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Aberrant attentional bias to sad faces in depression and the role of stressful life events: Evidence from an eye-tracking paradigm☆

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ABSTRACT

Attentional biases are thought to be involved in the etiopathogenesis of depressive disorders. Recent studies indicate eye-tracking techniques could overcome methodological issues of traditional reaction time bias measures and be used to reliably quantify biases in attention. In the current study, 50 participants with a current depressive disorder and 31 never-depressed individuals performed a free-viewing eye-tracking paradigm with two counterbalanced blocks; one contained four-by-four arrays of happy and neutral faces, the other arrays of sad and neutral faces. Average dwell-times were analyzed, and internal consistency was examined. Dwell-time measures had good to excellent internal consistency. Both groups were characterized by increased dwell-time to happy compared to neutral faces (i.e., bias toward positive faces). Never-depressed participants showed a bias away from sad stimuli (i.e., increased dwell-time to neutral compared to sad faces), that was not evident in the depressed group. Moreover, depressed individuals dwelled longer on sad stimuli than never-depressed participants. Within depressed participants, bias to sad faces was associated with both childhood trauma and recent negative life events. Results demonstrate that an attentional bias towards sad faces in depression can be reliably assessed using free-viewing eye-tracking technique and its magnitude is exacerbated by the experience of stressful life events.

Depressive disorders are among the most prevalent and impairing disorders worldwide (Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015; Kessler et al., 2003). According to cognitive models, attentional biases are assumed to play a significant role in the etiopathogenesis of depression (Beck, 1976; Clark, Beck, & Alford, 1999). Specifically, increased attention to negative stimuli and decreased attention to positive stimuli have been assumed to contribute to the cognitive distortions involved in the pathophysiology of depressive disorders (Beck & Clark, 1988; Koster, De Lissnyder, Derakshan, & De Raedt, 2011). Knowledge about depression-related alterations in attentional biases are relevant both for understanding the pathogenic processes in depression, and for the development of specific interventions that might directly target these biases, i.e., attentional modification trainings (Lazarov, Ben-Zion, Shamai, Pine, & Bar-Haim, 2018). Some evidence suggests that manipulating attention can improve depression-related symptoms (Wells & Beevers, 2010) and risk for recurrence (Browning, Holmes, Charles, Cowen, & Harmer, 2012). However, the nature of aberrant attentional patterns in depression is still not satisfactorily understood. Major aims of the current study therefore were to determine the presence of attentional biases in a rather large group of participants with current depression by directly contrasting positive and negative emotional stimuli to neutral, and to investigate associations between these biases and both early and recent stressors. Our overarching goal was to shed more light on the nature and role of attentional biases, as

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assessed by eye-tracking, in the etiopathogenesis of depression.

Most research to date on attentional biases in clinical disorders has employed experimental paradigms that assess reaction times to infer biases in attention (e.g., the dot probe task or emotional Stroop task). Studies that employ these behavioral measures of attentional bias suggest that individuals with depression focus attention more towards negative compared to positive stimuli (Gotlib, Kasch, et al., 2004; Gotlib, Krasnoperova, Yue, & Joormann, 2004; Peckham, McHugh, & Otto, 2010). However, inconsistencies in findings and non-replications (for reviews see: Mathews & MacLeod, 2005; Peckham et al., 2010) have given rise to concerns about the measurement quality of reaction time measures of attentional bias. Specifically, behavioral attentional bias measures have repeatedly been shown to have insufficient psychometric properties, including poor reliability and internal consistency (Kappenman, Farrens, Luck, & Proudfit, 2014; Rodebaugh et al., 2016; Schmukle, 2005; Waechter, Nelson, Wright, Hyatt, & Oakman, 2014).

A potentially more naturalistic and methodologically superior method for assessing attentional biases employs eye-tracking and calculates the amount of time individuals fixate on specific stimuli during picture viewing. For instance, participants are simultaneously shown multiple faces, and eye-tracking can be used to separately calculate how much time (i.e., dwell-time) participants spend on pleasant and neutral stimuli. A meta-analysis by Armstrong and Olatunji (2012) indicates that depressed individuals are mostly characterized by increased dwell-time to dysphoric/sad stimuli and decreased dwell-time to positive/happy stimuli. Four newer studies in depression using free-viewing paradigms confirmed alterations in attentional biases in depression, albeit with some variation in results: increased negative and decreased positive bias (Lu et al., 2017), increased negative in combination with normal positive bias (Lazarov et al., 2018) or marginally decreased positive bias (Duque & Vazquez, 2015), as well as reduced positive bias only (Isaac, Vrijsen, Rinck, Speckens, & Becker, 2014). A very recent systematic review on eye-tracking results in depression concludes moderate effects for both increases in maintained attention towards dysphoric stimuli and reduction in attention to positive stimuli (Suslow, Husslack, Kersting, & Bodenschatz, 2020).

Critically, free-viewing eye-tracking paradigms seem to outperform traditional behavioral bias measurements from a methodological perspective: initial results in both healthy (Skinner et al., 2018) and depressed individuals indicate that dwell-time bias measures derived from eye-tracking have good internal consistency (Lazarov et al., 2018; Sanchez, Romero, & De Raedt, 2017) as well as acceptable test-retest reliability (Lazarov et al., 2018). Collectively, these studies suggest the potential utility of eye-tracking approaches for examining attentional biases in depression.

Most studies to date have included relatively small clinical samples and results have varied somewhat across studies; thus, replications in larger clinical samples are needed. Moreover, previous studies often directly contrasted attention to positive versus negative stimuli – and have failed to include neutral stimuli. The separate assessment of attentional allocation in both a happy vs. neutral and sad vs. neutral condition is important in order to determine whether previously observed biases towards negative over positive stimuli in depression is driven by the presence of a negative bias, and/or the absence of a positive bias. A better understanding of the *specific* biases in depression could directly inform intervention efforts. Another potential methodological aspect that might have affected bias detection in depression in the past is the duration of stimulus presentation. Several studies suggest that attentional biases in depression are more likely to emerge when longer presentation times are employed (Armstrong & Olatunji, 2012), in line with cognitive models suggesting that these biases stem from deficits in top down processing (Kellough, Beevers, Ellis, & Wells, 2008; Sears, Thomas, LeHuquet, & Johnson, 2010). In the current study, we employed a presentation time of 6 s, utilizing a paradigm in line with Lazarov et al. (2018), to extend their findings in a larger group of individuals with depression to evaluate whether depression is associated with a negative bias, lack of a positive bias, or both. This presentation time is approximately intermediate with regard to what previous studies have utilized (i.e., some studies employing shorter, e.g., 1–5 s, but several also longer, e.g., 8–30 s, stimulus durations; for an overview see Suslow et al., 2020). Moreover, a study by Soltani et al. (2015) directly evaluated the time course of attentional differences between healthy participants and individuals with depression, and found that differences in attention allocation to sad stimuli may become apparent between depressed and healthy individuals only after 4–6 s of stimulus presentation.

Importantly, alterations in attentional biases are discussed as potential risk factors for depression, but only few studies so far (Browning et al., 2012) have linked altered biases to other risk factors and explored their potential association in individuals with depression. In the current study, we assessed two established risk factors for depression: self-reported childhood trauma and recent stressful life events. Childhood trauma has been shown to contribute to the development of depression in adult life (Kessler & Magee, 1993; Kessler et al., 2010) and a more chronic course of depressive disorders (Wiersma et al., 2009). Similarly, stressful life events during adulthood often precede the onset of depressive episodes (Kendler et al., 2010; Kendler, Thornton, & Gardner, 2000). Moreover, childhood adversity and negative life events later in life have been shown to interact, such that individuals with childhood trauma were specifically sensitive to the depressogenic effects of stressful life events (Kendler, Kuhn, & Prescott, 2004). One recent study found an association of childhood trauma with attentional biases assessed with eye-tracking in current depression (Bodenschatz, Skopinceva, Ruß, & Suslow, 2019); however, recent negative life events were not taken into account, and positive versus negative attentional biases were not separately evaluated. In the current study, we examined the impact of childhood trauma and recent negative life events on both positive and negative attentional biases in depression.

Overall, the current study sought to replicate previous findings while addressing limitations of existing work. We assessed attentional bias in a relatively large clinical sample of individuals with a current depressive disorder ($n = 50$) and a comparison group of never-depressed healthy individuals ($n = 31$). A methodological innovation is the use of a free-viewing eye-tracking technique with complex stimulus arrays displaying as many as 16 face stimuli simultaneously on each trial, but separately assessing attentional biases to happy and sad stimuli in comparison to neutral stimuli. This approach allows for an independent assessment of attentional biases toward sad and happy faces—as well as the psychometric properties of each type of bias. So, while the stimuli arrays used in the current study are complex and thus provide competition between stimuli (e.g., similar to visual exploration in naturalistic situations), each grid only contains two emotional stimulus types (one emotional, one neutral) at a time, thus enabling unambiguous interpretation of the results. Furthermore, we intended to investigate pathogenic mechanisms that might underlie aberrant attentional biases in depression and examined associations with self-reported childhood trauma and recent stressful life events. To contrast these potential risk-factor associations with disorder consequences, we also explored associations between depression-related attentional biases with self-reported symptom severity and number of previous depressive episodes.

1. Methods

1.1. Participants

Participants were recruited from the local community via online advertisement (i.e., Facebook.com), through the psychology clinic at Florida State University, word of mouth, and community postings. Participants were included in the depressed group (DEP) if they met diagnostic criteria for a current mood disorder, i.e., current major depressive episode (MDE) and/or persistent depressive disorder (PDD), and scored higher than 13 on the BDI-II (Beck, Steer, & Brown, 1996).

Exclusion criteria for the DEP group were a lifetime diagnosis of a bipolar or psychotic disorder, or current substance or alcohol use disorder. Participants were included in the healthy control group (HC) if they never met diagnostic criteria for a mood disorder and did not currently meet criteria for other psychiatric disorders. Participants were enrolled such that DEP and HC groups did not differ overall with regards to age, gender, and level of education. All participants had normal or corrected-to-normal vision, reported no history of head trauma or neurological disease, and were 18–60 years old. Participants received explanations of aims and procedures of the study and provided informed written consent. The study was conducted in accordance with ethical guidelines of the Declaration of Helsinki and approved by the Florida State University Institutional Review Board. All participants were compensated with $20/hour. Data were collected during one visit of a two-visit protocol, and results from other assessed measures (e.g., EEG, fMRI) are presented elsewhere (e.g., Klawohn, Burani, Bruchnak, Santopetro, & Hajcak, 2020a; Klawohn, Santopetro, Meyer, & Hajcak, 2020). Data from 52 participants with depression and 31 healthy participants were collected. Data of two participants in the DEP group were excluded due to insufficient data quality ($n = 1$) and extreme values, i.e., values > 3 SD from the mean ($n = 1$). The final study sample included 50 individuals with current depression and 31 healthy comparison participants.

1.2. Measures

The Structured Clinical Interview for DSM-5 (SCID-5-RV; First, Williams, Karg, & Spitzer, 2015) was administered by two PhD-level clinical psychologists to assess presence of current and past mood disorders. The SCID is a well-validated interview for DSM-5 diagnoses and allows for determination of MDE subtypes. For the sake of brevity, other past and present psychopathology was evaluated using the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998), updated for DSM-5 (version 7.0.2, Sheehan, 2015), a structured interview widely used for evaluating psychiatric diagnoses. Participants further rated current depressive symptoms with the Beck Depression Inventory–II (BDI-II; Beck et al., 1996). The BDI-II is a well-validated measure of depressive symptom severity with good psychometric properties. The total score derived from 21 items ranges from 0 to 63.

The Life Experiences Survey (LES; Sarason, Johnson, & Siegel, 1978) is a 57-item scale administered to assess the perceived impact of various life events (e.g., new job, divorce) that occurred within the previous 12 months. For the present study, the seven-item student portion of the survey was omitted, resulting in a total of 47 items and three additional fill-in-the-blank options to indicate further applicable events, if any. Scores were rated on a 7-point Likert scale (−3 = *extremely negative* to +3 = *extremely positive*). Following Sarason et al. (1978), separate scores for positive and negative life events were calculated by summing the total positive and negative (absolute value) impact rating of endorsed items, respectively.

In addition, the Childhood Trauma Questionnaire (CTQ; Pennebaker & Susman, 1988) was administered to assess history of traumatic experiences before the age of 17. The CTQ is a six-item scale assessing several types of potentially traumatic events (e.g., "death of a very close friend or family member") experienced during childhood. Scores were rated on a 7-point Likert scale (1 = *not traumatic at all* to 7 = *extremely traumatic*) and per Pennebaker and Susman (1988), only items rated ≥ 6 were scored as traumatic events.

1.3. Eye-tracking assessment

Gaze parameters were recorded using an Eyelink 1000+ (SR Research Ltd., Mississauga, Ontario, Canada) with a sampling rate of 500 Hz. Participants were seated approximately 60–63 cm from the desk-mounted eye-tracking device and 93–96 cm from the monitor. The device-to-screen distance was fixed at 33 cm. Stimuli were presented on a 24-inch monitor with a screen resolution of 1920x1080 pixels. The eye-tracking camera was set to pupil-corneal reflection mode, with thresholds set to 75 to 110 for the pupil and a maximum of 230 for the corneal reflex. Before each block, a 13-point calibration was performed followed by a 14-point validation. The calibration procedure was repeated if visual deviation was greater than 1.0° on the X or Y axis. All participants were able to meet this criterion.

1.4. Free-viewing paradigm

The viewing paradigm was administered using experiment-builder software (SR Research, Ontario, Canada; version 2.1.140). Two blocks were administered in counterbalanced order across participants; one block contained pictures of neutral and sad facial expressions, the other contained neutral and happy pictures. Each block encompassed 30 trials that lasted 6 s each. In order to ensure task-engagement, a centrally located fixation stimulus was presented between trials and a fixation duration of 1 s was required to begin the next trial, after a following 2 s ITI. On each trial, 16 different pictures of facial expressions (i.e., 8 emotional, 8 neutral expressions) were displayed in a 4x4 grid (see Fig. 1). One block employed 16 different actors (8 female) appearing with two expressions each, whereas 16 other actors (8 female) were used for the other block. Picture locations within the grid were counterbalanced with regards to gender and emotional expression; additionally, emotional expression and gender was equated in terms of distance from fixation. All pictures were taken from the KDEF Stimulus Set (Lundqvist, Flykt, & Öhman, 1998). Participants were instructed to freely view each grid until the inter-trial fixation was presented.

Eye-tracking data was processed using EyeLink Data Viewer (SR Research Ltd.; version 3.1.246). The pictures were defined as regions of interest within the whole grid and background. Dwell-times were exported based on the 6 s stimulus presentation. Mean dwell-times for emotional and neutral stimuli were extracted for each block, and separately for odd and even trials within each block to calculate split-half reliability; Δdwell-times were calculated as the emotional minus neutral dwell-times for each block. Percentage of missing gaze time per block was determined for all participants, (sad/neutral block, DEP: $M = 2.0\%$, $SD = 2.9$, HC: $M = 1.6\%$, $SD = 1.7$; happy/neutral block, DEP: $M = 1.7\%$, $SD = 2.6$, HC: $M = 1.1\%$, $SD = 1.0$), none of the participants had over 20% of gaze time missing in any block.

1.5. Data analysis

Internal consistency of dwell-times for the was examined with a split-half approach. The correlation between averages of odd- and even-numbered trials was determined, corrected using the Spearman-Brown prophecy formula (Nunnally, Bernstein, & Berge, 1967).

All statistical analyses were conducted with SPSS (IBM; version 23.0). Demographic and self-report data were analyzed with *t*-tests or X^2 tests. Comparison of dwell-times was performed using a mixed model repeated-measures ANOVA including the within-subjects factors block (happy, sad) and picture type (emotional, neutral), and the between-subjects factor group (DEP, HC). For significant interactions, follow-up ANOVAs and *t*-tests were conducted. Within the DEP group, exploratory multiple linear regression analyses were conducted with to examine whether endorsement of childhood traumatic events in the CTQ (dichotomous; trauma endorsed = 1; trauma not endorsed = 0), negative life events from the LES (mean-centered; continuous), or their interaction would predict Δdwell-time in the sad/neutral block. As a control analysis, we conducted the same linear regression with positive life events from the LES replacing negative life events as one predictor. Finally, Pearson correlation coefficients were determined in the DEP group to examine associations of Δdwell-times with BDI-II and number of previous depressive episodes. Methods and results regarding further clinical characteristics as potential moderators is presented in supplementary materials.

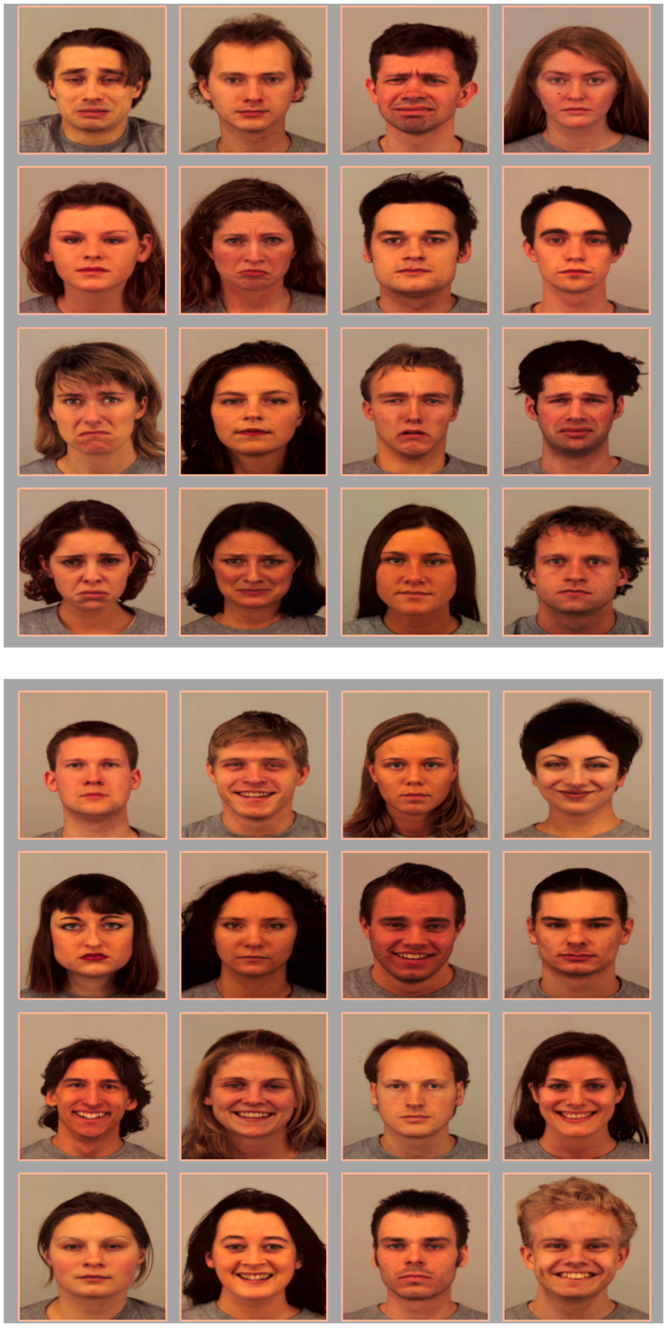

Fig. 1. Example arrays of emotional and neutral pictures from the sad/neutral block (upper panel) and the happy/neutral block (lower panel).

2. Results

Demographic and clinical characteristics of participants are presented in Table 1. The DEP and HC groups did not differ with respect to age, gender, ethnicity, or educational level. At the time of study participation, participants in the MDD group met diagnostic criteria either for a current episode of major depressive disorder (MDE, $n = 24$), or persistent depressive disorder (PDD, $n = 2$), or both ($n = 24$). Participants reported varying numbers of previous major depressive episodes (MDE), such as 1 to 3 ($n = 13$), 4 to 9 ($n = 16$), and 10 or more ($n = 13$), whereas some participants in the DEP group did not report previous MDE ($n = 8$). Within participants currently meeting diagnostic criteria for MDE, the following DSM-5 subtypes were present: with anxious distress ($n = 40$), mixed features ($n = 2$), melancholic features ($n = 28$), atypical features ($n = 7$). About half of the participants in the DEP group ($n = 26$) met diagnostic criteria for one or more of the following psychiatric disorders: generalized anxiety disorder ($n = 16$), social anxiety disorder ($n = 11$), specific phobia ($n = 3$), panic disorder ($n = 8$), agoraphobia ($n = 9$), obsessive-compulsive disorder ($n = 4$), post-traumatic stress disorder ($n = 2$), eating disorders ($n = 4$); resulting in 25 participants of the DEP group with a comorbid diagnosis of at least one current anxiety disorder (i.e., social anxiety disorder, generalized anxiety disorder, panic disorder, agoraphobia, or specific phobia). In the DEP group, 28 individuals (56%) were currently taking psychotropic medication (antidepressants, including SSRIs, $n = 23$; anxiolytics $n = 8$; anticonvulsants $n = 6$, stimulants $n = 2$, other $n = 3$).

Table 1
Demographic and Clinical Variables and Eye-tracking data for the Groups of Participants with a Current Diagnosis of Depression (DEP) and Participants without Current Psychiatric Disorder (HC).

	HC	DEP	*p*
Demographic and Clinical Variables			
N (% female)	31 (77.4)	50 (82.0)	.572
Age (years)	34.9 (13.5)	38.3 (12.1)	.247
Ethnicity (% Caucasian)	90.3	92.0	.346
Education (years)	4.61 (0.76)	4.52 (0.84)	.617
BDI-II	1.5 (2.2)	29.0 (9.5)	< .001
LES Negative Life Events	3.13 (2.75)	13.0 (8.31)	< .001
LES Positive Life Events	7.58 (4.91)	6.80 (6.88)	.584
CTQ (trauma endorsed/not endorsed)	7/24	33/17	< .001
Eye-tracking Measures			
Sad/neutral-block:			
Dwell-time sad (s)	68.24 (12.91)	76.63 (10.01)	.002
Dwell-time neutral (s)	82.59 (16.81)	75.09 (11.52)	.020
ΔDwell-time sad-neutral (s)	−14.35 (27.62)	1.55 (19.19)	.003
Happy/neutral-block			
Dwell-time happy (s)	85.83 (13.48)	82.06 (12.73)	.210
Dwell-time neutral (s)	67.95 (11.61)	69.88 (12.30)	.485
ΔDwell-time happy-neutral (s)	17.88 (24.50)	12.18 (23.28)	.297

Note. Means are displayed, standard deviations in parentheses, *p*-values for between-group t-tests or χ^2-tests are presented in the last column. BDI-II = Beck Depression Inventory-II, LES = Life Experiences Survey, CTQ = Childhood Trauma Questionnaire.

There were no group differences in impact of positive life events in the LES, $t(79) = 0.55$, $p = .584$, $d = 0.13$, 95% CI [-2.04, 3.61], between the DEP group ($M = 6.80$, $SD = 6.88$) and HC group ($M = 7.58$, $SD = 4.91$), but there was a significant group difference in self-reported impact of negative life events, $t(79) = 7.73$, $p < .001$, $d = 1.59$, 95% CI [6.78, 12.93], in that the DEP group reported a higher impact of negative life events ($M = 13.0$, $SD = 8.31$) compared to the HC group ($M = 3.13$, $SD = 2.75$). On the CTQ, a majority of individuals with current depression endorsed a childhood traumatic event ($n = 33$, 66%), compared to a significantly lower number of participants in the HC group ($n = 7$, 22.6, $X^2 = 14.33$, $p < .001$).

2.1. Eye-tracking results

The internal consistency analyses revealed good to excellent internal consistency of dwell-times for sad faces (DEP: $r = 0.75$, HC: $r = 0.96$) and neutral faces (DEP: $r = 0.64$, HC: $r = 0.93$) in the sad/neutral block, and dwell-times for happy faces (DEP: $r = 0.87$, HC: $r = 0.91$) and neutral faces (DEP: $r = 0.85$, HC: $r = 0.94$) in the happy/neutral block.

Mean dwell-times for both groups in the two experimental blocks are

displayed in Table 1, results of other measures (i.e., dwell count, first dwell latency and duration) are presented in a data supplement, Table S1. The block x picture type x group ANOVA on dwell-times yielded a significant three-way interaction, $F(1, 79) = 5.84$, $p = .018$, $\eta^2_p = .07$, indicating that differences in attentional biases between participants with and without current depression were block-dependent (see Fig. 2). Two separate ANOVAs with the factors picture type and group were conducted as follow-up. The results of the ANOVA on dwell-times in the sad/neutral block showed a significant main effect of picture type, $F(1, 79) = 6.05$, $p = .016$, $\eta^2_p = .07$, and interaction of picture type and group, $F(1, 79) = 9.34$, $p = .003$, $\eta^2_p = .11$. Follow-up tests indicated that healthy participants on average dwelled longer on neutral than on sad facial expressions, $t(30) = 2.89$, $p = .007$, $d = 0.52$, 95% CI [0.14, 0.89], whereas participants with depression did not, $t(49) = 0.57$, $p = .570$, $d = 0.08$, 95% CI [-0.19, 0.36]. Further analyses confirmed that depressed participants dwelled longer on sad facial expressions than healthy participants, $t(79) = 3.27$, $p = .002$, $d = 0.75$, 95% CI [0.28, 1.21].

For the happy/neutral block, the follow-up ANOVA indicated a significant effect of picture type, $F(1, 79) = 30.67$, $p < .001$, $\eta^2_p = .28$, but no significant effect of group, $F(1, 79) = 0.99$, $p = .322$, $\eta^2_p = .01$, nor interaction of picture type and group was present, $F(1, 79) = 1.10$, $p = .297$, $\eta^2_p = .01$. Thus, both groups showed longer dwell-times for happy compared to neutral facial expressions.

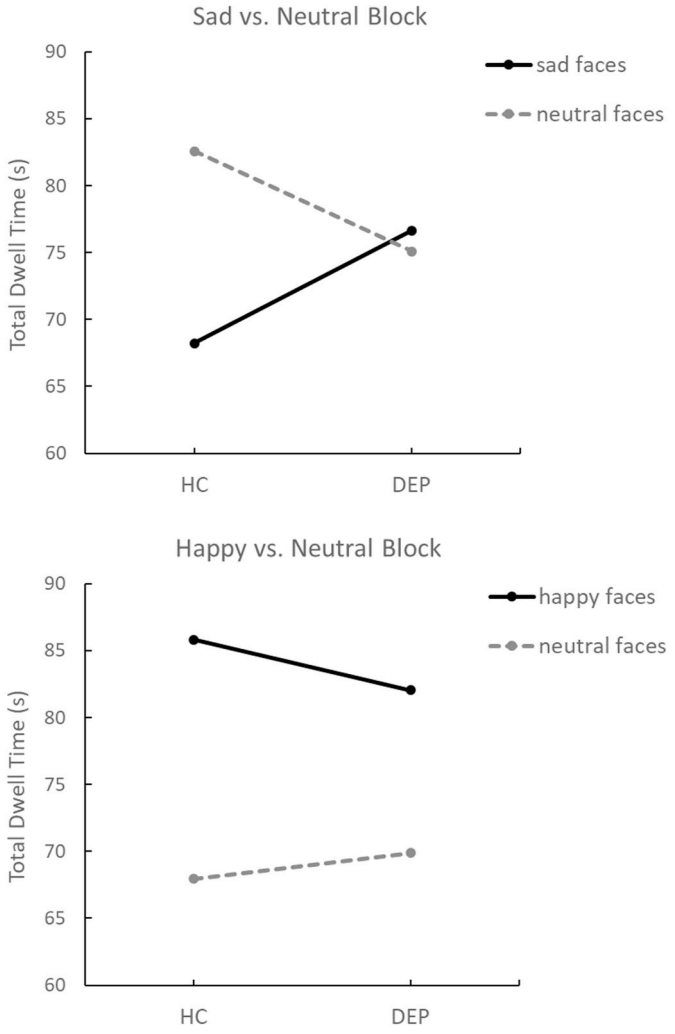

Fig. 2. Visualization of mean total dwell-times in the sad/neutral block (upper panel) and the happy/neutral block (lower panel) in the healthy participants group (HC) and the group of participants with current depression (DEP).

The linear regression within the DEP group with childhood trauma (CTQ) and recent negative life events (LES) scores[1] and their interaction as predictors of Δdwell-times in the sad/neutral block yielded a significant overall model, $F(1, 46) = 4.01$, R^2 (Nagelkerke) $= 0.207$, $p = .013$. Importantly, the interaction effect was significant in this model, indicating that the recent negative life events score interacted with the presence of childhood traumatic events to predict Δdwell-time on the sad/neutral block, $b = 1.87$, $SE = 0.65$, $p = .006$, 95% CI [0.55, 3.19]. Thus, endorsing a childhood traumatic event was a significant predictor of increased bias towards sad faces at average levels of negative life events, $b = 11.59$, $SE = 5.36$, $p = .036$, 95% CI [0.79, 22.39], and high levels (+1 *SD* above) of negative life events, $b = 27.12$, $SE = 8.05$, $p = .002$, 95% CI [10.91, 43.33], but not at low levels (−1 *SD* below), $b = -3.95$, $SE = 7.20$ $p = .586$, 95% CI [-18.44, 10.55]. This moderation effect is presented in Fig. 3.

Results of correlational analyses within the DEP group indicated no significant associations between Δdwell-time in the sad/neutral block and BDI-II, $r(49) = 0.113$, $p = .434$, or number of depressive episodes, $r(49) = 0.156$, $p = .280$, or between Δdwell-time in the happy/neutral block and BDI-II, $r(49) = -.054$, $p = .709$, or number of depressive episodes, $r(49) = 0.115$, $p = .425$, respectively. The analyses regarding further clinical characteristics as moderators of the attentional bias alteration in depression yielded no indication of such modulatory effects (see supplementary data).

3. Discussion

Results of the current study demonstrated that participants with a current depressive disorder dwelled longer on sad faces than a comparable group of healthy participants. Further, a relative bias away from

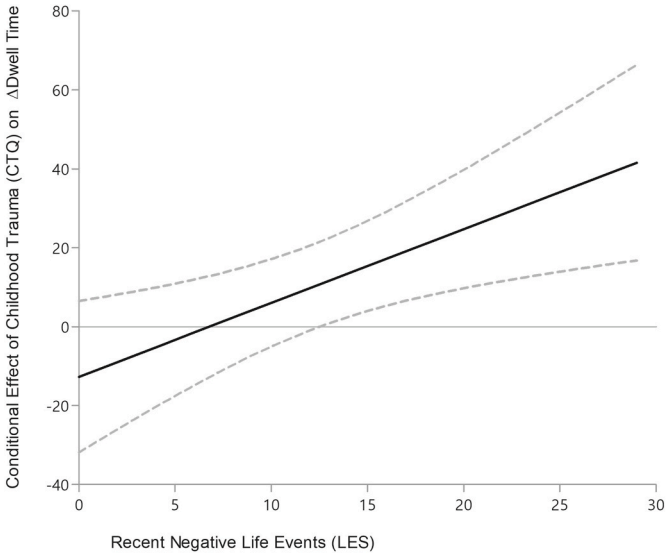

Fig. 3. Prediction of Δdwell-times in the sad vs. neutral block by childhood trauma (CTQ) as moderated by negative recent life events (LES) score in the group of participants with current depression (DEP, $n = 50$).

[1] To assess the specificity of these effects for negative stressors, we also examined whether Δdwell-time in the sad/neutral block would similarly be predicted by positive life events interacting with childhood trauma in the DEP group. The respective regression model including positive life events from LES and CTQ traumatic childhood events as well as their interaction as predictors did not yield a significant regression model, F^2 (3) = *1.53,* R^2 (Nagelkerke) = 0.091, $p = .283$.

sad and towards neutral faces, as observed in the healthy group, was not present in the group of participants with depression. In contrast, a relative attentional bias towards happy faces over neutral faces was evident in both groups. Finally, the dwell-time measures and associated bias scores were characterized by good to excellent internal consistency.

The alteration in negative bias found in the participants with current depression is in line with previous findings from free-viewing paradigms in participants with depression (Armstrong & Olatunji, 2012; Lazarov et al., 2018). Increased attentional allocation to sad stimuli has been interpreted as an index of increased elaborative processing of dysphoric content in individuals with current depression (Armstrong & Olatunji, 2012), potentially corresponding to a deficit in the ability to remove negative information from working memory (Levens & Gotlib, 2010). These findings are also consistent with the possibility that depression is characterized by impaired attentional disengagement from negative stimuli, although the current study did not directly test this mechanism (Sanchez, Vazquez, Marker, LeMoult, & Joormann, 2013).

The current study extends previous findings regarding an increased negative attentional bias to a comparatively large clinical population, thus allowing for the investigation of these effects in relation to clinical characteristics and well-known risk factors for depression. The identified alteration in attentional bias toward sad relative to neutral faces in the depressed group was not impacted by current comorbidity with an anxiety diagnosis, presence of persistent depressive disorder, or current medication (see supplementary data). Moreover, number of previous depressive episodes and self-reported symptom severity did not predict magnitude of negative attentional bias in depression, further suggesting that a negative bias in the DEP group is not exacerbated by increased symptoms or longer duration of the disorder. Collectively, these data from the investigation of potential clinical moderators and the lack of an association with disorder duration or severity point towards a rather generic, state-independent alteration in negative attentional bias within the depressed sample. This pattern seems in line with the notion that heightened negative attentional biases found in depression might be a marker of risk rather than a consequence of the disorder (Joormann, Talbot, & Gotlib, 2007). In line with this possibility, current results strongly suggested that life stressors, including both childhood trauma and recent negative life events, impact the magnitude of an attentional bias towards sad stimuli in the group of participants with current depression. That is, the presence of traumatic childhood experiences was only predictive of an increased attentional bias to sad stimuli when additional recent stressful life events were also experienced. As these critical life experiences themselves are established risk factors for depression, this association with negative attentional biases is consistent with the notion that attentional biases might represent markers of increased risk for depression (Joormann et al., 2007).

This association could emerge through either of two mechanisms. Heightened negative attentional biases could amplify the effects of stressful negative life events on the development or exacerbation of depressive symptomatology, thus functioning to mediate the impact of life events on depressive outcomes. Or, life stressors could result in an increase in negative attentional biases and depressive symptoms in a parallel fashion. Since the current data are cross-sectional in nature, no conclusions can be drawn about the direction of causality and longitudinal studies are needed to further examine these possible mechanisms. Nonetheless, the association shown in the current study provides novel insight in the complex interplay of risk factors for depression, and demonstrates the potential utility of negative attentional biases as indicators of risk markers for changes in depression.

To our knowledge, only one previous study investigated the association of attentional bias alterations assessed using a free-viewing paradigm, and childhood maltreatment experiences. Bodenschatz et al. (2019) used a paradigm with simultaneous presentation of four emotional expressions, and found that childhood maltreatment was associated with reduced attention to angry and sad expressions among participants with depression; these data were interpreted in terms of avoidance of these emotions. In contrast, the current results suggest that increased dwelling on negative (i.e., sad, dysphoric) stimuli in those depressed individuals with both childhood and recent stressful life events. Thus, our results do not suggest a pattern of avoidance, but rather point towards experience-induced salience of sad stimuli. There were several methodological differences between these studies, however. The present study included the assessment of recent negative life events, and only presented two face types per block. Further studies incorporating the investigation of childhood and recent critical life events will be needed for clarification.

In contrast to the observed increase in attention to sad faces, no alteration in attention to happy faces was found in the depressed group. This lack of a depression-related reduction in positive attentional bias is in contrast with several studies (Armstrong & Olatunji, 2012; Duque & Vazquez, 2015; Lu et al., 2017), albeit not all previous studies have found this effect (Eizenman et al., 2003). It is important to note that previous eye-tracking studies typically present a limited number of different stimuli at one time (e.g., often one positive versus one other stimulus type). In contrast, this is the first study to assess for a positive bias in depression separately while using complex stimuli arrays. Thus, the previously observed alterations in positive biases might be limited to task designs that directly contrast positive stimuli with alternative emotional stimuli (i.e., less complex arrays with fewer stimuli, usually 2 or 4). In addition, some previous eye-tracking studies on attentional biases in depression have used more complex emotional pictures as stimuli (Eizenman et al., 2003; Kellough et al., 2008; Wells, Clerkin, Ellis, & Beevers, 2014), which could further explain variation in findings. Future studies in clinical samples might directly compare these methodological differences in terms of their impact on positive attentional bias in depression.

A methodological innovation of the current study is the use of a free viewing paradigm with complex stimulus grids that present as many as 16 faces at a time, while separate experimental blocks were employed to contrast happy or sad face stimuli with neutral stimuli separately. Other studies have also employed displays of multiple stimuli in studies of depression, but usually show identical actors with different expressions simultaneously (e.g., Kellough et al., 2008). The use of these complex stimulus arrays might reflect a more naturalistic viewing behavior insofar as it allows for competition of several simultaneous stimuli (Lazarov et al., 2018); moreover, the presentation of several faces of each type on each trial could lead to a more sensitive and reliable assessment of attentional biases. Future studies should directly investigate the impact of such methodological choices on detection of bias alterations in clinical groups by comparing different stimulus types and presentation modes (i.e., 2, 4, or 16 stimuli simultaneously). Furthermore, the separate assessment of attentional biases in two counterbalanced blocks allowed us to determine that the predominant alteration in depressed individuals was the presence of a negative bias, while we did not observe the absence of a positive bias.

The current study suggests relative specificity of aberrant attentional allocation in depression for negative, specifically dysphoric stimuli, and thus contributes to a better understanding of the respective contribution of different biases to depressive pathophysiology. Furthermore, these data suggest that a lack of bias away from sad stimuli – but not necessarily a lack of bias toward positive stimuli – might be a potential target for intervention approaches that leverage eye-tracking, which have already been successfully applied in anxiety (Lazarov, Pine, & Bar-Haim, 2017). That is, methods described in Lazarov et al. (2017) could be employed to reduce bias toward sad faces in depression. Indeed, an according first approach in depression recently yielded promising results (Shamai-Leshem, Lazarov, Pine, & Bar-Haim, 2020). Eye-tracking based bias measures are an especially promising target for such interventional efforts, as the current study further demonstrated that alterations in attentional allocation in depression can be reliably assessed with an eye-tracking based, passive viewing paradigm (Lazarov et al., 2018).

One methodological limitation of the current study could be the use of a moderate stimulus presentation duration (i.e., 6 s) in comparison to other free-viewing studies in depression that use even longer presentation durations (Armstrong & Olatunji, 2012; Suslow et al., 2020). It is conceivable that a lack of a bias towards positive facial expressions might have emerged at longer presentation times. Future studies using similar experimental designs with complex stimulus grids should take this possibility into account and consider using longer presentation times. Another limitation of the current study is the lack of a clinical control group, such as one with pure anxiety disorders, which could help examine specificity of the observed effects for depression in contrast to psychopathology in general. Further, the current study was cross-sectional in nature, therefore we cannot infer whether alterations in attentional biases are a precursor or risk factor for the disorder or rather a result of increased symptoms of depression. Future studies in high-risk populations, like first-degree relatives of depressed individuals, are needed to shed light on this possibility. Similarly, prospective studies are necessary to determine whether aberrant attentional biases precede first-onset of depression. Longitudinal studies could also elucidate whether biases persist after remission or attenuate with symptom reduction. The existing literature conveys a rather inconsistent picture in this respect, with some studies showing persistent aberrant biases in individuals with remitted depression (Sears, Newman, Ference, & Thomas, 2011; Soltani et al., 2015), while others suggest no abnormality in negative attentional bias in individuals during remission (Isaac et al., 2014; Li et al., 2016). We are currently following participants from the current study to examine how the attentional bias to sad stimuli will relate to the persistence or remission of depressive symptoms over time.

In conclusion, the current study was able to parse potential alterations in positive and negative attentional biases in depression, using a free-viewing paradigm that employed more complex visual arrays (i.e., four by four grids) of faces using with eye-tracking. Depressed individuals were differentiated from healthy only in terms of attention to negative stimuli (i.e., sad facial expressions); specifically, depressed adults spent more time fixated on sad faces compared to healthy adults. While healthy adults attended less to sad compared to neutral faces, depressed adults spent roughly equal time attending to sad and neutral faces. On the other hand, both depressed and healthy adults equally attended more to happy facial expressions. Both sad and happy attentional bias measures had good to excellent psychometric properties. The results demonstrate that a free-viewing eye-tracking paradigm using complex arrays of faces can be used to reliably assess attentional biases toward sad stimuli in depression. Further, the magnitude of attentional bias to sad faces in depression was independent of depression severity and chronicity but was instead associated with the presence of both childhood trauma and recent negative life events— linking negative attentional bias to known risk factors for depression. Future studies might leverage this measure in the context of studies to evaluate risk for depression, and course of depressive episodes, to better examine the more specific mechanistic role of this measure of attentional bias in depression.

CRediT authorship contribution statement

Julia Klawohn: Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing. **Alec Bruchnak:** Formal analysis, Writing - original draft. **Kreshnik Burani:** Formal analysis, Writing - original draft. **Alexandria Meyer:** Conceptualization, Writing - review & editing. **Amit Lazarov:** Methodology, Writing - review & editing. **Yair Bar-Haim:** Methodology, Writing - review & editing. **Greg Hajcak:** Conceptualization, Methodology, Supervision, Writing - original draft, Writing - review & editing.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2020.103762.

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