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Neural Response to Pleasant Pictures Moderates Prospective Relationship between Stress and Depressive Symptoms in Adolescent Girls

Amanda R. Levinson[1], **Brittany C. Speed**[1], and **Greg Hajcak**[2]

[1]Department of Psychology, Stony Brook University, Florida State University

[2]Department of Psychology, Florida State University and Department of Biomedical Sciences, Florida State University

Abstract

Objective: Adolescent girls are at increased risk for depression, which is thought to result from the interaction of biological vulnerabilities and life stressors common to adolescent girls. A blunted LPP to emotional stimuli (i.e., pleasant and unpleasant) has been associated with depressive symptoms and risk. The current study of adolescent girls examines the moderating effects of the late positive potential (LPP), a candidate biomarker of depression, of the link between life stress and increases in depressive symptoms over 1 year.

Method: Measured LPP to pleasant and unpleasant pictures from the International Affective Picture Set among 143 predominantly Caucasian adolescent girls ages 8 to 14, who also reported on the frequency of common life stressors. Self-reported depressive symptoms were assessed both at baseline and 1 year after the initial lab visit.

Results: The LPP to pleasant pictures moderated the relationship between baseline life stressors and the change in depressive symptoms. Specifically, life stress was associated with increases in depressive symptoms when the LPP to pleasant pictures was blunted, whereas life stress was associated with decreases in depressive symptoms when the LPP to pleasant pictures was potentiated. These effects showed some specificity to family and school-related stressors, and to anhedonic and efficacy-related depressive symptoms. A similar pattern, though not statistically significant, was found for the LPP to unpleasant pictures.

Conclusions: Together, these findings suggest that the LPP to pleasant pictures may represent a useful biomarker in identifying individuals at greatest risk of experiencing depressive symptoms following stress.

Keywords

Late positive potential; depressive symptoms; stress; adolescence

Correspondence should be addressed to Amanda R. Levinson, Psychology B Building, Stony Brook University, Stony Brook, NY 11794-2500. amanda.levinson@stonybrook.edu.

Over the course of adolescence, the prevalence of depression increases from roughly 1% to between 17.1% and 25% (Kessler, Avenevoli, & Merikangas, 2001). These increases disproportionately affect adolescent girls, such that gender differences in depression rates first emerge in adolescence, rise to a ratio of approximately 2:1 female to male by age 15, and are maintained at this proportion for the next several decades (Avenevoli, Swendsen, He, Burstein, & Merikangas, 2015; Kessler et al., 2001). Throughout the lifespan, life stress plays a critical role in the genesis and maintenance of depression (Kendler, Karkowski, & Prescott, 1999; Kessler, 1997; Monroe, Rohde, Seeley, & Lewinsohn, 1999), including triggering a cascade of biological changes such as increasing immune activation and alterations to the structure of the hippocampus, amygdala, and prefrontal cortex (DellaGioia & Hannestad, 2010; McEwen, 2005; Segerstrom & Miller, 2004). Nolen-Hoeksema & Girgus' (1994) interactive model proposes that the emergence of sex differences in depression during adolescences results from the interaction of life stressors and biological vulnerabilities occurring during this stage of life (Bale & Epperson, 2015; Ge, Conger, & Elder Jr, 2001; Nolen-Hoeksema & Girgus, 1994).

Indeed, adolescent girls are uniquely vulnerable to the effects of life stressors due to a confluence of situational, psychological, and biological circumstances. Adolescence is a period of increased life stressors, including greater conflict with family (Allison & Schultz, 2004), new social pressures that include the beginning of romantic relationships and increased peer victimization (Csikszentmihalyi, Larson, & Prescott, 2014; Ge, Lorenz, Conger, Elder, & Simons, 1994; Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013; Rizzo, Daley, & Gunderson, 2006; Starr & Davila, 2009); this period is also characterized by greater challenges at school (Compas, Orosan, & Grant, 1993; Kaplan, Liu, & Kaplan, 2005). Consistent with epidemiological data on depression, adolescent girls display a stronger link between these stressors and the development of affective disorders (Nolen-Hoeksema & Girgus, 1994; Shih, Eberhart, Hammen, & Brennan, 2006). This gender difference has been attributed to the fact that adolescent girls report lower self-esteem and greater prioritization of interpersonal relationships, which may increase the negative impact of challenges to self-worth and interpersonal conflict, respectively (Moksnes, Moljord, Espnes, & Byrne, 2010; Robins, Trzesniewski, Tracy, Gosling, & Potter, 2002; Rudolph et al., 2000). In sum, adolescent girls represent a high-risk population for the depressogenic effects of life stressors. Little is known, however, about potential moderators of this effect of life stress on depression. Identifying moderating biomarkers could inform who among the high-risk population of adolescent girls is most vulnerable, and may provide insight into potential pathophysiological mechanisms and serve as targets for novel prevention efforts.

The Emotion Context Insensitivity (ECI) model of depression provides a suggestion for the types of biomarkers that may be of interest. The ECI model suggests that depression is associated with reduced engagement with emotional stimuli, regardless of their emotional valence (Rottenberg, Gross, & Gotlib, 2005; Rottenberg & Hindash, 2015). Put another way, strong engagement with emotionally salient environmental stimuli may reflect a propensity antithetical to depression. One neural measure that has been relevant to the predictions of the ECI model is a component of the event-related potential (ERP) waveform called the late positive potential (LPP). The LPP is a positive-going deflection that begins roughly 300ms after the onset of stimulus presentation, and is potentiated following stimuli with emotional

(i.e., pleasant or unpleasant compared to neutral) content (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Hajcak, Dunning, & Foti, 2009). The LPP is therefore thought to reflect sustained attentional engagement with emotionally salient stimulus content. Furthermore, the LPP is thought to be relatively trait-like, which is supported by its strong test-retest reliability (Bondy et al., 2017). The ECI model of depression, therefore, would predict attenuated LPPs to both pleasant and unpleasant emotional stimuli, reflecting generalized emotional disengagement among depressed individuals (Rottenberg et al., 2005; Rottenberg & Hindash, 2015).

Consistent with predictions from the ECI model, clinically depressed adults exhibit a reduced LPP to both pleasant and unpleasant emotional pictures (Foti, Olvet, Klein, & Hajcak, 2010; Weinberg, Perlman, Kotov, & Hajcak, 2016). Furthermore, a blunted LPP to both pleasant and unpleasant images have been associated with risk factors for depression. For example, the LPP to both positively and negatively-valenced emotional images was found to be attenuated in girls with a maternal history of depression or depression symptoms (Kujawa, Hajcak, Torpey, Kim, & Klein, 2012; Nelson, Perlman, Hajcak, Klein, & Kotov, 2015)[1]. Similarly, a blunted LPP to both pleasant and unpleasant emotional images was related to reduced positive emotionality (Speed et al., 2015), a personality trait linked to risk for depression (Dougherty, Klein, Durbin, Hayden, & Olino, 2010; Naragon-Gainey, Watson, & Markon, 2009; Watson, Clark, & Carey, 1988). Collectively, these data support the ECI model hypothesis that a blunted LPP to standardized emotional images may characterize individuals with depression as well as those at increased risk. That is, increased risk for depression may be reflected in a preexisting tendency toward reduced engagement with motivationally salient environmental stimuli.

Within the context of a diathesis-stress model, it is possible that greater emotional engagement, as reflected by a larger LPP to emotional images, is protective against the depressogenic effects of stress. Previous work on the relationship between life stress and depression suggests that depression is most strongly associated with life stressors that are at least partially self-generated, referred to as dependent stressors (Auerbach, Bigda-Peyton, Eberhart, Webb, & Ho, 2011; Shih et al., 2006), as opposed to independent, or fateful stressors, which are life stressors that cannot be attributed to the sufferer (e.g. a natural disaster). Dependent life stressors have also been the focus of previous moderation studies examining the relationship between stress and depression (Mazure, Bruce, Maciejewski, & Jacobs, 2000; Shahar, Joiner, Zuroff, & Blatt, 2004).

In the context of this background, the current study sought to examine the potential moderating role of the LPP on the relationship between life stress and depression. This study focuses on girls because we expect greater variability and a higher mean level of depression symptoms in an all-girl sample, allowing us to examine functioning at the higher end of the depression symptom spectrum. We focused on girls between the ages of 8 and 14, as this age

[1]In studies that examine the LPP to semantic self-relevant information using the Self-Referential Encoding Task (SRET) find that depression and depression risk factors are associated with a blunted LPP to positive words, and a potentiated LPP to negative words (Auerbach, Stanton, Proudfit, & Pizzagalli, 2015; Speed, Nelson, Auerbach, Klein, & Hajcak, 2016; Webb et al., 2017). This suggests that the link between depression and the LPP to self-referential information be better understood using a positivity attenuation or negative potentiation model. However, the current study focuses on the LPP elicited by nomothetic emotional scenes.

range (i.e., late childhood and early adolescence) has been suggested to be the peak period of risk for the depressogenic effects of life stress (Rudolph et al., 2000). We examined whether the LPP might interact with baseline age-relevant life stressors to prospectively predict changes in depression over the course of 1 year. We examined the effects of dependent life stressors separately, as well as in combination with independent stressors. We hypothesized that, consistent with the ECI model, individuals with blunted LPPs to both pleasant and unpleasant images would have a stronger association between baseline stressors and increases in depressive symptoms from baseline to year-1 follow up.

Method

Participants

A community sample of 317 adolescent girls ages 8 to 14 in the suburban area of Long Island, NY was recruited using direct mailings to likely households. Of the 317 total participants, 112 were missing at least one of the self-report measures, 110 of whom could not be included because the baseline measure of life stress (ALEQ) was added to the study while data collection was already ongoing and 2 of whom were lost to attrition between baseline and follow up. Additionally, 44 did not complete the baseline emotional interrupt task due to time constraints, 7 were excluded from analysis due to poor EEG data quality; 1 was excluded for insufficient number of useable trials on the EEG task; finally, 10 were excluded from analysis because their accuracy to identifying targets in the emotional interrupt task was less than 50%, suggesting that they were not engaged during task administration. Thus, a total of 143 participants were included in the final moderation analyses. Independent-samples t-tests indicate that the included and excluded participants did not differ significantly in self-reported depression symptoms or in ERP magnitude. The excluded sample was significantly younger than the included sample ($t = -4.49$, $p < .001$), which is a group difference driven by the participants who were excluded for poor EEG data quality and task performance. Finally, chi-squared tests comparing task-completers and non-completers find no group differences in race or ethnic group membership, and independent-samples t-tests comparing these groups indicate no group differences in self-reported depression symptoms. Task non-completers were, however, significantly younger than task completers ($t = -3.37$, $p = .001$).

The mean age of this final sample was 12.90 years (SD = 1.55 years). The sample was predominantly Caucasian (87%) with the remaining sample self-identified as 4% African American, 3% Hispanic, and 6% Other or Multiple Races. Finally, the sample was also of relatively high SES with a mean household income of 128K (±81K). Inclusion criteria were that the participant be a girl between the ages of 8 and 14, living with at least 1 biological parent who speaks English fluently. Participants were excluded if they had a diagnosis of pervasive developmental disorder. At baseline, 11 participants met criteria for a lifetime history of a depressive disorder, and 33 participants met criteria for lifetime history of an anxiety disorder. Participants were compensated $20/hour for their time in the study, including time spent completing questionnaires and the EEG tasks. All participants' parents completed informed consent procedures while adolescent participants completed assent procedures as approved by the Institutional Review Board at Stony Brook University.

Measures

Adolescent Life Events Questionnaire—The Adolescent Life Events Questionnaire (ALEQ) is a measure of stressful life events with good reported psychometric properties (Hankin & Abramson, 2002). The ALEQ asks respondents to rate the frequency with which each of 57 stressful life events has been experienced in the past 3 months. In this study, the ALEQ was completed by participants at the baseline study visit and participants reported on stressful life events that occurred in the 3-months prior to this visit. Each event is rated on a 5-point scale (0–4), where 0 represents never, and 4 represents always. Subscales for dependent and independent life stressors were calculated using the categorization system created by Auerbach and colleagues (2010). Dependent stressors (29 items) included events such as: "You had an argument with a close friend". Independent stressors (13 items) included events such as: "You and your family moved to a new town, but you didn't want to move". Subscales were also calculated based on the context in which the stressor was experienced. This yielded 4 subscales: 1) family stressors (e.g. "You fought with your parents over personal goals, desires, or choice of friends"; 23 items), 2) romantic life stressors (e.g. "A boyfriend or girlfriend broke up with you"; 8 items), 3) school stressors (e.g. "You got in trouble with the teacher of principal"; 11 items), and 4) peer stressors (e.g. "A close friend moved away"; 15 items).

Children's Depression Inventory—Depression was measured at both baseline and 1-year follow-up though adolescent self-report using the Children's Depression Inventory (CDI; Kovacs, 1992). This measure consists of 27 items rated on a 3-point scale (0–2), and yields 5 subscales: 1) Negative Mood (e.g. "I feel like crying every day"; 6 items), 2) Interpersonal Problems (e.g. "I get into fights all the time"; 4 items), 3) Ineffectiveness (e.g. "I can never be as good as other kids"; 4 items), 4) Anhedonic Symptoms (e.g. "I do not have any friends"; 8 items), 5) Negative Self-Esteem (e.g. "I am sure nobody loves me"; 5 items)[2].

CDI residualized change scores were calculated for the total score and each subscale using linear regression, as the unstandardized residual value of the score at year 1, adjusting for the corresponding score at baseline. Residualized change scores were selected based on literature that suggests residual scores may provide a more reliable estimate of change than traditional subtraction-based change scores (Cohen, Cohen, West, & Aiken, 2003; Cronbach & Furby, 1970; DuBois, 1957).

EEG Task

The LPP was elicited using a modified version of the emotional interrupt task (Kujawa, Klein, & Hajcak, 2012; Mitchell, Richell, Leonard, & Blair, 2006; Weinberg & Hajcak, 2011). Twenty neural, 20 pleasant, and 20 unpleasant pictures from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) were each presented 2

[2]. In a review of depression measures for children and adolescents, Klein and colleagues report that, across multiple studies, the CDI has good reported internal consistency, generally good reported test-retest reliability, strong concurrent validity when compared to other common measures (e.g. Children's Depression Rating Scale, CDRS), and is sensitive to change in symptoms as in a treatment study (Klein, Dougherty, & Olino, 2005). However, this review also notes that the CDI factor loadings on the CDI subscales vary as a function of age, indicating that the CDI subscales may not be consistent across all samples. Similarly, the factor structure of the CDI has also been found to vary between child and parent report (Cole, Hoffman, Tram, & Maxwell, 2000).

times in random order; each picture was presented once before any picture was repeated. This yielded a total of 120 trials (40 neutral picture trials, 40 pleasant picture trials, and 40 unpleasant picture trials[3]). The pictures used were selected to be age-appropriate. Neutral pictures displayed objects or scenes with people; pleasant pictures displayed affiliative scenes or cute animals; and unpleasant pictures displayed sad or threatening scenes. Each trial proceeded as follows: (i) a fixation point was presented for 800ms, (ii) one of the IAPS images was presented for 1000 ms, (iii) a black screen with either a left or right arrowhead at center (i.e., the target) was presented for 150 ms, at which time participants had been instructed to respond as quickly as possible to the target by clicking the corresponding left or right mouse button and finally, (iv) the same IAPS picture was presented for 400ms. Between trials, a blank screen was presented for 1500–2000ms. The images presented in the emotional interrupt task are task-irrelevant, where the task is the identification of the direction of the target arrow. Thus, the task can yield behavioral indices of emotional interference (i.e. reaction time to targets as a function of picture valence).

Physiological Recording and Data Processing

Continuous EEG was recorded throughout the emotional interrupt task from 34 electrodes positioned according to the 10/20 system, including FCz and Iz, using the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Vertical electrooculographic (VEOG) activity was monitored using electrodes placed above and below the left eye, while horizontal electrooculographic (HEOG) activity was monitored through electrodes placed adjacent to the outer canthi of the left and right eyes. The EEG signal was pre-amplified at the electrode to improve signal-to-noise ratio. Data were digitized at a sampling rate of 1024 Hz using a low-pass fifth order sinc filter with a 3dB cutoff of 208 Hz. Active electrodes were measured online with respect to a common mode sense active electrode constructing a monopolar channel. Raw EEG was re-referenced offline to the average of the left and right mastoids and band-pass filtered from 0.1 to 30 Hz. Eye blink and ocular-movement corrections were performed using established standards (Gratton, Coles, & Donchin, 1983). Artifact rejection was done using a semi-automated procedure in which the rejection of individual channels was enabled. First, if a voltage step of more than 50.0 mV between sample points was present in a channel, if a deflection of more than 300.0 mV occurred within a trial in one channel, or if a voltage difference of less than 50.0 mV was detected within 100ms, the channel was removed from that trial. A visual inspection of the remaining trials was then conducted to detect and reject any other artifacts; participants were included if they had at least 20 artifact-free trials of each trial type (neutral, pleasant, and unpleasant). The average number of trials included in ERP averages per subject was comparable across trials types (neutral: M = 34.71, SD = 6.70, pleasant: M = 35.82, SD = 6.07, and unpleasant: M = 35.31, SD = 6.53).

[3]. The following IAPS pictures were used in this task. Unpleasant: 1050, 1052, 6571, 1205, 1200, 1300, 1304, 1930, 2458, 9600, 2691, 2703, 2800, 2811, 2900, 3022, 6190, 6213, 6231, 6510. Pleasant: 1462, 1710, 1750, 1811, 2070, 2091, 2092, 2224, 2340, 2345, 2347, 7325, 8031, 8200, 8461, 8496, 8497, 8370, 7400, 7330. Neutral: 5395, 7026, 7130, 7190, 7175, 2514, 7038, 2580, 5390, 7090, 5500, 5731, 5740, 7100, 5900, 7000, 7002, 7009, 7010, 7039. The means and standard deviations of IAPS normative arousal scores for the selected pictures are as follows: unpleasant = 6.36 ± 0.55, pleasant = 5.22 ± 0.82, and neutral = 3.03 ± 0.63 (Lang et al, 2008).

Each trial was segmented beginning 200ms before the first presentation of the picture (i.e. pre-target presentation) and continuing until the end of the first picture presentation, resulting in 1200ms epochs. The LPP was scored separately for neutral, pleasant, and unpleasant trials as the average activity between 300–1000 ms after picture onset at parietal midline site Pz, and baseline-corrected using 200 ms before picture onset. Consistent with recommendations for best methods practices (Handy, 2005) electrode site (Pz) was selected *a priori* because it is the most typical location for the measurement of the LPP. Visual inspection of the LPP waveforms confirmed that this was a reasonable location at which to measure the LPP. Similarly, the window of 300–1000ms post-stimulus was chosen *a priori* both because it is a common window used in the literature that uses the full timeframe of the LPP (i.e. beginning at approximately 300ms and continuing throughout the duration of the picture presentation).

Residualized difference scores for each valence type (pleasant and unpleasant) were calculated using linear regression as the unstandardized residual of the LPP to each pleasant and unpleasant picture, adjusting for the LPP to neutral pictures. We refer to these measures as the residual LPP to pleasant pictures and residual LPP to unpleasant pictures. In addition to previously noted evidence that residualized change scores may broadly have better psychometric properties than subtraction-based change scores (Cohen et al., 2003; Cronbach & Furby, 1970; DuBois, 1957), a recent study found that residualized change scores of the LPP to emotional pictures were more heritable and had better psychometric properties than subtraction-based difference scores (Weinberg, Venables, Proudfit, & Patrick, 2015).

Procedure

The emotional interrupt task to elicit the LPP was completed in the lab at the baseline study visit, as was the ALEQ life stressor self-report measure. Self-reported depression, as measured using the CDI, was assessed at both the baseline visit and approximately 1 year later (M = 1.07 years, SD = 0.12) via an online survey.

Data Analytic Plan

Analyses were conducted using the statistical software package SPSS, Version 22 (SPSS Inc, Armonk, NY). We report descriptive statistics (means and standard deviations) of the LPPs to pleasant, unpleasant, and neutral pictures. We also computed split-half reliabilities of each LPP by calculating the correlation between averages based on odd- and even-numbered trials, corrected using the Spearman-Brown Prophecy Formula (Nunnally, Bernstein, & Berge, 1967). Moderation analyses were run within SPSS, using the PROCESS macro (version 2.13.2; Hayes, 2012). These analyses (model 1) used a bootstrapping approach with 1000 bootstrapped samples, and significance was determined at 95% bias-corrected confidence intervals. All variables were mean-centered products prior to analysis, and the estimated effects reported were unstandardized regression coefficients. The planned core interaction models used baseline ALEQ total life stressors as the independent variable, CDI residualized scores as the dependent variable, and residual LPP to either pleasant or unpleasant pictures as the moderator. Separate exploratory interaction models were conducted replacing either the total ALEQ score or the total CDI scores with each of each

measure's subscales score to examine whether any interactive effects were driven by subtypes of life stressors or were stronger for certain depression symptom categories.

Results

Waveforms of the LPPs to pleasant, unpleasant, and neutral pictures are depicted in Figure 1a. Also presented are 3D headmaps of the LPP difference scores for each valence type (1b: unpleasant minus neutral, 1c: pleasant minus neutral[4]). Finally, bivariante correlations among all study variables as well as descriptive statistics and indices of reliability for each measure are reported in Table 1.

The full results of the *a priori* interaction models are shown in Table 2, and interaction effects are depicted graphically in Figures 2a and 2b. The first model tested the relationship between baseline ALEQ total life stress scores and CDI total depression residualized scores moderated by the baseline residualized LPP to pleasant pictures. This model found a significant main effect of ALEQ life stress on residualized depression (b = .05, SE = .02, $p < .05$) as well as a significant interaction between stress and the LPP to pleasant pictures ($b = -.01$, SE = .00, $p < .01$). There was no main effect of the LPP to pleasant pictures in predicting residualized depression (b = .05, SE = .07, p = .51). The Johnson-Neyman technique suggested the moderation effects were significant at both high and low levels of the LPP to pleasant pictures. Specifically, an attenuated LPP to pleasant pictures corresponded to stronger effects of ALEQ life stress in predicting increases in depression. A larger LPP to pleasant pictures corresponded to a diminished effect of ALEQ life stress in predicting increases in depression (see Figure 2a).

The second *a priori* interaction model replicated the first model, substituting in the residualized LPP to unpleasant pictures as the moderator variable. This model produced the same overall pattern of associations as in the first model, but neither the main effect of stress on residualized depression (b = .04, SE = .02, p = .06) nor interaction between stress and the LPP to unpleasant pictures ($b = -.01$, SE = .00, p = .06) reached statistical significance[5].

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4. Because the LPP to pleasant minus neutral appeared to be of greatest magnitude on either side of the midline, we repeated moderation analyses using the residual LPP to pleasant pictures calculated as the averaged amplitude at left and right lateral sites P3, PO3, P4, and PO4. These analyses replicated the patterns we found when calculating the LPP to pleasant at midline site Pz.

5. To better examine what aspects of our model contribute to the current results, we conducted a series of supplemental analyses, as follows:

To address concerns about the confounding effects of age, we conducted exploratory analyses, replicating our core moderation model with age as a covariate. With the inclusion of this age covariate, the LPP to pleasant pictures continues to significantly interact with baseline ALEQ to predict residualized CDI at follow-up (F(1,138) = 6.86 p = .01) and the same interaction using the LPP to unpleasant pictures now reaches statistical significance (F(1,138) = 4.19 p = .04). Furthermore, we analyzed the bivariate associations between age and our model variables. We find that age is significantly positively correlated with CDI depression scores and ALEQ life stress scores. We also find that age is significantly negatively correlated with the LPP to negative pictures but is not significantly related to the LPP to positive pictures. Finally, we conducted the recommended three-way interaction models, adding age as a moderator of the original core moderation models. For the LPP to positive pictures, we find that age does not significantly moderate the effects of either core moderation model (i.e. age does not significantly interact with the LPP, ALEQ stressors, or their interaction term). For the LPP to negative pictures, we find that there is a significant three-way interaction between the LPP, ALEQ stressors, and age such that the interactive effects of the LPP and life stressors in predicting depression were only significant for participants closest the mean age of the sample. This analysis is exploratory; however, one possible interpretation is there may be a sensitive developmental period around the mean age of our sample (12.90 years old) during which a blunted LPP to negative pictures conveys more risk for stress-induced depression.

Anxiety has been associated with LPP magnitude (MacNamara, Ferri, & Hajcak, 2011) and thus anxiety symptoms may present a confound to the current analyses. In order to examine this potential confounding effect, we repeated our core moderation models with baseline anxiety symptoms, as measured by the total child self-reported anxiety at baseline using the Screen for Child Anxiety Related Disorders (SCARED; Birmaher et al., 1997). With the inclusion of this covariate, the LPP to pleasant pictures continues to

Exploratory moderation models assessed the interaction of each category of ALEQ stressor with the residualized LPP to pleasant predicting residualized CDI depression scores (Table 3). First, in examining the ALEQ subscales which separate stressors by context, we found the LPP to pleasant pictures significantly interacted with family stressors ($b = -.01$, SE = .01, $p < .05$) and school stressors ($b = -.02$, SE = .01, $p < .01$) to predict depression change. Other tested models did not reach significance. Examining the interpersonal dependent vs non-interpersonal independent stressors, as we expected, we found that dependent stressors significantly interacted with the LPP to pleasant pictures ($b = -.01$, SE = .01, $p < .05$) to predict change in depression. Surprisingly, we also found that the non-interpersonal independent stressors interacted significantly with the LPP to pleasant pictures ($b = -.02$, SE = .01, $p < .05$).

Finally, Table 4 presents exploratory moderation models assessing the changes in specific depression symptom types predicted by the interaction of ALEQ total stress and residual LPPs to pleasant pictures. These analyses found a significant interaction between residualized LPP to pleasant pictures and ALEQ total stress in predicting increases in symptoms of ineffectiveness ($b = -.00$, SE =.00, $p < .001$) and anhedonia ($b = -.00$, SE = .00, $p < .05$) to predict change in depression.

Discussion

In a community sample of 143 girls ages 8 to 14, the present study found that the LPP to pleasant pictures significantly moderated the relationship between baseline life stressors and changes in depressive symptoms a year after the baseline assessment. Specifically, we found that baseline life stress predicted increases in depressive symptoms a year later among adolescents who had a blunted LPP to pleasant pictures. The same pattern of moderation was found for the LPP to unpleasant pictures, though the model did not reach statistical significance, except when age was included as a covariate (see footnote for supplemental analyses).

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significantly interact with baseline ALEQ to predict residualized CDI at follow-up ($F(1,138) = 7.14$ $p = .01$) and the same interaction using the LPP to unpleasant pictures is trending toward, but does not achieve, statistical significance ($F(1,138) = 3.53$ $p = .06$).

It is common to divide the LPP into early (~300–600ms) and late (~600–1000ms) components, as these have been suggested to represent separable components (Foti, Hajcak, & Dien, 2009). To address the question of whether there was a significant effect of early (300–600ms) vs late (600–1000ms) LPP, we conducted a supplemental replication our core moderation analyses separately for each of these time windows. The early LPP to pleasant pictures continues to significantly interact with baseline ALEQ to predict residualized CDI at follow-up ($F(1,139) = 5.88$ $p = .02$) and the same interaction using the early LPP to unpleasant pictures approaches but does not reach statistical significance ($F(1,139) = 3.27$ $p = .07$). The late LPP to pleasant pictures also continues to significantly interact with baseline ALEQ to predict residualized CDI at follow-up ($F(1,139) = 6.66$ $p = .01$) and the same interaction using the late LPP to unpleasant pictures now reaches statistical significance ($F(1,139) = 4.01$ $p = .05$).

In order to understand whether the interaction effect with life stress was driven by the response to emotional or neutral pictures, we repeated out analyses, including each interaction term separately. These analyses indicate that the LPP to the emotional picture and not the neutral picture drives the interaction effect with ALEQ to predict depressive symptoms. Using pleasant pictures, ALEQxLPP to pleasant pictures significantly predicts CDI ($\beta = -0.39$, $p = .02$), while ALEQ*LPP to neutral pictures does not ($\beta = 0.17$, $p = .28$). Similarly, using unpleasant pictures, ALEQxLPP to unpleasant pictures is trending toward significance ($\beta = -0.30$, $p = .10$), while ALEQ*LPP to neutral pictures does not approach significance ($\beta = 0.10$, $p = .57$).

To assess whether behavioral measures of interference predict similar outcomes as the LPP, we replicated our core moderation models, substituting in reaction time measures of interference (i.e., residualized RT on pleasant trials adjusting for RT on neutral trials, residualized RT on unpleasant trials adjusting for RT on neutral trials) as the moderator in place of the LPP. These models found that moderating effects of interference on pleasant picture trials approach but do not reach statistical significance ($F(1,110)=-2.72$, $p=.10$). Moderating effects of Interference by unpleasant pictures does not significantly moderate this relationship ($F(1,110)=0.11$, $p = .74$. These analyses suggest that the moderating effects of the LPP cannot be comparably indexed using behavioral measures of emotional interference, though interference on pleasant picture trials trends in the same direction.

Exploratory analyses considered these moderation models with more narrowly-defined stressors, first by domain of functioning (family, peer, school, or romantic stressors) and then by the individual's potential role in creating the stressor (dependent vs. independent). Consistent with our hypothesis, we found that adolescents who had a blunted LPP experienced increases in depressive symptoms when exposed to greater *dependent* stressors (i.e. stressors to which they may have contributed). We found that these adolescents also experienced increased depressive symptoms following exposure to fateful or independent stressors. Additionally, we found that the effects were relatively specific to stressors that occurred in a family or school context.

Finally, we examined which types of depressive symptoms were predicted by the interaction of overall life stress with the LPPs to pleasant pictures. We found that adolescents with a blunted LPP experienced increases in the CDI ineffectiveness and anhedonia subscales following exposure to life stress. The ineffectiveness subscale indexes the adolescents' belief in their efficacy, while the anhedonia subscale indexes the somatic symptoms of depression, such as sleep and appetite disturbances. One study of the factor structure of the CDI across multiple sites suggested that the combination of these two subscales may reflect a unitary factor, indexing the tendency to withdraw or disengage from the environment (Logan et al., 2013). The specificity of this effect is consistent with the notion that a decreased LPP may reflect the tendency to disengage from the environment. Furthermore, these findings suggest that adolescents with a blunted LPP to pleasant pictures may be particularly susceptible to withdraw and disengage from the environment following stressors. The moderate to poor reliability of the ineffectiveness and interpersonal problems CDI subscales in this sample (see table 1) may limit the ability to detect significant relationship, thus these subscale-level results should be interpreted with caution. Overall, these findings highlight the LPP as a promising biomarker of risk for depression following life stress.

The LPP to pleasant and unpleasant pictures may be best understood to reflect two aspects of the same overarching construct: increased and sustained attention to emotional stimuli. Consistent with that interpretation, in the current study these two LPPs were highly correlated with one another (r=.64, $p < .01$). The literature on the LPP and depression largely indicates that depression is associated with blunting of the LPP to all *normative* emotional stimuli, regardless of valence (Kujawa et al, 2012; Speed et al, 2016; Weinberg et al, 2016; c.f. Auerbach et al, 2015; Webb et al, 2017, when the task involves self-referential evaluation of word stimuli). This literature is consistent with the ECI model of depression which builds on emotion theories that suggest that all emotions share the common function of directing action (Keltner & Gross, 1999). The ECI model argues that depression serves the evolutionary function of reducing the likelihood of action in the face of high-risk circumstances, and that this instinct not to act becomes pathological when the consequences of inaction are greater than those of action. The ECI model is borne out by findings, as summarized in one meta-analysis, that depression is associated with attenuated responses across various emotional stimuli (Bylsma, Morris, & Rottenberg, 2008).

To our knowledge, this is the first study to examine the LPP as a moderator between stress and depression and thus provides novel information about the utility of the LPP as a biomarker of depression risk. Consistent with the ECI model, in the current study, the

pattern of interactions with stress were similar for the LPP to pleasant and unpleasant stimuli. Nevertheless, the effects were more robust for pleasant pictures. Of note, the unpleasant and pleasant pictures were unevenly matched on emotional arousal, such that the unpleasant pictures were more arousing than the pleasant pictures, based both on normative ratings (Lang, Bradley, & Cuthbert, 2008) and LPP magnitude in our sample. It is possible that the less robust effects for unpleasant pictures ceiling effects on the LPP to unpleasant stimuli; future studies might test whether this is the case by including lower-arousal negative stimuli. Together, these findings are most consistent with a version of the ECI model in which reduced engagement with emotional stimuli in general is a risk factor for depression, with more robust reductions to pleasant stimuli. Furthermore, because these were interactive, and not main effects, the current findings also point to a possible mechanism by which a blunted LPP may confer risk for depression. Specifically, a reduced LPP to pleasant pictures may reflect a trait-like vulnerability indexing insufficient emotional engagement with pleasant, approach-motivating stimuli. Adolescent girls low in emotional engagement with pleasant stimuli may be more likely to withdraw from the environment – especially when stressed; because pleasant enriching stimuli in the environment are thought to provide important protections against the detrimental effects of stress (Crofton, Zhang, & Green, 2015), girls with reduced LPP to pleasant stimuli may be less likely to seek out pleasant comforting stimuli which might allow them to better cope with stressors.

We chose to use a moderation model based on an Interactive Model of depression in adolescent girls that suggests biological vulnerability and stressors in the environment interact to convey particular risk for depression (Nolen-Hoeksema & Girgus, 1994). One countervailing interpretation is that the more trait-like LPP may indicate risk for the generation of life stressors, as in the stress generation hypothesis (Hammen, 1991); in this view, stressors might mediate the link between the LPP and depressive symptoms. However, in our sample, the LPP variables were largely uncorrelated with ALEQ stress variables, which suggests that the mediation model is unlikely.

The timing of the stressors assessed by our administration of the ALEQ limit our conceptual interpretation of our data. Specifically, the ALEQ stress measures inquired about stressors that occurred in the three months prior to the baseline assessment of the LPP and CDI depression. Because stress is assessed at a single timepoint, our models are only able to assess the between-subjects effects of life stressors, rather that the within-subjects effect of changes in stressor frequency over the lifespan (Abela & Hankin, 2008; Hankin, Jenness, Abela, & Smolen, 2011; Stange, Hamilton, Olino, Fresco, & Alloy, 2016). Furthermore, we are unable to answer questions about the trajectory of these variables (LPP, stress, depression) over time and how the trajectory of each variable may influence the trajectory of the others.

Only one previous study, to our knowledge, has examined the interactive effects of the LPP and life stress predicting longitudinal changes in psychopathology (Kujawa et al., 2016). Kujawa and colleagues examined the interaction of LPP magnitude with exposure to Hurricane Sandy-related stressors and found that a larger LPP to unpleasant stimuli and a small LPP to pleasant stimuli each interacted with degree of stress exposure to prospectively predict greater *externalizing* symptoms (Kujawa et al., 2016). They found a similar, though

weaker interaction effect for a larger LPP to unpleasant stimuli predicting *internalizing* symptoms. Kujawa and colleagues' findings may diverge somewhat from the current study due to methodological differences. First, Kujawa and colleagues (2016) used a younger sample (mean age = 9.16), who had not yet begun to exhibit rapid increases in depression rates. Second, different types of stressors were assessed in the two studies. Specifically, previous work suggests that the link between stress and depression may be driven by dependent, as compared to independent, stressors (Auerbach et al., 2011; Auerbach et al., 2010; Shih et al., 2006) and chronic stressors, as compared to acute stressors (Hammen, Brennan, Keenan-Miller, Hazel, & Najman, 2010). For these reasons, the acute independent stressor (i.e. a natural disaster) assessed by Kujawa and colleagues (2016) may be less likely to predict *depression* than other forms of psychopathology.

This study adds to the literature on stress and depression in adolescent girls by pointing to one meaningful biomarker of vulnerability to experiencing depressive symptoms following stress. Consistent with previous work, stress predicted depressive symptoms; however, this effect was only evident among adolescents with a reduced baseline LPP to pleasant pictures. These findings help to shed light on one possible mechanism underlying the deeply entrenched relationship between life stress and depressive symptoms. That is, reduced processing of emotional stimuli may interfere with the ability to cope with life stressors and therefore increase the risk for stress-induced depression. The LPP may prove useful in the identification of those adolescents at increased risk for depression; moreover, interventions that increase the LPP to pleasant stimuli may protect adolescents against the depressogenic effects of stress.

There are several limitations to the current study worth noting. First, the study sample was predominantly Caucasian and relatively high in SES, and thus may not be the representative of adolescent girls more broadly. Second, we did not conduct an interview-based measure of life stress in order to address previously reported problems of bias in self-report stress measures (Liu, 2013; Monroe & Kelley, 1995). Alternative measures of stress would also be useful to address limitations of the structure of the ALEQ. Specifically, all ALEQ items are equally weighted, yet the ALEQ subscales have uneven item counts and the specific items in each subscale are not all equally likely to occur (e.g. a fight with a friend is more likely to occur frequently than a parents' divorce). Finally, though our all-girl sample was selected in order to better understand what factors convey vulnerability to depression in the higher risk population of adolescent girls, it does not allow ups to examine whether these vulnerabilities are unique to girls. Therefore, future research is needed to examine whether these interactive effects are also seen in boys. Because both life stress and the LPP have been associated with depression in co-ed samples, we would likely expect the same general pattern of moderation in boys and girls. Nevertheless, because boys generally experience lower levels of both stressors and depression (Avenevoli et al., 2015; Ge, Natsuaki, & Conger, 2006), we might predict in boys a relatively attenuated version of the same moderation pattern we see in the current all-girl sample.

Future work is needed to assess whether the residualized LPP continues to moderate the relationship between stress and depression over a longer time span, and whether the LPP moderates the relationship between stress and more severe, clinical levels of depressive

symptoms. Similarly, future research is needed to assess whether the current moderation model is replicated in boys. Finally, future research examining whether a potentiated LPP to emotional stimuli may confer risk for other forms of psychopathology. In conclusion, the current study points toward a promising biomarker for the prediction of vulnerability to depression following stressful life events, as well as a possible novel target for interventions that could increase resilience. Namely, interventions that increase the magnitude of LPP may buffer high-risk girls against the deleterious effects of life stress.

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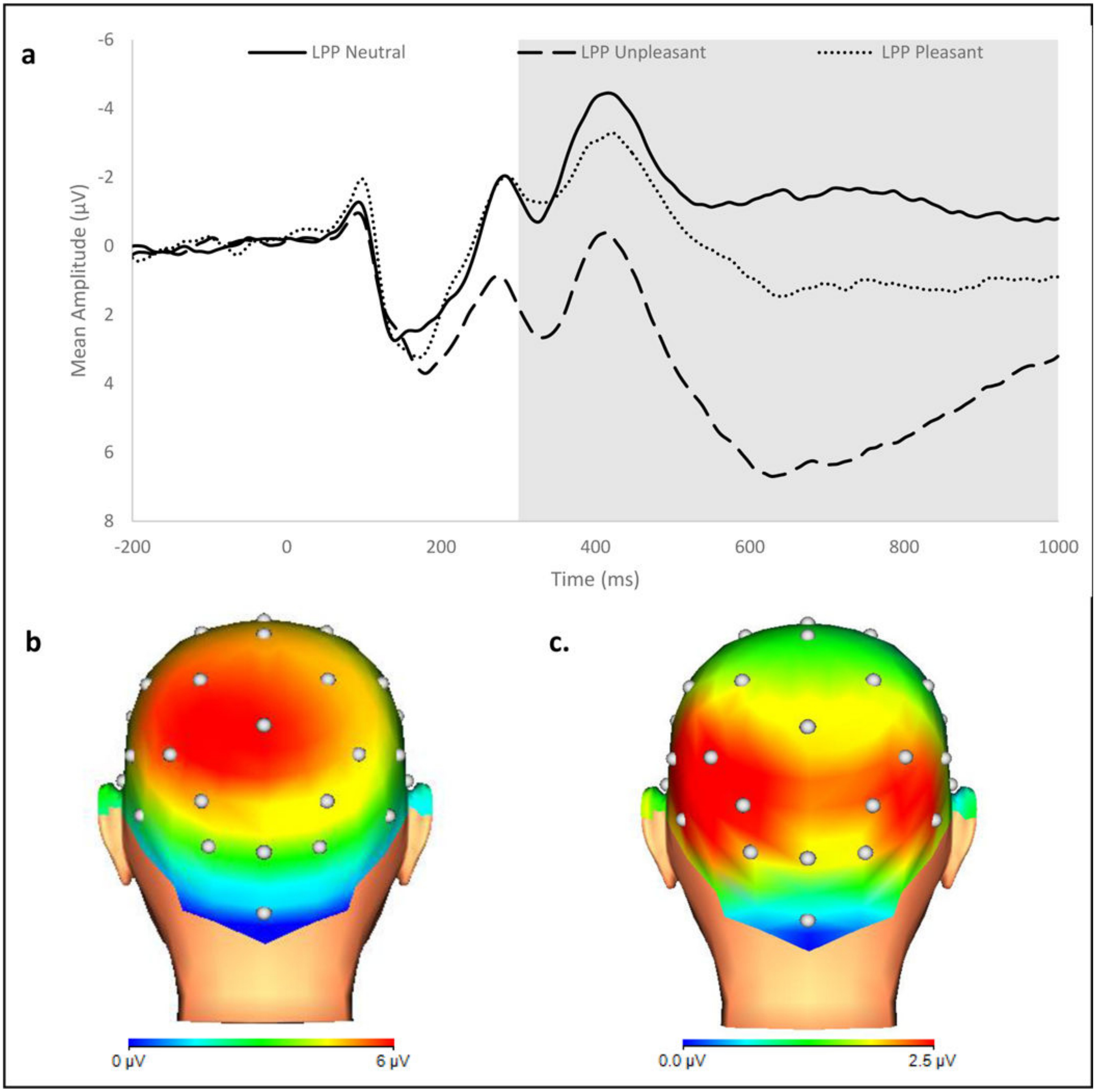

Figure 1.

Waveforms and headmaps of LPPs to IAPs pictures. (a) displays ERP waveforms for unpleasant, pleasant, and neutral pictures. The vertical axis represents µV, while the horizontal axis represents time in ms, such that zero indicates the onset of the picture presentation, (b) displays the headmap of the LPP to unpleasant pictures minus the LPP to neutral pictures in the time window of the LPP, (c) displays the headmap of the LPP to pleasant pictures minus the LPP to neutral pictures in the time window of the LPP. All LPPs measured at parietal midline site Pz.

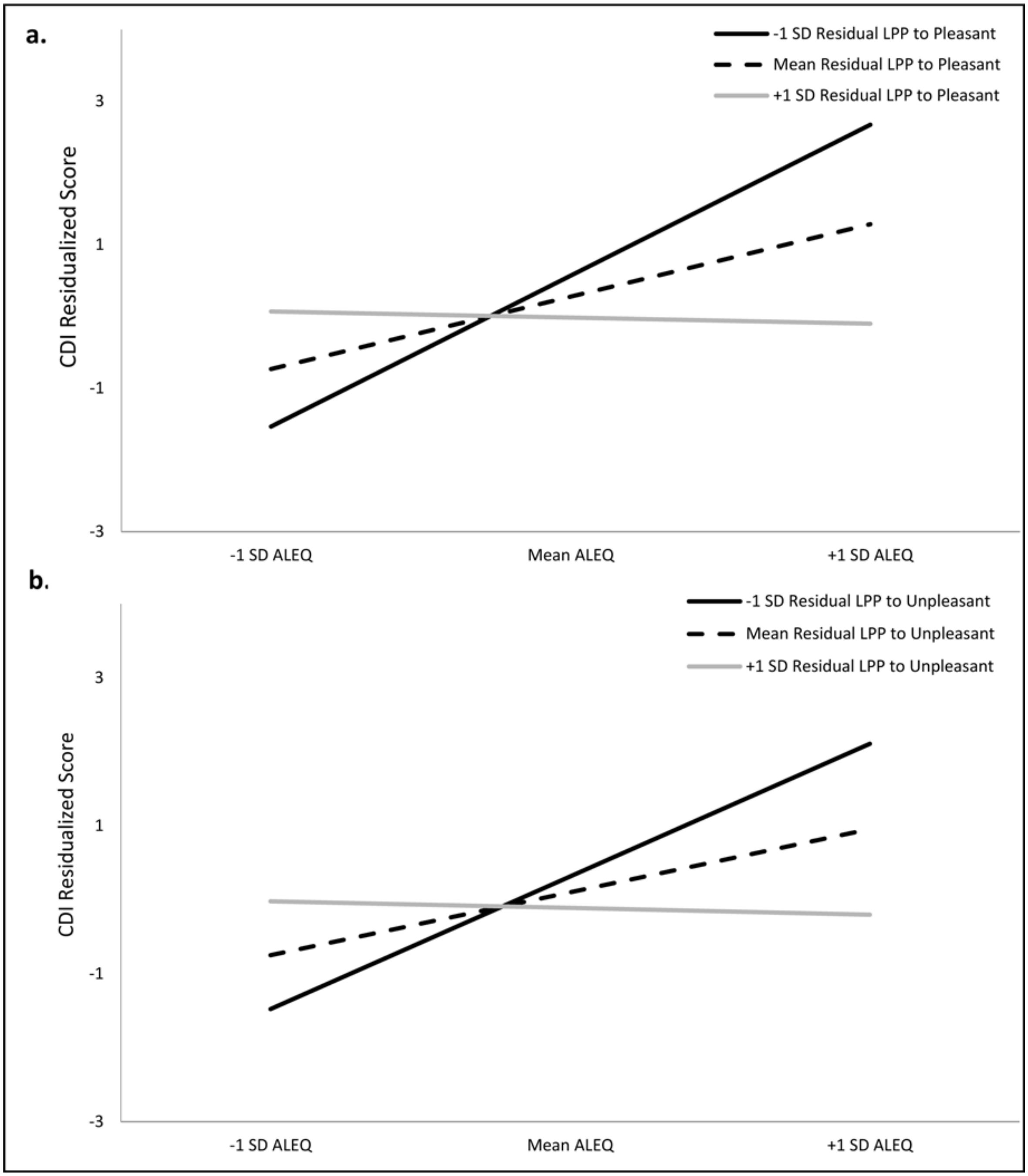

Figure 2.
Residualized self-reported depressive symptoms (CDI) from baseline to year 1 follow-up predicted by the interaction of baseline life stressors (ALEQ, Total Score) and (a) residualized LPP to pleasant pictures or (b) residualized LPP to unpleasant pictures.

Table 1

Bivariate correlations of ERPs, CDI scales, and ALEQ scales. LPP = Late Positive Potential; CDI = Children's Depression Inventory; ALEQ = Adolescent Life Events Questionnaire; Residual LPPs are calculated as the LPP to emotional pictures, adjusting for the LPP to neutral pictures. Reliability is calculated for all self-reports using Cronbach's alpha unless otherwise specified.

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	LPP to Neutral	--	.69**	.66**	.09	−.07	−.11	.02	−.11	−.04	.03	−.06	.04	.02	.05	.03	.04	.01	.03
2	LPP to Pleasant		--	.64**	.78**	.20*	−.14	−.03	−.14	.02	−.01	−.08	.14	.03	.20*	.03	.13	.16	.07
3	LPP to Unpleasant			--	.32**	.71**	−.10	−.03	−.11	.05	.05	−.03	.00	.00	.06	.00	.02	.02	.00
4	Residual LPP to Pleasant				--	.34**	−.10	−.06	−.09	.06	−.04	−.06	.16	.02	.22**	.02	.15	.21*	.07
5	Residual LPP to Unpleasant					--	−.03	−.06	−.04	.11	.04	.03	−.03	−.03	.02	−.02	−.02	.02	−.03
6	CDI, Negative Mood						--	.61**	.52**	.61**	.60**	.86**	.08	.02	.24**	.20*	.17*	.16	.20*
7	CDI, Interpersonal Problems							--	.44**	.52**	.41**	.70**	.20*	.09	.32**	.17*	.25**	.28**	.20*
8	CDI, Ineffectiveness								--	.52**	.47**	.72**	.13	.03	.23**	.17*	.18*	.21*	.18*
9	CDI, Anhedonia									--	.58**	.85**	.19*	.09	.30**	.17*	.23**	.24**	.21*
10	CDI, Negative Self-Esteem										--	.75**	.09	.01	.20*	.07	.12	.13	.10
11	CDI, Total											--	.09	.00	.25**	.13	.15	.18*	.14
12	ALEQ, Family Stressors												--	.52**	.74**	.75**	.95**	.79**	.86**
13	ALEQ, Romantic Stressors													--	.50**	.48**	.63**	.45**	.66**
14	ALEQ, School Stressors														--	.57**	.85**	.95**	.68**
15	ALEQ, Peer Stressors															--	.85**	.55**	.91**
16	ALEQ, Total Stress																--	.85**	.93**
17	ALEQ, Independent Stressors																	--	.64**
18	ALEQ, Dependent Stressors																		--
	Mean	−2.49	−0.81	3.46	−0.32	−0.21	0.07	−0.06	−0.04	0.09	−0.01	0.12	13.35	1.61	8.03	7.09	30.07	8.99	14.16
	Standard Deviation	7.60	8.85	7.93	6.40	5.99	1.78	0.77	1.14	1.96	1.08	5.33	10.04	2.39	6.60	6.51	22.20	6.74	12.55

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Reliability	.84[a]	.88[a]	.82[a]	--	--	.67, .75[b]	.46, .43[b]	.63, .62[b]	.70, .77[b]	.84, .79[b]	.90, .92[b]	.85	.60	.87	.80	.93	.83	.91

Note:

† $p < .1$

* $p < .05$

** $p < .01$

*** $p < .001$

[a] Split-half reliability coefficient with Spearman-Brown correction

[b] First value is Cronbach's α at baseline, second is at 1 year follow-up

Table 2

Moderation models with life stress and residualized LPPs prospectively predicting residualized CDI depressive symptoms. The top half of the graph presents main effects of baseline ALEQ life stress, baseline residualized LPPs, and their interaction predicting residualized CDI depressive symptoms at 1 year follow-up. The bottom half of the graph shows provides simple slopes and t-scores for the conditional effects of ALEQ on CDI at different levels of the LPPs to pleasant and unpleasant pictures.

	LPP to Pleasant Pictures				**LPP to Unpleasant Pictures**			
Predictor	B	SE	95% CIs Lower	95% CIs Upper	B	SE	95% CIs Lower	95% CIs Upper
LPP	−.05	.07	−.18	.09	−.04	.08	−.19	.12
ALEQ Total	.05 *	.02	.01	.08	.04 †	.02	−.00	.08
LPP * ALEQ Total	−.01 **	.00	−.01	−.00	−.01 †	.00	−.01	.00
	Simple slope		t		Simple slope		t	
−1 SD LPP	.09		3.31 **		.08		2.63 **	
Mean LPP	.05		2.28 *		.04		1.93 †	
+1 SD LPP	−.00		−0.15		−.00		−0.14	

Note:

† $p < .1$

* $p < .05$

** $p < .01$

*** $p < .001$

Table 3

Interaction models using each ALEQ subscale as the independent variable, interacting with residualized LPP to pleasant pictures to predict CDI residualized total depression symptoms score from baseline to year-1 follow-up.

	Moderation by Residual LPP to Pleasant Pictures	
Stressor Type (ALEQ Subscale)	**ΔR^2**	***F***
Family	.03	4.57 *
Romantic	.02	2.22
School	.05	7.59 **
Peers	.02	2.46
Dependent	.03	4.52 *
Independent	.04	5.71 *
Total	.05	7.17 **

$^{\dagger}p < .1$

$^{*}p < .05$

$^{**}p < .01$

$^{***}p < .001$

Table 4

Interaction models with ALEQ total scores interacting with residual LPP to pleasant pictures to predict change in each residualized CDI subscale (at year-1 follow-up adjusting for baseline)

CDI Subscale	Moderation by Residual LPP to Pleasant Pictures	
	ΔR^2	F
Negative Mood	.02	2.96 †
Interpersonal Problems	.01	1.60
Ineffectiveness	.08	12.58 ***
Anhedonia	.03	3.96 *
Negative Self-Evaluation	.02	2.18
Total	.05	7.17 **

$^{\dagger}p < .1$;

$^{*}p < .05$;

$^{**}p < .01$;

$^{***}p < .001$