

Increased error-related negativity (ERN) in childhood anxiety disorders: ERP and source localization

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Background: In this study we used event-related potentials (ERPs) and source localization analyses to track the time course of neural activity underlying response monitoring in children diagnosed with an anxiety disorder compared to age-matched low-risk normal controls. **Methods:** High-density ERPs were examined following errors on a flanker task from 12 children between 8 and 14 years old diagnosed with an anxiety disorder (ANX) and 13 age-matched low-risk normal controls (LRNC). **Results:** Children diagnosed with an anxiety disorder had increased error-related negativity (ERN) amplitude. The neural generators of the ERN in the ANX group were estimated to be localized in the anterior cingulate cortex (ACC). There were no significant group differences in P_E amplitude. **Conclusions:** These data provide evidence for increased ERN amplitude localized to the ACC in children diagnosed with an anxiety disorder, suggesting altered maturational patterns of the ACC circuitry early in the course of this illness. **Keywords:** Children, anxiety disorders, error-related negativity (ERN), error-related positivity (P_E), anterior cingulate cortex, event-related potentials, source localization. **Abbreviations:** ANX: Anxiety Disorder group; LRNC: Low-Risk Normal Control group; CBCL: Child Behavior Checklist; SCARED: Screen for Childhood Anxiety and Related Disorders; CDI: Children's Depression Inventory; BDI: Beck Depression Inventory.

Progress in understanding the neural mechanisms underlying cognitive and affective processes in childhood anxiety disorders may shed some light on the pathophysiology of these disorders in ways that ultimately can inform early intervention and prevention strategies (Pine, 1999). The field of cognitive neuroscience provides methods that allow us to investigate these neural mechanisms. One of these methods is high-density event-related potentials (ERPs). Although ERPs are limited in terms of spatial resolution compared to functional neuroimaging, they provide an excellent and more precise metric of the time course of neural activity.

Event-related potentials (ERPs) reflect the coordinated behavior of large populations of neurons measured by averaging segments of electroencephalogram (EEG) recordings that are time-locked to perceptual, cognitive, and motor events. The timing and size of ERPs along with their location on the scalp are used to make inferences about the time-course of processing in the brain. Source localization analyses, which are multivariate mathematical computations that allow researchers to estimate the location of the underlying neural generators of ERPs, are often included in ERP studies. Due to their millisecond-level temporal resolution, ERPs constitute a good neuroimaging method for investigating the time-course of higher-level cognitive processes (Rugg & Coles, 1997).

Using ERPs, researchers have identified a sharp negative deflection in the EEG approximately 50–150 ms after subjects make an error in speeded reaction time tasks – this negative deflection was coined the error-related negativity (ERN). The ERN is a response-locked ERP that is maximally distributed at fronto-central EEG recording sites. It has been observed across various stimulus and response modalities (Holroyd, Dien, & Coles, 1998). As such, it is considered as a generic neural index of response monitoring processes (Dehaene, Posner, & Tucker, 1994; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000). More specifically, the ERN has been interpreted to reflect an error signal that is generated when a comparator system detects a discrepancy or conflict between the emitted response and the correct response (Dehaene et al., 1994; Gehring, Coles, Meyer, & Donchin, 1995; van Veen & Carter, 2002). Recent evidence suggests that the ERN is late to mature, reaching adult amplitude levels in mid to late adolescence (Davies, Segalowitz, & Gavin, 2004; Ladouceur, Dahl, & Carter, 2004; Ladouceur, Dahl, & Carter, under review). Studies that have used source localization analyses suggest that the ERN is generated by a single neural source in the medial frontal cortex – specifically, the caudal region of the anterior cingulate cortex (ACC) (Dehaene et al., 1994; van Veen & Carter, 2002). These results have been supported by functional magnetic resonance imaging (fMRI) studies indicating increased activation of the ACC during error processing (Carter et al., 1998).

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Recently, researchers have found increased ERN amplitude in anxious adults. For example, Hajcak et al. (2003) reported increased ERN amplitude in college undergraduate students who scored high on general anxiety and worry self-report measures (Hajcak, McDonald, & Simons, 2003) and using fMRI Paulus et al. (2002) showed increased ACC activation in high-trait anxiety individuals processing errors on a decision-making task (Paulus, Hozack, Frank, & Brown, 2002). Furthermore, several studies have found increased ERN in adults diagnosed with obsessive-compulsive disorder (OCD) (e.g., Johannes et al., 2001) and significant correlations between ERN magnitude and OCD severity (Gehring, Himle, & Nisenson, 2000). Taken together these results were interpreted as indicating that anxiety disorders may be related to excessive error-related activity in the ACC (Hajcak et al., 2003). It remains unknown, however, whether such excessive error-related activity in the ACC is present early in the course of the illness – such as in pediatric anxiety disorders.

The goal of this study was to determine whether the increased ERN amplitude found in anxious adults would also be found in children diagnosed with an anxiety disorder. Given the existing literature showing that children with anxiety disorders have an attentional bias toward negative or threatening information (Vasey & MacLeod, 2001), we hypothesized that errors would be more salient for anxious children and as such, would engage greater response monitoring processes which would translate into increased ERN amplitude. We also hypothesized that ERN amplitude would be correlated with symptom severity and that the neural generators of the ERN would be located in a similar region of the ACC to that found in adult samples.

The ERN is generally followed by the P_E , which is a late positive deflection in the EEG that occurs at centro-parietal sites approximately 200–400 ms following response execution (Falkenstein et al., 2000). Little is known about the functional significance of the P_E . The current hypotheses suggest that the P_E is involved in processes that follow the detection of errors, possibly reflecting conscious recognition of having made an error or a subjective/emotional reaction to errors (Falkenstein et al., 2000). Source localization analyses suggest that the neural generators of the P_E are located in the rostral ACC, which is thought to be linked to affective processes (van Veen & Carter, 2002). Unlike the ERN, the P_E is clearly present in childhood (Davies et al., 2004; Ladouceur et al., 2004, under review). To our knowledge, no studies have examined the P_E in anxiety disorders. Nevertheless, given that ACC overactivity may play a role in the pathophysiology of anxiety disorders and that the P_E is generated in the ACC, it would seem plausible to expect increased P_E amplitude in anxious children.

In order to test these hypotheses, we measured ERPs while participants performed a speeded reaction time task. In particular, we compared ERN and P_E amplitude and the location of underlying neural generators in children diagnosed with an anxiety disorder and age-matched low-risk normal controls while they performed the Eriksen flanker task (Eriksen & Eriksen, 1974) – a speeded reaction time task often used to examine these ERPs. Given that the ERN has neural generators in the ACC and some evidence suggesting that it does not fully develop until late adolescence, finding an increased ERN in children diagnosed with an anxiety disorder could have important implications for elucidating the role of the ACC circuitry in some aspects of the pathophysiology of pediatric anxiety disorders.

Method

Participants

Twelve children diagnosed with an anxiety disorder (ANX) (8 males) and 13 age-matched low-risk normal controls (LRNC) (3 males) (mean age = 11.42 ± 2.15 ; range = 8.0–14.6 years) initially participated in the study. A total of 6 participants (3 ANX and 3 LRNC) were excluded from analyses for the following reasons: a) too few error trials (i.e., less than 20), b) too many errors (i.e., more than 200), or c) too few good EEG segments (i.e., less than 40 in each cell). Thus, a total of 19 participants are included in the current report. Of these 19 participants, there were nine in the ANX group (mean age = 11.12 ± 2.25 , 6 males) and 10 in the LRNC group (mean age = 12.16 ± 2.14 , 2 males). The majority were right-handed (90%), as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The overall mean score for socio-economic status (SES) was 44.50 ± 9.56 , as measured with the Hollingshead Four-Factor Index (Hollingshead, 1975).

Children in the ANX group were recruited from outpatient clinics at the Western Psychiatric Institute and Clinic, Pittsburgh, PA and through local newspaper and radio advertisements. They took part in a larger longitudinal project on the neurobiology of pediatric affective disorders (Birmaher et al., 2000) and were asked to participate before commencing any type of medication treatment. Diagnoses were established based on DSM-III-R and DSM-IV (American Psychiatric Association, 1994) criteria. All but one participant in the ANX group met criteria for Generalized Anxiety Disorder. Other diagnoses included Separation Anxiety Disorder ($n = 2$), Social Phobia ($n = 2$), and Specific Phobia ($n = 2$) as well as Dysthymia and Attentional Deficit Disorder ($n = 1$).

Children in the LRNC group were recruited through advertisement in the local newspaper. They were matched on age to participants in the ANX group according to a 2-year age interval. They were required to be free of any lifetime psychopathology. They were required also to have no first-degree relatives with a lifetime episode of any mood or psychotic disorder; no second-degree relatives could have a lifetime history of childhood-onset, recurrent, psychotic, or bipolar

depression or schizoaffective or schizophrenic disorder; and no more than 20% of their second-degree relatives could have a lifetime single episode of major depressive disorder (MDD) (Stein et al., 2000).

The University of Pittsburgh Institutional Review Board approved the study. To participate, children and their parents were required to sign assent and informed consent forms, respectively. Upon entry into the study, participants were admitted to the Child and Adolescent Sleep and Neurobehavioral Laboratory at Western Psychiatric Institute and Clinic for a three-day assessment that included ERP assessment.

Measures

Diagnostic interview. Diagnosis was established using The Schedule for Affective Disorders and Schizophrenia for School Aged Children – Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997). This interview provides assessments of present episode and lifetime history of psychiatric illness in children according to DSM-III-R and DSM-IV criteria. The interview was administered independently with the child and with one parent about the child by clinically experienced interviewers. All cases were staffed by a child psychiatrist who confirmed the diagnoses. In addition, monthly reliability meetings were conducted to establish reliability of clinical diagnoses. Interrater reliabilities for diagnoses assessed during the course of this study were estimated to be $k \geq .70$.

Self-reports. Participants and their parents or guardians completed the following self-report measures: a) the Behavior Checklist – parent form (CBCL) (Achenbach & Edelbrock, 1983), b) the Screen for Childhood Anxiety and Related Disorders (SCARED) child and parent versions (Birmaher et al., 1999; Birmaher et al., 1997), c) the Children's Depression Inventory (CDI) (Kovacs, 1985) (children, 8–12 years old), and the Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Muck, & Erbaugh, 1961) (adolescents, 13–18 years old).

Flanker task. EEG measures were taken while participants performed an arrow version of the Eriksen flanker task with congruent (i.e., $\rightarrow \rightarrow \rightarrow \rightarrow \rightarrow$ and $\leftarrow \leftarrow \leftarrow \leftarrow \leftarrow$) and incongruent (i.e., $\leftarrow \leftarrow \rightarrow \leftarrow \leftarrow$ and $\rightarrow \rightarrow \leftarrow \rightarrow \rightarrow$) conditions (Eriksen & Eriksen, 1974). The five-arrow stimulus arrays were presented using E-prime (Psychological Software Tools, Pittsburgh, PA). Each trial started with the presentation of a central fixation cross '+'. Following the fixation cross, one of the four stimulus arrays appeared on the computer screen. The probability of occurrence of each stimulus array was .25. Participants were asked to respond on a button box using their left index finger if the central arrow pointed to the left and their right index finger if the central arrow pointed to the right. In order to enhance the effect of the flankers with regard to priming incorrect responses in the incongruent condition, the flanker stimuli appeared 100 ms prior to the target stimulus, which appeared in the same location as the fixation cross. Flankers and the central arrow remained on the screen

until a response was made after which they disappeared simultaneously and a fixation cross appeared, which indicated the intertrial interval. The intertrial interval was randomized between 500 and 1500 ms. Each block of trials began with a fixation cross having a duration of 3000 ms.

Procedure

During the flanker task, each participant was seated .5 m directly in front of a computer monitor. After a description of the experiment, participants were given detailed instructions and asked to respond as quickly and as accurately as possible. To ensure that participants remained motivated throughout the task, they were told at the beginning of the task that they could win a 'cash bonus' if they performed extremely well on this task (all were told that they did very well and received an extra \$5). Participants completed a 60-trial practice block. The experimenter then applied the dense-array electrode net (Tucker, 1993). Participants received seven blocks of 120 trials (840 total trials) with each block initiated by the participant. The percentage of correct responses was computed between blocks informing the experimenter of the participants' performance; this information was used to guide the experimenter in providing feedback to participants about their performance to ensure that they kept being both fast and accurate throughout the task. Once testing was complete, participants were asked to complete a post-task questionnaire.

EEG data acquisition and processing

EEG data were recorded with a 128-channel dense-array Geodesic Sensor Net (Tucker, 1993) and analyzed using EGI software (EGI, Eugene, OR). EEG was recorded with a .1–100 Hz bandpass filter (3dB attenuation). The EEG signal was digitized at 250 Hz with a 12-bit A/D converter. During data acquisition, channels were referenced to channel 129 (Cz) and rereferenced, prior to data analyses, to the average reference. Impedances were measured prior to and following EEG recording. Before recording, impedances were below 50 K Ω . Channels with impedances above 100 K Ω at the end of the recording were noted and visually inspected. These channels were marked 'bad' if they were excessively noisy (i.e., differential amplitude of 100 μ V) through out the experiment.

EEG data processing involved the following steps. EEG data were digitally filtered using a .3–30 Hz bandpass filter. The EEG was then segmented –400 to +800 ms prior to and following response onset (button press) and divided according to correct and error trials. Response-locked epochs were baseline corrected at –150 to –50 ms. Artifacts were screened using automatic detection methods (Net Station, Electrical Geodesics, Inc.). Segments containing eye blinks and movement artifacts or that had reaction times lower than 100 ms and higher than 2000 ms were excluded from analyses. Bad channel data were replaced using spherical spline interpolation of neighboring channel values (Perrin, Bertrand, & Pernier, 1987). Analyses conducted to examine whether there were any

diagnostic group differences in the number of EEG segments excluded due to artifact (i.e., eye blinks, eye movements, or number of bad channels) did not yield any significant differences.

EEG data reduction and analyses

To quantify the response-locked ERN and P_E , averages of the maximum peak amplitudes were computed separately for correct and error trials for each subject. The ERN was defined as the maximum negative peak amplitude in the window 0–100 ms following response onset. The P_E was defined as the maximum positive peak amplitude in the window 100–500 ms following response onset.

Source localization analyses

The locations of the neural generators for the ERN and P_E were modeled using *Brain Electrical Source Analysis* software (BESA 5.0.8; MEGIS Software, Munich, Germany), a software program that estimates sources of electrical activity in a four-shell, spherical head model approximation with ellipsoidal correction (Scherg, 2003). Because bone conductivities are age dependent, we included in the model estimates provided by MEGIS software for bone thickness and conductivity for the ages of 10 to 12 years old. As such, bone thickness of 6 mm and bone conductivity of .01 were used in the model.

The BESA procedure (Scherg & Berg, 1996) was applied to the difference waveform grand averages of the ERN and P_E . The difference waveforms consisted of the correct-trial waveform subtracted from the error-trial waveform. The difference waveforms were fitted from the onset to the maximal peak using a sequential strategy. The appropriateness of the solutions was tested with the techniques outlined by Scherg and Berg (1996). These include, for example, verifying the consistency of the results by repeating the procedure with randomly-seeded initial dipole configurations, by comparing the solution with plausible alternatives, and by assessing the stability of the solution by including additional dipoles.

Results

Self-report measures

Results from independent *t*-test analyses indicated that the ANX group had significantly higher T scores than the LRNC group on the CBCL – externalizing (ANX: 59.89 ± 10.23 ; LRNC: 46.20 ± 6.80 , $t(17) = 3.47$, $p < .01$), CBCL – internalizing (ANX: 68.22 ± 5.43 ; LRNC: 46.30 ± 8.74 , $t(17) = 6.47$, $p < .001$), and CBCL – total scales (ANX: 67.33 ± 6.16 ; LRNC: 45.50 ± 9.43 , $t(17) = 5.90$, $p < .001$) as well as on the total scores of the SCARED-child (ANX: 31.20 ± 14.92 ; LRNC: 4.30 ± 4.03 , $t(17) = 5.50$, $p < .001$), SCARED-parent (ANX: 32.47 ± 6.96 ; LRNC: 6.78 ± 3.63 , $t(16) = 9.82$, $p < .001$) and the z-score CDI/BDI (ANX: $.84 \pm 1.03$; LRNC: $-.59 \pm .19$, $t(15) = 4.34$, $p < .01$).

Behavioral measures

Reaction time and accuracy. A mixed MANOVA model was performed on reaction times with diagnostic group (ANX, LRNC) as between-subject variable and trial type (congruent, incongruent) and response type (correct, error) as within-subject variables. Results did not reveal any significant main effects of diagnostic group, $F(1, 17) = .56$, $p = .47$. In addition, there were no significant diagnostic group by trial type, $F(1, 17) = .51$, $p = .49$, or diagnostic group by response type, $F(1, 17) = .66$, $p = .43$, interactions. As expected, however, results yielded a significant trial type main effect indicating that reaction times were slower on incongruent than congruent trials, $F(1, 17) = 74.68$, $p < .001$, and faster on errors than correct responses, $F(1, 17) = 79.96$, $p < .001$.

A similar MANOVA was performed on the overall percentage of errors. There were no significant diagnostic group main effect, $F(1, 17) = 1.44$, $p = .25$, or significant diagnostic group by trial type interactions, $F(1, 17) = .12$, $p = .73$. As expected, however, there was a significant trial type main effect indicating that all children made more errors for incongruent than congruent trials, $F(1, 17) = 83.89$, $p < .001$.

Post-error slowing. In addition to reaction times and accuracy, we examined children's response slowing following errors. Response slowing after having made an error is a well-known indicator of the recruitment of higher-order cognitive processes that support behavioral adjustment on a particular task (Rabbitt, 1966). We computed the difference in reaction times between correct trials following error trials and correct trials following correct trials and performed an independent *t*-test. Results indicated that there were no significant differences across diagnostic groups with regard to post-error slowing ($t(17) = -.53$, $p = .61$); both groups slowed down on correct trials following errors ($t(17) = 2.68$, $p < .05$).

These results indicate that the performance of the ANX group was not significantly different than that of the LRNC group (see Table 1).

ERP measures

Before conducting between-group analyses, we compared the amplitudes at the four fronto-central electrode sites where ERN and P_E activity have been located in previous studies (EGI sites 11 or Fz, 6 or FCz, 129 or Cz, and 62 or Pz) and selected the site that showed the greatest amplitude for each of the ERPs. This comparison involved computing difference waveforms for each electrode site by subtracting the signal elicited on correct trials from the signal elicited on error trials for the ERN and the P_E and performing a repeated measures ANOVA with channel as a within-subject variable. Results indicated

Table 1 Summary of the behavioral performance for the anxiety disorder and low-risk normal control groups

Variables	Group	
	Anxiety disorder (<i>n</i> = 9)	Low-risk normal control (<i>n</i> = 10)
Reaction time		
Overall	472.68 (52.70)	473.03 (65.31)
Correct	484.34 (53.68)	482.12 (64.95)
Incorrect	387.04 (58.20)	397.92 (96.47)
Congruent	439.11 (42.42)	436.74 (60.14)
Incongruent	506.26 (67.09)	509.32 (72.69)
Post-error slowing	31.71 (63.48)	23.40 (32.41)
Percentage of errors		
Overall	9.29 (4.67)	6.77 (2.56)
Congruent	3.54 (3.37)	2.07 (1.17)
Incongruent	15.03 (6.64)	11.48 (4.74)

Note: Standard deviations are in parentheses; there were no significant group differences.

that the largest amplitude was at site 6 (FCz) for the ERN and at site 62 (Pz) for the P_E , $F(3, 16) = 11.12$, $p < .001$. Therefore, amplitude data for these respective sites were used for statistical analyses.

Error-related negativity (ERN). To examine group differences in ERN amplitude, we performed a mixed MANOVA model with diagnostic group as a between-subject variable (ANX, LRNC) and response type (correct, error) as a within-subject variable on ERN amplitude. Consistent with our hypothesis, there was a significant diagnostic group by response type interaction, $F(1, 17) = 7.84$, $p < .05$, indicating that ERN amplitude was significantly more negative on error trials in the ANX compared to the LRNC group (see Figure 1). There was also a significant response type main effect, $F(1, 17) = 23.42$, $p < .001$, confirming that amplitude was more negative for error trials compared to correct trials.

Error-related positivity (P_E). The same mixed MANOVA model performed on ERN amplitude was performed on P_E amplitude. In contrast to ERN results, there was no significant diagnostic group by response type interaction, $F(1, 17) = .25$, $p = .62$. There was, however, a significant response type main effect, $F(1, 17) = 91.24$, $p < .001$, indicating that amplitude was significantly more positive for error trials compared to correct trials.

Dipole modeling of the ERN and the P_E

For the ANX group, a two-dipole model was obtained. One dipole located in mid-dorsal region of the ACC accounted for a large part of the variance in the observed data for the ERN (ERN location: $x = .13$, $y = -.05$, $z = .47$, Cartesian US; residual variance (RV): 6.5%). While holding constant the location and the orientation of the ERN dipole, a second dipole was obtained; it was located in the mid-dorsal region of the ACC rostral to the neural generators of the

ERN (P_E location: $x = -.07$, $y = .19$, $z = .46$; RV: 3.8%). For the LRNC group, a single dipole located in the mid-dorsal region of the ACC was able to account for a large part of the variance in the observed data for the P_E (location: $x = -.02$, $y = .19$, $z = .41$; RV: 5.0%). See Figure 2.

Correlation between ERN amplitude and symptom severity

We predicted that children with more severe anxiety symptoms would show increased ERN activity. In order to test this hypothesis, we restricted analyses to the ANX group and computed Kendall's Tau rank-order correlations between ERN amplitude and the total scores on the SCARED-child and SCARED-parent. There were no significant correlations between ERN amplitude and the total scores of the SCARED-child ($r = .22$) and SCARED-parent ($r = -.22$) self-report measures.

Discussion

Consistent with our hypothesis, results of this study show that anxious children have increased ERN amplitude compared to children at low risk of affective disorders. These results are in sharp contrast to normative developmental data showing that the ERN appears to mature during mid to late adolescence and is typically *not* observed in most children (Davies et al., 2004; Ladouceur et al., 2004, under review). The neural generators of the ERN in the ANX group were localized to the ACC, suggesting that pediatric anxiety disorders may be related to altered maturational patterns of ACC circuitry. Results did not yield significant group differences in P_E amplitude or significant correlations between ERN and symptom severity.

The increased ERN amplitude in the ANX group is consistent with the results of previous studies conducted in adults showing increased ERN amplitude in individuals with high-trait anxiety (Hajcak et al., 2003). Given that the ERN is typically not observed until mid to late adolescence (Davies et al., 2004; Ladouceur et al., 2004, under review), the fact that the anxious children in this study showed 'adult-like' ERN amplitude is noteworthy. Source localization analyses revealed that the neural generators of the ERN in the ANX group were estimated to be in the mid-dorsal region of the ACC, which is consistent with the results of previous studies (Ladouceur et al., under review; van Veen & Carter, 2002). Thus it is possible that the excessive error-related activity in the ACC observed in adult anxiety disorders may be present early in the course of the illness and play a role in the pathophysiology of anxiety disorders.

The increased ERN in the ANX group is consistent also with the results of other studies that have reported increased ERN in affectively distressed

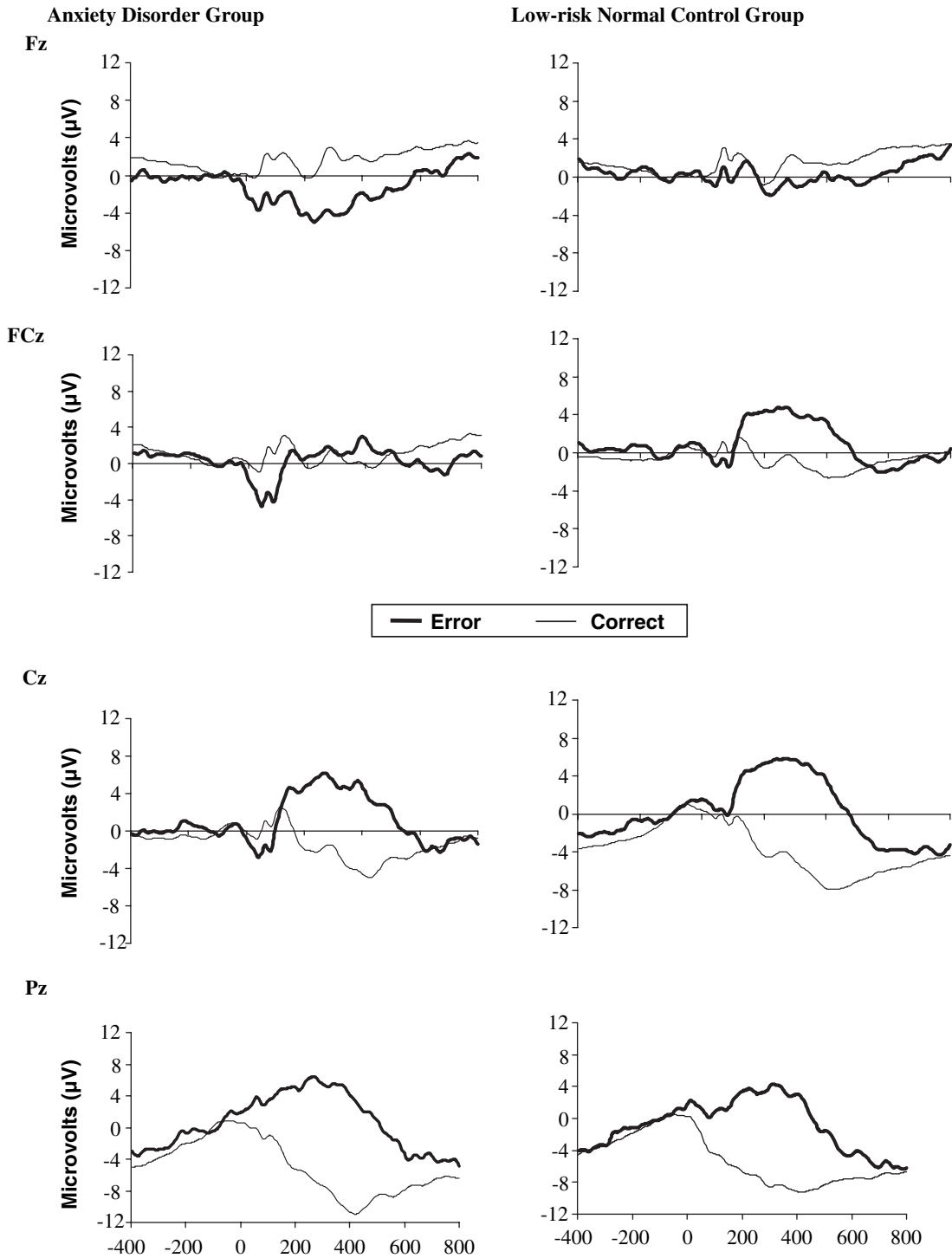


Figure 1 Grand averaged response-locked waveforms for the anxiety disorder and low-risk normal control groups

individuals. For instance, increased ERN amplitude has been found in college students who reported high levels of negative affect on the Positive and Negative Affect Schedule (Hajcak, McDonald, & Simons, 2004). The measure of negative affect has been conceptualized as ‘emotional distress’ according to Clark and Watson’s (1991) tripartite model of anxiety and depression. This model has been adapted for childhood affective disorders and proposes, similarly to the adult model, that childhood anxiety disorders are characterized by high levels of negative

affect whereas depression is characterized by both high levels of negative affect and low levels of positive affect (Joiner, Catanzaro, & Laurent, 1996). As such, one interpretation may be that the increased ERN amplitude in the ANX group is attributable to higher levels of negative affect. This notion of the ERN would be consistent with Luu and Tucker’s (2004) model suggesting that the ERN indexes an affective signal reflecting distress about detecting a discrepancy between an action and an emotionally-salient goal (Luu & Tucker, 2004). It would also be consistent

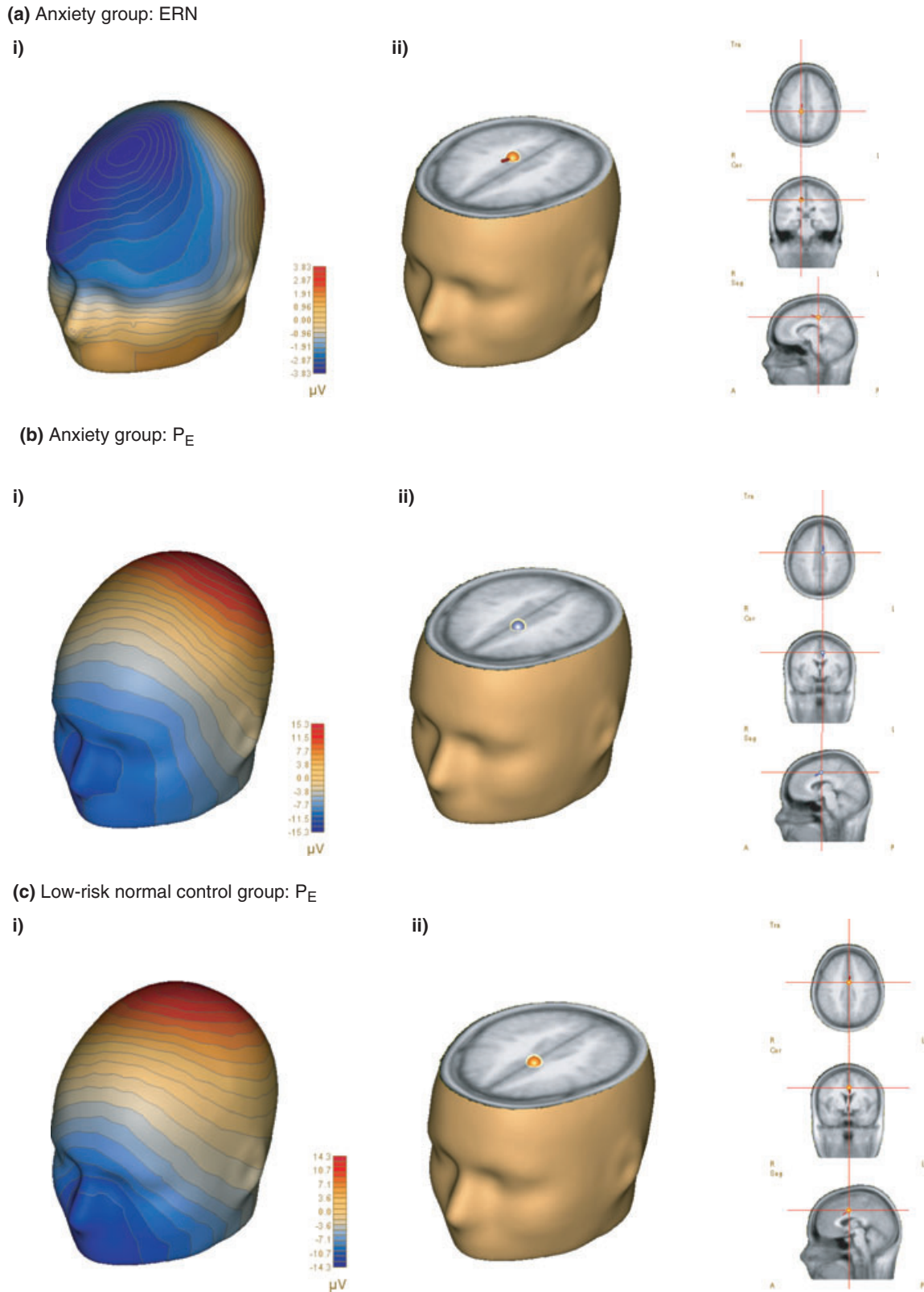


Figure 2 Three-dimensional maps illustrating the scalp distribution of the ERP difference waveforms at their maximal peaks (*note*: blue = more negative; red = more positive) (i) and dipole source models (large) with transversal, coronal, and sagittal views of dipole (small) superimposed on a standard realistic MR-based head model (ii) for a) the ERN in the ANX group, b) the P_E in the ANX group and, c) the P_E in the LRNC group

with Holroyd and Coles' (2002) model suggesting that the ERN represents a neural signal, generated by the midbrain dopaminergic system, that serves to

detect when outcomes occur that are 'worse than expected' (Holroyd & Coles, 2002). Our results do not support such an interpretation, however, as we did

not find any significant correlations between ERN amplitude and anxiety self-report measures. A recent study by Moser, Hajcak, and Simons (2005) also raises doubt about the influence of negative affect on the ERN. In their study, Moser et al. (2005) measured the ERN in college students during control and fear induction conditions and found that fear did not have any impact on ERN amplitude (Moser et al., 2005). It would thus appear that the notion of greater ERN amplitude resulting from high negative affect remains to be tested further.

According to the conflict monitoring model, the ERN indexes the detection of response conflict – which is considered to be high when errors occur – and serves as a signal to engage higher-order and more specialized cognitive control processes to come on-line to adjust performance (Botvinick, Braver, Barch, Carter, & Cohen, 2001). If we consider the functional role of the ERN according to the conflict monitoring model (Botvinick et al., 2001), then we would expect the increased ERN amplitude in the ANX group to be accompanied by changes in performance such as slower reaction times following errors. However, we did not find any significant group differences in post-error slowing or in any of the behavioral measures. These results could be interpreted as indicating that increased ERN amplitude in anxious children reflects a lower threshold in detecting response conflict but a higher threshold for signaling the need to engage higher-order cognitive processes. Another possible interpretation may be that performance adjustments can only be detected later in development. Having a sample with a wider age range would allow us to test these hypotheses further.

As for the P_E , its amplitude was visibly greater in the ANX group (8.38 microvolts) than the LRNC group (5.96 microvolts) but results did not yield statistically significant group differences – which may have been due to the size of our sample. Given that the neural generators of the P_E and the ERN were localized to the same region of the ACC for the ANX group, it is possible that these components share a common functional role. However, because little is known about the functional significance of the P_E in anxiety disorders these results are preliminary and need to be replicated in a larger sample.

Before considering the implications of our results, there are some methodological issues that merit discussion. Firstly, although results of this study are consistent with those found in anxious adults, they remain preliminary. For instance, the small sample of children in this study did not yield enough power to test whether ERN amplitude in the ANX group was correlated with symptom severity. Secondly, the groups were not matched on sex, yielding an unequal male to female ratio in each of the groups. However, our preliminary analyses supported previous studies showing that sex did not seem to impact ERN or P_E amplitudes. Thirdly, despite the fact that we took into consideration age-related differences in

bone thickness and bone conductivity in order to improve the validity of the source localization models in this study, these models remain approximations and would definitely need to be replicated in a different sample. Fourthly, source localization analyses are based on solving an inverse problem and as such, can only provide an estimate of the location of the neural generators for the ERN and the P_E . Future studies of response monitoring in childhood anxiety using complementary imaging techniques such as fMRI will be helpful not only to address these spatial resolution issues but also to determine whether the increase in ERN amplitude in the ANX group is due to differences in ACC structure or function.

In summary, the results of this study provide evidence that children diagnosed with an anxiety disorder have a larger ERN that is localized to the ACC, suggesting that altered maturational patterns of the ACC circuitry involved in response monitoring processes may contribute to the development of pediatric anxiety disorders. This increased neural signal indexing fast-occurring response monitoring processes reflected in the ERN in anxious children is consistent with the view of anxiety disorders as reflecting *active defensive systems* that involve a tendency toward withdrawal or avoidance of perceived threat (Mogenson, Jones, & Yim, 1980). Further research with a sample that spans through childhood and adolescence and that involves co-registering ERPs and fMRI would help to elucidate further the neuromechanisms of response monitoring leading to a better understanding of the pathophysiology of pediatric anxiety disorders.

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