Ratings of KIDSCREEN-52 Subscales of Internalized Symptoms

Subscale	Self-Ratings	Parental-Ratings
Psychologic Well- Being	M = 33.43 SD = 8.65	M = 34.76 SD = 9.09
Moods and Emotions	M = 31.14 SD = 4.34	M = 29.34 SD = 8.57
Self- Perception	M = 35.09 SD = 6.56	M = 36.95 SD = 7.17
Autonomy	M = 40.78 SD = 8.28	M = 49.06 SD = 9.36
Parent Relation and Home Life	M = 41.81 SD = 8.31	M = 43.95 SD = 5.74
Social Support and Peers	M = 35.01 SD = 12.04	M = 41.32 SD = 16.91

Psychologic Well-Being

A simple linear regression was conducted to explore concordance of self- and parental-ratings. The model was not found to be significant with $p_{uncorrected}$ = 0.15, $p_{adjusted}$ = 0.30 (multiple R^2 = 0.13, F (1,15) = 2.30, SE = 8.74). The intercept of the model was estimated to be 21.95 (SE = 8.71, t = 2.52, p = 0.024), suggesting the intercept to be statistically significant. The slope was estimated to be 0.38 (SE = 0.25, 95% CI [-0.15, 0.91], t =1.52). Furthermore, an examination of the residuals revealed a range from -11.62 to 19.66. The median residual was found to be -0.75 (Figure 9).

Moods and Emotions

The model was not statistically significant (F (1,15) = 1.08, residual SE = 8.55, multiple R^2 = 0.07, $p_{uncorrected}$ = 0.31, $p_{adjusted}$ = 0.40). The intercept (estimate = 13.41, SE = 15.47, t = 0.87, p = 0.40) remained non-significant as well. The slope coefficient was 0.51 (SE = 0.49, 95% CI [-0.53, 1.55], t = 1.04). Residuals ranged from -14.52 to 16.92 with a median of -0.97 (Figure 9).

Self-Perception

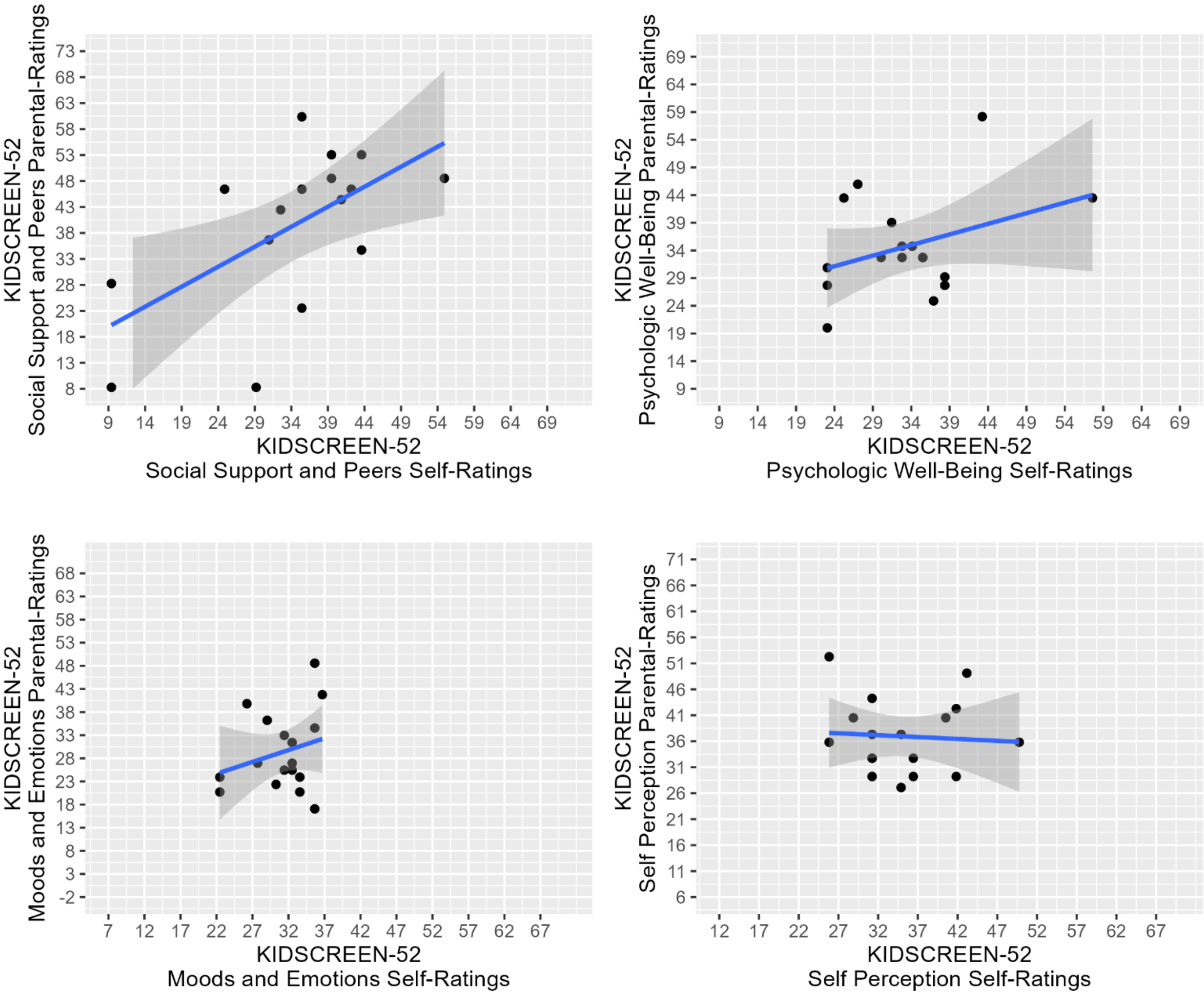
The linear regression model not found to be significant (F (1,15) = 0.07, residual SE = 7.39, multiple R^2 = 0.005, $p_{uncorrected}$ = 0.80, $p_{adjusted}$ = 0.80). The intercept was significant (estimate = 39.51, SE = 10.04, t = 3.93, p = 0.001). The non-significant slope coefficient was -0.07 (SE = 0.28, 95% CI [-0.67, 0.53], t = -0.26). Residuals ranged from -9.87 to 14.65 with a median of -0.07 (Figure 9).

Social Support and Peers

The linear regression model was significant (F (1,15) = 10.5, residual SE= 13.39, multiple R^2 = 0.41, $p_{uncorrected}$ = 0.006, $p_{adjusted}$ = 0.036), indicating the self-reports to account for 41.18 % of variance in parental-reports (Figure 9). The intercept was not significant (estimate = 9.77, SE = 10.26, t = 0.95, p = 0.36). Significant slope estimate was 0.90 (SE = 0.28, 95% CI [0.30, 1.5] t = 3.24). Residuals ranged quite broadly from -27.80 to 19.73 with a median of 3.16.

Figure 9

Scatterplots with Regression Line of KIDSCREEN-52 Social Support and Peers, Psychologic Well-Being, Moods and Emotions and Self-Perception Self- and Parental-Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores.

Autonomy

Another Spearman's rank-order correlation was performed. Results indicated no significant correlation ($p_{uncorrected}$ = 0.11, $p_{adjusted}$ = 0.33). The correlation coefficient ρ = 0.40 indicated a moderate association between self- and parental-reports.

Parent Relation and Home Life

For this subscale, Spearman's rank-order correlation was conducted and found not be significant ($p_{uncorrected}$ = 0.63, $p_{adjusted}$ = 0.63). A very weak association between self- and parental-ratings was instigated by the correlation coefficient ρ = 0.13.

Hypothesis 5: Total Fixation Durations of Sad and Neutral Faces are Expected to Differ in Adolescents Diagnosed with MDD in a Free-Viewing Eye-Tracking Task.

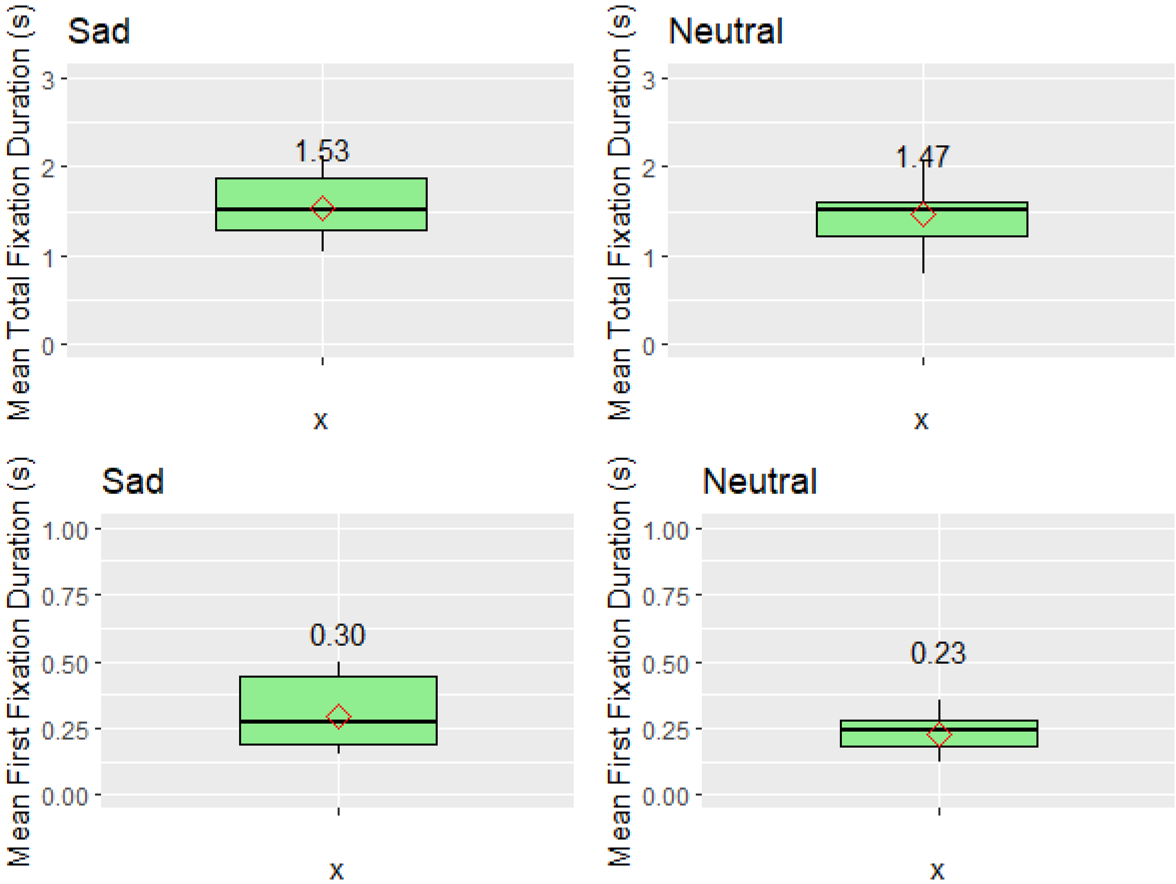
Results of a paired *t*-test revealed a difference in total fixation durations between sad and neutral AOIs (t = -0.54, p = 0.60, df = 12), which did not reach significance. As shown in Figure 10, mean total fixation duration of sad faces (M = 1.53 ± 0.35 s) was higher than of neutral faces (M = 1.47 ± 0.41 s) with a mean difference of -0.06 s (95 % *CI*: [-0.32, 0.19]).

Exploratory Hypothesis (EH) 1: Is Attentional Bias towards Sad Stimuli Manifested in First Fixation Duration in Adolescents Diagnosed with MDD, in a Free-Viewing Eye-Tracking Task?

Results of a paired *t*-test revealed a difference in first fixation duration between sad and neutral AOIs (t = -1.88, p = 0.09, df = 12), which marginally reached significance. Mean first fixation duration of sad faces (M = 0.30 ± 0.12 s) was higher than of neutral faces (M= 0.23 ± 0.07 s) with a mean difference of -0.07 s (95 % *CI*: [-0.14, 0.01]) (Figure 10).

Figure 10

Boxplots of Mean Total and First Fixation Durations of Sad-Neutral Face Pairs

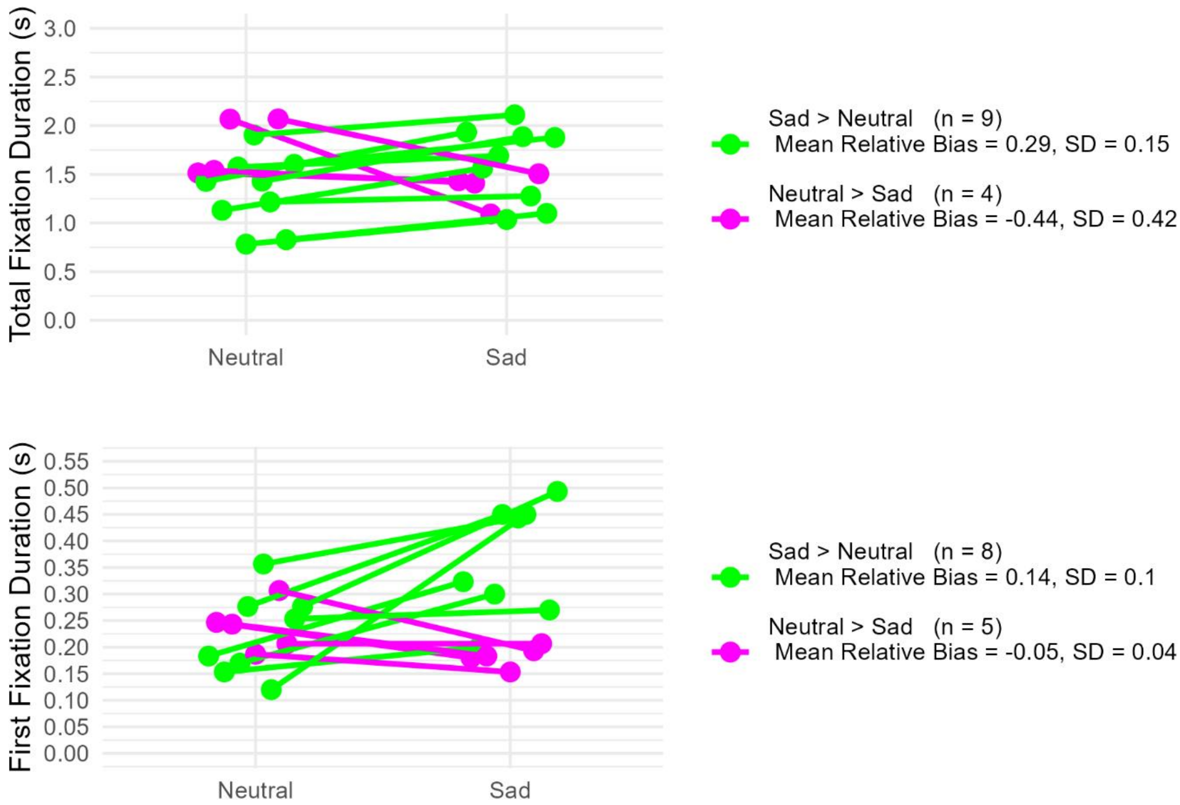


EH 4: Do Adolescents Diagnosed with MDD Exhibit Relative Bias towards Sad Faces?

As shown in Figure 11, calculation of relative bias scores of total fixation duration of sad-neutral face pairs found n = 9 participants to exhibit a bias towards sad faces, indicated by a relative bias score > 0 (M = 0.29, SD = 0.15, range [0.06, 0.51]), whereas n = 4 participants showed an attentional bias towards neutral faces (M = -0.44, SD = 0.42, range [-0.97,- 0.08]). Similarly, relative bias scores of first fixation duration found n = 8 participants to exhibit a bias towards sad faces (M = 0.14, SD = 0.1, range [0.02, 0.33]) and n = 5 to preferentially process neutral faces (M = -0.05, SD = 0.04, range [-0.11, -0.001]).

Figure 11

Connected Dot Plots of Individual Relative Bias in Total and First Fixation Duration of Sad and Neutral AOIs



Note. Connected dot plots of individual mean total and first fixation durations. Longer mean fixation durations of sad faces (sad bias) are indicated by green connected dots, whereas longer mean fixation durations of neutral faces (neutral bias) are indicated by pink connected dots. Mean magnitudes of relative bias (= individual differences in viewing times of sad and neutral faces) are depicted in the legends.

EH 2: Is Attentional Bias towards Angry Stimuli Manifested in Total Fixation Duration in Adolescents Diagnosed with MDD, in a Free-Viewing Eye-Tracking Task?

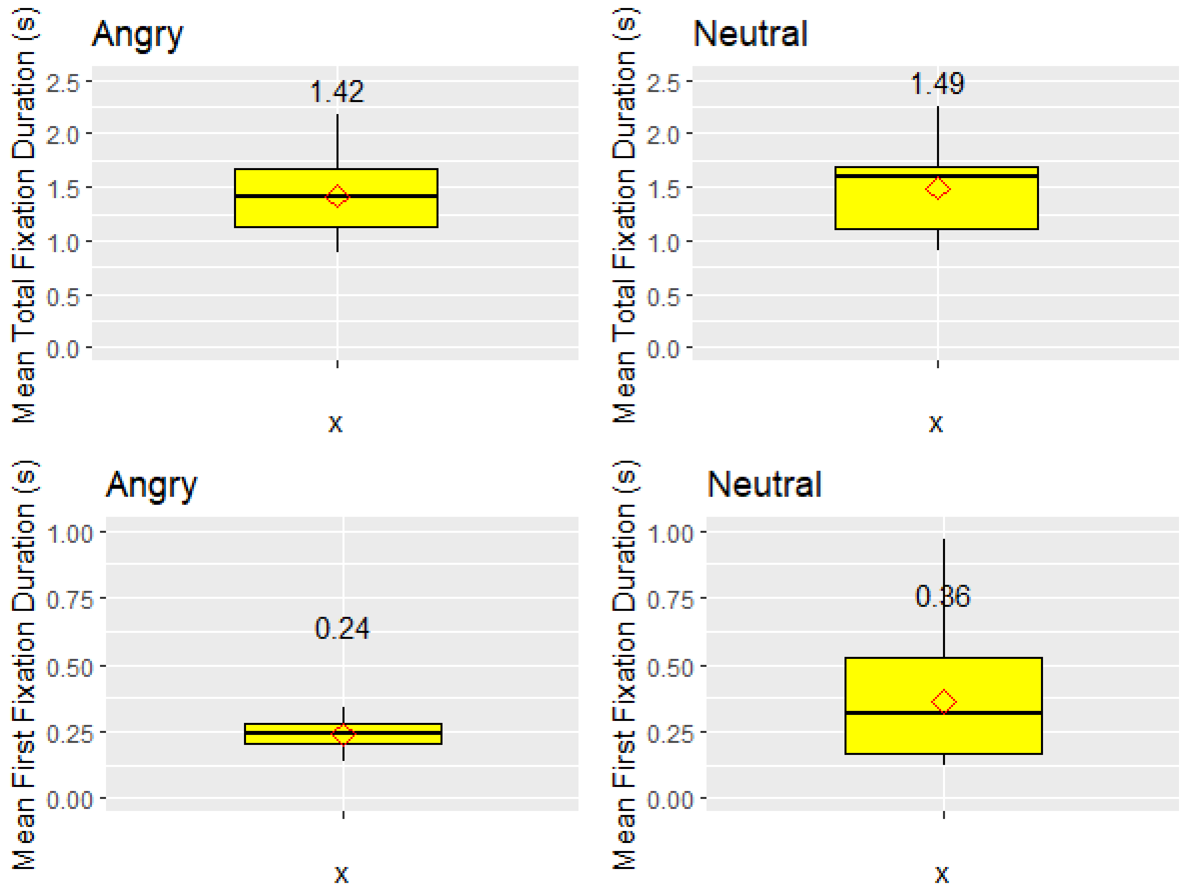
For angry-neutral face pairs, another paired samples *t*-test was conducted to compare total fixation duration scores of angry and neutral faces. Results revealed a difference in total fixation durations between the AOIs ($t = -0.74$, $p = 0.48$, $df = 12$), which did not reach statistical significance. The mean score for angry faces ($M = 1.42 \pm 0.39$ s) was lower than for neutral faces (*M* = 1.49 ± 0.42 s) with a mean difference of -0.08 s (95 % *CI*: [-0.30, 0.15]) (Figure 12).

EH 3: Is Attentional Bias towards Angry Stimuli Manifested in First Fixation Duration in Adolescents Diagnosed with MDD, in a Free-Viewing Eye-Tracking Task?

Similarly to the analysis of results of first fixation duration in sad faces, results of a paired *t*-test revealed a marginally non-significant difference in first fixation duration between angry and neutral AOIs (t = -1.97, p = 0.07, df = 12) The mean first fixation duration for angry faces (*M* = 0.24 ± 0.07 s) was lower than for neutral faces (*M*= 0.36 ± 0.25 s) as shown in Figure 12, with a mean difference of -0.12 s (95 % *CI*: [-0.25, 0.01]).

Figure 12

Boxplots of Mean Total and First Fixation Duration of Angry-Neutral Face Pairs

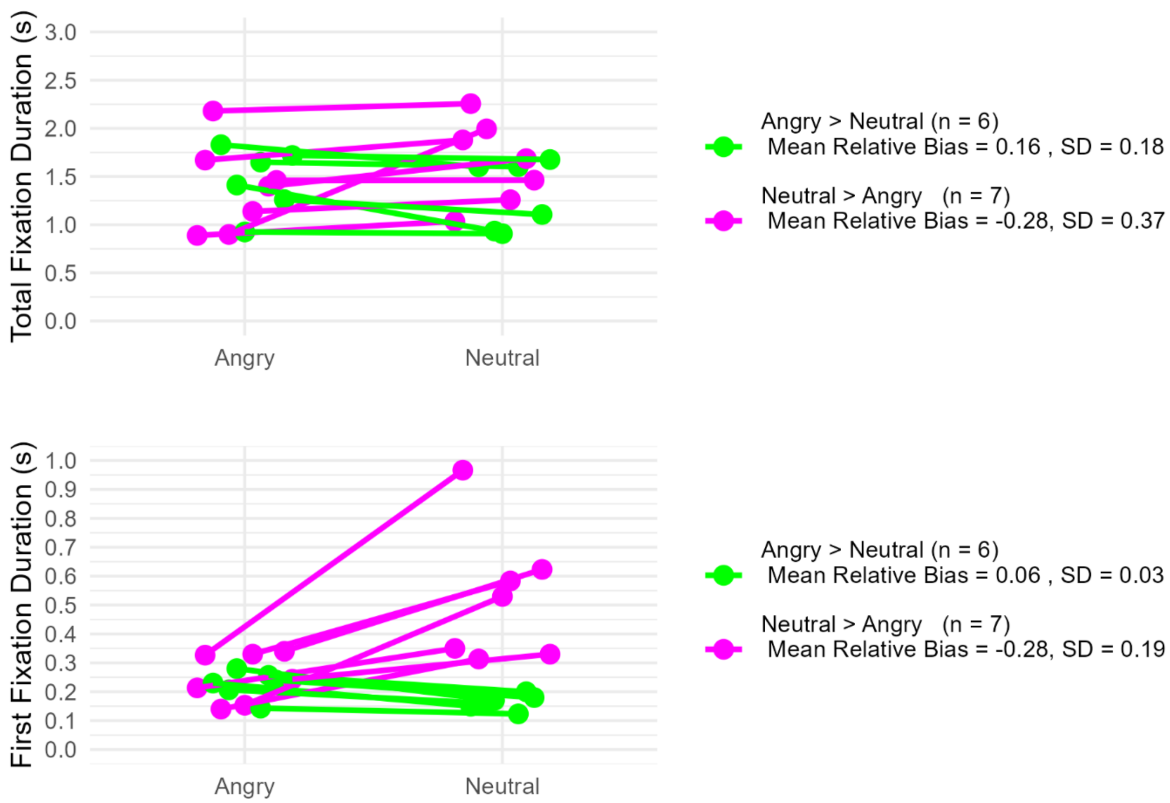


EH 4: Do Adolescents Diagnosed with MDD Exhibit Relative Bias towards Angry Faces?

As depicted in Figure 13, calculation of relative bias scores of angry-neutral face pairs found *n* = 7 participants to not exhibit a bias towards angry but towards neutral faces indicated by a relative bias score ≤ 0 (total fixation duration: *M* = -0.28 *SD* = 0.37, range [-1.10, -0.003]; first fixation duration: *M* = -0.28 *SD* = 0.19, range [-0.38, -0.09]), whereas *n* = 6 participants showed preferential processing of angry faces (total fixation duration: *M* = 0.16, *SD* = 0.18, range [0.02, 0.48], first fixation duration: *M* = 0.06, *SD* = 0.03, range [0.02, 0.11]).

Figure 13

Connected Dot Plots of Individual Relative Bias in Total and First Fixation Duration of Angry and Neutral AOIs



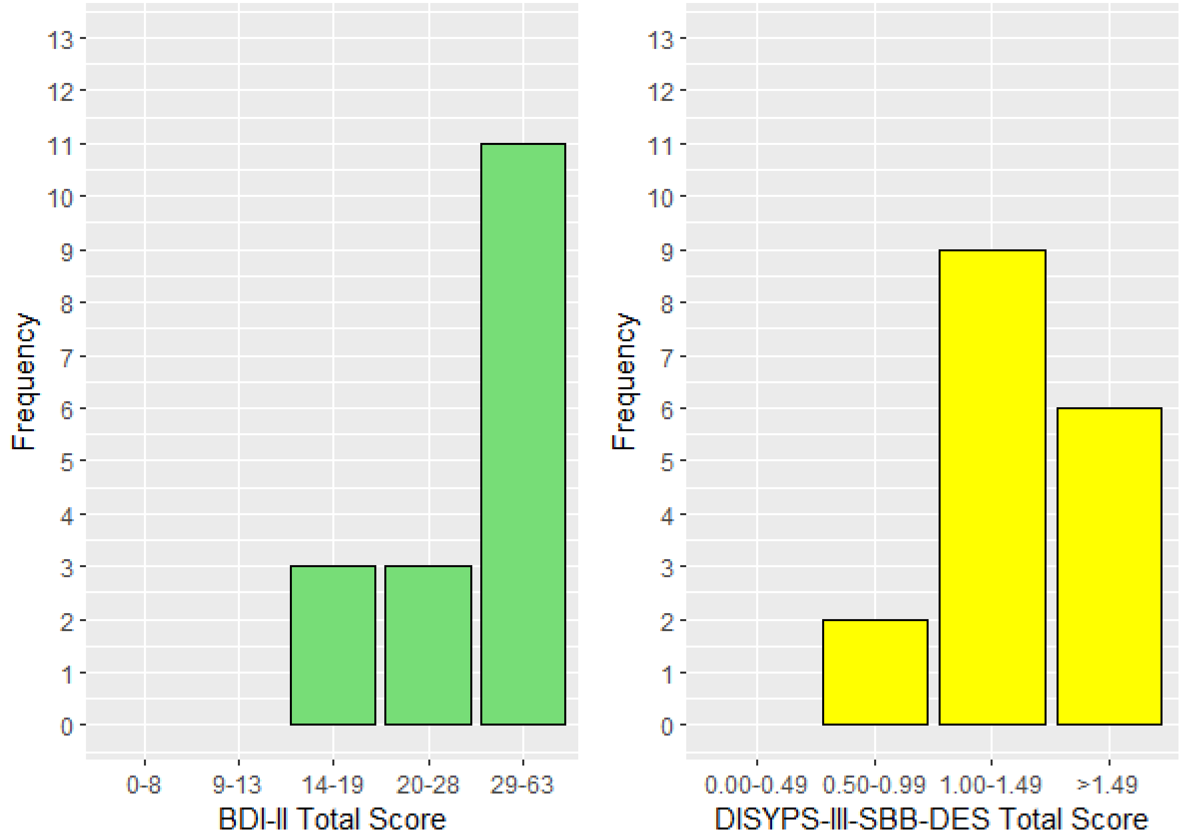
Note. Connected dot plots of individual mean total and first fixation durations. Longer mean fixation durations of angry faces (angry bias) are indicated by green connected dots, whereas longer mean fixation durations of neutral faces (neutral bias) are indicated by pink connected dots. Mean magnitudes of relative bias (= individual differences in viewing times of sad and neutral faces) are depicted in the legends.

EH 5: Is MDD Symptom Severity Congruent between BDI-II and DISYPS-III-SBB-DES assessments?

Depressive symptom ratings were assessed using BDI-II and DISYPS-III-DES self-rating questionnaires. Mean score of BDI-II and DISYPS-III-SBB-DES total scores were compared since they both aim to assess general MDD severity. For DISYPS-III-SBB-DES, the mean total score was 1.40 ± 0.39, which is interpreted as conspicuous, and ranked as second highest level of symptom severity. Mean of BDI-II being 32.18 ± 11.99 qualified for the highest symptom severity rating in BDI-II which is severe depression. As can be seen in Figure 14, in DISYPS-III-SBB-DES, out of $N = 17$, $n = 6$ participants fell into the highest category of very conspicuous, $n = 9$ showed conspicuous symptom severity and $n = 2$ fell in the mildly conspicuous category. For BDI-II, $n = 11$ fell into the category of severe depression, and $n = 3$ participants scored for each mild or moderate depression. Simple linear regression analysis was conducted to investigate the relationship between the scores on the two instruments. The linear regression model with BDI-II scores predicting DISYPS-III-SBB-DES total scores was statistically significant (F (1, 15) = 45.96, residual $SE = 0.20$, multiple $R^2 = 0.75$, $p < .001$). The significant slope coefficient for BDI-II was 0.03 (SE = 0.004, 95% CI [0.02, 0.04], $t = 6.78$, $p < .001$). The residuals ranged from -0.36 to 0.31, with a median value close to zero (-0.01), indicating that the model provided a good fit to the data (Figure 15).

Figure 14

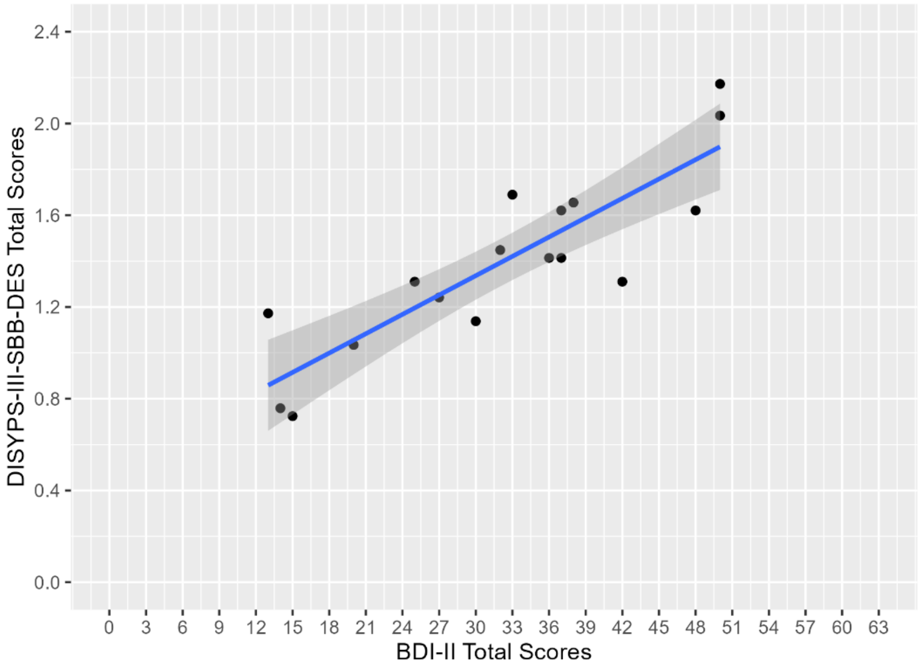
Histograms of Severity of BDI-II and DISYPS-III Self-Report Total Scores



Note. Histograms portraying the number of participants scoring in given severity categories of BDI-II and DISYPS-III-SBB-DES.

Figure 15

Scatterplot with Regression Line of BDI-II and DISYPS-III-SBB-DES Total Scores



Note. 95 % CIs of the regression model are depicted along the regression line. Intervals of x- and y-axis represent ranges of instrument scores.

Discussion

The objective of the current thesis was to investigate the relationship of MDD and HRQoL, concordance of self- and parental-ratings of depressive symptoms and HRQoL, as well as manifestation of MDD in negative attentional bias in adolescents. MDD was found to be significantly associated with HRQoL in one HRQoL subdimension. Concerning rater concordance in depressive symptoms, regression models did not find self-ratings to be significant predictors of parental-ratings. Self-ratings of HRQoL were found to be significant predictors of parental-ratings in one sub dimension only. Regarding attentional bias, data analysis yielded no statistically significant indications of attentional bias manifestation in differences between mean total, and first fixation durations sad-neutral and angry-neutral face pairs. The calculation of individual attentional bias revealed most participants to show negative attentional bias towards sad faces, when total fixation durations were considered.

Investigations of the Relationship of MDD and HRQoL

Addressing how MDD affects HRQoL, it was hypothesized that the two constructs are linked by a negative correlative relationship. For Mental Health/Subjective Well-Being and Physical Health, none of the regression models reached significance after correction for multiple testing, and R^2 values were small. Initially, in line with expectations, BDI-II and the KIDSCREEN-52 subscale Self Perception were found to be significantly associated with BDI-II scores ($p = 0.04$) explaining 24% of variance in the Self Perception subscale. This score equals Pearson's r of -.49, suggesting a moderate, negative correlation. The model did not remain significant after FDR correction ($p = 0.10$), which is against expectations. Since the model marginally reached significance, this association should be further investigated with a larger sample size. Against expectations, Psychologic Well-Being, Moods and Emotion, and Physical Well-Being were not found to be significantly associated with BDI-II or DISYPS-III-SBB-DES scores. Noteworthy, all non-significant slope parameters were found to be negative, which is in line with expectations. For Psychologic and Physical Well-Being, a possible explanation of the models not reaching significance is high variability in the data, which makes effects hard to detect with the small sample size. An additional explanation of the large variability in the KIDSCREEN-52 subscale Physical Well-Being amongst participants might be Physical Well-Being not being inherently affected by MDD. Concerning Psychologic Well-Being, drawing a similar conclusion does not seem plausible. Possibly, this KIDSCREEN-52 subscale assesses constructs of psychological well-being not affected by MDD. Therefore, high variability in this subscale might reflect unrelated, subjective variation. In the subscale Moods and Emotion, data variability was low and therefore, does not appear to distort findings. The slope parameters were small, indicating a weak association between the two dimensions, which is a possible explanation for the model not reaching significance. As stated for Psychologic Well-Being, possibly the Moods and Emotion subscale does not cover constructs directly affected by MDD. Concerning the subscale Social Support and Peers, scores of both, BDI-II and DISYPS-III-SBB-DES, have been found to be significant predictors, meaning that there is a significant negative association between the two measures. Besides the general association between social health and MDD (Cho et al., 2019; Katschnig, 2006), items of this KIDSCREEN-52 subscale might cover aspects of social functioning directly affected by MDD. Possibly, the relevance of social interaction for adolescents is high. The importance of social interaction and peer groups for the adolescent age group (Brown & Lohr, 1987; Harris, 1995; La Greca et al., 2001) might make it an especially suitable impact factor of their quality of life (Blakemore & Mills, 2013; Orben et al., 2020) which serves as a possible explanation for it to be affected by MDD and consequential impairments (Hawkley & Cacioppo, 2010.; Orben et al., 2020).

Investigations of the Relationship of Self- and Parental-Ratings of MDD and HRQoL

Low concordance of adolescent-self and parental-ratings of depressive symptoms was hypothesized (Kim et al., 2020; Lewis et al., 2014). None of the three fitted linear regression models were significant. For total scores, parental reports judged adolescents' symptom severity to be higher (very conspicuous) than self-ratings (conspicuous). This is in line with findings of Lewis and colleagues (2014) of parents estimating overall depressive symptoms of adolescents to be more severe, than the subjects themselves. For the Competencies, Confidence and Enjoyment subscale, means of both self- and parental-ratings, judged symptom severity to be average. For the Functional Impairment and Psychological Strain subscale, parents judged adolescents' impairment to be higher, meaning more severe than they did themselves. The non-significant models could indicate no significant association between self- and parental reports of MDD, as has previously been found comparing self- and parental-ratings (Kim et al., 2020; Lewis et al., 2014). Given the lack of significance, it remains questionable if any conclusions on relations of parental and self-reports can be drawn. Ranges of residuals were rather large and R^2 scores small, indicating poor model fit. Exclusion of outliers could have benefitted the model fit but was decided against in the underlying analysis due to the small sample size. As mentioned before, a larger sample might contribute to shed light on true effects.

For externalized dimensions of HRQoL, moderate concordance of self- and parental reports was hypothesized (Eiser & Morse, 2001; Northfield et al., 2023). Three subscales of KIDSCREEN-52 were identified as measuring externalized dimensions of HRQoL. A linear regression model for the subscale Physical Well-Being yielded no significant association between self- and parental reports. Mean scores of the two measures were similar as depicted in Table 6. For Financial Resources, Spearman's Rank Order Correlation revealed no significant correlation between self- and parental-ratings. These findings are against expectations of moderate concordance in externalised symptoms. Although the lack of significance of these models could demonstrate lacking concordance between ratings. Possibly, due to emerging individuality in adolescents leading to parents having reduced insight in adolescents' sentiments and experiences (Harris, 1995; Northfield et al., 2023; Tomé et al., 2012). The third simple linear regression analysis of self- and parental-ratings of School Environment yielded marginally significant findings after FDR correction ($p = 0.06$) with self-reports explaining 30.04% of variance in parental reports. Investigating this association with a larger sample could provide deeper insights in the true relationship. Possibly, ratings of school environment provide higher congruence due to parents not relying solely on adolescents for information retrieval, but also being informed by teachers.

For internalized dimensions of HRQoL, low concordance between self- and parental-ratings was hypothesized (Kim et al., 2020; Lewis et al., 2014). Data variability was quite high. The only significant finding of association between self and parental reports was found for the Social Support and Peers subscale. Self-reports were found to account for 41.18% of variance in parental reports ($p_{\text{adjusted}} = 0.036$), which equals a Pearson's r score of .64, indicating moderate to strong correlation. This finding even exceeds previous findings of concordance in self and parental reports of internalized symptoms (Kim et al., 2020; Lewis et al., 2014). As stated above, the importance of social interaction for teenagers might contribute for it to be a detrimental factor for quality of life (Brown & Lohr, 1987; Harris, 1995; La Greca et al., 2001; Orben et al., 2020). Parents being aware of its importance for their adolescent children might contribute to them more accurately judging their children's social sentiment. Northfield and colleagues (2023) have found indications of maternal ratings to contribute to relatively accurate estimations of internalized symptoms of their children. Qualitative characteristics of communication and interaction might cause these findings, as they are important for congruence of ratings, and are often more present in maternal interactions due to gender roles. This could have contributed to the correlation being stronger than expected since the current sample consisted of $n = 16$ female parental raters.

Summing up overall investigations of rater concordance, the lack of significant findings might stem from the emerging individuality in adolescence. This could result in adolescents sharing thoughts and sentiment with their parents to a lesser extent (Harris, 1995; Northfield et al., 2023; Tomé et al., 2012). In line with this thesis, Vierhaus and colleagues (2018) identified perceived observability of sentiment and behaviour to be critical for rater concordance, rather than actual observability. Social withdrawal from parents due to depressive symptoms and adolescence might decrease perceived observability of behaviours and consequently reduce concordance.

Investigations of Attentional Bias in Adolescents diagnosed with MDD

Attentional bias was hypothesized to be manifested in differing total fixation durations between sad and neutral faces during an attentional bias, eye-tracking paradigm. As the paired-samples *t*-test yielded no significant difference between total fixation durations of sad and neutral faces, findings did not confirm the expected attentional bias to be manifested in total fixation durations. Noteworthy, in line with results of Klawohn and colleagues (2020) and Vazquez and colleagues (2018), mean total fixation durations of sad faces ($M = 1.53 \pm 0.35$) were longer than on neutral faces ($M = 1.47 \pm 0.41$). Klawohn and colleagues (2020) found a mean difference of - 0.06 s ($M_{\text{Sad}} = 2.56 \pm 0.33$ s, $M_{\text{Neutral}} = 2.50 \pm 0.38$ s trial duration = 6 s) between the two AOIs. Vazquez and colleagues (2018) found a mean difference of - 0.08 s ($M_{\text{Sad}} = 1.41 \pm 0.36$ s, $M_{\text{Neutral}} = 1.33 \pm 0.35$ s trial duration = 3.5 s). The current thesis employed a similar experimental design to Vazquez et al., 2018. The mean difference of -0.06 s found in the current analysis is in line with both sources. It even exceeds the findings of Klawohn and colleagues (2020) if trial durations were matched. Additionally, approximately 70 % of participants exhibited relative biases towards sad faces, viewing sad-neutral face pairs. These findings indicate bias towards sad faces in most individuals of a sample of adolescents diagnosed with MDD. To further analyse relative bias scores, group comparisons are necessary for assessing whether this relative bias towards sad faces is unique to depressed adolescents as has previously been found (Duque & Vázquez, 2015; Klawohn et al., 2020; Shane & Peterson, 2007).

Concerning first fixation duration of sad faces, results of a paired-samples *t*-test revealed a marginally significant difference between first fixation duration of sad and neutral faces. As first fixation duration on sad faces was higher than on neutral AOIs, these findings point towards a negative attentional bias, similar to the results of the total fixation duration. Individual relative bias scores for first fixation duration were mixed, with half of the participants exhibiting relative bias towards sad, rather than neutral faces. Noteworthy, the magnitude of relative bias towards sad faces in first fixation durations was smaller than of total fixation duration. Findings, failing to reach the level of significance, could indicate that the attentional bias is not manifested in first fixation duration on sad faces, as has previously been found (Armstrong & Olatunji, 2012; Huang et al., 2022; Shane &Peterson, 2007; Suslow et al., 2020). This is contrary to findings of other studies investigating reaction-time-based measures reporting negative attentional bias in early stages of attention (de Voogd et al., 2016; Klein et al., 2018; Yang et al., 2016), as well as one study finding evidence for attentional bias in first fixation duration in eye-tracking paradigms with similar designs as in the current thesis (Duque & Vázquez, 2015).

Investigating attentional bias manifestation in total and first fixation duration of angry faces, fixation durations for both measures have been found to be lower for angry, than neutral faces. This is in line with previous findings of no bias in early orientation towards threatening stimuli in depressed compared to control groups (Armstrong & Olatunji, 2012; Duque & Vázquez, 2015; Suslow et al., 2020). To the contrary, de Voogd and colleagues (2016), Klein and colleagues (2018), and Platt and colleagues (2015) reported attentional bias for early orientation towards angry faces in adolescent samples. Firstly, the bias was found in visual search (de Voogd et al., 2016; Klein et al., 2018), and dot-probe tasks (Platt et al., 2015), whereas the current thesis employed a free-viewing eye-tracking paradigm. Furthermore, even though findings of this thesis concerning early orientation on angry-neutral face pairs did not reach significance, mean first fixation duration for angry faces was *lower* than for neutral faces. To the contrary, de Voogd and colleagues (2016), Klein and colleagues (2018), and Platt and colleagues (2015) identified biases *towards* angry faces, resulting in increased attention towards angry stimuli in early orientation. Previous studies rarely reported differences in attention on different AOIs as has been analysed in this thesis, but rather group differences were investigated.

As a second outcome, total fixation durations on angry faces were assessed and indicated less fixation time spent on angry, as opposed to neutral faces. This is in line with prior findings (Armstrong & Olatunji, 2012; Bodenschatz et al., 2019; Duque & Vázquez, 2015) of no bias in depressed individuals in maintained attention towards threatening stimuli. Supporting the assumption of no bias manifestation towards angry faces in total fixation durations, Vazquez and colleagues (2018) found total fixation durations in angry and neutral facial AOIs to hardly differ in baseline measures of a free-viewing eye-tracking paradigm, using a similar experimental setup to the underlying thesis, but did not further statistically analyse within-subjects baseline assessments.

In the current thesis, relative bias scores for angry faces assessed for each participant individually were rather inconclusive for both outcome measures over the whole sample, as equal ratios of participants exhibited relative bias towards neutral and angry faces. Intraindividual differences of total fixation duration between angry and neutral faces were relatively small. Noteworthy, in first fixation duration, for participants exhibiting relative bias towards neutral rather than angry faces, the magnitude of intraindividual differences between first fixation durations was rather big, whereas it remained small for participants exhibiting relative bias towards angry faces. This could be interpreted as relative bias towards angry faces in first fixation duration being characterized by rather small differences in first fixation durations between AOIs, whereas the opposite is the case for relative bias towards neutral.

To synthesize findings of ABT regarding the overall bias towards sad faces in depressed adolescents, paired samples *t*-tests did not find robust evidence of attentional bias manifesting in differences between AOI fixation durations. Attentional bias towards sad faces still seems inherent after analysis of individual relative bias. Therefore, negative attentional bias might not manifest in large differences of fixation durations in AOIs, but rather in comparisons between healthy participants and those diagnosed with MDD. Concerning angry faces, no significant results of bias manifestation were found. Noteworthy, findings indicate avoidance of angry faces rather than orientation towards them. The overall non-significance of findings of negative attentional bias could be due to the small sample size after data preprocessing. Concerning first fixation duration of sad faces, Suslow and colleagues (2020) found effect sizes of bias towards sad stimuli manifested in early orientation to be rather small, which further impedes effect detection, especially with a small sample. Moreover, reliability of attentional bias in early stages of facial stimuli exposure has been found to be low. Therefore, manifestations of attentional bias as first fixation duration can only be interpreted carefully (Sears et al., 2019). Future studies should investigate attentional bias towards sad and angry faces using larger samples, for example operationalised through relative bias scores or bias differentials as proposed by Shane and Peterson (2007). Additionally, group comparisons of individuals with MDD and healthy individuals should be performed to further investigate bias manifestations. Furthermore, more studies on attentional bias employing eye-tracking paradigms in depressed adolescents are needed since current evidence is scarce.

Concordance of MDD Severity in BDI-II and DISYPS-III-SBB-DES

The significant regression model showed high concordance of BDI-II and DISYPS-III-SBB-DES ratings. Analysis indicated a very strong correlation between the two instruments (Pearson's $r = .87$). This exceeds previous findings of Besier and colleagues (2006). They found moderate to high correlation in analyses of concordances between BDI-II and subscales of the German version of the Child Behavior Checklist (CBCL, Döpfner & Melchers, 1993), SPS-J ("Screening Psychischer Störungen im Jugendalter", Hampel & Petermann, 2005), and ILK-J ("Inventar zur Erfassung der Lebensqualität von Kindern und Jugendlichen", Mattejat et al., 1998). Concerning external validity of DISYPS-III-DES, no previous investigations could be retrieved. Therefore, findings of the current thesis of high correlation between BDI-II and DISYPS-III-SBB-DES gain even more relevance.

Taking all the above-mentioned findings into consideration, the current thesis found a significant negative association between MDD and a social functioning as a subdimension of HRQoL. Contrary to expectations, no other correlation between the constructs reached the level of significance. Concerning concordance between self- and parental-ratings, the only significant congruence of ratings was found for social functioning, which even exceeded the expectations of moderate congruence. Future studies could further investigate the apparent high impact of social functioning / interactions on adolescents' mental health and quality of life. Negative attentional bias towards sad faces was found in relative bias scores, and differences in fixation durations in AOIs was found to be rather small. As only few previous studies analysed differences in fixation durations in adolescents employing eye tracking, future studies should further investigate fixation durations in AOIs with larger adolescent sample sizes.

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Abbreviations

ABT .... Attentional Bias Task

AOI .... Area of Interest

BDI-II .... Beck’s Depression Inventory II

CBT .... Cognitive Behavioural Therapy

CI .... Confidence Interval

DLPFC .... Dorsolateral Prefrontal Cortex

DSM-4 / 5 .... Diagnostic and Statistical Manual of Mental Disorders Fourth / Fifth Edition

HRQoL .... Health-Related Quality of Life

ICD-10...... International Statistical Classification of Diseases and Related Health Problems, 10th edition

MDD.. Major Depressive Disorder

OR... Odds Ratio

SSRI .... Selective Serotonin Reuptake Inhibitor

RCT.. Randomized Controlled Trial

Appendix

Abstracts

The prevalence of depressive disorders in adolescents has surged recently, necessitating expanded treatment options. Understanding symptoms, manifestations, and assessment of depressive disorders is vital for innovative therapeutic strategies. Clinical depression is linked to negative attentional bias and reduced Health-Related Quality of Life. Commonly, self- as well as parental reports are considered for assessing clinical depression. In the current thesis, a negative correlation between clinical depression and Health-Related Quality of Life was hypothesized. Concordance between self- and parental ratings of depressive symptoms and internalized Health-Related Quality of Life dimensions was expected to be low. In externalized dimensions of Health-Related Quality of Life moderate concordance was expected. Negative attentional bias was anticipated to be reflected in differing fixation durations on sad versus neutral faces. Exploratory analysis addressed biases in first fixation duration on sad versus neutral faces and differing fixation durations on angry versus neutral faces. Cross-sectional data from $N = 17$ adolescents was analysed. Simple linear regression models revealed negative associations between Health-Related Quality of Life and clinical depression. Overall agreement between self- and parental-ratings was low. Associations were strongest in models employing the social functioning dimension, suggesting its importance for adolescents' well-being. For the first time in adolescents with Major Depressive Disorder, an eye-tracking task was employed for assessing negative attentional bias. While paired t-tests showed no significant differences between viewing times of negative and neutral faces, mean fixation durations and individual biases suggest bias towards sad over neutral and neutral over angry faces.

Die Prävalenz depressiver Störungen von Jugendlichen zeigt einen ansteigenden Trend, was erweiterte Therapieangebote erforderlich macht. Die Auseinandersetzung mit Symptomen, Manifestationen und Diagnostik depressiver Störungen ist entscheidend für innovative therapeutische Strategien. Klinische Depression steht im Zusammenhang mit negativer Aufmerksamkeitsverzerrung und verminderter, gesundheitsbezogener Lebensqualität. In der vorliegenden Arbeit wurde ein negativer Zusammenhang zwischen klinischer Depression und gesundheitsbezogener Lebensqualität antizipiert. Niedrige Übereinstimmung zwischen Selbst- und Elternberichten depressiver Symptome und internalisierter Dimensionen gesundheitsbezogener Lebensqualität wurde angenommen. In externalisierten Dimensionen der gesundheitsbezogenen Lebensqualität wurde moderate Übereinstimmung erwartet. Eine Manifestierung negativer Aufmerksamkeitsverzerrung wurde als unterschiedliche Fixierungszeiten auf traurige, verglichen mit neutralen Gesichtern erwartet. Explorative Analysen untersuchten die Manifestierung von Aufmerksamkeitsverzerrung in der Dauer der ersten Fixation von traurigen, im Vergleich zu neutralen Gesichtern sowie unterschiedliche Fixierungszeiten auf wütende, verglichen mit neutralen Gesichtern. Querschnittsdaten von N = 17 Jugendlichen wurden analysiert. Einfache lineare Regressionsmodelle zeigten negative Assoziationen zwischen der gesundheitsbezogenen Lebensqualität und klinischer Depression. Insgesamt war die Übereinstimmung von Selbst- und Elternberichten gering. Modelle, die Dimensionen der sozialen Funktionsfähigkeit inkludierten, zeigten aber hohe Korrelationen, was auf ihre Bedeutung für die gesundheitsbezogene Lebensqualität von Jugendlichen schließen lässt. Erstmalig wurde bei Jugendlichen mit klinischer Depression ein Eye-Tracking Experiment zur Erhebung negativer Aufmerksamkeitsverzerrungen eingesetzt. Während *t*-Differenzentests keine signifikanten Unterschiede zwischen den Fixierungszeiten von negativen und neutralen Gesichtern zeigten, legen mittlere Fixierungszeiten und relative Verzerrungen präferierte Verarbeitung von traurigen, im Vergleich zu neutralen und neutralen, verglichen mit wütenden Gesichtern nahe.