Differentiating Anxiety and Depression in Children and Adolescents: Evidence From Event-Related Brain Potentials

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The current study, which was a reanalysis of previous data, focused on the error-related negativity (ERN)—an event-related potential (ERP) associated with error monitoring— and the feedback negativity (FN)—an ERP associated with reward processing. Two objectives motivated this study: first, to illustrate the relationship between the ERN and anxious symptoms, and the relationship between the FN and depressive symptoms; second, to explore whether the ERN and the FN relate *uniquely* to anxiety and depression, respectively, in children. EEG was collected from twenty-five 11- to 13-year-old participants (12 female; 23 Caucasian, 1 Asian, 1 of Caucasian and Hispanic ethnicity) during tasks designed to elicit an ERN and an FN. Participants and a parent completed questionnaires assessing the participant's anxious and depressive symptomatology. Increasing anxiety was related to a larger ERN, and increasing depression was related to a smaller FN. Further analysis demonstrated that these relationships remained significant when controlling for the contribution of other variables; that is, the ERN continued to predict anxiety when controlling for the FN and depression, and the FN continued to predict depression when controlling for the ERN and anxiety. Thus, in late childhood and early adolescence, the ERN and the FN appear to relate uniquely to anxious and depressive symptoms, respectively. Although this research is still in early stages, the ERN and the FN have the potential to inform trajectories of risk for anxiety and depression, and could be utilized in clinical settings as cost- and labor-efficient neural biomarkers.

By the age of 16, more than 35% of children will have met criteria for a psychiatric illness at some point in their lives (e.g., Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Beyond the distress this causes the child, childhood psychopathology is associated with increased economic burden for the child's family; parents of children with mental disorders are more likely to cut hours at work or quit their jobs to take care of their children (Busch & Barry, 2007). Anxiety and depression represent a substantial portion of mental disorders in children and adolescents, and cumulative prevalence rates increase over the course of adolescence, each reaching approximately 10% by age 16 (Costello et al., 2003).

In addition to the immediate consequences to children and their parents, the negative effects of childhood mental illness persist. Children diagnosed with

anxiety disorders, for instance, are at increased risk for anxiety disorders later in life (Last, Perrin, Hersen, & Kazdin, 1996). Furthermore, young people with anxiety disorders are at increased risk for subsequent early parenthood and academic problems (Woodward & Fergusson, 2001), and may also be at increased risk for later substance abuse disorders (Compton, Burns, Helen, & Robertson, 2002; Kendall, Safford, Flannery-Schroeder, & Webb, 2004; Woodward & Fergusson, 2001). Childhood depression, too, is associated with lasting consequences. Earlier onset of depression in childhood is linked to a longer episode duration (Kovacs, Feinberg, Crousenovak, Paulauskas, & Finkelstein, 1984), and, like childhood anxiety disorders, childhood depressive disorders are associated with increased risk for adult psychopathology as well as early parenthood (Fergusson & Woodward, 2002) and impaired academic performance (Birmaher et al., 1996). Furthermore, children and adolescents who have experienced depression

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are at higher risk for suicide in adulthood (Harrington et al., 1994).

Given the high prevalence rates and lasting consequences of childhood anxiety and depression, effective prevention efforts are essential. Existing preventive interventions for anxiety and depression in children and adolescents have been somewhat successful (Clarke et al., 1995; Dadds et al., 1999; Gillham et al., 2006; Neil & Christensen, 2009). One study of a universal school-based anxiety intervention program for sixth- and ninth-grade children found that the intervention decreased anxiety in all children, although it was more successful among younger children (Barrett, Lock, & Farrell, 2005). In fact, there may be a benefit to targeting children at even younger ages; it has been suggested that children of preschool and early primary school age may be more likely to benefit from therapy given their increased neural and behavioral flexibility (Hirshfeld-Becker & Biederman, 2002). Moreover, targeting preschool-age children for treatment may provide them with coping skills for anxiety that arises during the transition to elementary school (Hirshfeld-Becker & Biederman, 2002). Likewise, preventive interventions can reduce the incidence of depression by 22% (Cuijpers, van Straten, Smit, Mihalopoulos, & Beekman, 2008) and may reduce economic burden by obviating more serious measures such as hospitalization (Clarke et al., 1995).

OVERLAP OF ANXIETY AND DEPRESSION

As research on preventive intervention for anxiety and depression continues, it will be important to identify markers of risk in order to focus efforts on the children who are most likely to benefit. However, anxiety and depression are highly comorbid and have been notoriously difficult to disentangle. Of adults with major depressive disorder, 50% to 60% report having experienced an anxiety disorder (Kaufman & Charney, 2000), and approximately 70% of those with a lifetime history of an anxiety disorder have experienced major depressive disorder (Moffitt et al., 2007). Comorbidity rates are similar in young people: Among children and adolescents with a depressive disorder, 30% to 75% have comorbid anxiety (Angold & Costello, 1993; Birmaher et al., 1996). Contributing to this overlap is the fact that the criteria for anxiety and depressive disorders in the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev. [*DSM-IV-TR*]; American Psychiatric Association, 2000) share a number of symptoms. Some have even argued that depression and some forms of anxiety may, in fact, be manifestations of the same disorder (Kendler, Neale, Kessler, Heath, & Eaves, 1992; Tyrer, 1996; Vollebergh et al., 2001; Watson, 2005).

Despite their commonalities, however, there are reasons to believe that anxiety and depression are separable. Both factor-analytic models (Brown, Chorpita, & Barlow, 1998; Clark & Watson, 1991; Joiner, Catanzaro, & Laurent, 1996; Turner & Barrett, 2003; Watson, Clark, Weber, & Assenheimer, 1995) and genetic studies (Mineka, Watson, & Clark, 1998; Thapar & McGuffin, 1997) suggest that in addition to shared characteristics, anxiety and depression are associated with specific factors related to hyperarousal and low positive affectivity, respectively. Therefore, the current diagnostic system may simply not be optimized to capture features that differentiate the two.

A promising alternative to the current system is an approach that characterizes psychopathology in terms of underlying core neural processes and systems (e.g., Insel et al., 2010). In the current article, we focus on brain systems that have been implicated in anxiety and depression (i.e., error-monitoring and reward processing), which we measure using event-related brain potentials (ERPs). ERPs are collected by recording electroencephalographic (EEG) activity while presenting the subject with a series of stimuli. By averaging together multiple EEG epochs following the same type of event (e.g., a stimulus or the person's response), the trial-to-trial electrical noise is averaged out and more reliable patterns of electrocortical activity—or ERPs—become apparent.

In relation to anxiety and depression, two ERPs are of particular interest: the error-related negativity (ERN) and the feedback negativity (FN). Recent work has provided evidence that these ERPs relate to anxious and depressive symptomatology, respectively. Moreover, data suggest that these ERPs may reflect biomarkers of risk.

THE ERN

The ERN arises shortly after the commission of an error (Carter & van Veen, 2007; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring, Goss, Coles, Meyer, & Donchin, 1993; Holroyd, Dien, & Coles, 1998; Nieuwenhuis, Ridderinkhof, Blow, Band, & Kok, 2001). Typically, the ERN is elicited using tasks in which the participant is likely to make an occasional incorrect response. In a letter version of the flankers task, for instance, participants might be asked to identify a central letter surrounded by other letters ("HHSHH" or "HHHHH"). When the EEG is time-locked to the average of all errors, a negative-going deflection in the ERP waveform—the ERN—emerges approximately 50 ms after the onset of the response (Carter & van Veen, 2007).

The ERN has been conceptualized as an error-monitoring signal originating in the anterior cingulate cortex (ACC; Carter & van Veen, 2007; Holroyd & Coles, 2002; van Veen & Carter, 2002). Errors lead to increases in skin conductance and changes in heart rate (Hajcak, McDonald, & Simons, 2003), pupil dilation (Critchley, Tang, Glaser, Butterworth, & Dolan, 2005), and potentiation of the defensive startle reflex (Hajcak & Foti, 2008); these findings are consistent with the notion that errors activate defensive motivational systems. Moreover, amplitude of the ERN is modulated by the threat-value of errors; for instance, it is larger when errors are more financially costly and when performance is being evaluated (Hajcak, Moser, Yeung, & Simons, 2005). The ERN is also enhanced when errors are punished (Riesel, Weinberg, Endrass, Kathmann, & Hajcak, 2012). Collectively, the data suggest that the ERN is not purely a reflection of behavioral performance but rather that the ERN also reflects the degree to which errors are aversive or threatening (Weinberg, Riesel, & Hajcak, 2012).

Relative to healthy controls, an enhanced (i.e., more negative) ERN has also been observed in adults with both obsessive-compulsive disorder (OCD; Endrass, Klawohn, Schuster, & Kathmann, 2008; Gehring, Himle, & Nisenson, 2000) and generalized anxiety disorder (Weinberg, Olvet, & Hajcak, 2010). Developmental studies have produced similar results: Children with OCD show an enhanced ERN compared to controls (Hajcak, Franklin, Foa, & Simons, 2008). Ladouceur, Dahl, Birmaher, Axelson, and Ryan (2006) found that 8- to 14-year-old children with anxiety disorders (most of whom met criteria for generalized anxiety disorder) also showed relatively large ERNs. An enhanced ERN has been observed in clinically anxious children as young as 6 years old (Meyer et al., 2013). Likewise, Meyer, Weinberg, Klein, and Hajcak (2012) found that among 11- to 13-year-old children, there was an association between trait anxiety and ERN, such that more anxious children had a larger ERN. We have argued that errors are threatening to the individual and that variation in the ERN in part reflects the degree to which errors are aversive; thus, the relationship between ERN and anxiety is consistent with the well-established association between anxiety and hypervigilance to threat (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007; Mogg & Bradley, 1998).

Moreover, fMRI studies have found that OCD (Fitzgerald et al., 2005; Stern et al., 2011; Ursu, Stenger, Shear, Jones, & Carter, 2003) and high trait anxiety (Paulus, Feinstein, Simmons, & Stein, 2004) are associated with hyperactivation of neural circuits involved in error monitoring. Thus, evidence from both ERPs and fMRI suggests a link between anxiety and hyperactive error-monitoring activity of the ACC.

The ERN also appears to relate to *risk* for anxiety. Among adolescents who had high behavioral inhibition—a risk factor for anxiety disorders—during childhood, a larger ERN is associated with an increased likelihood of clinically significant anxiety; this effect is not present in adolescents who had low behavioral inhibition during childhood (McDermott et al., 2009). Variation in the ERN has also been related to familial risk for anxiety among 6-year-old children (Torpey et al., 2013).

THE FN

In contrast to the ERN, which is associated with the internal detection of errors, the FN is elicited by external feedback. The FN is frequently elicited using a gambling task in which participants can win or lose money on each trial; these outcomes are often completely random, and thus feedback is not contingent on performance. The FN emerges as an apparent negative deflection in the ERP waveform approximately 250 to 300 ms after the presentation of feedback indicating loss compared to gain (Bellebaum & Daum, 2008; Hajcak, Moser, Holroyd, & Simons, 2006, 2007).

Historically, the FN has been thought to arise from similar processes as the ERN, originating from the ACC (Holroyd & Coles, 2002). In fact, researchers have referred to the FN as the feedback ERN (fERN; Holroyd, Nieuwenhuis, Yeung, & Cohen, 2003), and conceptualized it as signaling that outcomes were worse than anticipated (Hajcak et al., 2006; Holroyd & Coles, 2002). More recent evidence, however, suggests that the FN may actually reflect neural response to *desired* outcomes; that is, there is a reward-related positive ERP that is absent on nonreward trials (Baker & Holroyd, 2011; Bernat, Nelson, Steele, Gehring, & Patrick, 2011; Carlson, Foti, Mujica-Parodi, Harmon-Jones, & Hajcak, 2011; Foti, Weinberg, Dien, & Hajcak, 2011). In a recent study by Carlson et al. (2011), the amplitude of the FN was found to correlate with blood oxygenation level dependent activation in reward-related brain areas using fMRI. Furthermore, variations in the amplitude of the FN have been tied to genetic factors related to extrasynaptic dopamine (Foti & Hajcak, 2012), which is involved in reward-related processing.

The relationship between the FN and reward makes it an excellent candidate to investigate with regard to depression. One of the primary *DSM-IV-TR* criteria for a major depressive episode is anhedonia, or diminished interest or pleasure in activities (American Psychiatric Association, 2000)—in other words, reduced reward sensitivity. Indeed, evidence links depression with a reduced FN. A blunted FN has been observed in adults with higher self-reported depression (Foti & Hajcak, 2009) and in relation to greater state levels of sadness (Foti & Hajcak, 2010). Among 8- to 13-year-olds,

those who are more depressed have a blunted FN (Bress, Smith, Foti, Klein, & Hajcak, 2012). These findings are consistent with evidence from fMRI (Forbes et al., 2006) and behavioral studies (Forbes, Shaw, & Dahl, 2007), which have found that depressed children are characterized by decreased reward-related neural activity and reduced behavioral differentiation between low- and high-magnitude rewards. Thus, as with anxiety and dysfunctional error monitoring, evidence from both ERP and fMRI studies has converged on the same finding: Depression is associated with dysfunction in neural systems responsible for processing reward.

In addition to the association between FN and *current* depression, adolescents at familial *risk* for depression have a stronger association between sadness and FN amplitude than peers who are not at familial risk (Foti, Kotov, Klein, & Hajcak, 2011). Moreover, a smaller FN has been found to predict subsequent increased depressive symptoms and major depressive episodes in previously nondepressed adolescents (Bress, Foti, Kotov, Klein, & Hajcak, 2013). Even at a very young age, temperamental risk for depression (i.e., low positive emotionality and maternal history of depression) is associated with a smaller FN (Kujawa, Hajcak, Dyson, Olino, & Klein, 2013). Together, these findings suggest that, beyond its association with current depressive symptomatology, a blunted FN may constitute a risk factor for depression in healthy children.

ERN AND FN AS UNIQUE BIOMARKERS

Existing research lends fairly strong support to associations between an increased ERN and anxiety, and between a reduced FN and depression. However, considering the extensive comorbidity between anxiety and depression, as well as the overlap in symptomatology and genetic variation between the two disorders, it would be useful to explore the extent to which the ERN and the FN may relate differentially to anxiety and depression in children. As a first pass at addressing this question, we conducted an exploratory reanalysis of previously reported data (Bress et al., 2012; Meyer et al., 2012) with two goals: first, to illustrate the relationship between the FN and depressive symptoms, and the relationship between the ERN and anxious symptoms; second, to explore the specificity of these relationships. That is, our aim was to determine whether the ERN and the FN might relate *uniquely* to anxiety and depression, respectively, in children.

METHOD

Participants

Participants were recruited using a commercial mailing list of families from Stony Brook and the surrounding community—suburban areas approximately 60 miles from New York City—with children between the ages of 8 and 13. Children were considered eligible for participation if they fell within this age range. Recruitment letters were sent to 800 families, which were followed by phone calls. Of those contacted, 69 children participated in the overall study; further details about the original sample may be found elsewhere (Bress et al., 2012; Meyer et al., 2012).

Participants with low-quality data recordings were excluded. We previously found that the FN related to depressive symptoms in 8- to 13-year-olds (Bress et al., 2012); in the same sample, we found that the ERN was related to anxiety in older—but not younger—children (Meyer et al., 2012). Because the goal of the current study was to assess the specificity of the relationships between the ERN and anxiety, and between the FN and depressive symptoms, we analyzed both components among the older 28 participants. The younger participants (ages 8–10, $M = 9.24$, $SD = .74$) were not included in the current analysis.

Three additional participants were excluded because their ERN, FN, or score on one of the questionnaire measures fell more than 3 standard deviations from the mean. The final data set included 25 participants (12 female) between the ages of 11 and 13 ($M = 12.12$, $SD = .78$). Of those participants, 23 were of Caucasian ethnicity, one was of Asian ethnicity, and one was of mixed Caucasian and Hispanic ethnicity. Participants were paid $40.00 for their participation, plus $5.00 in earnings from the doors task.

Tasks

ERPs were elicited using two computer tasks: an arrow version of the flankers task, and a guessing task (i.e., the doors task). Both tasks were administered on a Pentium D Class computer with a 19-in. (48.3 cm) monitor, using Presentation software (Neurobehavioral Systems, Inc., Albany, CA).

Flankers task. To elicit an ERN, participants completed an arrow version of the flankers task (Eriksen & Eriksen, 1974) consisting of 11 blocks of 30 trials each (330 trials in total). On each trial, a row of five arrowheads was displayed for 200 ms, and participants were asked to determine the direction of the center arrowhead by pressing the corresponding mouse button. On half of the trials, the center arrowhead was compatible with the surrounding arrowheads ($<<<<<$ or $>>>>>$); on the other half, it was incompatible ($<<><<$ or $>><>>$). Each stimulus presentation was followed by an intertrial interval (ITI) of a random duration ranging from 2,300 to 2,800 ms.

Participants were encouraged to complete the task both quickly and accurately. At the end of each block, they were given on-screen feedback about their performance. If accuracy was less than 75%, participants were presented with the message, "Please try to be more accurate"; if accuracy was greater than 90%, they saw the message, "Please try to respond faster." For blocks on which their accuracy was between 75% and 90%, participants were given the message, "You're doing a great job." The flankers task lasted approximately 10 to 12 min.

Doors task.   To elicit an FN, participants completed a guessing task similar to those used in previous studies (Dunning & Hajcak, 2007; Foti & Hajcak, 2009, 2010), consisting of three blocks of 20 trials each (60 trials in total). Before the task began, participants were told that they would have the chance to win actual money and that the goal of the task was to win as much money as possible. On each trial, participants viewed an image of two doors and were instructed to choose either the right or left door by clicking the corresponding mouse button; the image of the doors remained on the screen until a response was made. After a delay of 1,000 ms, participants were presented with feedback indicating that they had either won $0.50 (represented by a green ↑) or lost $0.25 (represented by a red ↓); these values were chosen such that the subjective values would be perceived as equivalent to participants (Tversky & Kahneman, 1981, 1992). Feedback remained on the screen for 2,000 ms, followed by a fixation mark presented for 1,500 ms. Finally, the message "click for next round" appeared and remained onscreen indefinitely until the participant clicked a mouse button. The doors task lasted approximately 5 to 7 min.

Questionnaires

Participants completed the Screen for Child Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997), a measure of anxiety symptoms. The self-rated version of the SCARED (SCARED:SR) consists of 38 items rated on a scale from 0 (*not true or hardly ever true*) to 2 (*very true or often true*), with items summed to produce a total score. Test–retest reliability of the SCARED, measured in terms of intraclass correlations, ranges from .70 to .90, with good internal consistency ($\alpha = .74$–.93) and discriminant validity (Birmaher et al., 1997).

Participants were also given the short version of the Children's Depression Inventory self-report (CDI:SR; Kovacs, 1992), a measure used to assess depressive symptoms. The CDI:SR consists of 10 items with responses rated on a scale from 0 (e.g., *I am sad once in a while*) to 2 (e.g., *I am sad all the time*). Items are

summed to produce a total score. Test–retest reliability of the CDI long form ranges from .56 to .87, and correlations between the short and long versions of the CDI are high (Sitarenios & Kovacs, 1999). A wide range of studies indicate that the CDI has strong construct validity (Sitarenios & Kovacs, 1999).

Parents completed informant versions of both the SCARED (SCARED:P) and the CDI (CDI:P). The SCARED:P follows the same format as the SCARED:SR, with a total of 38 items scored from 0 to 2. Like the SCARED:SR, the SCARED:P has good test–retest reliability, internal consistency, and discriminant validity (Birmaher et al., 1997).The CDI:P consists of 17 questions similar to the CDI:SR, which are scored from 0 (*not at all*) to 3 (*much or most of the time*). Test–retest reliability of the CDI:P is high, and it shows good agreement with teachers' ratings on the Children's Depression Rating Scale (Wierzbicki, 1987).

Because agreement between self- and parent reports tends to be low (Achenbach, Mcconaughy, & Howell, 1987), interpretation of parent versus self-ratings can be problematic. In fact, both may be viewed as contributing different and useful information regarding the construct being measured. Therefore, for both measures, self-report and parent-report data were aggregated into a single total measure (SCARED and CDI, respectively). Aggregate measures were calculated as the sum of the Z scores from the child and parent reports.

Procedure

Participants gave informed assent, and their parents gave informed consent, for their participation in the study. After the consenting process, participants completed a series of questionnaires including the SCARED: SR and the CDI:SR. The computer tasks were explained to the participants, and EEG electrodes were applied. Participants completed several computer tasks that included the flankers and doors tasks; task order was counterbalanced across participants. This study was formally approved by the Stony Brook University Institutional Review Board.

Psychophysiological Recording and Data Reduction

EEG was recorded from a custom 34-electrode elastic cap configured according to the 10/20 system, using the ActiveTwo BioSemi System (BioSemi, Amsterdam, the Netherlands). Additional data were recorded from the mastoids, and an electrooculogram was collected from electrodes placed 1 cm from the outer corners of the eyes and 1 cm above and below the right eye. Recordings were amplified at the electrode with a gain of 1, and the data were digitized at 24-bit resolution with a sampling rate of 1024 Hz using a low-pass fifth-order

sinc filter with a half-power cutoff of 204 Hz. EEG was measured online with respect to a common mode sense active electrode, forming a monopolar channel.

BrainVision Analyzer (Brain Products, Munich, Germany) was used for offline analysis. Data were rereferenced to the average of the recordings from the left and right mastoid channels, and a band-pass filter with cutoffs of .1 and 30 Hz was applied. Ocular artifacts were corrected using the procedure developed by Gratton and colleagues (Gratton, Coles, & Donchin, 1983). Physiological artifacts were corrected using a semiautomated procedure with a maximum allowed voltage step of 50 μV between sampling points, a maximal voltage difference of 300 μV in a given trial, and a maximum allowed voltage of .5 μV within an interval of 100 ms. Remaining artifacts were rejected manually using visual inspection of the data.

For the ERN, EEG recordings were segmented into response-locked epochs from −300 to 1,000 ms relative to the onset of the response. Segments were baseline-corrected using mean amplitude in the window from −300 to −100 ms relative to response onset. In addition to the ERN, a smaller negative deflection—the correct-related negativity (CRN)—frequently appears within the same time window after correct responses (Ford, 1999; Mathalon, Whitfield, & Ford, 2003; Scheffers & Coles, 2000); therefore, both the ERN and the CRN were measured. Separate averages were created for error and correct trials, and the ERN and the CRN were defined as the mean activity in a 50-ms window surrounding the most negative peak between −50 and 100 ms relative to response onset for error and correct trials, respectively. Error-related activity was maximal at frontocentral sites (Fz, FCz, Cz, FC1, and FC2); therefore, data from these sites were pooled.

For the FN, EEG was segmented into feedback-locked epochs from −200 to 600 ms relative to the onset of feedback. Segments were baseline corrected using mean amplitude of the EEG within the 200 ms before feedback onset. Separate averages were created for loss and win trials. ERPs were quantified as the mean activity from 275 to 375 ms after feedback onset at a pooling of Fz and FCz sites. The FN was defined as the mean amplitude of the response to losses minus the mean amplitude of the response to gains.

RESULTS

In the flankers task, participants committed a mean of 47.88 errors ($SD = 23.80$) and made correct responses on a mean of 83.89% ($SD = 9.03$) of trials. Consistent with prior research, a negative deflection in the waveform was apparent approximately 50 ms after error and correct responses (i.e., the ERN and the CRN, respectively). As expected based on the results of other studies and on previous analyses from the current data set (Meyer et al., 2012), the ERN was significantly more negative ($M = -2.65\,\mu V$, $SD = 5.42$) than the CRN ($M = 2.53\,\mu V$, $SD = 4.44$), $t(24) = -4.14$, $p < .001$.

In the doors task, also consistent with prior work, a negative deflection in the ERP waveform (i.e., the FN) was apparent approximately 330 ms after feedback onset. Response to losses ($M = 5.54\,\mu V$, $SD = 7.13$) was significantly less positive than response to gains ($M = 10.43\,\mu V$, $SD = 7.86$), $t(27) = -4.51$, $p < .001$. The mean amplitude of the FN (i.e., losses minus gains) was $-4.89\,\mu V$ ($SD = 5.42$).

Mean SCARED:P and SCARED:SR were 11.76 ($SD = 6.39$) and 18.08 ($SD = 7.14$), respectively; mean CDI:P and CDI:SR were 8.58 ($SD = 5.66$) and .94 ($SD = 1.47$), respectively. Cronbach's alphas for the SCARED:P, SCARED:SR, CDI:P, and CDI:SR were .78, .74, .82, and .68, respectively. SCARED and CDI were not significantly correlated ($r = .28$, $p = .17$), and ERN and FN were not significantly correlated ($r = .16$, $p = .44$).

A scatter plot of the relationship between the ERN and the SCARED is depicted in Figure 1 (left). ERN was negatively associated with SCARED ($r = -.47$, $p < .05$), such that participants with greater SCARED
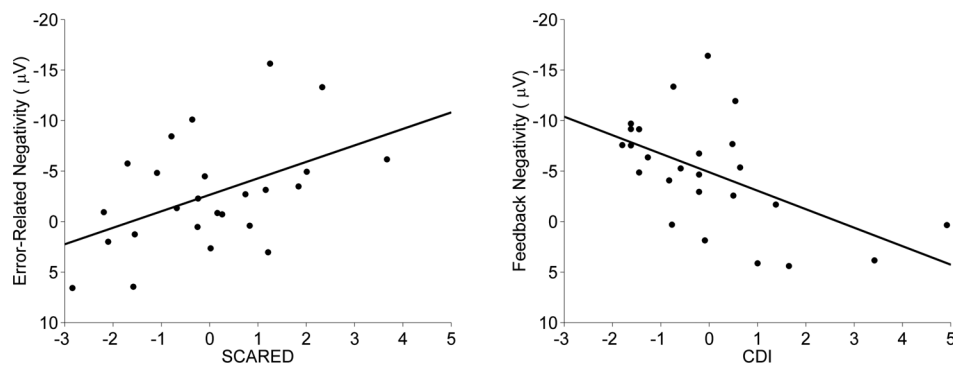

FIGURE 1 Scatter plots depicting the relationship between the error-related negativity and the Screen for Child Anxiety Related Emotional Disorders (SCARED; left) and the relationship between the feedback negativity and the Children's Depression Inventory (CDI; right).

scores had a larger (i.e., more negative) ERN. ERN did not correlate significantly with CDI ($r = -.26$, $p = .22$). A scatter plot of the relationship between the FN and the CDI is depicted in Figure 1 (right). FN was positively associated with CDI ($r = .54$, $p < .01$), such that participants with greater CDI scores had a smaller (i.e., less negative) FN. FN did not correlate significantly with SCARED ($r = .21$, $p = .31$).[1]

When ERN, FN, and CDI were entered as simultaneous predictors of SCARED in a multiple regression, the overall model was significant ($R^2 = .31$), $F(3, 21) = 3.16$, $p < .05$. ERN contributed significantly to the variation in SCARED ($\beta = -.53$, $p < .05$); FN ($\beta = .31$, $p = .20$), and CDI ($\beta = -.02$, $p = .93$) did not.

When the ERN, FN, and SCARED were entered into a regression predicting CDI, a complementary result emerged. Again, the overall model was significant ($R^2 = .42$), $F(3, 21) = 5.00$, $p < .01$. In contrast to the previous regression, however, ERN ($\beta = -.36$, $p = .08$) and SCARED ($\beta = -.02$, $p = .93$) did not significantly predict CDI, but FN did ($\beta = .61$, $p < .01$).

DISCUSSION

As reported previously (Bress et al., 2012; Meyer et al., 2012), children with higher anxiety scores showed an enhanced ERN, and children with higher depression scores showed a blunted FN. However, novel analyses presented here found that the ERN *uniquely* predicted anxiety when controlling for FN and depression, and the FN *uniquely* predicted depression when controlling for ERN and anxiety. This finding suggests that the ERN and the FN may index relatively unique cognitive processes that underlie anxiety and depression.

In the context of functional hypotheses of the ERN and the FN, the current results suggest that anxiety may be uniquely characterized by enhanced performance monitoring and error detection subserved by the ACC and related neural circuits; on the other hand, depression may be uniquely characterized by diminished reward sensitivity related to mesocorticolimbic dopamine circuits. The sample size used in the current analyses was small, and these results will need to be replicated in a larger sample. However, the current findings are consistent with factor analytic (Clark & Watson, 1991) and genetic studies (Mineka et al., 1998; Thapar &

McGuffin, 1997), which have demonstrated specific factors associated with anxiety and depression.

The value of physiological indicators of psychopathology such as ERPs has been emphasized by the Research Domain Criteria (RDoC; Insel et al., 2010), an initiative that is being developed with the aim of addressing some inadequacies of the current categorical diagnostic system (i.e., the *DSM-IV-TR*; American Psychiatric Association, 2000). In contrast to the *DSM-IV-TR*, which is based largely on apparent symptoms rather than on the underlying mechanisms of psychopathology, the goal of RDoC is to understand the pathophysiology of mental disorders, which are conceptualized in terms of brain disorders (Insel et al., 2010). According to this conceptualization, all domains are grounded in neural systems. Although the RDoC matrix encompasses measures of those systems at various levels of analysis, neural measures such as ERPs constitute a major area of focus. Thus, measures that index dysfunction of core neural circuits implicated in psychopathology might serve as relatively pure measures of disease-relevant processes (i.e., biomarkers or biosignatures; Insel et al., 2010)—and the ERN and the FN may represent two such biomarkers. Inasmuch as each appears to relate uniquely to anxiety or depression, respectively, the ERN and the FN may be aligned more closely than standard measures with the processes that distinguish these overlapping disorders.

Biomarkers hold a particularly important advantage over self- and informant reports for evaluating children: namely, they provide a relatively objective measure of the child's cognitive and neural processes, which can be measured reliably regardless of the child's ability to provide an accurate self-report. Particularly in younger children, self-reports are not always reliable (Edelbrock, Costello, Dulcan, Kalas, & Conover, 1985). Moreover, agreement between self- and parent reports tends to be low, particularly during midchildhood (Achenbach et al., 1987). Young people tend to report more internalizing disorders than their parents, whereas parents tend to report more externalizing (Grills & Ollendick, 2002; Jensen et al., 1999). These inconsistencies make interpretation difficult, as it is unclear whether the child's true level of symptomatology is most accurately represented by the child's self-report, the parent's report, or some combination of the two.

The use of ERPs such as the ERN and the FN also carries a number of practical advantages. The relatively low price point of EEG systems makes them a more affordable option than more expensive imaging techniques such as fMRI. Moreover, many fMRI scanners require a dedicated specialist or technician to run an imaging session, whereas EEG can be collected by a research assistant. With appropriate software and training, it can take less than 15 min for a research

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[1]When the analyses were run separately for parent- and child-reported symptoms, the results were similar to the correlations using the aggregate scores, but effect sizes and significance levels varied. SCARED:P was significantly correlated with the ERN ($r = -.48$, $p < .05$), but SCARED:SR was not ($r = -.27$, $p = .20$). On the other hand, CDI:SR was significantly correlated with FN ($r = .51$, $p < .05$), whereas the CDI:P was only marginally significantly correlated ($r = .37$, $p = .07$).

assistant to apply an EEG cap and begin recording. Once setup is completed, many tasks used to elicit ERP components last 10 min or less. Finally, the processing of EEG data can be substantially less time and labor intensive than the processing of fMRI data. As indicated in the aims of the current issue, there is a need for affordable and labor-efficient psychophysiological measures that transcend research settings and could be used in a clinical context. In these regards, EEG is a particularly suitable technique.

The current findings regarding the ERN and the FN provide one example of how ERPs could be used to study core neural dysfunctions that relate to psychopathology in an objective, cost- and labor-efficient way. The ERN (Olvet & Hajcak, 2009b; Pontifex et al., 2010) and the FN (Marco-Pallares, Cucurell, Munte, Strien, & Rodriguez-Fornells, 2011) both become stable after relatively few trials, making them quick to collect and therefore especially useful for clinical contexts in which time is a limited commodity. EEG setup takes 15 min, and the ERN and FN tasks each last less than 15 min; therefore, within 45 min, two different biomarkers can be collected. After data collection, processing takes no more than 15 min for each ERP. Moreover, the ERN has excellent psychometric properties, with high test–retest reliability over a period of weeks (Olvet & Hajcak, 2009a; Segalowitz et al., 2010) and as long as 2 years (Weinberg & Hajcak, 2011). The existing evidence suggests that the FN shows similar reliability (Segalowitz et al., 2010), although further research will be needed to replicate these effects. The stability of these ERPs over time supports the possibility of their use as biomarkers of risk.

As research into the specificity of the ERN and the FN progresses, a variety of relevant questions need to be addressed. The current study used an unselected sample; it would be informative to investigate the same associations in a psychiatric sample. Existing evidence suggests that a similar finding might emerge: the increased ERN has been found to be specific to anxiety in clinically anxious individuals compared to individuals with comorbid anxiety and depression (Weinberg, Klein, & Hajcak, 2012). In addition, it is not yet clear at what point during the course of development the ERN and the FN begin to reliably relate to anxiety and depression, respectively. Moreover, the current study took place at a single time point and related ERPs to *current* symptoms. Prior research suggests that both the ERN and the FN may relate to risk for later psychopathology (Bress et al., 2013; Foti, Kotov, et al., 2011; Kujawa et al., 2013; McDermott et al., 2009; Torpey et al., 2013), but the extent of these relationships is not yet clear, and it remains to be seen whether the ERN and FN have unique predictive ability. We are currently conducting a large-scale longitudinal study with children

and adolescents across a range of ages and stages of pubertal development that will address some of these questions.

If the current results are replicated, they could have substantial clinical utility; the ERN, the FN, and other ERPs could be used to guide both preventive interventions and treatment. Current preventive interventions are effective, but the number needed to treat (i.e., the number of people who would need be treated for one additional person to improve compared to an untreated group) is still relatively high (Cuijpers et al., 2008). Future research might investigate whether psychopathology prevention efforts in children could be informed by neurobiological measures such as the ERN and FN. For instance, it could be cost effective to select children for a depression prevention program based, in part, on the magnitude of their FN.

Moreover, clinical cutoffs would need to be determined before ERPs could be used in clinical practice. Similar to a body mass index above 30 indicating obesity (WHO Expert Committee on Physical Status, 1995) or an IQ score below 70 indicating intellectual disability (Grossman, 1973), an ERP amplitude that crosses a particular threshold might be seen as an indicator of risk for psychopathology. Given idiosyncratic differences in scalp-measured brain activity between individuals, the cutoffs might require more complicated calculations based on the child's baseline levels. Furthermore, the sample used in the current study was relatively homogeneous; therefore, norms would need to be established in a large-scale study spanning a wide range of age groups, ethnic groups, and socioeconomic statuses— which, given the relatively low price point of EEG systems, might be feasible.

The current study was limited by the fact that the analyses included only the older subset of participants. The decision to exclude the younger participants was based on previously reported results from the current data set (Meyer et al., 2012) in which no association was found between the ERN and anxiety in the subset of 8- to 10-year-old children. Given this decision, the interpretation of the results is necessarily more limited; the same results might not be found in a younger sample.

However, evidence from separate research suggests that the relationship between the ERN and anxiety may, in fact, exist even in very young children. Meyer and colleagues recently reported an enhanced ERN in 6-year-old children with diagnosed anxiety disorders (Meyer et al., in press). It is possible that the relationship between ERN and normative variation in anxiety does not emerge until later, in early adolescence; further work with larger samples will be needed to clarify this question. To the extent that abnormalities in the ERN may precede the observable symptoms of anxiety— much as a reduced FN precedes the onset of clinically

diagnosable depressive episodes (Bress et al., 2013)—the ERN might serve as a useful predictor of emerging anxiety disorders in adolescence.

Given the extensive overlap between anxiety and depression in children (Angold & Costello, 1993; Birmaher et al., 1996), there is a need to understand dysfunction of brain systems that uniquely characterize these disorders. ERPs represent an objective, reliable, cost-effective, and relatively easy-to-use means of indexing core neural systems in children. The current findings suggest that the ERN and the FN, in particular, may relate uniquely to specific psychological processes underlying anxiety and depression. Although this research is still in its early stages, the current results provide an exciting first step toward the use of ERPs as unique biomarkers of psychopathology.

The advantages of ERP methodology are not limited to the ERN and the FN; other components might be used to assess additional processes underlying psychopathology. For instance, the P1, N2 pc, P300, and late positive potential have been used to index aspects of the heightened attentional bias toward threat that is associated with anxiety (Macnamara, Kappenman, Black, Bress, & Hajcak, 2013). The incorporation of the ERN, the FN, and other ERPs into research and clinical practice has the potential to aid in the differentiation and prediction of anxiety and depression, and might eventually contribute to improved screening procedures, treatment, or prevention programs for children.

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