Error-related brain activity in pediatric major depressive disorder: An ERP and time-frequency investigation

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ABSTRACT

Background: The error-related negativity (ERN) reflects individual differences in error monitoring. However, findings on the ERN in adult and adolescent depression have been inconsistent. Analyzing electroencephalographic (EEG) data in both the time- and time-frequency domain can be useful to better quantify neural response to errors. The present study aimed at examining electrocortical measures of error monitoring in early adolescents with and without depression.

Method: EEG activity was collected during an arrowhead version of the flanker task in 29 (25 females) early adolescents with depression and 34 without MDD (29 females).

Results: The depression group showed reduced ERN amplitude, reduced error-related theta power and increased error-related beta power compared to the control group. When all variables that related to MDD diagnosis were considered simultaneously, both theta and beta power, but not the ERN, were independently related to an increased likelihood of being diagnosed with depression.

Conclusions: By examining both time-domain and separate time-frequency measures, the present study provided novel evidence on error monitoring alterations in youth depression, suggesting that depression during adolescence may be characterized by reduced error monitoring (i.e., reduced ERN and error-related theta) and post-error inhibition (i.e., greater error-related beta power). These results support that time-frequency measures might be better suited for examining error-related neural activity in MDD relative to time-domain measures.

1. Introduction

Ranked among the most prevalent and costly disorders worldwide, major depressive disorder (MDD) is characterized by a persistent state of sadness and/or loss of interest or pleasure that affects cognition, behavior, and physical health (Kessler, 2012; Lim et al., 2012). MDD that occurs during adolescence is a particularly severe condition characterized by poor emotional, social, and academic functioning (Lewinsohn et al., 2003) that often persists into adulthood (Fombonne et al., 2001). Earlier onset depression disposes youth to a greater risk of suicide, which represents the second leading cause of death in adolescence (Heron, 2014; Keenan-Miller et al., 2007). Therefore, identifying biomarkers implicated in adolescent-onset MDD that might contribute to its etiology and the recurrent course is of great importance.

A process that appears to underlie MDD is a pattern of emotional disengagement from pleasant and unpleasant stimuli, consistent with the Emotion Context Insensitivity (ECI) hypothesis (Bylsma et al., 2008; Bylsma, 2021; Rottenberg and Hindash, 2015). The motivational disengagement that characterizes MDD is evident in reductions in physiological arousal to emotional stimuli (e.g., Foti et al., 2010; Lang et al., 2007; Klawohn et al., 2021; Messerotti Benvenuti et al., 2015; Messerotti Benvenuti et al., 2019; Rottenberg et al., 2005; Weinberg et al., 2016a). Reactivity to pleasant and unpleasant content can be viewed as components of the Positive and Negative Valence Systems of the U.S. National Institute of Mental Health’s (NIMH) Research Domain Criteria (RDoC), respectively (Insel et al., 2010). Much of the evidence for the ECI hypothesis comes from studies examining the Positive Valence System, showing a strong association between MDD and...
A physiological response to the commission of an error (i.e., error monitoring) may be a way to assess the Negative Valence System. Indeed, making a mistake is generally perceived as subjectively unpleasant and, at times, it can be perilous and threatening to one’s life (Weinberg et al., 2016b). For example, at the physiological level, like other threats, the commission of an error elicits a cascade of defensive responses: greater startle reflex (Hajcak and Foti, 2008), higher skin conductance levels, and slower heart rate (Hajcak et al., 2003; Hajcak et al., 2004).

A physiological measure of error monitoring is the error-related negativity (ERN), which arises as a negative electrocortical deflection in the event-related potential (ERP) at fronto-central scalp sites within 100 ms following the commission of an error versus correct response (Falkenstein et al., 1991; Gehring et al., 1995). To date, findings on the ERN in depression have been less consistent, with studies reporting enhanced (Chiu and Deldin, 2007; Holmes and Pizzagalli, 2010) and reduced (Weinberg et al., 2015b; Ruchsocial et al., 2004, 2006; Schrijvers et al., 2008) amplitude relative to healthy controls, or no differences (Olvet et al., 2010). In addition, reduced ERN was reported in the offspring of mothers with a history of MDD (Meyer et al., 2018). To date, only a few studies have assessed the ERN in children with depression—and those studies have reported either reduced (Ladouceur et al., 2012) amplitude or no differences in amplitude when compared to non-depressed youth (Bress et al., 2015). One study reported that youths with MDD did not show the normative increase in ERN amplitude as a function of age, suggesting that depression may alter the development of neural systems associated with error monitoring (Ladouceur et al., 2012).

Given the mixed findings on the ERN in depression, analyzing EEG data in both the time- and time-frequency domain can be a useful approach to better quantify neural response to errors (Morales et al., 2022). Indeed, the utilization of both time and frequency data of the EEG signal allows the extrapolation of information that is not accessible using only time-domain analysis and reflects distinctive aspects of information processing (Cohen, 2014; Munneke et al., 2015). For example, time-domain analyses assume temporal consistency across trials, while the time-frequency data in both the time- and time-frequency domain can be a useful approach to better quantify neural response to errors (Morales et al., 2022).

Error monitoring can be examined in terms of power across several frequency bands. Greater power in the delta (1–3 Hz) and theta (4–8 Hz) frequency bands in response to error relative to correct responses has been consistently reported, suggesting that these frequency bands are involved in error monitoring processes (e.g., Beatty et al., 2020; Cavanagh et al., 2009; Cavanagh et al., 2017; Lu et al., 2004; Muir et al., 2020; Munneke et al., 2015; Riesel et al., 2013; Sandra and Weinberg, 2019; Trujillo and Allen, 2007). In addition, a few studies have examined alpha power (8–14 Hz) in the context of error monitoring in healthy participants (Carp and Compton, 2009; Li et al., 2020; van Driel et al., 2012), mainly reporting reduced alpha power to errors relative to correct responses. Given evidence indicating that alpha power changes reflect transient modifications of cortical activation during attentional tasks (e.g., Klimesch et al., 1998; Klimesch et al., 2007; Sauseng et al., 2005; Thut et al., 2006; specifically in error processing tasks, see Carp and Compton, 2009; Li et al., 2020), this alpha suppression is thought to reflect greater attentional engagement following the commission of an error.

The beta frequency band (15–20 Hz), generated in sensorimotor areas (Tzagarakis et al., 2015) and linked to motor functions (Klarevik et al., 2013), has been less investigated in the context of error monitoring. Some studies suggested that beta power might enable motor-action preparation by increasing flexibility allowing responses to be more appropriately adjusted (Gable et al., 2016; Engel and Fries, 2010; Jenkinson and Brown, 2011; Glazer et al., 2018; Wilhelm et al., 2021, 2022). Beta oscillations are suppressed during action preparation (McFarland et al., 2000; Pfurtscheller et al., 1994; Yang et al., 2015), while increased beta power reflects inhibition of prepared actions in multiple tasks also related to error monitoring (Li et al., 2020; Rosin et al., 2011; Swann et al., 2012; Wessel et al., 2016).

Despite the utility of time-frequency data in outlining separate mechanisms associated with error monitoring, to date, time-frequency patterns of error monitoring in depression remain unexplored. To fill this gap, the objective of the present study was to examine error monitoring in early adolescence, among individuals with and without MDD. The ERN as well as time-frequency power within the delta, theta, alpha, and beta bands during a flanker task were analyzed to quantify neural correlates of error monitoring. Consistent with the ECI hypothesis, we hypothesized that MDD would be characterized by a reduced ERN, delta, and theta power to errors relative to healthy controls. Considering the lack of previous studies examining alpha and beta bands even in healthy individuals, no a priori hypotheses were formulated for these frequency bands. Lastly, an exploratory aim of this study was to examine whether using a combination of the ERN and time-frequency measures would explain unique variance in MDD status.

### 2. Methods

#### 2.1. Participants

The current study used data from a longitudinal study funded by the NIMH (MH106477) aimed to examine the effectiveness of a computerized adaptive attention bias modification training in modifying neural activity associated with errors and anxiety symptoms in a large sample of early adolescents. The present study included data collected from a subset of participants at the baseline visit. Families were recruited via a commercial mailing list, referrals, and other advertisements from the New York/Long Island, Tallahassee, and San Diego area communities. Eligible participants had to be fluent in English and a parent or legal guardian needed to be present at the lab visit. Exclusion criteria included any medical or developmental disability, severe suicidality, history of severe brain injury, and colour blindness, based on an ad-hoc anamnestic interview. The present study included data from a subset of participants with MDD and a control group, consisting of 63 participants overall (9 males) between the ages of 11 and 14 years ($M = 13.60$ years; $SD = 1.03$).

Participants were divided into two groups matched for age and gender: an MDD group (n = 29, 25 females) and a healthy control group (n = 34, 29 females). The presence of MDD was determined by a trained clinical interviewer using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Kaufman et al., 1997). Table 1 includes the characteristics of the sample. Six

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic, clinical variables, and EEG data for the group with depression (MDD) and the healthy control group (HC).</th>
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<tbody>
<tr>
<td></td>
<td>HC group (n = 34)</td>
</tr>
<tr>
<td>Age</td>
<td>13.5 (1.01)</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>85.3</td>
</tr>
<tr>
<td>Ethnicity (% White)</td>
<td>58.2</td>
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<tr>
<td>CDI scores</td>
<td>7.17 (7.34)</td>
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</table>
participants were previously included in a recently published work on error-related brain activity in obsessive-compulsive disorder that employed a similar procedure and methods (Dell Acqua et al., 2022a; 4 concurrently met the diagnostic criteria for MDD and OCD, and 2 healthy participants, namely free from any mental disorder, were included in both control groups). Moreover, 38 % of MDD participants (n = 11) had GAD, 28 % (n = 8) had social anxiety, 31 % (n = 9) had separation anxiety, 38 % (n = 11) met for specific phobia, 7 % (n = 2) had panic disorders, 10 % (n = 3) had OCD, and 3 % (n = 1) had a non-specified anxiety disorder. All participants had normal or corrected-to-normal vision and were naive to the purpose of the experiment. Participants were compensated for their participation ($20 per hour). Parents/guardians and participants provided consent and assent before participating. The present study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Reviews Boards of Florida State University, Stony Brook University and San Diego State University.

2.2. Measures

2.2.1. Self-reports

The Children’s Depression Inventory (CDI) is a well-established and widely used self-report measure to assess depressive symptoms in children and adolescents (Kovacs, 1992). This scale is composed of 27 items, each scored on a 3-point scale (ranging from 0 to 2) with 0 being no presence of the symptom, 1 being mild presentation of the symptom, and 2 representing severe symptoms. The CDI has good internal consistency and convergent validity with clinical diagnoses of depression in various adolescent samples (Ivarsson et al., 2006; Rivera et al., 2005). In the present sample, the CDI total score had excellent internal consistency with a Cronbach’s alpha value of 0.93.

2.2.2. Flanker Task and behavioral data reduction

An arrowhead version of the flanker task was administered through the Presentation software (Neurobehavioral Systems, Inc., Albany, CA). On each trial, five horizontally aligned arrowheads were presented for 200 ms, followed by an ITI that varied between 2300 and 2800 ms. Congruent flankers were displayed in half of the trials (“<<<<<< or “>>>>>>”), while the other half displayed incongruent flankers (“<<<<<< or “>>>>>>”) in random order. Participants were instructed to respond with their right hand as quickly and as accurately as possible by pressing the right mouse button if the central arrow was pointing to the right, and the left mouse button if the central arrow was pointing left. A practice block of 30 trials preceded the task to ensure an adequate understanding of the task. The task consisted of 11 blocks of 30 trials (330 trials total). At the end of each block, participants received feedback based on their performance. If performance was 75 % correct or lower, the message “Please try to be more accurate” was presented; if performance was above 90 % correct, the message “Please try to respond faster” was displayed; otherwise, the message “You’re doing a great job” was shown.

The first trial of each block and trials with no response were not included in the analyses. Considering their elevated skewness (skewness before transformation = 1.70; skewness after transformation = 0.43), RTs were log-transformed to produce a normal distribution.

2.2.3. Electroencephalogram recording

Continuous EEG was recorded during the flanker task using a 34-channel system (ActiChamp system, Brain Products) placed according to the 10/20 system; two electrodes on the left and right mastoid, Cz was used as the online reference, and Fpz served as the ground electrode. Electrooculogram was recorded from electrodes placed above and below the left eye and two placed on the outer canthus of both eyes. The EEG was digitized with a sampling rate of 1000 Hz, utilizing a low-pass fifth-order sinc filter with a half-power cutoff set at 100 Hz.

2.3. Procedure

Lab visits lasted approximately 4–5 h and participants were asked to complete multiple tasks (i.e., including self-report questionnaires, psychophysiological and neuroimaging tasks). Current and lifetime psychiatric history were evaluated with the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version (KSADS; Kaufman et al., 1997). Diagnosis was made consistent with the DSM-IV. The KSADS is a semi-structured clinical interview with good psychometric properties (Birmaher et al., 2009). The KSADS was conducted with parents and participants, separately, by trained interviewers under the supervision of experienced, Ph.D.-level clinical psychologists (Amir et al., 2023). Relevant to the current study, participants completed a flanker task while continuous EEG data were collected. Some of the participants’ stimulus-locked data from the flanker task has been previously published elsewhere (see Santopetro et al., 2021) and the main aims of the study, which included analyzing ERN in the entire sample, are presented elsewhere (Amir et al., 2023).

2.4. EEG data processing

2.4.1. Time-domain analysis

For time-domain analyses, data were processed offline with Brain Vision Analyzer (Brain Products, Gilching, Germany). Raw EEG signals were referenced to the average of mastoid electrodes and filtered with low and high filter cutoffs set at 0.01 Hz and 30 Hz, respectively. For analyses of ERPs time-locked to the responses (i.e., ERN, CRN), EEG segments of 1500 ms were extracted from the continuous EEG, beginning 500 ms before responses. Data were then corrected for ocular movements and blinks (Gratton et al., 1983). Then, segments containing residual artifacts exceeding voltage steps >50 μV between sample points, a voltage difference of 300 μV within a single trial, or a maximum voltage difference of <0.5 μV within 100-ms intervals were automatically rejected and additional artifacts were identified and removed based on visual inspection. ERP averages were created for error and correct trials and a baseline of the average activity from –500 to –300 ms before the response was subtracted from each data point. Only participants with at least six usable error trials were included (Olvet and Hajcak, 2009). Based on previous research (e.g., Meyer and Klein, 2018; Klawohn et al., 2020), the error-related negativity (ERN) and correct-related negativity (CRN) were scored as the average voltage in the window between 0 ms and 100 ms after response commission on an error and correct trials, respectively; the CRN and ERN were quantified at electrode site FCz, where error-related brain activity was maximal.

2.4.2. Time-frequency analysis

The processing pipeline for the time-frequency domain was similar to the one conducted for the time domain. For this analysis, EEG data were processed offline in Brainstorm (Tadel et al., 2011). The signal was filtered with a band-pass filter of 0.3–30 Hz, to minimize slow drifts that could have adverse effects on time-frequency decomposition (Cohen, 2014; Debnath et al., 2020). Blink artifacts were removed using independent component analysis (ICA). The signal was then segmented into 1500 ms epochs, from 500 ms before stimulus onset to 1000 ms after onset. Then, segments containing residual artifacts exceeding ±70 μV (peak-to-peak) were excluded. Time-frequency analysis was performed using Morlet wavelet transformation on individual trials for each 1-Hz frequency bin between 1 and 30 Hz, using a mother wavelet at 1 Hz with 3-s time resolution (as calculated by the full width at half maximum, FWHM). Time-frequency decompositions were then averaged for each participant and condition (error and correct trials), and the event-related spectral perturbation (ERSP) was computed as the change in power expressed in decibels (dB) relative to the baseline (~300 to –100 ms) in each frequency bin at each time point (i.e., baseline normalization). Then, data were grand averaged across each participant for each condition.
2.4.3. Statistical analyses

Statistical analyses were conducted using Rstudio (R Core Team, 2012), JAMOVI, and Matlab using a two-tailed α = 0.05. Group differences in demographics, self-report CDI scores, and error rates were examined using independent samples t-tests or χ²-tests. A repeated measures analysis of variance (ANOVA) was utilized to determine differences within- and between groups in RTs to correct vs. error trials.

2.4.4. Time-domain

Regarding the time-domain data, residualized difference scores were computed to isolate variance specific to each measure by saving the unstandardized residuals in linear regressions predicting values on error trials from values on correct trials (Meyer et al., 2017). A one-way ANOVA was used to compare the ERN resid between the two groups.

2.4.5. Time-frequency

For time-frequency data, a cluster-based permutation approach was conducted to identify trial-type (error vs. correct trials) effects in event-related delta (1–3 Hz), theta (4–8 Hz), alpha (9–14 Hz), and beta (15–20 Hz) within the whole sample as implemented by the FieldTrip toolbox (Oostenveld et al., 2011). This method effectively controls for the proportion of clusters in the null distribution. With cluster-based permutation tests, the theoretical underlying distribution of the test statistics under the null hypothesis is generated by the data itself by an iterative shuffle of the condition labels over trials. If the test statistic associated with the non-shuffled data falls within the distribution of the null hypothesis, the null hypothesis cannot be rejected and this would indicate that the observed data could have been randomly generated (Cohen, 2014; Luck, 2014). With cluster-based correction, at each iteration of the null-hypothesis distribution generation, the outcome is units of clusters instead of single pixels (i.e., electrodes; Cohen, 2014). In this work, the differences within conditions (correct versus error trials) across the whole sample were shuffled pseudo-randomly 2000 times. For each significant cluster in the (non-shuffled) data, the cluster-corrected p-value was computed as the statistics of the proportion of clusters in the null distribution that exceeded the one obtained for the cluster in question. Clusters with a pcorr < .05 were considered statistically significant. Cluster-based repeated measures ANOVAs were conducted to extract within-subjects differences in event-related power changes between conditions (error vs. correct).

Then, time-frequency power within each frequency band that emerged as significant from the cluster-based analyses was extracted as the averaged power in the specific time window and location (i.e., electrodes). Using the same approach as above, residualized difference scores were created for each significant time-frequency measure (Meyer et al., 2017). To compare the two groups on each significant time-frequency measure, separate one-way ANOVAs were computed.

2.4.6. Correlations

Pearson and point-biserial correlations were conducted across the sample for neural (i.e., the ERN and time-frequency measures), behavioral (i.e., RTs), and clinical (i.e., diagnostic group and CDI scores) data. Then, logistic regression was conducted to examine the amount of unique variance explained by each significant time-frequency and time-domain measure in determining the likelihood of MDD diagnosis. Collinearity was tested by calculating the Variance Inflation Factors (VIF) with the vif function of the car package (Fox et al., 2019).

To examine internal consistency in the flanker task of the ERN and time-frequency measures, split-half reliability was computed by taking the correlation between even and odd error and correct trials and then adjusting with the Spearman-Brown prediction formula (Meyer et al., 2014). This approach uses all event-related data from each participant to estimate the stability of the EEG measures across the task.

3. Results

3.1. Demographic and behavioral results

Demographic and self-report measures for the MDD and HC groups are presented in Table 1. There were no significant differences between groups with respect to age, gender, or ethnicity, while the two groups differed in terms of total CDI scores.

The two groups did not differ in terms of number of errors performed (HC: M · err = 40.1, SD · err = 17.9; MDD: M · err = 32.6, SD · err = 13.4; t(61) = 1.90, p = .07). Overall, all participants were faster on error trials compared to correct trials (M · err = 2.52; SD · err = 0.06; M · cont = 2.64; SD · cont = 0.07; F1,61 = 407.6, p < .001). Participants with MDD were generally slower than healthy controls (M · cont = 2.61, SD · cont = 0.07, M · ddd = 2.64, SD · ddd = 0.06; F1,61 = 5.72, p = .020), while no interaction between group and trial type emerged for reaction time (F1,61 = 0.45, p = .56).

3.2. ERPs

The ERN was larger (more negative) than the CRN (F1,62 = 49.2, p < .001) across the whole sample. As shown in Fig. 1, the MDD group showed a smaller (i.e., more positive) ERN resid compared to the HC group (Control: M = −1.27, SD = 6.08; MDD: M = 1.49; SD = 4.48; F1,61 = 4.26, p = .043).

Time-frequency differences between error and correct trials.

3.3. Delta power (1–3 Hz)

The cluster-based analysis on event-related delta power showed a significantly greater delta power to error trials relative to correct trials (electrodes FP1 FZ F3 F7 FCZ FC5 FC1 C3 T7 CP5 CP1 P3 P7 O1 OZ O2 P4 P8 CP6 CP2 C4 T8 FC6 FC2 F4 F8 FP2 CZ; cluster F-value = 271,439.87, pcorr < .001, time window 0 to 1000 ms; Fig. 2, panel a, b, and c).

3.4. Theta power (4–8 Hz)

The cluster-based analysis on event-related theta power showed a significantly greater theta suppression to error trials relative to correct trials (electrodes FP1 FZ F3 F7 FCZ FC5 FC1 C3 T7 CP5 CP1 PZ P3 P7 O1 OZ O2 P4 P8 CP6 CP2 C4 T8 FC6 FC2 F4 F8 FP2 CZ; cluster F-value = 224,937.32, pcorr < .001, time window 0 to 436 ms; Fig. 2, panel d, e, and f).

3.5. Alpha power (9–14 Hz)

The cluster-based analysis on event-related alpha power showed a significantly greater alpha suppression (i.e., decreased power) to error relative to correct trials (electrodes FP1 FZ F3 F7 FCZ FC5 FC1 C3 T7 CP5 CP1 PZ P3 P7 O1 OZ O2 P4 P8 CP6 CP2 C4 T8 FC6 FC2 F4 F8 FP2 CZ; cluster F-value = 157,947.15, pcorr < .001, time window 0 to 1000 ms; Fig. 2, panel g, h, and i).

3.6. Beta power (15–20 Hz)

The cluster-based analysis on event-related beta power showed a significantly greater beta suppression (i.e., decreased power) to error relative to correct trials (electrodes FP1 FZ F3 F7 FCZ FC5 FC1 C3 T7 CP5 CP1 PZ P3 P7 O1 OZ O2 P4 P8 CP6 CP2 C4 T8 FC6 FC2 F4 F8 FP2 CZ; cluster F-value = 76,900.55, pcorr < .001, time window 0 to 470 ms; Fig. 2, panel j, m, and n).

3.7. Time-frequency differences between groups

As shown in Fig. 3, the MDD group showed reduced theta resid power (F1,61 = 4.00, p = .050, panel a) and greater beta resid power (F1,61 = 6.05,
p = .018, panel b) than the HC group. No delta or alpha power differences emerged between the two groups (all ps > .35).

3.8. Correlations

Correlations between EEG measures and behavioral and clinical variables across the whole sample are shown in Table 2. The \( \Delta \text{ERN}_{\text{resid}} \) and \( \Delta \text{theta}_{\text{resid}} \) power were negatively correlated (i.e., more negative \( \text{ERN}_{\text{resid}} \) corresponded to increased error-related \( \text{theta}_{\text{resid}} \)). \( \text{Theta}_{\text{resid}} \) and \( \text{beta}_{\text{resid}} \) power were also positively correlated. \( \text{Beta}_{\text{resid}} \) was positively correlated with \( \text{alpha}_{\text{resid}} \) and negatively correlated with \( \text{delta}_{\text{resid}} \). The \( \text{ERN}_{\text{resid}} \) was positively correlated with RTs on error trials (i.e., a more negative \( \text{ERN}_{\text{resid}} \) corresponded to slower RTs). Both being depressed and increased continuous CDI scores were related to increased \( \text{beta}_{\text{resid}} \). There were no other significant correlations among time-frequency, time-domain, and behavioral measures. Regarding internal consistency of EEG measures, Table 4 illustrates results of split-half reliability computations, which resulted moderate to high for most indices.

3.9. Regressions

Results of the logistic regressions are shown in Table 3. When all the ERP variables that related to MDD diagnosis were considered simultaneously, both \( \text{theta}_{\text{resid}} \) and \( \text{beta}_{\text{resid}} \) power, but not the \( \text{ERN}_{\text{resid}} \) were related to an increased likelihood of being diagnosed with MDD. Specifically, MDD was associated with reduced error-related theta and increased error-related beta; however, the previous effect of \( \text{ERN}_{\text{resid}} \) was no longer significant in this regression, suggesting that variance in MDD status related to a smaller \( \text{ERN}_{\text{resid}} \) was accounted for by \( \text{theta}_{\text{resid}} \) and/or \( \text{beta}_{\text{resid}} \).\(^1\) VIF values were all <1.43, indicating low multicollinearity.\(^2\)

4. Discussion

The primary aim of the present study was to explore electrocortical measures of error monitoring, as indexed by the ERN and time-frequency power, in a sample of adolescents with and without MDD. As hypothesized, the MDD group showed reduced ERN and error-related theta relative to the control group. In addition, the MDD group was characterized by increased error-related beta power relative to the control group.

Regarding time-frequency within-groups patterns, in line with previous literature (Cavanagh et al., 2009; Cavanagh et al., 2017; Dell’Acqua et al., 2022b; Lui et al., 2004; Muir et al., 2020; Munneke et al., 2015; Sandre and Weinberg, 2019; Trujillo and Allen, 2007), the entire sample was characterized by greater delta and theta power following error compared to correct trials. This supports the view that both delta and theta power might be linked to error monitoring processes. Nevertheless, these measures were not correlated, and the MDD group had reduced error-related theta but not delta power. Taken together, these findings suggest that error-related delta and theta might reflect distinct processes relevant to error monitoring. For instance, previous studies suggest that theta power may index an initial error detection and primary response outcome (Cavanagh et al., 2009; Cavanagh and Frank, 2014), whereas error-related delta may reflect more elaborative processes during error monitoring (Bernat et al., 2015; Watts and Bernat, 2018), such as the processing of higher-level aspects of outcomes (e.g., relative outcome, outcome magnitude, expectancy). Further studies are warranted to clarify this potential functional dissociation between error-related delta and theta power. Moreover, contrary to what was hypothesized, no group difference emerged in error-related delta power. This finding provides further evidence for a potential dissociation between error-related delta and theta power (e.g., Sandre and Weinberg, 2019), although error-related delta dysfunctions in MDD may develop later with increasing duration and chronicity of the condition.

In addition, in line with a previous study that explored error-related time-frequency patterns (Li et al., 2020), alpha power decreased following the commission of an error relative to a correct response. Given that alpha activity is inversely related to cortical activity, this alpha power decrease might reflect increased cortical arousal and engagement of attentional resources required to adjust behavior following an error (Carp and Compton, 2009; Li et al., 2020). Moreover, the sample showed reduced beta power to error relative to correct trials. Based on previous investigations suggesting that beta suppression facilitates motivational processes to prepare and execute upcoming responses and to allow responses to be adjusted appropriately (e.g., Gable et al., 2016; Glazer et al., 2018; Meyniel and Pessiglione, 2014; Li et al., 2020; Wessel et al., 2016; Wilhelm et al., 2022), this result may reflect the engagement of greater motor preparation for the subsequent trial following the commission of an error.

In line with some previous studies (Weinberg et al., 2015b; Ruchsow et al., 2004, 2006), the group with MDD showed reduced ERN amplitude.
relative to controls. As suggested by Weinberg et al. (2015a, 2016), the magnitude of the ERN might reflect the degree to which errors are evaluated as threatening which, in turn, mobilizes defensive systems to respond adaptively. Hence, the present findings may support the ECI model, showing that MDD is related to reduced functioning of the Negative Valence System. In addition to the reduced ERN, individuals with depression showed reduced error-related theta relative to controls; increased error-related theta power was associated with a larger (i.e., more negative) error-related negativity, although ERN amplitude was not associated with other time-frequency measures. These results suggest that theta power and the ERN might share a functional role in error processing (e.g., Cavanagh et al., 2009; Dell’Acqua et al., 2022a). In this way, the current study provides evidence for the inclusion of not only the ERN but also error-related theta as a potential unit of measurement in the sustained threat construct of the Negative Valence System.

This was the first study to show greater error-related beta power in the MDD group relative to the control group. Based on previous literature (e.g., Li et al., 2020; Wessel et al., 2016; Wilhelm et al., 2022), this finding could indicate that participants with MDD are characterized by
reduced motor preparation following errors (i.e., greater inhibition). Besides, the group with MDD showed longer response times than the control group to all trial types and not just following errors, suggesting that they might be characterized by overall motivational inertia in performing the task. In addition to error-related beta, future ad-hoc studies should be designed to explore the link between beta power and other ERPs associated with action preparation, such as the lateralized readiness potential (Dayan et al., 2017; Morand-Beaulieu et al., 2021; Schurger et al., 2021).

A second aim of the present study was to examine whether using a combination of the ERN and time-frequency measures would explain unique variance in MDD status. In a logistic regression model, time-frequency measures that differed between the two groups and the ERN were included as predictors of group status. Greater error-related beta and reduced error-related theta emerged as significant predictors of MDD over and above ERN, suggesting that the variance in MDD group status associated with a smaller ERN was accounted for by the time-frequency measures. Considering that error-related theta and the ERN were strongly correlated, and both reduced in MDD, it could be that, in this model, the variance related to their underlying shared process in MDD was better explained by theta power. From these results, it appears that ERN deficits in youth MDD are better explained by variance in theta and beta power, which may explain why prior work examining only ERN

![Fig. 3. (Panel a and b) Mean differences in event-related theta (panel a) and beta (panel b) power between the MDD group and the HC group. Error-related theta and beta are residualized scores (i.e., residualized differences scores computed by saving the unstandardized residuals in linear regressions predicting values on error trials from values on correct trial).](image)

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<td>Note. ERN = error-related negativity; RTs = response times. *p &lt; .05.</td>
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| Table 3 | Results of the logistic regression analysis predicting diagnostic status (MDD, HC) from the ERN and theta and beta power to error trials. |
| Measure | Prediction of diagnostic status (MDD, HC) |
|  | R² | χ² | OR | 95% CI | p |
| ERN | 0.31 | 16.4 | 1.05 | 0.94–1.18 | .42 |
| Theta | 0.37 | 0.15–0.90 | .03 |
| Bet | 2.82 | 1.26–6.30 | .01 |
| Note. Logistic regression was used to predict the dichotomous dependent variable diagnosis of MDD (0 = absent, 1 = present) from both time-frequency measures that emerged as significant from the cluster-based analyses (beta and theta power) and the ERN. The Nagelkerke R² and χ² statistics are reported for the logistic regression models. CI = confidence intervals; OR = odds ratio. |

| Table 4 | Results of split-half reliability computed by taking the correlation between even and odd trials and then adjusting with the Spearman-Brown prediction formula. |
| Measure | r (p-value) |
| Delta error trials | 0.358 (.004) |
| Delta correct trials | 0.739 (<.001) |
| Theta error trials | 0.473 (<.001) |
| Theta correct trials | 0.823 (<.001) |
| Alpha error trials | 0.525 (<.001) |
| Alpha correct trials | 0.956 (<.001) |
| Beta error trials | 0.374 (<.001) |
| Beta correct trials | 0.889 (<.001) |
| ERP error trials | 0.695 (<.001) |
| ERP correct trials | 0.970 (<.001) |
| Note. | |
amplitudes in depression has led to inconsistencies. Taken together, these findings suggest that reduced error-related theta and greater error-related beta represent unique correlates of MDD in youth.

The adopted time-frequency method provided additional information on error monitoring deficits in MDD – namely reduced error-related theta and greater error-related beta. Regarding the methodology, the present investigation explored time-frequency patterns associated with error monitoring with a cluster-based permutation approach, an ad hoc data-driven method that avoids selection biases (Cohen, 2014; Luck, 2014).

The present study has some limitations worth noting. First, most of the participants were female and White. Future studies should replicate our findings in more diverse samples. Lastly, the current study was cross-sectional. Longitudinal studies should be conducted in the future to determine whether these abnormal error-related EEG patterns could represent a risk factor for the onset of depression instead of just being a mere correlate of the disorder.

Taken together, by examining both time-domain and separate time-frequency measures, the present study provided novel evidence on error monitoring alterations in youth MDD, suggesting that depression during adolescence may be characterized by reduced error monitoring (i.e., reduced ERN and error-related theta) and post-error inhibition (i.e., greater error-related beta power). Despite the evident need for replication, these findings may set the stage for the hypothesis that MDD is related to reduced error monitoring and, consequently, to a potential reduced Negative Valence Systems activity in depression. This study was the first to examine whether the ERN and time-frequency indices related to error monitoring predict unique variance in MDD. The results provided further information on the pathophysiology of MDD in youth and might be useful to enhance the clinical utility of ERP measures.

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Data availability
Data or other materials are available through correspondence with the first author.

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CRediT authorship contribution statement
G.H., N.A., and A.M. conceived and designed the study; G.H., N.A., N.J.S., C.J.B., and A.M. conducted the study; C.D.A., N.J.S., and C.J.B. analyzed the data; C.D.A. and C.J.B. wrote the paper, and all authors reviewed the manuscript.

References


