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Neural markers of emotion regulation difficulties in adolescent depression and risk for depression

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Abstract

Depressed individuals tend to use maladaptive emotion regulation strategies more frequently than non-depressed individuals while using adaptive strategies (e.g., reappraisal) less frequently. Objective neural markers of emotion regulation ability could aid in identifying youth at greatest risk for depression and functional impairment more broadly. We used electroencephalography to examine emotion regulation in adolescents (aged 14–17; $N = 201$) with current depression ($n = 94$) and without any history of depression ($n = 107$) at high ($n = 54$) and low ($n = 53$) risk for depression based on a maternal history of depression. Results revealed group differences in event-related potential markers of emotion regulation using multiple scoring approaches. Never-depressed adolescents had significant reductions in mean-activity and principal component analysis-identified late positive potential responses to dysphoric stimuli under reappraisal instructions compared to passive viewing. There was no significant difference in neural responses between conditions among depressed adolescents. The magnitude of the reappraisal effects appeared slightly stronger for low-risk adolescents relative to high-risk. Exploratory analyses further demonstrated that the association between neural markers of emotion regulation and overall functioning was moderated by age, such that impaired emotion regulation abilities predicted poorer functioning among older adolescents. Findings support the sensitivity of the late positive potential to emotion regulation impairments in depression and psychopathology more broadly.

Keywords

Emotion regulation; Depression; Adolescence; Event-related potential; Late-positive potential

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.xjmad.2024.100051.

1. Introduction

Earlier onsets of depression are associated with a more debilitating course of the disorder across the lifespan [6,70]. Identifying vulnerability factors is crucial for targeted early intervention in adolescence, a high-risk period for the development of depression [14,40,75]. Emotion dysregulation is common across internalizing disorders [78], and impairments in the ability to regulate responses to dysphoric emotions are central to the onset and maintenance of depression in particular [45,50]. Given evidence that some alterations in emotion processing may precede the development of depression [51], the dysregulated processing of dysphoric stimuli may be a candidate vulnerability marker that could aid in identifying youth at greatest risk for depression, as well as functional impairment due to internalizing symptoms more broadly.

Prior research links depression with low responses to positive stimuli and minimal up-regulation of positive emotion ([1,10,19,33]; Kujawa et al., 2020; [77]). However, the literature on the regulation of negative emotions in depression is more complex, particularly across methods (e. g., self-report versus neural responses). Depressed individuals tend to endorse using emotion regulation strategies such as rumination and suppression more frequently than non-depressed individuals, and using strategies such as reappraisal, less frequently [45,46,50,60]. Meta-analytic evidence suggests reappraisal is associated with lower psychopathology symptoms while suppression and rumination are associated with elevated levels of psychopathology [13]. It is important to note, however, that the adaptiveness of a given strategy is dependent upon the interaction between the person and context [2,7]. Dysregulated processing of negative content may also be a pre-existing vulnerability for depression observable in those at high risk. Research has shown non-depressed youth at risk for depression due to a parental history of depression selectively attend more towards negative stimuli and interpret ambiguous stimuli more negatively than their low-risk peers [15,48].

Importantly, associations between depression and difficulties regulating negative emotions appears to vary across methods. For example, under explicit emotion regulation instructions, self-report ratings of affect generally show minimal differences between depressed and non-depressed adults [23,33,47], though a recent adolescent study found depressed adolescents reported less of a reduction in negative affectivity for reappraised compared with passively viewed negative images than healthy controls [25]. Findings from neuroimaging research examining emotion regulation in depressed youth are mixed. Some evidence indicates depressed youth can engage regulatory regions and reduce amygdala responses under explicit emotion regulation instructions [63, 64], while another study found depressed individuals showed less of a reduction of amygdala activation during emotion regulation compared to healthy peers [74]. Considering sustained dysphoric mood is one of the hallmark symptoms of depression, it is important to clarify our understanding of emotion regulation in clinical depression and depression risk across methods, particularly methods suitable to capturing the time course of emotion regulation.

Electroencephalography (EEG) is optimally suited for studying emotion regulation due to the high temporal resolution at the scale of milliseconds, recording the dynamics of initial reactivity and controlled recovery from emotional stimuli. Event-related potentials (ERPs) are time-locked to the presentation of circumscribed stimuli and index cognitive and affective processing [55]. One specific ERP, the late positive potential (LPP), is a sustained positive deflection in the ERP waveform beginning around 300 ms after stimulus onset over centroparietal sites and persisting throughout stimulus presentation [66]. The LPP reflects the sustained attention and elaborative processing of salient stimuli and is consistently enhanced for emotional stimuli compared to neutral [38]. Combined neuroimaging and EEG research has linked the scalp recorded LPP to activation of a broadly distributed network of cortical and subcortical regions, as well as bi-directional coupling between occipitoparietal and prefrontal regions [54,58,9]. Reciprocal projections between the medial and ventrolateral prefrontal cortices and the amygdala are central to the development of emotion regulation skills [11,68].

Critically, research utilizing emotion regulation tasks reveal the LPP is modulated by emotion regulation efforts, although the timing and topography of effects varies across studies [28,37,36,59]. Adult studies have shown reductions in parietal LPPs under explicit emotion regulation instructions compared to LPP amplitudes when passively viewing negative stimuli [28,37,36]. Others have shown reappraisal-related modulations over frontal sites [27,28], with one study showing a relative LPP enhancement for reappraisal during a mid-latency window [59]. Concordant with neuroimaging research on changes in the neural circuitry underlying emotion regulation across development [69], neurophysiological research has found differences in the ability to modulate the LPP under explicit emotion regulation instructions with age. Specifically, studies have shown minimal modulation of the LPP during reappraisal compared to passive viewing in late childhood and early adolescence, while significant LPP reductions during emotion regulation emerge by mid- to late adolescence [16,18,76]. These findings support the sensitivity of the LPP to individual differences in emotion regulation abilities, which could potentially help identify those at greatest risk for depression.

Several previous studies have shown depression is associated with reduced LPPs when passively viewing broad types of negative stimuli compared to healthy controls in both youth and adult samples [30,34, 41]. However, in studies examining LPP responses to personally relevant stimuli, namely adjectives from a self-referential encoding task, currently depressed and high-risk youth showed enhanced LPP amplitudes to negative words compared to non-depressed, low-risk youth [4, 71]. These findings support the possibility that dysregulated responses to negative stimuli may precede the development of depression and confer vulnerability for the disorder. However, to date there has been minimal research examining LPP modulations during explicit emotion regulation in adolescent depression and depression risk. One recent study comparing LPP amplitudes during reappraisal and passive viewing among depressed and control youth did not find any group differences at the neural level [25]. Additional research on this topic could clarify whether neural alterations in emotion regulation may reflect a concurrent marker of depression or a vulnerability predictive of future symptoms.

Despite the promise of the LPP for characterizing emotion regulation abilities, there are also challenges to the study of emotion regulation using traditional ERP approaches involving the visual inspection of grand averaged waveforms to identify components based on both consistency with prior research and maximal peaks and distributions on the observed data. This traditional approach has resulted in discrepancies across studies regarding the time window and electrodes used to quantify ERPs and may overlook relevant components that may not be expected based on the prior literature. Ambiguities surrounding the quantification of specific ERPs are particularly problematic for complex emotion regulation tasks, where stimuli presentation times are extended for several seconds. Principal component analysis (PCA) is a data-driven approach that systematically disentangles ERPs sensitive to emotion across development [22,29,62]. Research leveraging multiple scoring approaches could help in characterizing the temporal dynamics of emotion regulation in depressed youth.

The current study sought to examine the temporal dynamics of neurophysiological responses during an established emotion regulation task and compare whether modulations in identified ERP components and ratings of emotional intensity differed between currently depressed and never-depressed adolescents. During the task, participants viewed a series of dysphoric and neutral images with instructions to either passively view or reappraise the images while EEG data were recorded and subjective ratings of emotional intensity were collected. Secondary aims included testing potential group differences between relatively high-risk (based on maternal history of depression) and low-risk adolescents within the never depressed group. We addressed prior limitations in ERP scoring methods by examining both traditional mean activity approaches to scoring the LPP and ERPs identified using temporospatial PCA. Given the mixed literature, we hypothesized that either a parietal or frontal LPP component would be modulated by emotion regulation, with currently depressed adolescents showing less modulation of this component between conditions. We also hypothesized the effect of reappraisal would be strongest among the low-risk adolescents, indicative of a vulnerability for depression in never-depressed adolescents at relatively high risk. We expected the group differences to be relatively specific to neural measures, though some group differences for task-based ratings of emotional intensity may be observed. Finally, considering recent research suggests emotion dysregulation may represent a transdiagnostic superspectrum [78] and the diagnostic heterogeneity within our sample (see clinical description below), we conducted exploratory analyses examining whether the associations between the reappraisal-related LPP and self-reported depressive symptoms and clinician-rated functioning varied as a function of age. Given evidence for improved emotion regulation with age, we hypothesized less modulation of the LPP during reappraisal compared to passive viewing among older adolescents would be associated with more symptoms and poorer functioning.

2. Method

2.1. Participants

Participants (N = 201) were recruited from two larger studies of neural markers of emotionality in adolescent depression and risk and included 94 currently depressed

adolescents and 107 never-depressed adolescents at high (n = 54) or low (n = 53) risk for depression based on a biological maternal history of depression. Eligible participants were adolescents (aged 14–17 years) with either a current diagnosis of major depressive disorder, persistent depressive disorder, or clinically significant unspecified depression (current depression group) or adolescents without any history of a clinically significant depressive disorder (never-depressed groups). Adolescents with a past but not current diagnosis of depression were ineligible. Additional exclusion criteria included adolescent or maternal diagnoses of mania, bipolar disorder, or psychosis, as well as adolescents with pervasive developmental or autism spectrum disorders. Informed consent was obtained from caregivers and assent for participation was obtained from the adolescents. All study procedures were approved by the Institutional Review Board at Vanderbilt University.

Graduate-level research assistants administered the Kiddie Schedule for Affective Disorders and Schizophrenia present and lifetime version (KSADS-PL; [49]) to determine adolescent depression diagnoses baseline. Interviews were first conducted with the adolescents, and the adolescents' biological mothers were subsequently interviewed to obtain a parent-report of the adolescents' symptoms. Summary symptom ratings were based on the combined parent- and adolescent-report. Based on the diagnostic interview, adolescents' overall functioning was rated by the interviewer using the Children's Global Assessment Scale (CGAS; [67]), which ranges from 0–100 with lower scores reflecting greater functional impairment (overall observed range: 40–95). Maternal histories of major depressive disorder, persistent depressive disorder, or clinically significant unspecified depression were ascertained using the clinician version of the Structured Clinical Interview for the DSM-5 (SCID; [26]). All diagnoses and CGAS ratings were reviewed in supervision with a licensed psychologist (AK). Inter-rater reliabilities for adolescent and maternal depression diagnoses were excellent (adolescent diagnoses kappa = 1.0, n = 20; maternal diagnoses kappa =.88, n = 17). After initial interviews to determine eligibility and adolescent and maternal depression diagnoses, adolescents were scheduled for a visit to the lab to complete an EEG assessment including the emotion regulation task.

2.2. Measures

2.2.1. Emotion regulation task—The emotion regulation task was adapted from previous ERP studies on emotion regulation [57,59]. Participants viewed a series of neutral and sad or dysphoric images obtained from the International Affective Picture System ([53]. Sad and dysphoric images were intentionally selected rather than broadly unpleasant or threatening images to capture emotional experiences relevant to depression more specifically. Participants were instructed to respond to these images by either passively viewing the image and responding to it naturally (LOOK NEGATIVE trials) or trying to change the way they think about the image to decrease their emotional reaction (DECREASE NEGATIVE trials). The researcher first provided examples of cognitive reappraisal to demonstrate how a participant might change their interpretation of an image. Participants then completed two LOOK NEGATIVE and two DECREASE NEGATIVE trials, after which they described the strategies used to decrease their emotional responses on the decrease trial to ensure comprehension of the task. Participants were also prompted to rate the intensity of their emotional response from 0 (none) to 7 (very strong) following

the presentation of images on each trial. Participants completed 4 additional practice trials including the emotional intensity rating prior to beginning the task. The task included 25 trials per condition (LOOK NEUTRAL; LOOK NEGATIVE; DECREASE NEGATIVE) for 75 total trials. Consistent with prior work [59], the same set of 25 dysphoric images were used for both look and decrease trials to isolate differences attributable to the participant's attempts to regulate responses to the image, rather than differences in the content of the images. Images were presented in a random order. For each trial, instructions were presented for 2 s, followed by a fixation mark (+) for 500 ms, followed by a neutral or sad/dysphoric image presented for 6 s (see Supplemental Fig. S1 for a visual depiction of the task) and then the prompt to rate emotional intensity. 13 participants were missing EEG and 14 were missing behavioral data from the emotion regulation task.

2.2.2. Self-reported depressive symptoms—The 33-item Mood and Feelings Questionnaire (MFQ; [3] was administered to obtain dimensional ratings of current depressive symptoms. Participants were asked to rate the extent to which they had experienced each item in the past two weeks on a scale of 0 (*not true*), 1 (*sometimes true*), or 2 (*true*). MFQ scores were computed by summing all items. Internal consistency for the MFQ was excellent (Cronbach's alpha =.96).

2.2.3. EEG data collection and processing—EEG data were continuously recorded using a 32-channel acti-CHamp system from BrainProducts (Munich, Germany). However, for a subset of participants the number of channels was temporarily reduced to 16 to minimize contact during the initial stages of the COVID-19 pandemic (see Supplemental Information Fig. S2 for a schematic of the reduced electrode scheme and the analyses showing our results were consistent when covarying for the number of recorded channels). Impedances were lowered below 30 kΩ and voltages from active electrodes were referenced online to Cz. Data were digitized at a sampling rate of 1000 ms, and then processed offline using BrainVision Analyzer software (BrainProducts, Munich, Germany). Data were band pass filtered with cutoffs at.01 and 30 Hz, consistent with prior LPP work and given evidence that a more stringent high pass cutoff can attenuate later portions of the LPP [39], and re-referenced to the averaged mastoid recordings (TP9/TP10). For most participants, electrooculogram was recorded via facial electrodes placed 1 cm above and below one eye and 1 cm from the outer corner of each eye and referenced to an electrode placed on the back of the neck of the participant, per the BrainProducts bipolar-to-auxiliary adapter design. Ocular correction was performed using Gratton's algorithm with a common reference [32]. For the subset of participants for whom data were collected using the reduced electrode scheme, ocular correction was performed using FT9/FT10 in lieu of the horizontal facial electrodes, and FP1 in lieu of the vertical facial electrodes with a common reference. EEG data were segmented from 200 ms prior to stimulus onset to 6000 ms post stimulus onset and baseline corrected to 200 ms pre-stimulus onset. Interpolation by spherical splines was used to resolve faulty recordings at a single electrode based on the signal from the surrounding electrodes (spline order = 4; maximum degree of the Legendre polynomials = 10; lambda = 1E-05). Artifact rejection and eye-blink correction were completed using semi-automatic procedures identifying voltage steps of more than 40 μV between sampling points, voltage differences of 150 μV within 500 ms intervals, and voltage differences less

than.50 μV within 100 ms intervals. Trials were visually inspected for remaining artifacts and averaged within each condition. Nineteen participants were excluded from analyses due to the presence of excessive artifacts in the EEG data and 1 participant was excluded due to a technical error during recording.

The LPP was scored across frontal (Fz, FC1, FC2) and centroparietal (Pz, Cz, CP1, CP2) electrode sites (these sites were available for all participants regardless of electrode montage used) and are consistent with prior research examining LPP alterations during explicit emotion regulation [17,59]. Though the exact time frame of the LPP windows varies across studies depending upon the duration of the stimuli presentations, previous LPP research on emotion regulation consistently divides the LPP into relative early, middle, and late time windows [16, 17,25,61,72,76]. We quantified the early LPP using a window that is commonly used in the literature examining emotional reactivity to images presented for relatively short durations (400–1000 ms; [8,41,73, 79]), and then split the remaining 5000 ms into middle (1000–3500 ms) and late (3500–6000 ms) windows (see Fig. 1).

At Fz, participants had an average of 23.80 (SD = 2.25) artifact-free trials for the passive viewing condition, 23.18 (SD = 2.80) for the reappraisal condition, and 22.72 (SD = 3.69) for the neutral condition. At Pz, participants had an average of 23.45 (SD = 2.82) artifact-free trials for the passive viewing condition, 24.03 (SD = 1.98) for the reappraisal condition, and 23.74 (SD = 2.50) for the neutral condition. There were no significant differences between groups on the number of artifact-free trials, ps > .239. The averaged conditions in each time window were further examined for outliers and extreme values were removed [43]; the number of outliers ranged from one to seven across conditions and time windows (usable EEG data n = 149). Split-half reliabilities varied from acceptable to borderline across the examined time windows and electrode poolings (Spearman Brown coefficients: 0.52–0.78; see Supplemental Table S1 for more detailed information). The LPP was generally more reliable for the early LPP, while reliability was lower in later windows, consistent with recent psychometric research demonstrating the LPP is characterized by more residual variance, or noise, across time (Hill et al., 2023).

2.3. Data analysis

2.3.1. Self-report analyses—Mixed design ANOVAs were conducted to test within-subjects effects of condition (passive viewing, reappraisal, neutral), between-subjects effects of group (currently depressed vs. never-depressed in the first model, followed by analyses of currently depressed vs. high-risk vs. low-risk), and the group × condition interaction on emotional intensity ratings.

2.3.2. Neural analyses with traditional LPP scoring—A series of mixed design ANOVAs were similarly conducted to test the main effects of time (400–1000 ms, 1000–3500 ms, 3500–6000 ms), condition (passive viewing, reappraisal, neutral), group, and group × time, condition × time, group × condition, and group × condition × time interaction effects for both frontal and centroparietal electrode poolings. To account for multiple comparisons, False Discovery Rate (FDR) corrections using the Benjamini-Hochberg method were applied (2 tests; [5]). Condition and time were specified as a within-subjects

factors while group was specified as a between-subjects factor (currently depressed vs. never-depressed in the first model, followed by analyses of currently depressed vs. high-risk vs. low-risk). Greenhouse-Geisser corrections were applied when assumptions of sphericity were violated for all ANOVAs. A post-hoc sensitivity analysis conducted with G*Power for the group (currently depressed vs. never-depressed) × condition (reappraisal, passive viewing, neutral) mixed ANOVAs indicated our sample with usable EEG data (n = 149) with an alpha = .05 and power = 0.80 was sufficient detect even relatively small effect sizes, Cohen's $f = 0.10$.

2.3.3. Neural analyses with PCA scoring—Of the 16-electrodes collected from all participants, 12 were included in the temporospatial PCA analyses. Fp1, Fp2, FT9, and FT9 were excluded from the analysis since Fp1, FT9, and FT10 were used for ocular correction for a subset of participants. The processed EEG data for these channels were exported from BVA and subjected to temporospatial PCA using the ERP PCA Toolkit following established recommendations [22]. To determine the number of components to retain, we used a combined approach examining the amount of variance accounted for by the components and a parallel analysis [42] comparing the Scree plots for the observed data with randomly generated data [12]. Since the primary goal of PCA is to reduce the dimensionality of the data, only those components above the random Scree line that account for 90% of the data will be retained. First, a PCA using promax rotation was applied to the covariance matrix in the temporal domain [21]. Of the 27 components above the random Scree, 3 temporal factors (TFs) accounted for 90% of the variability in the data and were retained. The 3 TFs were subsequently subjected to a second PCA for the spatial domain [21]. 2 spatial factors (SFs) emerged above the random Scree and were retained. The overall temporospatial PCA resulted in 6 TF/SF combinations that accounted for 71.48% of the variance (40.90% unique variance) in the ERP waves. Microvolt-scaled PCA factor scores for these components (peak electrode and time point) were then exported for further analysis using mixed design ANOVAs to determine whether there were significant group differences in emotion regulation effects. To account for multiple comparisons, False Discovery Rate (FDR) corrections using the Benjamini-Hochberg method were applied (4 tests; [5]).

2.3.4. Age-related change analyses—Exploratory multiple linear regression analyses were conducted to examine the main and interactive effects of age and LPP residuals during reappraisal on self-reported depressive symptoms and CGAS ratings of overall functioning. Residual scores for late frontal LPPs during reappraisal adjusting for LPPs while passively viewing sad/dysphoric images were computed according to established recommendations [56]. Age was mean centered prior to computing the interaction term. Full information maximum likelihood was used to account for missing data with the correlational and multiple linear regression analyses. The analyses were conducted using the lavaan package in R [65].

3. Results

Demographic and clinical information for currently depressed, high-risk, and low-risk adolescents are presented in Table 1 (additional clinical information is provided in Table S2 and bivariate correlations in Table S3 in the Supplemental Information). One-way ANOVAs

and chi-square tests for these variables between groups are also presented. As expected, the currently depressed group had higher levels of depressive symptoms and lower ratings of overall functioning, as well as higher rates of comorbid anxiety disorders. Although, it is notable that 22–35% of adolescents in the never-depressed groups also met criteria for comorbid anxiety disorders. Means, standard deviations, and contrasts between reappraisal and passive viewing for each measure within each group are presented in Table 2.

3.1. Self-report results

Mixed method ANOVA results revealed a main effect of condition, $F(1.63, 285.05) = 788.74$, $p < .001$, $\eta_p^2 = .82$, such that emotional intensity ratings were highest for the passive viewing condition compared to both reappraisal, $F(1, 175) = 244.62$, $p < .001$, $\eta_p^2 = .58$, and neutral, $F(1, 175) = 1057.14$, $p < .001$, $\eta_p^2 = .86$. Intensity ratings for the reappraisal condition were higher than the neutral condition, $F(1, 175) = 730.96$, $p < .001$ $\eta_p^2 = .81$. The group × condition interaction was not significant when examining depression diagnoses (currently depressed vs. never-depressed) or depression risk groups (currently depressed vs. high-risk vs. low-risk), ps > .184, η_p^2s < .01.

3.2. Neural results with traditional LPP scoring

For the frontal electrode pooling, mixed ANOVA results revealed a significant three-way interaction between time (400–1000 ms, 1000–3500 ms, 3500–6000 ms), condition (negative reappraisal, negative passive viewing, neutral), and group (currently depressed, never-depressed), $F(3, 441.16) = 3.31$, $p = .020$, Benjamini-Hochberg adjusted $p = .020$, $\eta_p^2 = .02$. Follow-up analyses revealed a significant group × condition interaction in the late time window (3500–6000 ms), $F(2, 308) = 3.85$, $p = .022$, $\eta_p^2 = .02$, but the group × condition interaction was not significant in either of the earlier time windows (ps > .571). Within group repeated-measures ANOVAs indicated that LPP amplitudes were significantly reduced for the reappraisal condition relative to the passive viewing condition for never-depressed adolescents, $F(1, 84) = 11.43$, $p < .001$, $\eta_p^2 = .12$, but not for currently depressed adolescents, $F(1, 70) = 1.83$, $p = .181$, $\eta_p^2 = .03$. Further examination within the never-depressed group showed the effect of reappraisal on the late LPP was slightly stronger among the low-risk adolescents, $F(1, 44) = 6.60$, $p = .014$, $\eta_p^2 = .13$, compared to the high-risk adolescents, $F(1, 39) = 4.72$, $p = .036$, $\eta_p^2 = .11$. However, direct comparisons between the groups using the LPP residuals during reappraisal did not reach significance (results are presented in Supplemental Table S4).

For the centroparietal electrode pooling, a mixed ANOVA similarly revealed a significant three-way time × condition × group interaction when comparing currently depressed versus never-depressed, $F(3.13, 462.91) = 3.41$, $p = .016$, Benjamini-Hochberg adjusted $p = .020$, $\eta_p^2 = .02$. Follow-up analyses showed a trending group × condition interaction in the late time window (3500–6000 ms) for currently depressed versus never-depressed, $F(2, 308) = 2.70$, $p = .069$, $\eta_p^2 = .02$ (earlier time windows ps > .342). Within group repeated-measures ANOVAs indicated LPP amplitudes were reduced for the reappraisal condition relative to passive viewing at a trend level for never-depressed adolescents overall, $F(1, 86) = 3.36$, $p = .070$, $\eta_p^2 = .04$, but not currently depressed adolescents, $p = .978$. The trending reduction

during reappraisal was observed only for the low-risk adolescents, $F(1, 44) = 3.48$, $p = .069$, $\eta_p^2 = .07$, but not for the high-risk, $p = .598$ (see Fig. 2).

3.3. Neural results with principal component analysis

PCA yielded 4 TF/SF components consistent with a typical LPP that were sensitive to emotional condition (presented in Table 3) based on results of repeated-measures ANOVAs. In general, results showed a relatively early emerging occipital component consistent with an early LPP/P3, with enhancements for both emotional conditions relative to neutral. Two mid-latency components were also identified, with patterns showing enhancements for both emotional conditions relative to neutral. These components appear to reflect the transition of the LPP from posterior to anterior regions. Finally, a late frontal component emerged with trending reductions for the reappraisal condition relative to passive viewing. This latter component accounted for the most unique variance in the data (19.29%).

For mixed ANOVA analyses testing for potential group × condition interactions in the four PCA-identified components, only the late frontal component (TF1SF1: FC2, 5760 ms) demonstrated a significant group (currently depressed versus never-depressed) × condition interaction, $F(2, 264) = 3.34$, $p = .042$, that did not survive correction for multiple comparisons, Benjamini-Hochberg adjusted $p = .168$, $\eta_p^2 = .03$. The group × condition interactions for the remaining PCA components were non-significant, ps > .152, Benjamini-Hochberg adjusted ps > .304. The late frontal TF1SF1 component results were generally consistent with the findings for the traditionally scored LPP. Repeated measure ANOVAs examining the effect of task condition within each group indicated that TF1SF1 amplitudes were significantly reduced during reappraisal relative to passive viewing among never-depressed adolescents, $F(1, 75) = 5.47$, $p = .022$, $\eta_p^2 = .07$, but not currently depressed adolescents, $F(1, 57) = 0.10$, $p = .750$, $\eta_p^2 < .01$. However, unlike the traditionally scored LPP, the comparison between reappraisal and passive viewing did not reach significance for either the high-risk or low-risk groups, ps > .082 (see Fig. 3).

We conducted additional group × condition mixed ANOVAs for the traditionally scored late frontal LPP and the PCA-identified late frontal LPP covarying for a concurrent anxiety disorder given the high levels of comorbidity and for pubertal development stage based on the significant differences between groups. The results were largely consistent with the primary findings, with the exception that the results were trending when covarying pubertal stage for the traditionally scored late frontal LPP, $F(2, 306) = 2.92$, $p = .056$, $\eta_p^2 = .02$, and when covarying anxiety for the PCA-identified late frontal LPP, $F(2, 262) = 2.93$, $p = .055$, $\eta_p^2 = .02$.

3.4. Age-related change results

Model results for CGAS ratings of overall functioning are presented in Table 4 and results for self-reported depressive symptoms are presented in Table 5. Age significantly predicted self-reported depressive symptoms, with older adolescents reporting higher levels of symptoms, but the interaction between LPP residuals during reappraisal and age was not significant. In the model for CGAS ratings of overall functioning, the conditional main effects for age and late frontal LPP residuals during reappraisal were not significant, but

there was a significant cross-over interaction between age and the LPP. The interaction was probed by examining the simple slopes between late frontal LPP residuals during reappraisal and overall functioning at the 50th percentile for age (15 years, $n = 56$), as well as the 25th (14 years, $n = 63$) and 75th percentiles for age (16 years, $n = 45$) in our sample (see Fig. 4). The Johnson-Neyman regions of significance were also examined. Results indicated a significant negative relationship between the reappraisal-related LPP and functioning among older adolescents (16 years; $b = -0.65$, SE =0.23, $t = -2.87$, $p = .005$), but not younger adolescents at 15 years ($b = -0.16$, SE = 0.20, $t = -0.80$, $p = .426$) or 14years ($b = 0.33$, SE = 0.32, $t = 1.03$, $p = .305$). Johnson-Neyman results show the relationship between late frontal LPP residuals during reappraisal and functioning was significantly negative for adolescents aged 15.44 or older.

4. Discussion

This study was among the first to examine whether clinically depressed adolescents significantly differed from never-depressed adolescents at high and low risk for depression in their ability to regulate neurophysiological responses to dysphoric stimuli. We leveraged multiple approaches to scoring ERPs and examined the temporal dynamics of emotion regulation. Across the time course and topography of emotion processing captured by the LPP, our findings revealed significant LPP reductions at relatively late stages of processing (3500–6000 ms) over frontal sites during explicit emotion regulation instructions compared to passive viewing among never-depressed adolescents. No differentiation between the conditions was observed among currently depressed adolescents, likely reflecting impairments in emotion regulation abilities. Notably, this pattern of results converged across both traditional mean activity and PCA-derived LPP scoring approaches. Further LPP analyses comparing adolescents at high versus low risk for depression showed a pattern with mildly stronger and more widespread reappraisal effects among the low-risk adolescents, though further prospective research is needed to determine whether the reappraisal-related LPP may be a viable marker of risk for depression. Finally, exploratory analyses showed the association between the reappraisal-related LPP and overall functioning was moderated by age, such that emotion regulation difficulties indexed by the LPP was associated with poorer overall functioning among older adolescents.

Sustained dysphoric mood is a cardinal symptom of depression, and research shows emotion dysregulation in depression, including increased rumination and suppression along with limited use of reappraisal [45,46,50,60]. Leveraging the high temporal precision of EEG/ERP methods, our findings indicate that under explicit instructions to regulate responses to dysphoric images using reappraisal, depressed individuals showed difficulty sustaining reductions in neural responses indexed by the LPP. Conversely, adolescents without any history of depression were able to successfully modulate their neural responses, displaying significantly reduced LPP amplitudes during reappraisal compared to passive viewing. These patterns are most apparent at relatively late stages of processing (i.e., 3500–6000 ms) across frontal electrodes. These findings diverge from a recent study examining the effect of reappraisal on LPP amplitudes among depressed and non-depressed youth [25]. This study did not find any evidence of group differences in LPP amplitudes during reappraisal versus passive viewing across central, parietal, or occipital poolings. Similar

to the findings of Feldmann et al. [25], we did not observe significant differences across centroparietal sites, but the group differences were apparent across frontal sites, consistent with research demonstrating the LPP shifts from posterior to anterior sites across time [29,38]. Thus, the discrepant results could be due to differences in the examined electrode poolings, differences in the task stimuli, or differences in sample sizes. Our findings are also broadly consistent with adult neuroimaging research showing reduced activation in prefrontal regions and impaired fron-to-limbic coupling among depressed individuals [24,33,44] and a study of youth showing depressed individuals showed less differentiation in amygdala activation during reappraisal and passive viewing compared to controls [74]. However, some adolescent neuroimaging research has shown adolescents with depression can engage regulatory regions and reduce amygdala responses under explicit emotion regulation instructions [63,64]. Inconsistencies between our findings and these studies could be attributable to differences in sample size, task design, or the clinical characteristics of the samples.

Similar to prior adult research showing explicit emotion regulation instructions yield minimal differences between depressed and non-depressed individuals on self-report ratings of affect [23,33,47], we did not find group differences in self-reported emotional intensity ratings. However, one recent study of youth did find group differences in self-reported affect, with psychiatrically healthy youth rating the stimuli as less negative on reappraisal trials relative to passive viewing trials compared to depressed youth [25]. The discrepancy between our findings and this study of youth could be attributable to differences in the clinical characteristics of the non-depressed groups, the types of stimuli used, or the format of the scale used to obtain subjective ratings. Cumulatively, this suggests depression may be typified by a discrepancy in emotion regulation efficacy between self-reports and the modulation of neural responses. Depressed individuals may perceive themselves as effectively engaging in emotion regulation while yielding limited effects on neural responses. Considering LPP amplitudes for both reappraisal and passive viewing were significantly enhanced compared to LPPs to neutral images, it is unlikely that depressed individuals may engage in more efficient emotion regulation. However, it is also possible that the discrepancy between the self-report and neural responses are the result of participants self-reporting reductions due to bias based on researcher expectations. These results highlight the potential for EEG/ERP measures to capture more subtle alterations in emotionality that may not be apparent when using other methodological approaches.

The findings from the current study also show the effect of reappraisal on the LPP was slightly stronger among low-risk adolescents compared to adolescents at high risk based on a maternal history of depression, though it is possible that impaired LPP alterations during emotion regulation may only emerge after the onset of depression rather than preceding. Given the modest differences that emerged when examining effects within groups rather than directly comparing groups, as well as the cross-sectional study design, future within-subjects, longitudinal research is warranted to conclusively determine whether the reappraisal-related LPP may be a marker of vulnerability or a marker of current disorder. That said, some of our prior work examining a subset of the current sample assessed before the start of the COVID-19 pandemic showed impaired emotion regulation ability indexed by the late frontal LPP prospectively predicted depressive symptom increases following

exposure to pandemic-related interpersonal stressors [35]. Relatedly, emotion regulation ability indexed by the late frontal LPP has also been shown to predict response to cognitive behavioral therapy for depression, such that those with greater difficulty modulating neural responses during reappraisal pre-treatment showing greater clinician-rated improvement post-treatment [20].

Recent research suggests emotion dysregulation may represent a higher order, transdiagnostic factor contributing to a range of internalizing symptoms [78]. Given the diagnostic heterogeneity in our sample, with approximately half of both the depressed and never depressed groups also meeting criteria for an anxiety disorder, it is plausible that LPP alterations following explicit emotion regulation instructions may correlate more with measures of functional impairment based on an individual's entire psychopathology profile. In support of this, our exploratory analyses revealed a significant interaction between age and the LPP in the prediction of adolescents' overall functioning, such that larger LPP residuals during reappraisal, reflecting more impaired emotion regulation abilities, was associated with poorer overall functioning specifically among older adolescents. This generally aligns with developmental neuroimaging research showing age-related changes in fronto-limbic circuitry underlying emotion regulation, with reductions in amygdala reactivity and increased recruitment of prefrontal regions with age [11,31,69]. The specificity of our results to overall functioning and not self-reported depressive symptoms also corresponds with findings from a systematic review indicating attenuated activation of ventrolateral and dorsolateral prefrontal cortices during cognitive reappraisal was a common deficit across patients with a variety of disorders [81]. Cumulatively, the evidence suggests typical developmental trajectories are characterized by improved emotion regulation abilities across adolescence, but our findings suggest disruptions in this normative pathway are associated with functional impairment due to psychopathology more broadly.

However, since the current study is cross-sectional, the directionality and causality of these associations cannot be determined. Future developmental research is needed to clarify the longitudinal associations between neural markers of emotional regulation, depression, and overall functioning. Other limitations to the current study include the focus on the down-regulation of negative stimuli. Considering depression has been specifically linked with blunted responses to positive stimuli and limited up-regulation of positive emotions [1,10,19,33,52, 77] coupled with recent research demonstrating the LPP to positive stimuli is enhanced when participants were explicitly instructed to engage in savoring [80], future research on emotion regulation in depressed youth should examine both the ability to down-regulate neural responses to negative stimuli *and* up-regulate responses to positive stimuli. The reliability of the LPP notably decreased across time, consistent with prior findings (Hill et al., 2023). However, it is unclear whether the lower reliabilities at later stages of processing reflect psychometric issues with the LPP or meaningful differences in individuals' abilities to regulate responses to specific images. Research examining more specific types of stimuli with greater personal relevance and ecological validity, as well as trial-by-trial analyses of emotion regulation are critical areas warranting further investigation.

5. Conclusion

This study was among the first to examine alterations in neurophysiological markers of emotion regulation in clinically depressed adolescents. Our results showed that while self-reported emotional intensity ratings during the emotion regulation task were comparable between currently depressed and never depressed adolescents, only the never depressed adolescents demonstrated significant emotion regulation-related reductions in neural responses to dysphoric images, as measured by the LPP. Further, the magnitude and breadth of the LPP reduction was slightly larger among adolescents at low-risk for depression. Finally, our findings, though cross-sectional, indicate that impaired emotion regulation abilities indexed by the LPP may be associated with a poorer prognosis and more functional impairment across adolescence. Future prospective research examining longitudinal changes in neural markers of emotion regulation ability across critical developmental periods in combination with changes in internalizing symptoms is needed. Findings from this study advance ERP methods for objectively quantifying emotion regulation in adolescence and further our understanding of alterations in emotion regulation ability in adolescent depression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The data that support the findings from this study are available by request to the corresponding author.

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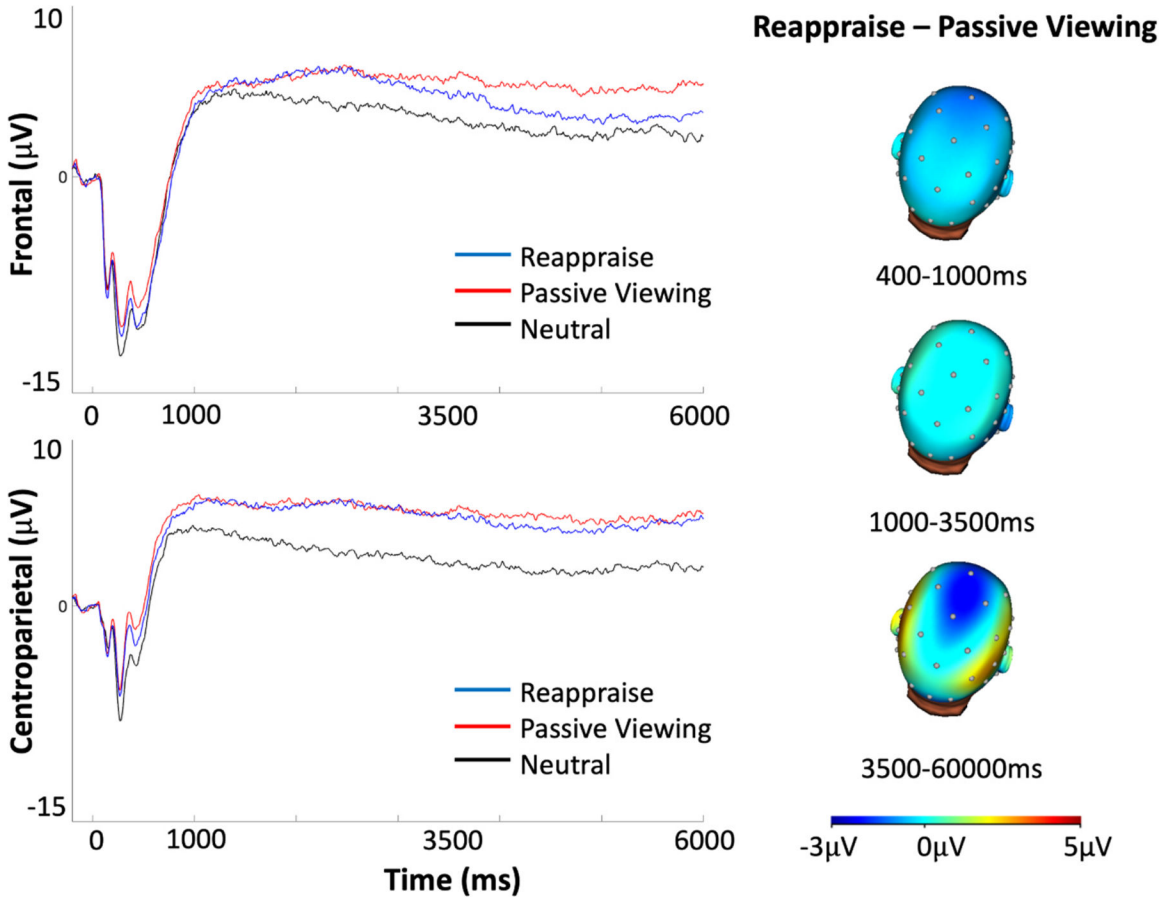

Fig. 1.

Overall ERP waveforms depicting responses in the reappraisal (blue), passive viewing (red), and neutral (black) conditions over frontal (top left) and centroparietal (bottom left) electrodes. Scalp distributions depict responses on reappraisal trials minus the passive viewing trials in the early (top right), middle (middle right), and late (bottom right) time windows. **Note:** 25 participants had data recorded from a reduced 16-channel electrode scheme during the early stages of the COVID-19 pandemic, which may impact the appearance of the scalp distributions.

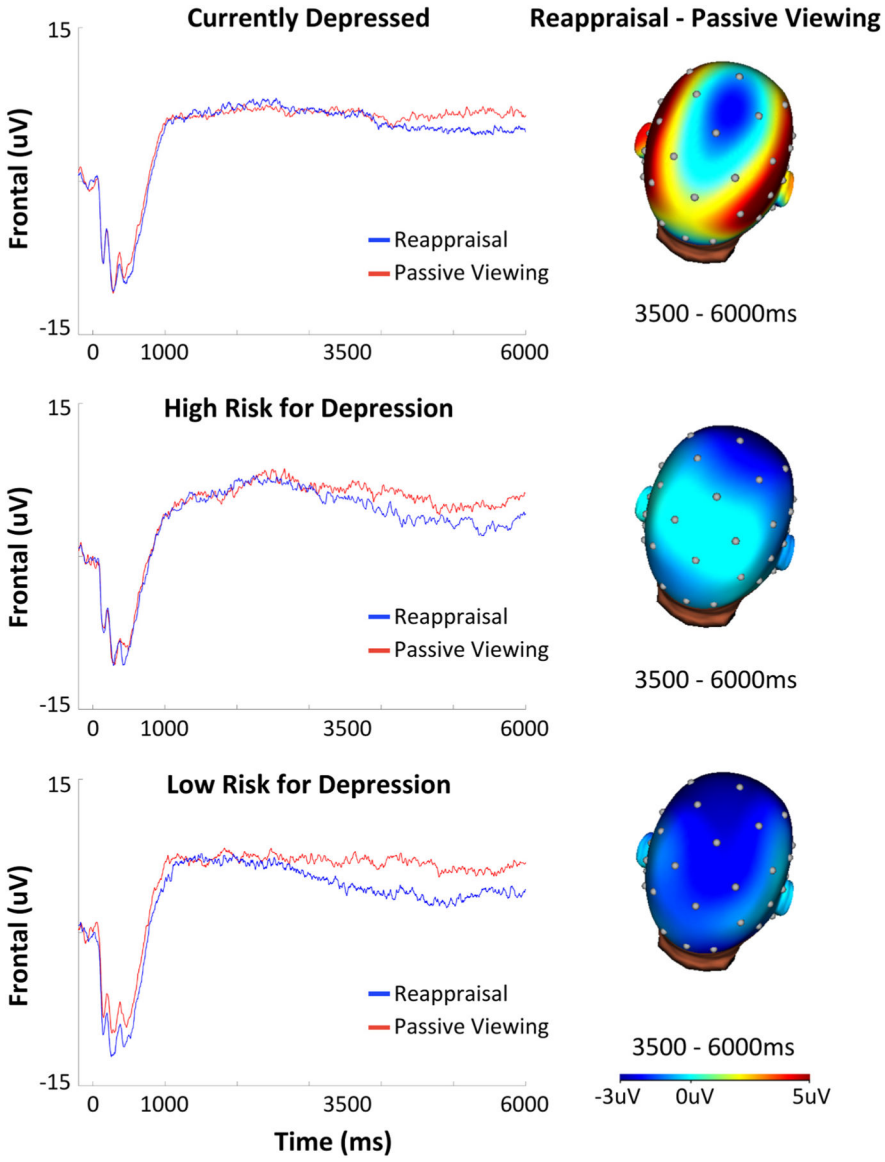

Fig. 2.

ERP waveforms depicting responses in the reappraisal (blue) and passive viewing (red) conditions for currently depressed adolescents (top), never-depressed adolescents at high risk (middle), and never-depressed adolescents at low risk (bottom). Scalp distributions depict the reappraisal condition minus the passive viewing condition in the late time window for each group. **Note:** 25 participants had data recorded from a reduced 16-channel electrode scheme during the early stages of the COVID-19 pandemic, which may impact the appearance of the scalp distributions.

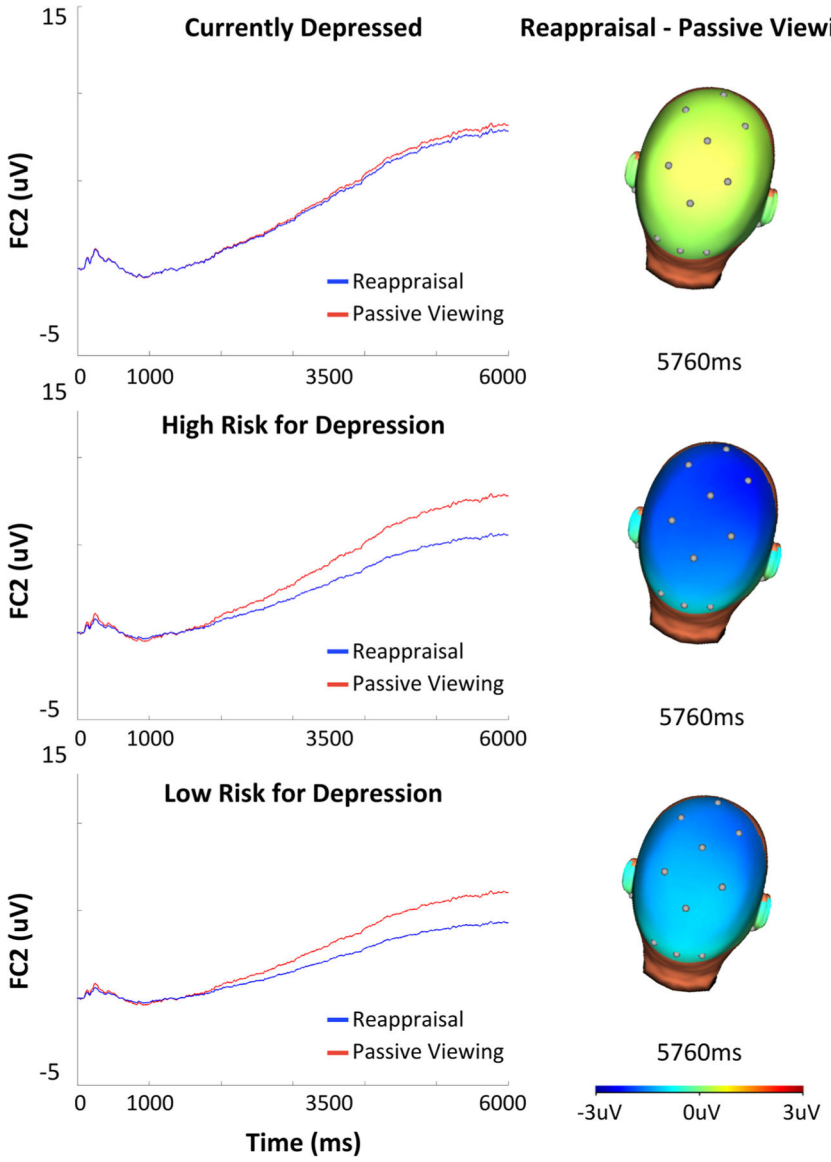

Fig. 3.

TF1SF1 PCA component waveforms depicting responses on reappraisal (blue) and passive viewing (red) trials in currently depressed adolescents (top), never-depressed adolescents at high risk (middle), and never-depressed adolescents at low risk (bottom). Scalp distributions depict the reappraisal condition minus the passive viewing condition at the peak latency for the TF1SF1 PCA component for each group.

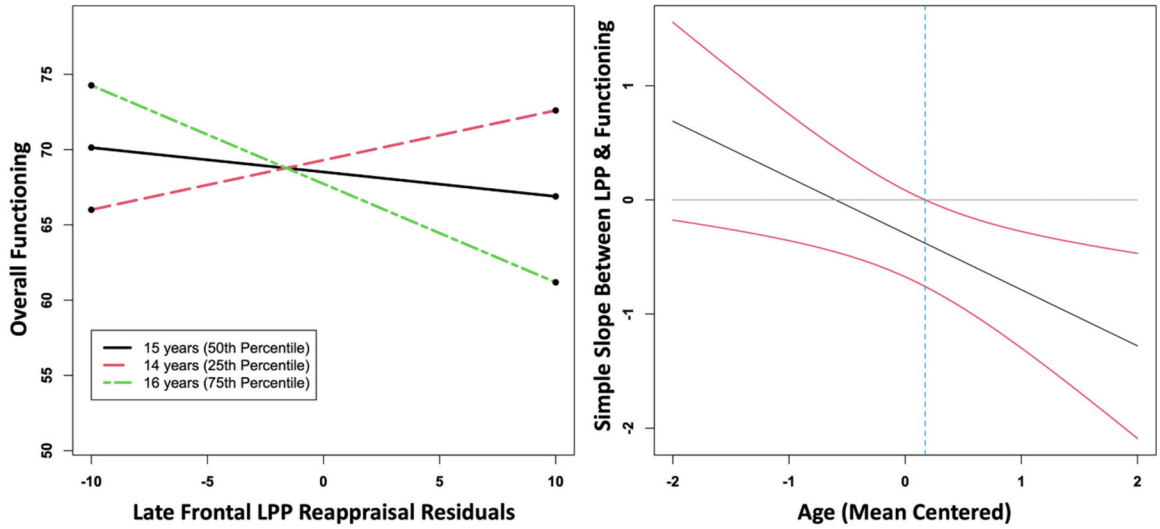

Fig. 4.

Left: simple slopes of the association between late frontal LPP residuals during reappraisal and overall functioning at ages 15 (black), 14 (red), and 16 (green). Right: confidence bands (red) and Johnson-Neyman regions of significance (blue) for the simple slope between late frontal LPP residuals during reappraisal and overall functioning across the sample age range. **Note:** more negative LPP residuals reflect more of a reduction in the LPP when prompted to use reappraisal to decrease their response to the image.

Table 1

Demographic information, clinical characteristics, and group comparisons for currently depression, high-risk, and low-risk adolescents.

	Currently Depressed (*n* = 94)	High-Risk for Depression (*n* = 54)	Low-Risk for Depression (*n* = 53)	*F* or χ^2	*p*
Demographics					
Age	15.43 (1.14)	15.19 (1.07)	15.09 (1.06)	$F = 1.83$	.146
Pubertal Development Scale	3.46 (0.65)	3.19 (0.72)	3.11 (0.95)	$F = 4.40$	.014
Sex (% Female)	66.67	59.62	58.00	$\chi^2(4) = 4.04$	.401
Race (% Caucasian)	78.72	72.22	69.81	$\chi^2(10) = 20.84$	.022
Ethnicity (% Hispanic)	3.19	9.26	7.55	$\chi^2(2) = 2.57$	.277
Clinical Characteristics					
MFQ	31.57 (14.60)	10.49 (8.07)	7.52 (7.27)	$F = 94.34$	<.001
CGAS	53.60 (7.12)	78.43 (9.85)	81.52 (9.14)	$F = 235.45$	<.001
Current ADHD (%)	13.83	14.81	9.43	$\chi^2(2) = 0.81$	.666
Current Anxiety Disorder (%)	60.64	35.19	22.64	$\chi^2(2) = 22.10$	<.001
Current Therapy Only (%)	19.35	7.55	0.00	$\chi^2(6) = 74.45^{\wedge}$	<.001
Current Medication Only (%)	15.05	5.66	3.77		
Current Therapy & Medication (%)	35.48	1.89	1.89		

$^{\wedge}$The Chi-Square statistic represents the results for group (currently depressed, high-risk, low-risk) × current treatment (none, therapy only, medication only, combined medication and therapy).

Notes: MFQ: mood and feelings questionnaire; CGAS: clinical global assessment scale; ADHD: attention-deficit/hyperactivity disorder. Pubertal Development Scale (Peterson et al., 1988) scores range from 1–4, with higher scores reflecting more development.

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Table 2

Means, standard deviations, and simple contrasts results between the reappraisal and passive viewing condition.

	Reappraisal	Passive Viewing	Neutral	*F*	*p*	η_p^2
Currently Depressed (*n* = 94)						
Late Frontal LPP	5.45 (8.30)	6.84 (8.88)	2.54 (8.21)	1.83	.181	.025
Late Parietal LPP	6.56 (8.06)	6.58 (7.64)	2.34 (7.76)	0.00	.978	.000
PCA-defined LPP	6.62 (10.23)	7.09 (10.36)	2.02 (8.82)	0.10	.750	.002
Intensity Ratings	3.03 (1.15)	4.03 (1.40)	1.00 (0.93)	104.81	<.001	.552
Never Depressed (*n* = 107)						
Late Frontal LPP	3.87 (7.28)	6.45 (8.73)	4.53 (8.45)	11.43	.001	.120
Late Parietal LPP	4.91 (7.81)	6.31 (8.14)	3.67 (8.75)	3.36	.070	.038
PCA-defined LPP	5.05 (9.59)	6.99 (10.24)	4.80 (10.81)	5.47	.022	.068
Intensity Ratings	3.42 (1.25)	4.38 (1.32)	1.10 (1.32)	134.19	<.001	.586
High Risk for Depression (*n* = 54)						
Late Frontal LPP	4.05 (7.21)	6.29 (8.67)	4.13 (8.76)	4.72	.036	.108
Late Parietal LPP	5.68 (7.47)	6.16 (8.15)	3.26 (9.14)	0.28	.598	.007
PCA-defined LPP	5.04 (8.80)	7.26 (10.81)	4.09 (10.56)	3.20	.082	.080
Intensity Ratings	3.35 (1.01)	4.41 (0.96)	1.00 (0.84)	73.30	<.001	.609
Low Risk for Depression (*n* = 53)						
Late Frontal LPP	3.70 (7.42)	6.59 (8.88)	4.89 (8.25)	6.60	.014	.130
Late Parietal LPP	4.19 (8.14)	6.45 (8.23)	4.04 (8.47)	3.48	.069	.073
PCA-defined LPP	5.05 (10.45)	6.72 (9.76)	5.51 (11.14)	2.21	.146	.056
Intensity Ratings	3.49 (1.46)	4.35 (1.62)	1.20 (1.68)	61.35	<.001	.566

Note: The *F* statistic represents the contrast between the reappraisal and passive viewing conditions, since that contrast is the primary research interest. The high risk vs. low risk groups are subsets of the never-depressed group examined in secondary analyses. The PCA-defined LPP corresponds to the TF1SF1 component detailed in Table 3.

Table 3

Resulting temporal and spatial factor combinations derived through PCA.

Temporospatial Factors	Variance	Unique Variance	Temporal Peak (ms)	Peak Electrode	Emotional Modulation
TF3SF2	0.03	0.03	328	O2	Enhanced for reappraise and passive viewing vs. neutral, *p*s < .001 Reappraise vs. passive viewing, *p* = .142
TF2SF2	0.05	0.03	1757	O2	Enhanced for reappraise vs. neutral, *p* = .031 and trending for passive viewing vs. neutral, *p* = .051 Reappraise vs. passive viewing, *p* = .885
TF2SF1	0.15	0.07	1757	FC2	Enhanced for reappraise and passive viewing vs. neutral, *p*s < .002 Reappraise vs. passive viewing, *p* = .631
TF1SF1	0.36	0.19	5760	FC2	Enhanced for reappraise and passive viewing vs. neutral, *p*s < .015 Reappraise vs. passive viewing, *p* = .104

Table 4

Multiple linear regression results for the conditional main effects and interactive effect of age and late frontal LPP reappraisal residuals in the prediction of overall functioning.

	B (SE)	95% CI	*β*	*p*
Dependent Variable: CGAS				
Age	−0.79 (1.03)	[−2.80, 1.23]	−0.06	.443
Late Frontal LPP Reappraisal Residuals	−0.30 (0.19)	[−0.67, 0.08]	−0.12	.124
Age × LPP Residuals	−0.49 (0.19)	[−0.87, −0.12]	−0.20	.010
R^2 = 0.06				

Table 5

Multiple linear regression results for the conditional main effects and interactive effect of age and late frontal LPP reappraisal residuals in the prediction of self-reported depressive symptoms.

	B (SE)	95% CI	*β*	*p*
Dependent Variable: MFQ				
Age	2.22 (1.05)	[0.17, 4.28]	0.15	.034
Late Frontal LPP Reappraisal Residuals	0.07 (0.20)	[−0.33, 0.47]	0.03	.742
Age × LPP Residuals	0.14 (0.20)	[−0.25, 0.54]	0.06	.473
R^2 = 0.03				