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The late positive potential during affective picture processing: Associations with daily life emotional functioning among adolescents with anxiety disorders☆

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Abstract

Pediatric anxiety disorders are characterized by potentiated threat responses and maladaptive emotion regulation (ER). The Late Positive Potential (LPP) is a neural index of heightened attention to emotional stimuli. Anxious individuals typically exhibit a larger LPP to unpleasant stimuli, but the LPP may also be blunted to unpleasant and pleasant stimuli for those with co-morbid depression. While a larger LPP is thought to reflect greater emotional reactivity, it is unknown to what extent variation in the LPP to laboratory stimuli corresponds to daily emotional functioning. We assessed the LPP in the laboratory in response to unpleasant, pleasant, and neutral images in combination with ecological momentary assessment of emotional reactivity and regulation in daily life among youth (9–14 years old; 55 % female) with anxiety disorders (ANX, N = 130) and no psychiatric diagnoses (ND, N = 47). We tested whether LPP amplitudes to unpleasant and pleasant stimuli (vs. neutral) are greater in ANX (vs. ND) youth and whether LPP amplitudes inversely correlate with co-morbid depression symptoms. We also examined associations between the LPP and daily life emotional functioning among ANX and ND youth. We found no group-by-valence effects on LPP amplitudes. Within ANX youth, higher depression symptoms were associated with smaller LPP amplitudes to unpleasant, but not pleasant, stimuli relative to neutral stimuli. Larger LPP amplitudes to emotional (relative to neutral) stimuli were correlated with use of specific ER strategies among ANX and ND youth but not emotional reactivity. While the LPP may reflect initial emotional reactivity to laboratory stimuli, it is associated with ER behaviors, and not emotional reactivity, in daily life.

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Declaration of competing interest
The authors have declared that they have no competing or potential conflicts of interest.

Appendix I. Supplementary analyses
Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2022.09.009.

Keywords

Anxiety; Adolescence; Late positive potential; Emotion regulation; Emotion reactivity; Ecological momentary assessment; Brain-behavior relationships

1. Introduction

Anxiety disorders are among the most prevalent of childhood psychiatric disorders and are associated with increased risk for later depression, suicidality, and problematic substance use (e.g., Eisenberg et al., 2009; Kessler et al., 2005; Lonigan et al., 2004). These disorders are characterized by alterations in the processing of negative emotional information, including heightened neural activity in cortical and subcortical regions in response to threatening stimuli and greater subjective negative emotional reactivity (see Bar-Haim et al., 2007; Dillon et al., 2014; Price et al., 2013; Wieser and Keil, 2020). In additional to alterations in initial emotional responses, anxiety disorders are also associated with difficulties in emotion regulation (ER), including greater use of maladaptive ER strategies (e.g., avoidance, suppression) and less use of adaptive ER strategies (e.g., reappraisal, acceptance) to modulate negative emotion, which may further exacerbate or maintain distress (Amstadter, 2008; Bardeen and Fergus, 2014; Cisler et al., 2010; Price et al., 2013; White et al., 2009).

The Late Positive Potential (LPP) has been conceptualized as a neural index reflecting individuals differences in emotional reactivity and regulation in both adults and youth (Brooker et al., 2020; Dennis, 2010; Hajcak and Foti, 2020; Hajcak et al., 2010; McLean et al., 2020), including sustained engagement with threatening stimuli in individuals with anxiety disorders (Hajcak et al., 2010; Hajcak and Foti, 2020; Wieser and Keil, 2020). Specifically, the LPP is a sustained positive-going event-related potential (ERP) maximal at centro-parietal sites beginning around 400 ms post-stimulus onset and extending for the duration of a stimulus that reflects attentional processing of emotional stimuli (see Hajcak et al., 2010; Hajcak and Foti, 2020). The LPP originates in both cortical and subcortical neural regions that support emotional processing, including activation of cortico-limbic appetitive or aversive motivational systems (see Hajcak et al., 2010; Hajcak and Foti, 2020). LPP amplitudes are reliably greater for high-arousing unpleasant and pleasant emotional (relative to neutral) stimuli (i.e., based on subjective arousal ratings; e.g., Junghöfer et al., 2001; Schupp et al., 2000; Schupp et al., 2003; Schupp et al., 2006; Hajcak et al., 2010), correlate with measures of autonomic and self-rated arousal to emotional stimuli (e.g., Schupp et al., 2000), and are stable across time and development (e.g., Auerbach et al., 2016; Bondy et al., 2018; Kujawa et al., 2013; Moran et al., 2013).

In addition to reflecting initial emotional reactions, LPP amplitudes are also sensitive to laboratory-instructed regulation strategies in both adults and youth aimed at up-regulating or down-regulating emotional responses to unpleasant and pleasant picture stimuli (e.g., DeCicco et al., 2014; Dickey et al., 2021b; Dennis and Hajcak, 2009; Hajcak et al., 2010; Lewis et al., 2015). Along these lines, the LPP is particularly useful in examining in emotional processing and regulation as it is a sustained response typically present for the duration of an emotional stimulus that can be divided into epochs (i.e., time windows) to examine the time course of emotional responding, e.g., relative “early” vs. “late” stages in emotional processing, although specific LPP time windows have not yet been consistently defined or standardized (e.g., Dennis and Hajcak, 2009; Dickey et al., 2021b; Gable et al., 2015; Hajcak et al., 2009; Hajcak and Foti, 2020), particularly in youth where spatial and temporal characteristics of ERP components such as the LPP may change with development (Brooker et al., 2020; Dickey et al., 2021b).

With regards to anxiety disorders, the LPP has been associated with increased attention to high-arousing negatively-valenced (unpleasant) stimuli, with a number of studies reporting increased LPP amplitudes to threatening stimuli in anxious adults (MacNamara and Hajcak, 2010; Michalowski et al., 2009; Moser et al., 2008; Pauli et al., 1997) and youth (Kujawa et al., 2015; Leutgeb et al., 2010; DeCicco et al., 2014). Because few studies included positively-valenced (pleasant) stimuli during the assessment of the LPP in youth with anxiety disorders, it remains unclear to what extent attentional resources are being recruited to all highly arousing stimuli (both pleasant and unpleasant) or only to unpleasant stimuli. Only one study with a sample of non-clinical emerging adults found that social anxiety symptoms predicted a larger LPP to both unpleasant and pleasant stimuli (Dickey et al., 2021a), but it is unknown whether similar associations are present among youth diagnosed with anxiety disorders.

Depression is highly comorbid with anxiety disorders (Kendall et al., 1992; Kaufman and Charney, 2000) and is also associated with alterations in emotion processing, including alterations in processing of positively-valenced stimuli. In particular, major depressive disorder has been associated with emotion context insensitivity (Rottenberg et al., 2005; Bylsma et al., 2008; Bylsma, 2021), including blunted (i.e., reduced) emotional reactivity to both pleasant and unpleasant affective stimuli across multiple response systems (e.g., behavioral, neural, physiological, subjective), indicating overall disengagement with the environment. Also consistent with emotion context insensitivity, higher depression symptoms have been linked to blunted neural response to unpleasant (Foti et al., 2010) and pleasant emotional stimuli (Weinberg et al., 2016). Fewer studies have examined co-morbid depression in the context of anxiety disorders, but there is some limited evidence that co-morbid depression is also associated with lower LPP amplitudes in response to both rewarding and threatening stimuli among anxious adults (Weinberg et al., 2016).

In one of the few studies to examine associations with co-morbid depression symptoms among youth with anxiety disorders, Kujawa et al. (2015) found that although adolescents (aged 7–19) with anxiety disorders had a larger LPP to threatening vs. neutral faces, those with higher levels of depression symptoms showed a reduced LPP to threatening stimuli as compared to those with lower depression symptoms. These findings suggest that depression and anxiety may have distinct effects on neural threat processing, such that depression symptoms moderate the magnitude of responses to unpleasant stimuli among adolescents with anxiety disorders. Thus, characterizing associations with both anxiety and co-morbid depression symptoms in the same sample may better characterize emotional processing among youth with a range of depression symptoms.

To understand how neural activity to emotional stimuli, as reflected in the LPP, is related to symptoms of anxiety or depression, researchers have examined correlations between LPP amplitudes and self-report symptom measures or trait self-report measures of ER. For example, Harrison and Chassy (2019) found that habitual use of cognitive reappraisal is associated with lower LPP amplitudes in response to threatening pictures in a very small (N = 15) unselected sample of adults. Yet, whether LPP amplitudes to emotional stimuli relate to daily life emotional functioning (i.e., emotional reactivity and regulation) remains unknown, particularly among youth clinical samples, which may help reveal important information about mechanisms contributing to anxiety and depression among youth. Ecological momentary assessment (EMA) studies and earlier daily diary designs have aimed to characterize the nature of emotional difficulties that anxious adults and youth experience in the real world (see Walz et al., 2014, for review). In particular, youth with anxious disorders report greater daily life negative affect (Mor et al., 2010), greater negative emotional and self-reported physiological reactivity to daily life negative events (Tan et al., 2012), more frequent maladaptive ER responses (e.g., avoidance, rumination), and less frequent use of adaptive ER responses (e.g., acceptance) to daily life negative events (Beidel et al., 1999).

However, the association between neural and daily life indices of emotional reactivity and regulation remain to be fully characterized across youth with and without anxiety disorders and co-morbid depression symptoms. Specifically, little is known about how neural processing of emotion to standardized stimuli in the laboratory setting relates to daily life negative reactivity or ER responses to daily life negative events in the real world. A limitation of laboratory studies examining associations between the LPP and ER in adults and youth is the use of specific ER instructions or provided pre-appraisals of stimuli rather than spontaneous use of a range of self-reported ER strategies in various contexts. It remains to be tested whether the LPP in response to emotional stimuli during controlled laboratory conditions would be associated with naturalistic use of ER strategies in daily life. Characterizing these brain-behavior relationships during early adolescence - when neural networks implicated in emotion processing and regulation undergo important maturational changes (e.g., Ladouceur, 2012; Silvers et al., 2017) - is critical to understanding the neural correlates of real-world emotional functioning in ways that could have implications for improving interventions and targeted prevention programs aimed at reducing depressive disorders in youth with anxiety disorders.

To address these gaps in the literature, we examined LPP to both unpleasant and pleasant affective picture stimuli in youth with anxiety disorders relative to youth without a psychiatric disorder and the contribution of depression symptoms to LPP amplitude in pediatric anxiety. We hypothesized that youth diagnosed with an anxiety disorder (ANX) would show larger LPP amplitudes following unpleasant images (relative to neutral images), compared to youth without a psychiatric diagnosis (ND). We further hypothesized that higher levels of depression symptoms in ANX youth would be associated with blunted LPP amplitudes to both pleasant and unpleasant images (relative to neutral images). We also sought to characterize associations between LPP amplitudes in response to emotional (pleasant and unpleasant relative to neutral) stimuli in the laboratory and daily life emotional reactivity and ER responses among ANX youth. Specifically, we focused primarily on associations between the LPP and daily life negative reactivity (peak negative affect or self-reported physiological reactivity following a negative event) and regulation (i.e., use of specific ER responses following a negative event) among ANX youth. For associations with negative reactivity, we hypothesized that greater LPP amplitude to unpleasant stimuli would be associated with more frequently reported EMA measures of emotional and physiological reactivity in daily life among ANX youth. We also hypothesized that LPP amplitudes to pleasant and unpleasant picture stimuli would be associated with EMA measures of ER strategies in response to daily life negative events. For example, we expected that lower LPP amplitudes to unpleasant pictures in the laboratory would be associated with ER strategies aimed at reducing negative affect (e.g., distraction, reappraisal).

2. Method

2.1. Participants

Participants included 9–14-year-old youth (55 % female) with either a current anxiety disorder (ANX, N = 130) or no lifetime history of any DSM-IV disorders (ND, N = 47). Youth with anxiety were required to meet DSM-IV criteria for one of the following current anxiety disorders: generalized anxiety disorder, social anxiety disorder, or separation anxiety disorder. Exclusion criteria were as follows: IQ < 70, current use of psychoactive medications, presence of metal in the body, presence of neurological impairment, developmental disorder (e.g., autism spectrum disorder), current primary diagnosis of major depressive disorder; current diagnosis of obsessive-compulsive disorder, post-traumatic stress disorder, attention-deficit hyperactivity disorder-hyperactive subtype, or substance use disorder; or lifetime history of psychosis or mania. The current ANX and ND youth are sub-samples recruited as part of a randomized clinical trial study examining neurobehavioral mechanisms of treatment for pediatric anxiety (see Silk et al., 2018; Ladouceur et al., 2018; ClinicalTrials.gov identifier is NCT00774150) who were included in the current study if they completed both the EEG and EMA protocols. Participants in the original treatment study were recruited through community advertisements (84 %) or referrals from pediatricians, school counselors, or mental health professionals (16 %) from an American midwestern metropolitan city. Only baseline measures completed prior to treatment were included in the present study. See Table 1 for a summary of sample characteristics.

2.2. Procedures

Written consent was obtained from the primary caregiver and written assent from the participant, were approved by the local University Institutional Review Board. Interviews and rating scales were administered to the child and his/her primary caregiver by an independent evaluator unaware of treatment assignment condition. Following the intake assessment, participants completed an ecological momentary assessment (EMA) protocol to assess their day-to-day emotional functioning in their natural social environments and an electroencephalography (EEG) assessment at a pre-treatment baseline assessment.

2.2.1. Clinical assessment—The *Schedule for Affective Disorders and Schizophrenia in School-Age Children—Present and Lifetime version* (Kaufman et al., 1997) semistructured clinical interview was administered by independent clinical evaluators to determine the presence of other Axis-I disorders. Parents and youth were interviewed separately, with independent evaluators (trained BA- and MA-level research clinicians) integrating data from both informants to arrive at final diagnoses (Silk et al., 2018). Youth also completed a set of questionnaires assessing affective traits, symptom severity, and functional impairment.

2.2.2. Self-report measures—Youth anxiety and depression symptoms were assessed via parent self-report using the Screen for Anxiety Related Disorders (SCARED-P) (Birmaher et al., 1999) and the Mood and Feelings Questionnaire (MFQ-P) (Costello and Angold, 1988).

2.2.3. Daily life EMA assessment—A cellphone-based Ecological Momentary Assessment (EMA) protocol was used to examine youths' day-to-day emotional functioning (see Silk et al., 2018; Tan et al., 2012). Youth received a total of 14 calls per week over five 14-day blocks (up to 70 calls in total) from trained research assistants: two calls each day on weekdays and four calls each day on weekends randomly within pre-specified 3-h time windows (see Silk et al., 2018). For each call, youth were asked to rate their current (momentary affect) positive and negative affect, as well as their peak negative affect (during their self-rated “worst” negative event that occurred within the past hour). As we were interested in emotional reactivity and regulation to more intense negative emotions, we focused on peak negative affect in the current manuscript. Specifically, based on prior work (Laurent et al., 1999; Silk et al., 2003; Tan et al., 2012), youth rated four negative emotions (nervous, upset, sad, and angry) for peak negative affect (i.e., negative emotion reactivity) on a Likert scale from 1 (very slightly or not at all) to 5 (extremely).

At each assessment, youth also rated on a dichotomous choice (i.e., yes/no) scale whether or not they experienced physiological symptoms (physiological reactivity), as well as their use of specific emotion regulation (ER) responses to their peak negative affect based on prior work (Silk et al., 2011), adapted from the Responses to Stress Questionnaire (RSQ; Connor-Smith et al., 2000). Specifically, the following ER responses (responses to negative affect) were assessed at each timepoint: acceptance, rumination, distraction, cognitive restructuring, avoidance, and problem solving (Silk et al., 2011; Stone et al., 2019). Participants could select one or more ER responses and could also choose “Other” if none of the listed responses were used. We did not group ER responses into maladaptive and adaptive categories, as more recent work as suggested that the appropriateness of an ER response is context-dependent (Aldao et al., 2015). Although rumination is not always considered an explicit ER strategy, we included it here as some work as conceptualized rumination as a maladaptive cognitive emotion regulation strategy aimed at suppressing the experience of negative affect (e.g., Liverant et al., 2011). Consistent with prior work, youth could endorse multiple responses for the same event (Silk et al., 2011; Tan et al., 2012). A total of 177 eligible youth completed the EMA protocol (130 anxious, 47 controls). Overall, the compliance rate for call completion during the EMA protocol was high (>90 %), with no difference in compliance rates between ANX and ND youth ($t = 0.27$, $p = .39$).

2.2.4. Computation of EMA variables—Peak negative emotion ratings were averaged to create a peak negative affect composite variable (see Laurent et al., 1999; Silk et al., 2003; Tan et al., 2012). Aggregate within-person means were then computed for peak negative affect. For analyses of ER responses to negative events, consistent with Tan et al., 2012, we focused on only timepoints where at least one peak negative emotion was rated 3 or higher (76.5 % of events for anxious; 75.7 % of events for controls, see Table 2). This was to ensure that youth were responding to events that were at least moderately distressing where ER responses would be expected to occur (see Tan et al., 2012). One participant in the anxious group did not report any events rated 3 or higher and was excluded from analyses of ER responses. Also consistent with Tan et al. (2012), within-person aggregate ER responses were created for each strategy, calculated as the mean proportion of timepoints the response was endorsed as used relative to the total number of available reports (i.e., where at least one peak negative emotion was rated 3 or higher) for each participant.

2.2.5. Laboratory EEG assessment—During the EEG laboratory assessment, youth completed 3 tasks in counterbalanced order. Here we focus on an affective picture viewing task where neural responses to pleasant, unpleasant, and neutral pictures were assessed. Stimuli included 24 pleasant, 24 unpleasant and 24 neutral affective picture stimuli from the International Affective Picture System (IAPS, Lang et al., 1997).[1] Pictures were presented in random order with several breaks in between blocks. Each trial began with 500 ms fixation followed by 6000 ms picture stimulus presentation; trials ended with a 6000 ms mask presentation (included for collection of pupil data not included in the current study) and an intertrial interval that ranged from 0 to 2000 ms. Youth were asked to attend to the pictures and click a mouse button as quickly as possible in response to each picture (to assess attentiveness during the task). Mean button response time was as follows: 712.76 (95 % CI: 661.50–764.03), with comparable response times across groups (ANX_{mean} = 713.02, ND_{mean} = 712.08; $t = -0.02$, $p = .987$). Following the EEG assessment, youth were asked to rate the arousal and valence of each of the picture stimuli presented in random order using the Self-Assessment Manikin (SAM; Lang, 1980) on a 1–9 scale using a keypad, where lower numbers reflect lower arousal ratings or more pleasant valence, respectively.

2.2.6. EEG acquisition and data reduction—Continuous EEG activity was recorded using an ActiveTwo head cap and the ActiveTwo 128-channel BioSemi system sampled at 512 Hz. An elastic Lycra cap was placed on the child's head and 128 Ag/AgCl-tipped electrodes were attached to the cap. In addition, 7 flat electrodes were used to measure electrical activity generated by eye and muscle movements, such that 2 electrodes were placed at supra and infra orbital sites of the right eye to monitor vertical eye movements and 2 on the outer canthi of the left and right eyes to monitor horizontal eye movements. In addition, 2 electrodes were placed on the mastoid (right and left) and 1 on the tip of the nose. Offline, all data processing was performed using Brain Electrical Signal Analysis (BESA) software. EEG data were rereferenced to the average reference and filtered (0.1-30

[1]Pleasant image stimuli: 8409, 1750, 7250, 8260, 7510, 1920, 2650, 2660, 2070, 5020, 2311, 5450, 5480, 5910, 7330, 7390, 1710, 2340, 2306, 7410, 7430, 2332, 2310, 8620. Unpleasant image stimuli: 1120, 1300, 1930, 1525, 2455, 2703, 2120, 2205, 1274, 1280, 9421, 2900, 3230, 3280, 3500, 3530, 5950, 6230, 9830, 6370, 7380, 1040, 6940, 1201. Neutral image stimuli: 2190, 7053, 2595, 2514, 2850, 2890, 2980, 5471, 5510, 2385, 7705, 7000, 7010, 7030, 7040, 7080, 7090, 7096, 7130, 7150, 7170, 7175, 7185, 7190.

Hz). Eye blinks and movements were corrected using the method developed by Gratton et al. (1983). After visual inspection to identify bad channels, segments were extracted from −200 to 2000 ms prior to and following the onset of the picture stimuli. Baseline correction was applied using −200 to 0 ms prior to picture onset. A semi-automatic procedure was used to detect and reject artifact according to the following criteria: a voltage step of >50 μV between data points, voltage gradient of 150 μV within trials, signal of <0.1 μV across the trial. Trials with button press response times (mouse click in response to picture onset) <100 ms (5.6 % of trials) and >2000 ms (4.3 % of trials) were also excluded from ERP analyses. Participants with fewer than 10 good trials per condition (pleasant, unpleasant, neutral) were excluded from analysis. Of the 177 eligible youth who completed the EMA protocol, 120 had sufficient valid EEG data and were retained in the final analyses (86 ANX and 34 ND).

Time windows and electrode sites for the LPP were based on a combination of guidance from prior literature and visual inspection of the waveforms across the full sample (both ANX and ND groups), an approach that is consistent with recommended ERP publication guidelines (Keil et al., 2014) and developmental considerations (Brooker et al., 2020). Given the sustained nature of the LPP, as in prior research on the LPP in response to emotional pictures, we extracted the LPP for the following time windows (by dividing the larger time window in half to create two equal-sized windows) to assess relative early and late affective processing: 500–800 ms (early) and 800–1100 ms (late) post-stimulus onset from an average of the following electrode sites (Biosemi ABCD layout): A05-A10, A15-A23, A28-A32, B03-B7, B11-B13, D29-D31 (See Fig. 1). Although prior studies suggest the LPP typically onsets around 400 ms, we used a slightly later windows because initial visual inspection suggested that the LPP did not begin to emerge until around 500 ms (see Fig. 2). Cluster averages were computed when at least 75 % of the selected electrode sites contained valid data. Internal reliability of the LPP electrode clusters by condition was high (α = 0.94–96). Residual-based difference scores (i.e., residualized scores) were created for neural responses to pleasant and unpleasant pictures controlling for response to neutral images, based on prior recommendations that residualized scores are more reliable than change scores (e. g., Meyer et al., 2017), particularly when the constituent ERPs are expected to be highly correlated (Clayson et al., 2020), as would be expected for LPP scores to pleasant, unpleasant, and neutral stimuli. We first examined raw LPP amplitudes for each valence condition (pleasant, unpleasant, neutral) in our manipulation checks and preliminary analyses separately before using residualized scores in our primary analyses, as difference scores may obscure group differences in response to neutral stimuli (see Usler et al., 2020).

2.2.7. Statistical analyses—Prior to testing our primary hypotheses, we first conducted manipulation checks across the entire sample to test whether the picture valence categories showed the expected patterns for both subjective self-ratings and LPP amplitudes. First, we examined whether there was a main effect of picture valence (pleasant, unpleasant, neutral) on the self-reported valence and arousal ratings, with unpleasant and pleasant pictures being rated as negatively and positively-valenced, respectively, and more arousing compared to the neutral condition. Second, we examined whether LPP amplitudes would show the expected main effect of picture valence with larger LPP amplitudes for unpleasant and pleasant valence compared to neutral valence using a 3 (valence: pleasant, unpleasant, neutral) x 2 (time window: early vs late) RM ANOVA. In follow-up post-hoc comparisons, we also explored any potential time-window effects (early vs. late LPP) using Fisher's least significant differences (LSD). As there are known effects of age and sex on emotional processing, preliminary analyses examined associations between LPP amplitudes with age (correlational analyses) and sex (independent samples t-test) to determine appropriateness for inclusion as covariates in subsequent analyses. Only variables showing significant associations with LPP amplitudes (for dimensional variables) or group differences in LPP amplitudes (for categorical variables) were included in subsequent analyses.

To test our hypothesis that ANX youth would show hyper-reactivity (larger LPP amplitudes) specifically to unpleasant vs. neutral images, we added group status (ANX vs. ND) as a between-subjects predictor in a 3 (valence: neutral, pleasant, unpleasant) × 2 (time window: early vs late) RM ANCOVA (including any identified covariates). Follow-up contrasts were then used to further characterize any group effects and explore any time window effects.

To test our hypothesis that anxiety symptoms would be correlated with greater LPP amplitudes to negative stimuli (vs neutral), while co-morbid depressive symptoms would be associated with blunted LPP amplitudes to both pleasant and unpleasant images (vs neutral), we tested partial correlations (including identified co-variates) between LPP residualized scores (LPP to pleasant or unpleasant controlling for neutral) and parent-reported youth depression and anxiety symptoms within the ANX youth sample.

To test our hypothesis that ANX youth would show associations between laboratory neural processing of unpleasant emotional stimuli and daily life negative emotional reactivity and ER responses, we used a linear regression model predicting LPP unpleasant residualized scores as the dependent variable, with EMA variables (peak negative affect and self-reported physiological responses to daily negative events; frequency of reported use of ER strategies of acceptance, rumination, distraction, cognitive restructuring, and avoidance) entered separately as independent predictors, along with identified co-variates. All EMA variables were entered simultaneously to control for Type I error and to examine unique variance associated with each variable while controlling for the other predictors. A second exploratory regression model predicting LPP pleasant residualized scores (LPP amplitudes in response to pleasant stimuli controlling for response to neutral) as the dependent variable with the same set of independent predictor variables was also conducted to explore possible associations between neural response to pleasant emotional stimuli and daily life emotional reactivity and ER responses. To control for Type I error, initial models for both LPP unpleasant and pleasant residualized scores collapsed LPP amplitudes across early and late time windows. Then in exploratory follow-up analyses, we explored whether results varied by early vs. late LPP time windows.

In addition, in supplemental exploratory analyses, we compared LPP-EMA associations (using residualized scores) among healthy (ND) youth to explore whether these were specific to youth with anxiety disorders or whether they might also replicate in healthy youth as well (see Supplemental materials). We examined associations in the ND group separately from the ANX group rather than combining both groups given that these subgroups were based on pre-defined inclusion criteria, are different sample sizes, and have unequal variance across study measures. Thus it would not be appropriate to combine them in one omnibus analysis.

3. Results

3.1. Preliminary analyses

A summary of descriptive statistics for EMA and ERP variables by group are shown in Table 2.

Affective Ratings: as expected, valence and arousal subjective self-report ratings significantly differed by picture valence category (i.e., pleasant, unpleasant, neutral), such that positive and negative valence and arousal ratings for pleasant and unpleasant relative to neural pictures all significantly differed for both valence (pleasant vs. neutral: $t = 24.43$, unpleasant vs. neutral: $t = 17.34$; $ps < 0.001$) and arousal (pleasant vs. neutral: $t = 14.69$, unpleasant vs. neutral: $t = 12.06$; $ps < 0.001$). Importantly, arousal ratings did not differ between the pleasant and unpleasant pictures ($t = -0.22$, $p = .82$). See Table 2.

Age and Sex effects: Independent samples t-tests were used to examine whether there were any sex effects on LPP pleasant and unpleasant residualized scores. Since there were no significant sex differences on LPP pleasant and unpleasant residualized scores in either time window (highest $t = 0.44$; $ps > 0.05$), sex was not considered further in subsequent analyses. Similarly, bi-variate correlation analyses examined whether age was associated with LPP pleasant and unpleasant residualized scores. Because age was negatively correlated with LPP unpleasant residualized scores ($r = -0.22$, $p = .02$) and trended toward a negative association with LPP pleasant residualized scores ($r = -0.17$, $p = .07$) in the later time windows, age was included as a co-variate in subsequent LPP regression analyses.

LPP amplitudes: RM ANOVA analyses revealed significant main effects of valence ($F = 9.25$ $p < .001$) and time window ($F = 133.83$, $p < .001$) on LPP amplitudes across subjects, as well as a valence by time window interaction ($F = 22.34$, $p < .001$) (see Table 3). Follow-up post-hoc LSD comparisons showed that, as expected, the LPP amplitudes to the emotion picture conditions (pleasant, unpleasant) were significantly greater relative to neutral ($F = 18.75$, $p < .001$). Further, the pleasant and unpleasant conditions did not significantly differ in LPP amplitude ($F = 0.16$, $p = .69$), suggesting that our pleasant and unpleasant picture stimuli were appropriately matched on arousal. Post-hoc LSD comparisons were exploring the time window effect revealed that LPP amplitudes were higher on average in the earlier time window relative to the later time window (mean differences ranged from 2.9 to 3.9) across all valence conditions ($ps < 0.001$), further supporting our use of two time windows. See also Fig. 2 for LPP waveforms by valence condition.

3.2. LPP amplitudes by group status

There was no significant between-subjects group effect, but there was a significant group by time window interaction ($F = 11.70$, $p < .001$), such that relative to ND, ANX youth had larger LPP amplitudes across valence conditions in the later time window relative to the earlier time window; the group x time x valence interaction was not significant ($p > .05$). See Table 3.

An additional follow-up model considered inclusion of age as a co-variate, which was significant as a between-subjects effect ($F = 17.11$, $p < .001$). However, there were no interactions of age with valence, time window, or group ($ps > 0.05$), and the overall pattern of findings did not change with age included in the model. Thus, age was dropped as a covariate in the final model for parsimony.

3.3. LPP amplitude associations with dimensional measures of anxiety and depression symptoms among ANX youth

For correlations with anxiety and depression symptoms within the ANX group (see Table 4), anxiety symptoms were not correlated with LPP amplitudes to pleasant or unpleasant relative to neutral stimuli ($ps < 0.05$). Partially supporting our hypothesis, higher levels of depression symptoms were associated with reduced LPP unpleasant residualized scores (LPP amplitudes to unpleasant stimuli relative to neutral), with significant moderate associations for both time windows (early: $r = -0.33$, $p \geq 0.01$; late: $r = -0.25$, $p < .05$). However, depression symptoms reported by ANX youth were not associated with LPP pleasant residualized scores (LPP amplitudes to pleasant relative to neutral pictures, $ps > 0.05$). See Supplemental materials for exploratory correlation analyses of anxiety and depression symptoms with LPP amplitudes within the ND group (Table 1S).

3.3.1. LPP associations with daily life emotional reactivity to negative events among ANX youth—Regression analyses indicated no significant associations between LPP pleasant and unpleasant residualized scores with daily life negative reactivity (i.e., self-reported peak negative affect and physiological responses to negative events) ($ps > 0.05$). See Supplemental materials for exploratory analyses of LPP associations with daily life emotion reactivity within the ND group.

3.3.2. LPP associations with daily life ER following negative events among ANX youth—The model with LPP unpleasant residualized scores across time windows indicated that reported use of distraction ($t = -2.23$, $p = .02$) and rumination ($t = -2.44$, $p = .02$) in daily life were both associated with a lower LPP amplitude to unpleasant images in the laboratory. Depression symptoms were associated with lower LPP unpleasant residualized scores ($t = -3.12$, $p < .01$). In exploratory follow-up analyses for LPP unpleasant residualized scores in early and late time windows, the distraction effect was significant only in the early time window ($t = -2.33$, $p = .02$), while the rumination effect was significant only in the later time window ($t = -2.42$, $p = .02$). Regression analyses within ANX youth are shown in Table 5. See Supplemental materials for exploratory analyses of LPP associations with daily life ER within the ND group (Table 2S).

4. Discussion

Findings from the current study indicate that the LPP could represent an important neurophysiological marker of emotional functioning in the real world, consistent with the conceptualization of the LPP as an index of ER (e.g., Myruski et al., 2019). Specifically, we found several associations between the neural response to emotional images in the laboratory and use of specific ER strategies in daily life among anxious youth. Findings are broadly consistent with prior research linking the LPP response to emotional stimuli in the laboratory with psychiatric symptoms, trait emotion regulation, problematic behaviors, and social functioning (Bunford et al., 2017; Harrison and Chassy, 2019; Myruski et al., 2019).

Regarding the use of specific ER responses to daily life negative events, among anxious youth, more frequent use of distraction was associated with lower LPP amplitudes to unpleasant images (relative to response to neutral images). These findings are also consistent with prior research demonstrating that increased attentional vigilance to threat in the laboratory (assessed via fMRI and behaviorally using a dot-probe task) is related to greater self-reported use of distraction to regulate emotions in daily life among anxious youth (Price et al., 2016). We also found that more frequent use of rumination was associated with lower LPP amplitudes to unpleasant images, which is consistent with prior research showing that habitual self-reported use of rumination is associated with reduced LPP amplitudes in response to threatening images (Harrison and Chassy, 2019). The association of self-reported use of distraction and rumination in daily life with reduced LPP amplitude to unpleasant images in the laboratory may indicate that youth with anxiety disorders engage less with negatively-valenced laboratory stimuli as their attention is focused elsewhere.

We also explored in supplemental analyses whether associations between LPP amplitudes and daily life use of ER strategies in response to negative events among anxious youth would replicate in a small sample of youth with no psychiatric diagnoses (ND). A somewhat different pattern emerged for ND youth where distraction was positively associated with higher LPP amplitudes to unpleasant images relative to neutral images. Results suggest that for ND youth, the use of distraction in daily life in response to negative events is associated with increased neural response to negatively-valenced stimuli in the laboratory. It may be that healthy youth who tend to have larger neural responses to unpleasant stimuli may utilize distraction more often in daily life to manage negative emotional reactions. Youth with anxiety disorders may tend to utilize these strategies more chronically and pervasively to a broader range of situations, ultimately leading to associations with reduced neural processing of unpleasant stimuli. However, these results partially in contrast to those of Price et al. (2016), which found significant associations between greater threat vigilance in the laboratory and greater use of distraction in daily life among both anxious and non-anxious youth.

In terms of LPP responses to pleasant images, for ND youth, lower LPP amplitudes following pleasant images were associated with greater use of avoidance in daily life, suggesting that habitual avoidance in daily life is associated with blunted neural response to pleasant stimuli among healthy youth. Although anxious youth did not show a significant association between avoidance and LPP responses to pleasant images, there was a trend effect in the same direction among anxious youth. These findings are consistent with Bunford et al. (2017) who observed that a blunted LPP to pleasant images was associated with increased self-reported social and behavioral problems in daily life, as these youth may have difficulty with appropriately engaging with rewarding daily life activities. These findings are also consistent with the broader anxiety literature demonstrating the avoidance of both positive and negative emotions may contribute to higher anxiety and depression symptoms (Salters-Pedneault et al., 2004; Bardeen and Fergus, 2014; Buhk et al., 2020), and avoidance associated with anxiety may predict subsequent depression longitudinally (Jacobson and Newman, 2014).

Notably, some differential patterns emerged in exploration of early versus late LPP time windows, which may reflect different temporal effects of specific ER responses. Specifically, in exploratory follow-up analyses for LPP unpleasant residualized scores in early vs. late time windows, the distraction effect was significant only in the early time window while the rumination effect was significant only in the later time window. Prior reviews of attentional processes in anxiety have called for the need for more temporally sensitive approaches (Rosen et al., 2019). Examining the LPP may be particularly relevant for understanding the etiology of anxiety disorders, as early LPP time windows may reflect an early orienting or selective attention response (i.e., such as threat bias or heightened vigilance), whereas LPP amplitudes in later time windows may reflect more sustained difficulties with disengaging sustained attention from unpleasant information that may underlie perseverative negative thought processes such as worry and rumination. Relative to other ERP components that are relatively brief in response to a target stimulus, the LPP is more protracted, and as such, researchers examine its magnitude across multiple time-windows (e.g., Foti et al., 2009; Hajcak et al., 2011; Hajcak et al., 2010; Hajcak and Foti, 2020). For example, MacNamara et al. (2019) found that adults with social anxiety disorder exhibited a larger LPP to unpleasant stimuli in both time windows, whereas those with panic disorder showed an initial increase in the early time window with a reduction in the late time window, which was interpreted as possibly due to avoidance of physiological arousal (i. e., a defining characteristic of panic disorder). While our exploration of early and late LPP time windows in relation to daily life emotional reactivity and ER was preliminary, future studies should continue to characterize these potentially important temporal effects.

Contrary to predications, there were no associations with daily life emotional reactivity (peak negative affect or self-reported physiological reactivity) among ANX or ND youth. Despite the LPP being considered an index of emotional reactivity that is evoked milliseconds following an emotional stimulus, greater LPP magnitudes in response to laboratory stimuli do not appear to translate to greater emotional reactivity in daily life. It may be that the LPP reflects earlier attentional processing of emotional stimuli that is not reflected in subsequent emotional reactivity across other emotion response systems (e.g., subjective reactivity, experience of physiological arousal, behavior) or at much longer time scales (e.g., minutes to hours). However, initial neural processing of emotional stimuli may influence selection of ER strategies deployed in daily life.

It was somewhat surprising that ANX and ND youth did not show a difference in LPP response to unpleasant versus neutral images, as has been found in prior studies, nor was there any association with anxiety symptom severity among ANX youth. However, findings revealed that ANX youth show a relative increase in sustained affective processing across pleasant, unpleasant, and neutral stimuli, as reflected in their relatively higher LPP amplitudes (particularly in the later time window) across conditions, suggesting that anxious youth may show hyper-reactivity to all stimuli regardless of valence. One reason we may not have observed hyper-reactivity to negative stimuli in the anxious youth may be that prior studies generally included threat-related negative stimuli, particularly threatening faces, but this study included a broader range of negative high-arousing stimuli.

Our findings that youth with anxiety disorders with higher depressive symptoms showed an attenuated LPP in response to unpleasant images relative to youth with anxiety disorders who reported lower levels of depression is consistent with prior literature (Weinberg et al., 2016) and predictions of emotion context insensitivity (see Bylsma, 2021). Thus, these results highlight the importance of considering co-morbid depressive symptoms in studies examining neural processing of negatively-valenced emotional information in anxiety disorders to better characterize the heterogeneity of emotional processing among youth with pediatric anxiety. However, our observed associations between daily life ER and the LPP were not fully explained by depression symptoms, as these associations remained significant with co-morbid depression symptoms included as a co-variate in analyses. In contrast to our hypothesis that co-morbid depression would predict reduced reactivity to both pleasant and unpleasant stimuli (i.e., as predicted by emotion context insensitivity), depressive symptoms levels did not predict blunted LPP amplitudes in response to pleasant images. However, most prior findings examining LPP responses to emotional stimuli in depression have focused on unpleasant stimuli (e.g., Foti et al., 2010) without consideration of co-morbid anxiety.

Strengths of this study include the large and well-characterized sample of adolescents with diagnosed anxiety disorders and healthy controls and assessment of both laboratory neural responses to standardized emotional stimuli and daily life emotional functioning using EMA. Although findings are preliminary and require replication, this study is the first to provide evidence that neural processing of emotion in the laboratory using the LPP are associated with measures of emotional functioning daily life among youth with anxiety disorders and those without psychiatric disorders. Our use of cell-phone based EMA has notable strengths and weaknesses. In terms of strengths, this method allows for better validation of participant responses, but a limitation is that it may be less generalizable to the majority of more recent research that uses smartphone-based EMA. In addition, limitations of this study include the relatively smaller sample size of the healthy control group, which limited our ability to test additional potential moderators of these results. Our exclusion of some co-morbid conditions among the ANX youth also may limit generalizability of findings. We also did not include a depression-only group, so findings related to co-morbid depression symptoms should be interpreted in the context of anxiety disorders. We are also unable to rule out the possibility that differences in insight and emotional awareness may contribute to our findings. The design of our task including a button press during the presentation of stimuli that overlapped with our LPP time windows may have also potentially introduced additional noise or affected the latency of the LPP response. Finally, given that our healthy control sample was quite small and comparisons tested within this group were exploratory and in need of replication. Further research is needed to confirm these associations in larger transdiagnostic samples to fully characterize how individual differences and dimensions of psychopathology relate to brain-behavior relationships.

It is also important to note that a broader limitation of the current study, as well as prior research on the LPP to understand the time course of emotional processing and regulation, is a lack of standardization or clear guidelines for determining appropriate epochs for analysis (see Clayson et al., 2021 for a general review of these issues in ERP research). For example, prior studies of the LPP have defined epochs beginning as early as 200 ms (e.g., Myruski et al., 2019) and as late as 5000 ms (Cao et al., 2020) with the number of epochs of varying sizes ranging anywhere from one large epoch (e.g., Bautista et al., 2022) to as many as 9 epochs (Myruski et al., 2019), with most prior studies using 2–3 epochs (e.g., Dennis and Hajcak, 2009; Kujawa et al., 2012; McLean et al., 2020). Standardization of these processing decisions is a particular challenge for affective science research on the LPP relative to other ERP components as the LPP is a sustained response that is present for the duration of an emotional stimulus (with some evidence it may extend even beyond that; e.g., Hajcak and Foti, 2020), and thus it is sensitive to differences in study design (e.g., length or type of stimuli, ER instructions). Further, the specific spatial and temporal characteristics of the LPP are known to change with development and may need to be adjusted to be appropriate for specific developmental and clinical samples (Brooker et al., 2020; Dickey et al., 2021; Deng et al., 2019). However, it will be important for research to consider how to provide guidelines for standardization of LPP processing decisions that are also sensitive to developmental changes and methodological differences in task design.

In sum, these results provide evidence in support of the LPP in response to emotional stimuli in the laboratory as a neurophysiological marker of emotional functioning in daily life, such that the LPP responses to emotional stimuli in the laboratory setting was associated with the use of specific ER strategies in the context of daily life. Findings contribute to a deeper understanding of how neural responses to emotional information in the lab relate to daily life emotional functioning and to expanding the conceptualization of the LPP as an ecologically-valid marker of ER among both anxious and healthy youth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

Data will be made available on request.

Abbreviations:

EMA	Ecological Momentary Assessment
ER	Emotion Regulation
ERP	Event Related Potential
LPP	Late Positive Potential
ANX	Anxious
ND	No Diagnosis

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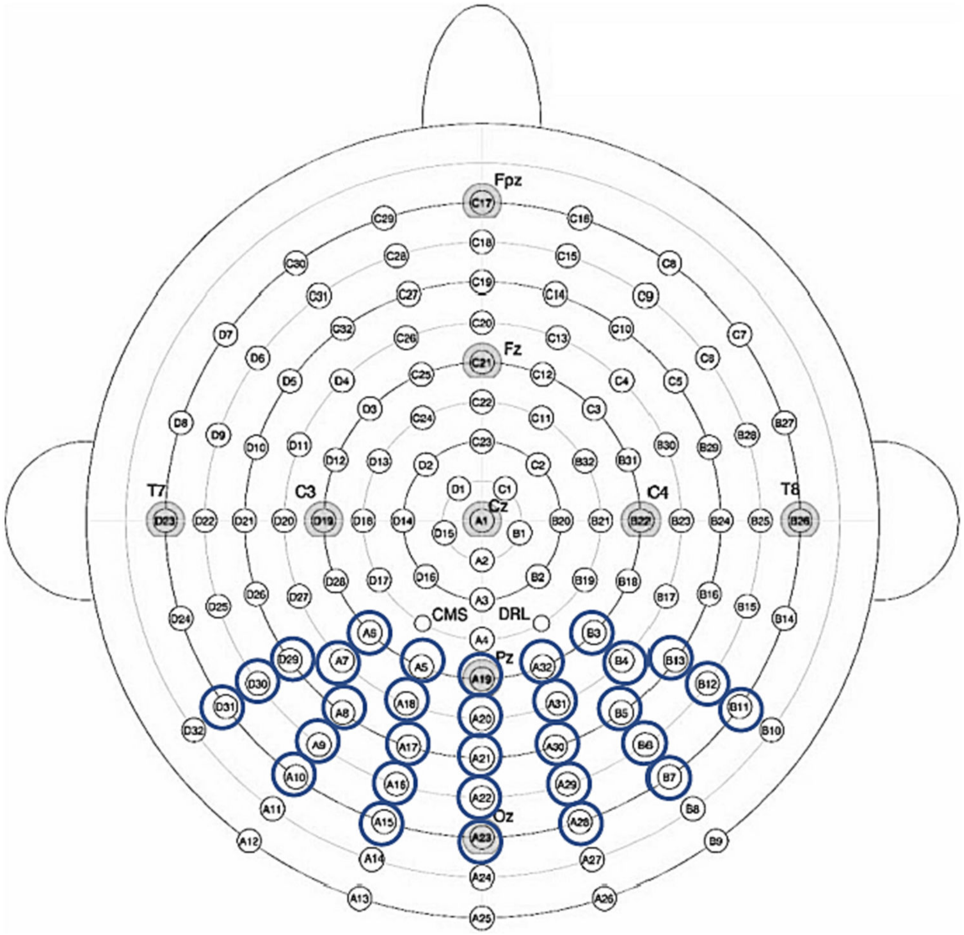

Fig. 1.

Biosemi 128-channel electrode mapping schematic. The following parietal-occipital electrode sites were averaged for computation of the LPP: A05-A10, A15-A23, A28-A32, B03-B7, B11-B13, D29-D31.

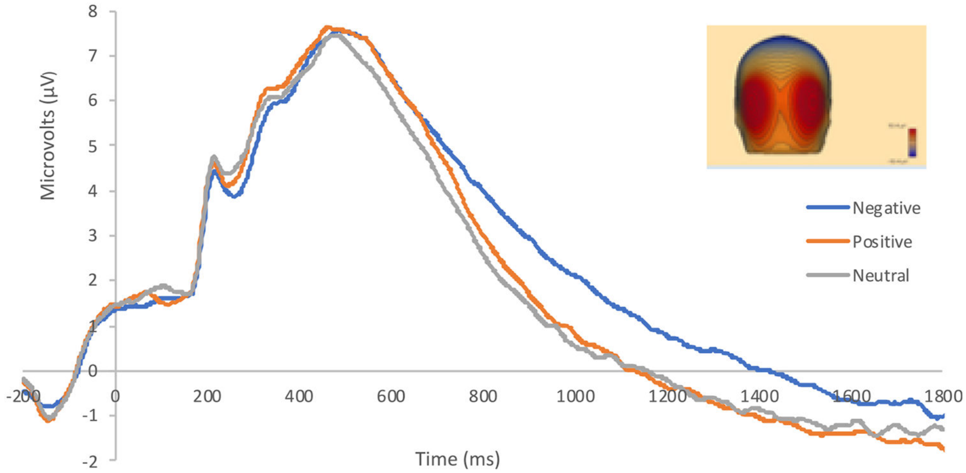

Fig. 2.

Grand average event-related potential (ERP) waveforms plotted following positive, negative, and neutral stimuli in ANX youth. Grand average ERP waveforms were computed using an average of the time series extracted from the following electrode sites: A05-A10, A15-A23, A28-A32, B03-B7, B11-B13, D29-D31.

Table 1

Sample characteristics.

Variable	ANX (N = 129)	ND (N = 47)
Age	10.95 (1.47)	11.36 (1.66)
Female, %	55.0	55.3
White, Non-Hispanic, %	89.1	76.1
SCARED-P	36.28 (11.63)	3.50 (3.71)
MFQ-P	14.51 (9.72)	1.39 (1.79)

Note: Data presented as mean *(SD)* unless otherwise noted. SCARED-P: Screen for Childhood Anxiety and Related Disorders Parent Report, MFQ-P: Mood and Feelings Questionnaire-Parent Report.

Table 2

Summary of descriptive statistics for ERP and EMA variables.

Variable	ANX (N = 85)	ND (N = 34)
Valence self-ratings of stimuli		
Neutral	5.15 (1.02)	4.89 (1.01)
Positive	2.90 (1.17)	3.15 (1.11)
Negative	7.02 (1.12)	6.40 (1.32)
Arousal self-ratings of stimuli		
Neutral	2.51 (1.43)	2.32 (1.50)
Positive	4.42 (2.16)	4.22 (2.15)
Negative	4.68 (2.05)	3.68 (1.76)
LPP mean amplitudes (μV)		
Neutral	5.11 (2.57)	4.09 (4.22)
Positive	5.59 (2.92)	5.32 (4.21)
Negative	5.76 (2.79)	5.17 (4.11)
EMA variables		
# Events REPORTS	55.54 (12.44)	58.65 (12.44)
# Intense negative events	35.27 (17.90)	28.47 (17.22)
Range negative intense events	1–70	1–61
Peak negative affect[a]	2.24 (0.58)	1.97 (0.47)
ER strategy use[b]		
Physiological	0.13 (0.18)	0.03 (0.06)
Acceptance	0.71 (0.34)	0.74 (0.28)
Rumination	0.21 (0.26)	0.37 (0.29)
Distraction	0.24 (0.22)	0.29 (0.24)
Reappraisal	0.56 (0.31)	0.55 (0.34)
Avoidance	0.64 (0.30)	0.53 (0.37)

Note: Values are presented as means (SD) unless otherwise specified. Valence and arousal self-ratings are based on the Self-Assessment Manikin (SAM), with lower numbers reflecting lower arousal ratings and more positive valence ratings, respectively. LPP: Late Positive Potential, mean amplitudes in microvolts (μV). EMA = Ecological Momentary Assessment.

[a] Aggregate means. ER = Emotion Regulation.

[b] Mean proportion frequency of occurrence following identified intense negative events.

Table 3

RM ANOVA of LPP amplitudes by valence (Pleasant, Unpleasant) and time (Early, Late) with group effect (ANX vs. ND).

Source	*df*	*F*	*p*	$\eta 2$
Group	1,118	1.09	.30	0.01
Valence	2, 236	10.33	<.001	0.08
Time window	1,118	151.51	<.001	0.56
Valence * time window	2, 236	19.74	<.001	0.14
Valence * group	2	1.49	.23	0.01
Time window * group	1	11.16	.001	0.09
Valence * time window * group	1	0.03	.89	<0.01

Table 4

Bivariate correlations among study variables among ANX youth.

	Age	SCARED-P	MFQ-P	LPP Neut Early Raw	LPP Neut Late Raw	LPP Pos Early Raw	LPP Pos Early Resid	LPP Pos Late Raw	LPP Pos Late Resid	LPP Neg Early Raw	LPP Neg Early Resid	LPP Neg Late Raw	LPP Neg Late Resid
Age	–												
SCARED-P	−0.06	–											
MFQ-P	0.07	0.42 **	–										
LPP Neut Early Raw	−0.23 *	0.08	−0.01	–									
LPP Neut Late Raw	0.29 **	0.21	0.03	0.57 **	–								
LPP Pos Early Raw	−0.21	0.13	−0.06	0.85 **	0.51 **	–							
LPP Pos Early Resid	−0.02	0.12	−0.10	−0.02	0.04	0.52 **	–						
LPP Pos Late Raw	−0.25 *	0.23 *	0.00	0.44 **	0.85 **	0.61 **	0.43 **	–					
LPP Pos Late Resid	−0.15	0.19	−0.03	0.19	0.46 **	0.52 **	0.68 **	0.86 **	–				
LPP Neg Early Raw	−0.22 *	0.09	−0.16	0.89 **	0.49 **	0.90 **	0.26 *	0.46 **	0.30 **	–			
LPP Neg Early Resid	−0.08	0.06	−0.33 **	0.15	0.04	0.44 **	0.59 **	0.22 *	0.32 **	0.58 **	–		
LPP Neg Late Raw	0.31 **	0.24 *	−0.15	0.68 **	0.74 **	0.69 **	0.21	0.73 **	0.52 **	0.76 **	0.44 **	–	
LPP Neg Late Resid	−0.19	0.16	−0.25 *	0.48 **	0.19	0.56 **	0.27 *	0.32 **	0.35 **	0.68 **	0.61 **	0.80 **	–

Note: Bivariate correlation coefficients are represented using Pearson's *r*. Abbreviations: LPP = Late Positive Potential; Pos = Positive (pleasant) valence; Neg = Negative (unpleasant) valence; Neut = Neutral valence; Raw = unadjusted mean amplitudes; Resid = residualized difference scores adjusting for LPP mean amplitudes in the Neutral condition. SCARED-P: Screen for Childhood Anxiety and Related Disorders Parent Report, MFQ-P: Mood and Feelings Questionnaire-Parent Report.

* Significant at the 0.05 level (2-tailed).

** Significant at the 0.01 level (2-tailed).

Table 5

Summary of regression models for LPP-EMA associations among ANX youth.

LPP negative residualized scores				
	B	***SE***	***t***	***p***
Age	−0.092	0.06	−1.64	.105
MFQ-P	−0.024	0.01	−3.12	.003**
Acceptance	0.223	0.37	0.60	.551
Rumination	−0.708	0.29	−2.44	.017*
Distraction	−0.938	0.42	−2.23	.029*
Reappraisal	−0.550	0.45	−1.21	.229
Avoidance	0.830	0.44	1.90	.061
LPP positive residualized scores				
	B	***SE***	***t***	***p***
Age	−0.066	0.06	−1.11	.270
MFQ-P	−0.007	0.01	−0.90	.369
Acceptance	−0.130	0.40	−0.33	.743
Rumination	−0.343	0.31	−1.12	.268
Distraction	−0.349	0.45	−0.78	.437
Reappraisal	0.054	0.48	0.11	.912
Avoidance	−0.292	0.46	−0.63	.531

Note: MFQ-P: Mood and Feelings Questionnaire-Parent Report.

* Significant at the 0.05 level (2-tailed).

** Significant at the 0.01 level (2-tailed).