



The development of the error-related negativity in large sample of adolescent females: Associations with anxiety symptoms[☆]

Alexandria Meyer^{*}, Corinne Carlton, Sierah Crisler, Alex Kallen

Department of Psychology, Florida State University, 1107W Call St., Tallahassee, FL, 32304, United States



ARTICLE INFO

Keywords:

Error-related negativity (ERN)
Anxiety
Biomarker
Development
Children
Adolescents
Event-related potentials (ERPs)

ABSTRACT

Anxiety is the most common form of psychopathology and tends to begin early in the course of development. Given this, there is great interest in identifying developmental changes in neural systems that may delineate healthy versus anxious trajectories. A substantial amount of work has focused on the error-related negativity as a neural marker of anxiety. The ERN is a negative deflection in the event-related potential that occurs when individuals make mistakes and is increased in anxious individuals. A separate body of work has focused on normative developmental changes in the ERN - demonstrating an age-related increase in the ERN that occurs across childhood and adolescence. In the current study, we examine the ERN in relation to specific phenotypic expressions of anxiety during a core risk period in a sample of females (N = 220) ranging from 8 to 14 years old. Results from the current study suggest that error-related brain activity is related to both parent and child report of social anxiety symptoms, even when controlling for all other symptom scales. Additionally, mediation models suggest that the normative developmental increase observed in the ERN is partially mediated by increases in social anxiety symptoms. The current results are novel insofar as they identify a specific phenotypic expression of anxiety that underlies developmental increases in this neural biomarker.

1. Introduction

Anxiety is the most common form of psychopathology (Kessler, DuPont, Berglund, & Wittchen, 1999, 2005) and tends to begin early in the course of development (Beesdo, 2010; Beesdo, Knappe, & Pine, 2009; Last, Perrin, Hersen, & Kazdin, 1996). Given that the transition from late childhood to adolescence appears to be a core risk period for increases in anxiety (Beesdo et al., 2009; Copeland, Angold, Shanahan, & Costello, 2014), there is substantial interest in identifying developmental changes in neural systems that may delineate healthy versus anxious trajectories. Identifying neural markers that underlie the development of anxiety may improve prevention and intervention strategies. For example, some have proposed that neuroimaging methods may have direct clinical application insofar as they may predict treatment outcomes and/or guide clinical decisions about who needs treatment and what type of treatment they may benefit from (Ball, Stein, & Paulus, 2014; Bunford et al., 2017; Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015; Whitfield-Gabrieli et al., 2016).

A substantial amount of work has focused on the error-related negativity (i.e., ERN) as a neural marker of anxiety (Cavanagh &

Shackman, 2014; Hajcak, 2012; Meyer, 2016; Weinberg, Riesel, & Hajcak, 2012). The ERN is a negative deflection in the event-related potential waveform that occurs when individuals make mistakes on speeded reaction-time tasks (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring, Goss, Coles, Meyer, & Donchin, 1993) and is generated in the anterior cingulate cortex (ACC) – a region of the brain that integrates information about threat, punishment, and pain (Shackman et al., 2011). The ERN has been shown to be increased in anxious individuals in over 50 studies to date and is thought to index increased reactivity to making mistakes (Cavanagh & Shackman, 2014; Hajcak, 2012; Meyer, 2016; Weinberg, Klein, & Hajcak, 2012; Weinberg, Riesel et al., 2012).

Consistent with this, the ERN has been shown to be increased in adults with obsessive-compulsive disorder (OCD; Riesel, Kathmann, & Endrass, 2014),¹ generalized anxiety disorder (GAD; Weinberg, Klein et al., 2012), and social anxiety disorder (SAD; Endrass, Riesel, Kathmann, & Buhlmann, 2014). Additionally, the ERN can differentiate anxiety early in the course of development – 6-year-old children with anxiety disorders are characterized by an increased ERN (Meyer et al., 2013). Importantly, the ERN also indexes risk for anxiety. For example,

[☆] This study was funded by a National Institute of Mental Health (NIMH)-funded grant R01 MH097767.

^{*} Corresponding author.

E-mail address: meyer@psy.fsu.edu (A. Meyer).

¹ It should be noted that OCD is not included as an anxiety disorder in the DSM 5.

an increased ERN in young children (Meyer, Hajcak, Torpey-Newman, Kujawa, & Klein, 2015) and adolescents (Meyer, Nelson, Perlman, Klein, & Kotov, 2018) can predict the new onset of anxiety disorders, while controlling for baseline anxiety symptoms.

While the ERN indexes anxiety, it also appears to undergo normative changes across development. Indeed, Davies, Segalowitz, and Gavin (2004) observed an age-related increase in the magnitude of the ERN in a large sample between the ages of 7 and 18-years-old. Since this initial study, 14 studies have replicated this finding – suggesting that the ERN increases across childhood and adolescence, reaching stability in early adulthood (Tamnes, Walhovd, Torstveit, Sells, & Fjell, 2013). While age-related changes in the ERN have consistently been observed across a number of studies, little work has been done to elucidate the psychological processes that this developmental increase in the ERN may reflect. In light of the fact that the ERN indexes anxiety, the developmental increase in the ERN may, in part, reflect normative developmental changes in anxiety symptoms.

In the current study, we utilize a large sample of child and adolescent females ($N = 220$) to examine the ERN in relation to anxiety symptoms during a core risk period for developmental increases in anxiety (ages range from 8 to 14 years-old). We focus on females based on previous work suggesting they are more likely to experience anxiety (Pine, Cohen, Gurley, Brook, & Ma, 1998; Wittchen, Nelson, & Lachner, 1998). While the ERN has been linked to anxiety, few studies have examined the relationship between the ERN and specific facets of clinical anxiety symptoms. Furthermore, few studies have investigated this relationship in the context of late childhood and adolescence – a developmental stage wherein both anxiety symptoms and the ERN are increasing. In the current study, self-report measures completed by both the child and the parent were used to assess symptoms related to: panic, general anxiety, separation anxiety, social anxiety, and school phobia. Using the ERN measured while participants completed the flankers task, we used correlational and regression techniques to examine what specific subscale of anxiety symptoms the ERN relates to during this developmental period. In light of the fact that the ERN is thought to reflect sensitivity to making mistakes, as well as evidence that normative increases in social anxiety are particularly pronounced during adolescence (La Greca & Lopez, 1998; Wittchen, Stein, & Kessler, 1999), we hypothesized that while the ERN may relate to multiple symptom scales, it would have the strongest relationship with social anxiety. This hypothesis is based on previous work finding an increased ERN in individuals with social anxiety (Endrass et al., 2014; Kujawa et al., 2016), as well as work suggesting the ERN is specifically sensitive to social contexts (Barker, Troller-Renfree, Pine, & Fox, 2015). Importantly, a previous study in adolescents found that the ERN was associated with social anxiety, but not generalized anxiety (Kujawa et al., 2016) – suggesting that the ERN may have specific relationships with social anxiety during adolescence.

To examine whether age-related increases in the ERN reflect, in part, normative developmental changes in anxiety symptoms, we conducted mediation analyses. In the first model we examined whether the relationship between age and the ERN was mediated by parent-reported anxiety symptoms. In the second model, we examined the same pattern using child-reported anxiety symptoms. We hypothesized that the indirect path from age via anxiety symptoms to the ERN would be significant, suggesting that the developmental increase observed in the ERN is partially due to developmental increases in anxiety.

2. Method

2.1. Participant recruitment

Participants in the proposed research included 220 females between the ages of 8 and 14. Overall, 4% of participants were 8 years-old, 7% were 9 years old, 7% were 10 years-old, 35% were 11 years-old, 17% were 12 years-old, 15% were 13 years-old, and 15% were 14 years-old.

We recruited children and adolescents via a commercial mailing list of families that have a 8–14 year-old female living at home. We sent letters describing the study prior to an initial call, and screened families based on the following criteria: the child must live with at least one biological parent, the child and caretaker must speak English, and the child must not have a significant developmental or medical disability. Participants were paid \$20 per hour for their participation. The sample identified as 9% Hispanic, 8% African American, 83% Caucasian, and 6% as Other.

2.2. Protocol

During the lab visit, when families arrived in the laboratory, parents and children were consented by a graduate student. The current study was part of a larger NIMH-funded longitudinal study (R01 MH097767) focusing on neural markers of risk for depression. The assessment consisted of a variety of behavioral and psychophysiological measures, as well as the Flankers task described below. During the laboratory visit, children and parents both completed self-report measures, including the Screen for Child Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997).

2.3. Self-report

The current proposal focuses on dimensional measures of symptoms measured by the Screen for Child Anxiety Related Emotional Disorders (SCARED) questionnaire (Birmaher et al., 1997). Two versions of the SCARED were administered: one to the child or adolescent (C-SCARED) and one to the parent who accompanied the child or adolescent to the laboratory (P-SCARED). Both versions of the SCARED broadly assess symptoms of anxiety as they manifest in children, including symptoms of panic, general anxiety, separation anxiety, social phobia, and school phobia. Each version contains a 38 item scale on which the participant can answer: 0 (“not true or hardly ever true”), 1 (“sometimes true”), or 2 (“true or often true”). The maximum score for each version is 76 and both versions include 5 subscales scores: Panic/Somatic, General Anxiety, Separation Anxiety, Social phobia, and School Phobia.

Internal reliability for the SCARED has been shown to be satisfactory in previous studies (Birmaher et al., 1997; Muris, Merckelbach, Van Brakel, Mayer, & Birgit, 1999), for both parent and child reports of the total score (Cronbach's alphas: .92 and .92), as well as the subscales: Panic/Somatic (.83 and .76), General Anxiety (.79 and .82), Separation Anxiety (.76 and .74), and Social phobia (.70 and .80) (Muris et al., 1999). In the current study, internal reliability was as follows for the parent report: total, Cronbach's alpha = .92, Panic/Somatic = .80, General Anxiety = .86, Separation Anxiety = .74, Social phobia = .90, and School phobia = .69. Internal reliability was as follows for the child report: total, Cronbach's alpha = .97, Panic/Somatic = .83, General Anxiety = .85, Separation Anxiety = .73, Social phobia = .83, and School Phobia = .67.

2.4. Tasks and materials

The EEG was recorded while participants engage in a computer task used frequently in our lab to study error related brain activity: an arrowhead version of the Flankers task (Eriksen & Eriksen, 1974). During the task, participants were shown five arrowheads, and instructed to press the left or right mouse button as quickly as possible depending on the direction of the central arrowhead. There were two “compatible” conditions (“< < < < > > >”) and two “incompatible” conditions (“< < > < > >”). The stimuli were presented randomly such that 50% are incompatible. Each stimulus was presented for 200 ms, and the interval between the offset of one stimulus and the onset of the subsequent stimulus varied randomly between 2300–2800 ms. Participants completed a practice block containing 30 trials during which they were instructed to be both accurate and as fast

as possible. The actual task consisted of 11 blocks of 30 trials (330 trials total) with each block initiated by the participant. To encourage both fast and accurate responding, participants received feedback based on their performance at the end of each block. If performance was 75% correct or lower, the message “Please try to be more accurate” was displayed; performance above 90% correct was followed by “Please try to respond faster”; otherwise the message “You’re doing a great job” was displayed.

2.5. Psychophysiological recording and data analysis

Continuous EEG recordings were collected using an elastic cap and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Thirty-four electrode sites were used, as well as two electrodes on the left and right mastoids. Electrooculogram (EOG) generated from eye movements and eye blinks was recorded using four facial electrodes: horizontal eye movements were measured via two electrodes located approximately 1 cm outside the outer edge of the right and left eyes. Vertical eye movements and blinks were measured via two electrodes approximately 1 cm above and below the right eye. The EEG signal was preamplified at the electrode to improve the signal-to-noise ratio and amplified with a gain of one by a BioSemi ActiveTwo system. The data was digitized at a 24 bit resolution with a sampling rate of 1024 Hz using a low-pass fifth order sinc filter with a half-power cutoff of 204.8 Hz. Each active electrode was measured online with respect to a common mode sense (CMS) active electrode producing a monopolar (non-differential) channel. Offline, all data was referenced to the average of the left and right mastoids, and band-pass filtered between 0.1 and 30 Hz; eye-blink and ocular corrections were conducted per Gratton, Coles, and Donchin (1983). A semi-automatic procedure was employed to detect and reject artifacts. The criteria applied was a voltage step of more than 50.0 μV between sample points, a voltage difference of 300.0 μV within a trial, and a maximum voltage difference of less than .50 μV within 100 ms intervals. These intervals were rejected from individual channels in each trial. Visual inspection of the data were then conducted to detect and reject any remaining artifacts.

The EEG data were segmented for each trial beginning 500 ms before the response and continuing for 1000 ms after the response. The response-locked ERPs were averaged separately for each trial type (e.g., correct and incorrect responses) to derive the correct response negativity (i.e., CRN)² and the error related negativity (i.e., ERN), and baseline correction was performed using the interval from –500 to –300 ms. Average activity at Fz, FCz, and Cz between 0–100 ms after response was exported for each subject. In order to obtain a measure of differentiation between errors and correct responses, the average activity related to correct responses was subtracted from the average activity related to errors (i.e., the ΔERN). Additionally, we also utilized a regression-based method of calculating the difference between error and correct trials based on recent work suggesting this approach may provide a superior measure of within-subject variance (Meyer, Lerner, De Los Reyes, Laird, & Hajcak, 2017). Behavioral measures included both the number of error trials for each subject, as well as accuracy expressed as a percentage of all valid trials. Average reaction times (RTs) on error and correct trials were calculated separately, as well as RTs on correct trials following correct and error trials to evaluate post-error RT slowing.

Statistical analyses were conducted using SPSS (Version 17.0) General Linear Model software, with Greenhouse-Geisser correction applied to p values associated with multiple-df, repeated-measures comparisons when necessitated by the violation of the assumption of sphericity. A repeated-measures ANOVA was utilized to examine error-

related brain activity. The Pearson correlation coefficient (r) was used to examine associations between anxiety symptoms and ERPs measures. To examine the specificity of the anxiety subscales and the ERN magnitude, we completed two separate stepwise regressions wherein all of the anxiety subscales (as reported by parent and child) were entered predicting the ERN. We then conducted a follow-up regression wherein we examined the relationship between anxiety symptoms and the ERN, while controlling for age, correct RT, error RT, accuracy, and post-error slowing. Additionally, we conducted two mediation models wherein the relationship between age and the ERN was mediated by anxiety symptoms. These were conducted using the SPSS Hayes macro PROCESS (Preacher & Hayes, 2004), model number 4, which provided a bootstrap estimate of the indirect effect between the independent and dependent variable, an estimated standard error, and 95% confidence intervals for the population value of the indirect effect. When confidence intervals for the indirect effect do not include zero, this indicates a significant indirect effect at the $p < .05$ level. Direct and indirect effects were tested using 5000 bootstrap samples.

3. Results

3.1. Self-Report

The means and standard deviations for the parent and child-reported SCARED totals and subscales are presented in Table 1. Overall, the scores between the parent-reported SCARED and child-reported SCARED were correlated, $r(218) = 0.43$, $p < .001$. Additionally, among the child-SCARED subscales, age related to increased generalized anxiety, $r(218) = .23$, $p < .01$ and increased social anxiety, $r(218) = .14$, $p < .05$. However, age related to *decreases* in separation anxiety as reported by the child, $r(218) = -.36$, $p < .01$. Among the parent-SCARED subscales, age related to increased social anxiety, $r(218) = .19$, $p < .01$, and increased school phobia, $r(218) = .17$, $p < .05$. However, age related to *decreases* in separation anxiety as reported by the parent, $r(218) = -.20$, $p < .01$.

3.2. Behavioral data

Overall, participants committed an average of 54.37, $SD = 30.57$, range = 6–166, errors, and were correct on 82.3%, $SD = 11.4$, range = 33–100%, of trials.³ Participants were faster on error trials compared to correct trials, $F(1,217) = 578.55$, $p < .001$, $M = 371.51$, $SD = 76.93$, and $M = 484.12$, $SD = 110.64$, respectively. Additionally, participants were slower to generate a correct response on trials that occurred after an error compared to trials that occurred after a correct response, $F(1,217) = 23.61$, $p < .001$, $M = 475.06$, $SD = 105.29$, and $M = 461.31$, $SD = 102.14$, respectively.

Accuracy related to the parent-SCARED separation anxiety subscale, $r(218) = -.18$, $p < .01$; however accuracy was not significantly related to any other parent or children reported anxiety subscales, all $ps > .10$. Reaction time on correct trials related to the child-SCARED generalized anxiety subscale, $r(218) = -.21$, $p < .01$, as well as the child-SCARED separation anxiety subscale, $r(218) = .20$, $p < .01$. Additionally, reaction time on error trials was also related to the child-SCARED generalized anxiety subscale, as well as the child-SCARED separation anxiety subscale, $r(218) = -.19$, $p < .01$, and $r(218) = .16$, $p < .05$, respectively. Additionally, the parent-SCARED school phobia subscale related to reaction time on error trials, $r(218) = -.15$, $p < .05$. However, it should be noted that when analyses were completed controlling for age, there were no significant relationships between any anxiety subscales and reaction times on error or correct

² While some CRN/anxiety relationships have been observed in previous studies (Meyer et al., 2012; Olvet & Hajcak, 2009; Riesel et al., 2011), it is more typical to observe ERN or ΔERN relationships with anxiety.

³ Six participants had accuracy rates under 50%. When they were removed from analyses, the pattern of results stayed the same. Therefore, they were included in the current analyses.

Table 1

Means and standard deviations for the parent and child-reported SCARED totals and subscales are presented.

	Mean	SD
Child-SCARED:		
Total	20.69	10.13
Panic	4.55	3.90
Generalized Anxiety	5.60	3.96
Separation Anxiety	3.90	2.92
Social Anxiety	5.14	3.50
School Avoidance	1.51	1.54
Parent-SCARED:		
Total	11.16	8.18
Panic	1.37	2.41
Generalized Anxiety	3.60	3.50
Separation Anxiety	1.77	2.27
Social Anxiety	3.57	3.41
School Avoidance	.86	1.18

trials. Additionally, post-error slowing was not significantly related to any of the anxiety subscales, all $ps > .10$.

Age related to reaction times in both correct and error trials, $r(216) = -.48, p < .01$ and $r(216) = -.43, p < .01$, respectively, such that older children were faster. However, post-error slowing did not relate to age, $r(216) = .12, p = .08$. Accuracy also related to age, $r(216) = .34, p < .01$, such that older children made fewer errors.

3.3. Error-related brain activity and total anxiety symptoms

Consistent with previous work, the ERN was significantly more negative than the CRN, $F(1,219) = 81.52, p < .001$. A response by electrode interaction suggested that the difference between error and correct differed by electrode site, $F(2, 438) = 22.73, p < .001$, and follow-up analyses suggested that while the Δ ERN differed between Fz and Cz, $t(219) = -4.36, p < .001$, and between Cz and FCz, $t(219) = 7.24, p < .001$, it did not differ between Fz and FCz, $t(219) = .52, p = .61$. Based on this, we created a pooling of activity on error and correct trials at electrodes FCz and Cz and subsequent analyses focus on this measure of the ERN, CRN, and Δ ERN. As an alternative to the subtraction-based difference score (error minus correct; i.e., Δ ERN), we created a regression-based difference measure. The ERN_{resid} was created by saving the variance leftover in a regression equation wherein the CRN was entered predicting the ERN.

To examine the relationships between error-related brain activity and child anxiety, we conducted bivariate correlations between the child and parent-SCARED total scores. As can be seen in Table 2, total anxiety symptoms as reported by the parent were significantly related to the ERN, such that more anxious children were characterized by a larger ERN. Moreover, total anxiety symptoms as reported by the child were significantly related to the ERN and the ERN_{resid} at a trend level, $p = .06$. The subtraction-based difference score was not significantly related to the child-SCARED or the parent-SCARED total scores, both $ps > .10$. When analyses were conducted controlling for child age, the relationships between the ERN and both child-SCARED and parent-SCARED remained significant, $r(217) = -.14, p < .05$, and $r(217) = -.19, p < .01$, respectively. Additionally, it should be noted that the CRN also related to the parent-SCARED total score.

Regarding symptoms subscales, the child-SCARED social anxiety symptoms subscale significantly related to both the ERN and ERN_{resid} (see Table 2). However, no other child-reported SCARED subscales related to error-related brain activity. For the parent-reported SCARED subscales – panic, generalized anxiety, social anxiety, and school phobia symptoms related to an increased ERN. Additionally, parent-reported social anxiety symptoms related to an increased ERN_{resid} as well. Additionally, panic, generalized anxiety, and separation anxiety parent-reported subscales also related to the CRN.

Table 2

Correlations between the CRN (correct-related negativity), ERN (error-related negativity), Δ ERN (error minus correct), ERN_{resid} (residualized measures of error-related activity) and anxiety symptoms as reported by both children and parents.

	CRN	ERN	Δ ERN	ERN_{resid}
Child-SCARED:				
Total	-.08	-.14*	-.08	-.13 ^t
Panic	-.05	-.09	-.05	-.08
Generalized Anxiety	-.05	-.11	-.07	-.10
Separation Anxiety	-.06	-.07	-.01	-.03
Social Anxiety	-.06	-.16*	-.12	-.16*
School Avoidance	-.09	-.12	-.04	-.09
Parent-SCARED:				
Total	-.17**	-.20**	-.02	-.10
Panic	-.17*	-.16*	.01	-.06
Generalized Anxiety	-.14*	-.15*	-.01	-.08
Separation Anxiety	-.15*	-.09	.07	.01
Social Anxiety	-.09	-.17**	-.09	-.15*
School Avoidance	-.13	-.14*	-.01	-.07

^t $p < .06$; * $p < .05$; ** $p < .01$.

3.4. Error-related brain activity and anxiety symptom subscales

To examine the specificity of the anxiety subscales and the ERN magnitude, we completed two separate stepwise regressions wherein all of the anxiety subscales (as reported by parent and child) were entered predicting the ERN. In the first, we entered all child-reported SCARED subscales predicting the ERN. Results suggested that only the social anxiety subscale uniquely predicted the ERN, $\beta = -.14, F(1,219) = 5.37, p < .05$, while all other subscales were excluded from the model. In the second, we entered all parent-reported SCARED subscales predicting the ERN. Results again suggested that only the social anxiety subscale uniquely predicted the ERN, $\beta = -.13, F(1,219) = 6.70, p < .01$, while all other subscales were excluded from the model. Fig. 1 depicts topographical headmaps (error minus correct for 0–100 ms) and waveforms for error, correct, and the difference (error minus correct) for high and low quartile social anxiety groups based on parent report.

We conducted a follow-up regression wherein child-reported Social Anxiety symptoms were entered predicting the ERN, while controlling for age, correct RT, error RT, accuracy, and post-error slowing. Results suggested that the relationship between Social Anxiety symptoms and the ERN remained significant, $\beta = -.14, t(213) = -2.07, p < .05$. Additionally, in the model, age, accuracy, and correct RT all uniquely predicted the magnitude of the ERN, $\beta = -.20, t(213) = -2.42, p < .05, \beta = .24, t(213) = 3.33, p < .01$, and $\beta = -.18, t(213) = -2.31, p < .05$.

We conducted a follow-up regression wherein parent-reported Social Anxiety symptoms were entered predicting the ERN, while controlling for age, correct RT, error RT, accuracy, and post-error slowing. Results suggested that the relationship between Social Anxiety symptoms and the ERN remained significant, $\beta = -.14, t(213) = -1.98, p < .05$. Additionally, in the model, age, accuracy, and correct RT all uniquely predicted the magnitude of the ERN, $\beta = -.19, t(213) = -2.12, p < .05, \beta = .23, t(213) = 3.23, p < .01$, and $\beta = -.18, t(213) = -2.08, p < .05$, respectively.

Additionally, we wished to examine the extent to which the relationships with social anxiety symptoms were specific to the ERN versus the CRN. To address this issue, we conducted a simultaneous multiple regression wherein both the ERN and CRN were entered predicting child-reported Social Anxiety symptoms. Results suggested that the ERN uniquely related to child-reported Social Anxiety symptoms, $B = -.21, t = -2.31, p < .05$, while the CRN did not reach significance, $B = .08, t = .88, p = .38$. Moreover, we conducted this same model predicting parent-reported Social Anxiety symptoms. Again, the

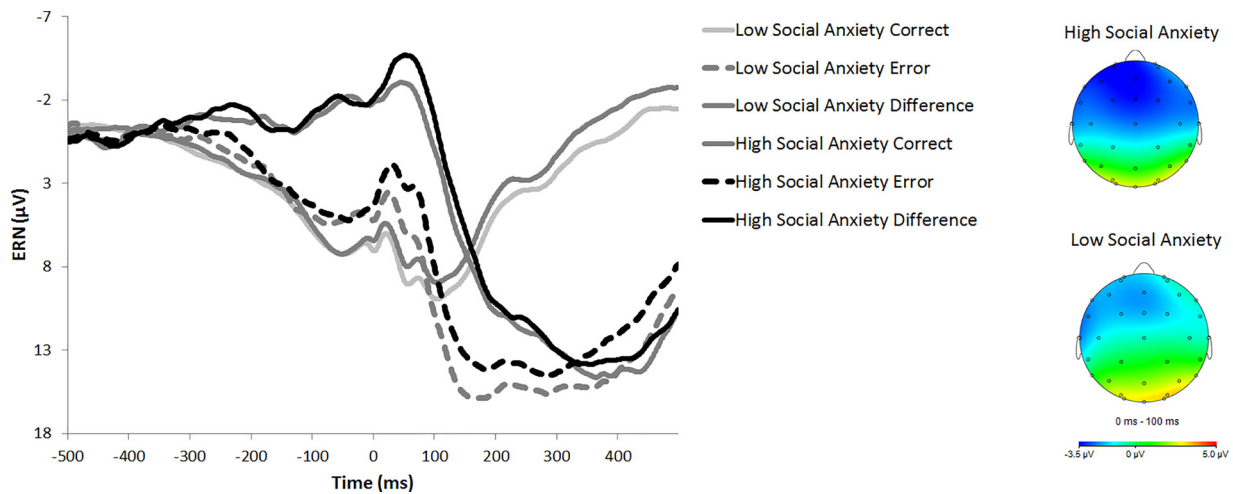


Fig. 1. On the right, topographical headmaps (error minus correct for 0–100 ms) and waveforms (on the left) for error, correct, and the difference (error minus correct) for high and low quartile social anxiety groups based on parent report.

ERN significantly predicted social anxiety symptoms, $B = -.20$, $t = -2.21$, $p < .05$, while the CRN did not reach significance, $B = .04$, $t = .43$, $p = .67$.

3.5. Developmental analyses – a mediation model

To examine whether age-related changes in error-related brain activity were partially mediated by anxiety symptoms, we conducted two mediation models wherein the relationship between age and the ERN was mediated by social anxiety symptoms as reported by the parent (model 1) and the child (model 2; see Fig. 2). We focused on social anxiety symptoms based on the results from the stepwise-regressions reported previously. In the first model, results suggested that the overall model was significant, $F(1,218) = 8.09$, $p < .01$. Additionally, the direct path between age and the ERN was significant, $effect = -.08$, $t = -2.21$, $p < .05$, 95% CI[-.16, -.01], consistent with previous work suggesting that the ERN increases across development. Moreover, results were consistent with a mediation model - the indirect effect of age on the ERN via social anxiety symptoms was significant, $effect = -.03$, 95%CI[-.09, -.01], suggesting that developmental increases in social anxiety symptoms as reported by parents underlies, in part, the developmental increase in the ERN. To test specificity of the model, the mediator and outcome were reversed (i.e., social anxiety symptoms were entered as the outcome variable and the ERN was entered as the

mediator; Agler & De Boeck, 2017). Results suggested that the indirect path did not reach significance, $effect = .005$, 95%CI[-.02, .09].

In the second model, we examined a mediation model wherein the relationship between age and the ERN was mediated by child-reported social anxiety symptoms. Results suggested that the overall model was significant, $F(1,218) = 4.04$, $p < .05$. Additionally, the direct path between age and the ERN was significant, $effect = -.09$, $t = -2.31$, $p < .05$, 95%CI[-.16, -.01]. Similar to the results reported above, results suggested that the mediation model was significant - the indirect effect of age on the ERN via child-reported Social Anxiety symptoms was significant, $effect = -.01$, 95%CI[-.04, -.01], suggesting that developmental increases in social anxiety symptoms as reported by children underlies, in part, the developmental increase in the ERN. To test specificity of the model, the mediator and outcome were reversed (i.e., social anxiety symptoms were entered as the outcome variable and the ERN was entered as the mediator). Results suggested that the indirect path did not reach significance, 95%CI[-.02, .08].^{4,5}

4. Discussion

Results from the current study suggest that during the transition from late childhood to adolescence, increased error-related brain activity indexes increases in social anxiety symptoms. The relationship between the ERN and social anxiety was significant using both parent and child report of symptoms. Furthermore, results suggested that the relationship between social anxiety and the ERN is more robust than the relationship between the ERN and any other anxiety symptom scale. Additionally, two mediation models (using parent and child report of social anxiety symptoms) suggested that the normative developmental increase observed in the ERN is partially mediated by increases in social anxiety symptoms. The current results are novel insofar as they identify

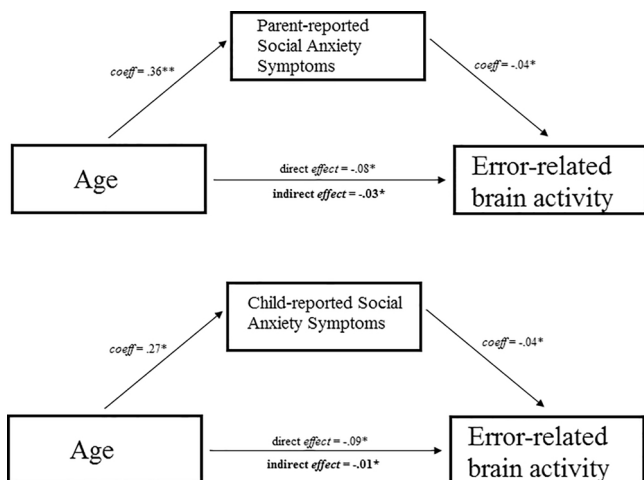


Fig. 2. Mediation model wherein social anxiety partially mediates the relationship between the ERN and age.

⁴ It should be noted, that in these analyses we focused on social anxiety given the robust relationship between social anxiety and the ERN in this sample. However, we also conducted follow-up analyses wherein all SCARED anxiety subscales were entered as simultaneous mediators in both of these models (parent and child SCARED). Results suggested that for the parent SCARED, when all symptom subscales are entered into the model, only the pathway via social anxiety symptoms was significant, $effect = -.01$, 95%CI[-.04, -.01]. However, for the child SCARED, when all symptom subscales are entered into the model, none of the indirect pathways reached significance.

⁵ Results suggested that a moderation model was not significant - i.e., the interaction between age and anxiety (total or social anxiety SCARED; reported by either child or parent) predicting the ERN did not reach significance, all $ps > .10$.

a specific facet of anxiety that underlies developmental increases in this neural biomarker.

While a substantial amount of research has found the ERN to be increased in anxious individuals (Cavanagh & Shackman, 2014; Meyer, 2016, 2017a, 2017b), few studies have examined the specific anxious phenotype that the ERN indexes. Results from the current study suggest that social anxiety symptoms had the most robust relationship with the ERN in a sample of females during a core risk period. This is consistent with the notion that the ERN may index sensitivity to making mistakes insofar as socially anxious individuals display enhanced monitoring of their own behavior. This finding is also consistent with previous work that has found an increased ERN in individuals with social anxiety disorder (Endrass et al., 2014; Kujawa et al., 2016), and work suggesting that the ERN is increased in social contexts (Barker, Troller-Renfree, Bowman, Pine, & Fox, 2018), especially in individuals high in social anxiety (Barker et al., 2015).

Moreover, while social anxiety symptoms had the strongest relationship with the ERN, parent-reported panic, generalized anxiety, and school phobia symptoms also correlated with the ERN. However, separation anxiety was not significantly related to the ERN. These findings are consistent with other work suggesting that an enhanced ERN is not associated with all forms of anxiety – individuals with simple phobias and PTSD do not differ from healthy controls in ERN magnitude (Moser, Hajcak, & Simons, 2005; Rabinak et al., 2013). Indeed, the ERN appears to relate to a transdiagnostic phenotype characterized by anxious apprehension (i.e., cognitive symptoms of anxiety) as opposed to one characterized by anxious arousal (i.e., acute fear response; Moser, Moran, Schroder, Donnellan, & Yeung, 2013). Results from the current study are consistent with this insofar as separation anxiety is not typically characterized by cognitive symptoms or concern over one's own behavior.

Consistent with previous work (Davies et al., 2004; Tamnes et al., 2013), there was a positive association between the ERN and age. This developmental increase in the ERN was significant even when accuracy and reaction time during the task were controlled for – suggesting that the ERN/age relationship cannot be fully attributed to older children completing the task more effectively (going faster and making less errors). While correlations with age and the ERN have been found in many studies to date, few studies have controlled for behavior on tasks – leaving room for the possibility that behavioral differences may have accounted for the developmental increase observed in the ERN. Results from the current study support the notion that the ERN increases across development and that this is not fully explained by increased performance on the task. In light of this, it stands to reason that developmental increases in the ERN may, in part, index normative changes in psychological phenomena – such as increased anxiety or sensitivity to making mistakes.

Despite this possibility, no study to date has yet examined the psychological processes that may underlie the developmental increase in the ERN. In the current study, results from a mediation model suggest that normative developmental increases in social anxiety may underlie developmental increases in the ERN. As children transition from childhood to adolescence, anxiety tends to transition from fear of external threat (e.g., the dark, animals, insects, weather) to self-conscious shyness and worry about behavioral competence and social evaluation (i.e., internal threat; Copeland et al., 2014; Crozier & Burnham, 1990; Gullone, 2000; Spence, Rapee, McDonald, & Ingram, 2001; Vasey, Crnic, & Carter, 1994). Indeed, in the current study, social anxiety symptoms increased with age. Furthermore, results from the current study suggest that developmental increases in the ERN may index this normative developmental increase in social anxiety or sensitivity to internal threat.

Moreover, results from the current study are consistent with other recent findings from Barker et al. (2018), wherein the ERN was increased during a social condition in girls between the ages of 9 and 17 years old (i.e., adolescents were told that two other adolescents would

be observing them complete the task and provide feedback about their performance). While younger adolescents displayed a larger ERN during the social condition compared to the non-social condition, older adolescents did not. Additionally, the enhancement of the ERN in the social condition diminished the ERN/age relationship amongst the younger adolescents. Similar to the current study, these findings suggest that at least part of the developmental increase observed in the ERN is due to normative developmental increases in social anxiety or worry about social evaluation.

Interestingly, while developmental increases in social anxiety accounted for some of the variance in age-related increases in the ERN observed, we did not find evidence of full mediation. In other words, developmental increases in the ERN were not entirely due to increases in social anxiety symptoms. Future work should examine to what extent other factors may play a role in the development of the ERN. For example, pubertal hormones may relate to the development of the ERN.

It should be noted that while the strongest relationships with anxiety symptoms were evident using the ERN alone, the ERN derived using a regression-based approach (ERN_{resid}) appeared to be a better index of individual variation in anxiety than the subtraction-based ERN (ΔERN). This is consistent with previous work suggesting that a regression-based approach may be superior to a subtraction-based approach in creating difference scores between conditions (Meyer et al., 2017). Future studies should utilize regression-based, as well as subtraction-based approaches, to further explore this possibility.

Additionally, while the ERN_{resid} appeared to be a better index of variation in anxiety compared to the subtraction-based ERN (ΔERN), the ERN and CRN alone displayed the most robust relationships with parent-reported anxiety symptoms (this pattern was not observed for child-reported anxiety symptoms). While some CRN/anxiety relationships have been observed in previous studies (Meyer, Weinberg, Klein, & Hajcak, 2012; Olvet & Hajcak, 2009; Riesel, Endrass, Kaufmann, & Kathmann, 2011), it is more typical to observe ERN or ΔERN relationships with anxiety. Indeed, in a previous study conducted in children, we did observe a CRN/anxiety relationship (Meyer et al., 2012). It is possible that developmental changes in the CRN, or even error awareness, may underlie these findings.

The current study focuses on a neural biomarker that indexes sensitivity to internal threat or behavioral monitoring, suggesting that these processes increase during the transition from late childhood to adolescence. Future studies should examine the developmental trajectories of neural biomarkers that index other types of threat. For example, certain types of threat sensitivity decrease during late childhood (e.g., fear of the dark or weather) and future work could link these changes to neural markers, further elucidating developmental pathways leading to healthy versus anxious outcomes.

The current study focuses on normative developmental trajectories of the ERN and anxiety. While this is an important first step in mapping healthy versus anxious trajectories, future work should explore whether specific developmental patterns of the ERN predict the onset of *clinical* anxiety later in development. For example, it is possible that the ERN normatively increases during the transition from late childhood to adolescence, but children characterized by an early-emerging adult-like ERN, before this transition, may be particularly at risk for clinical anxiety. Indeed, an increased ERN at 6-years-old does place children at risk for developing anxiety later in development (Meyer, Hajcak et al., 2015). Future work should examine whether there are certain developmental periods wherein an increased ERN is a particularly robust marker of risk.

Another limitation of the current study is that it is cross-sectional and therefore focuses on between-subject differences. Future work should utilize longitudinal designs to examine whether these proposed developmental shifts in the ERN and anxiety symptoms occur *within* individuals across time. For example, with multiple time points, the extent to which changes in the ERN track changes in social anxiety symptoms could be examined. Additionally, the current study includes

only females. Future work should examine whether the development of the ERN and anxiety may differ in males during the transition from childhood to adolescence.

It should also be noted that while the internal reliability for the SCARED subscales based on both parent and child report was generally good (between .7–.9), the school phobia subscale only reached modest reliability (.67 for child report and .69 for parent report). Although the results from the current study did not suggest the ERN was uniquely related to school phobia, results should be interpreted with caution given the low reliability of this subscale.

It should also be noted that numerous correlations were conducted (presented in Table 2) to explore potential relationships between both parent and child report on all subscales of the SCARED, as well as the ERN, CRN, ΔERN, and ERN_{resid}. While we viewed these preliminary analyses as exploratory, we did not correct p-values for multiple comparisons. Indeed, we followed-up on these initial findings with regression-based approaches, as well as mediation models. In fact, some have argued that correcting for multiple comparisons in such a context (exploratory analyses that are followed by more complex analytic approaches) are unnecessary and may increase the possibility for Type II error (Rothman, 1990; Saville, 1990). Given this, future studies are needed to replicate the current pattern of results.

According to the Biomarkers Definition Working Group (Colburn et al., 2001), a biomarker can be used as a “diagnostic tool for identification of those patients with a disease.” In the current study, the ERN was related to a number of anxiety symptom dimensions. However, it should be noted that these relationships were relatively small. We did not include anxiety disorder diagnostic status in the current study. However, other work does suggest that the ERN is increased in individuals with anxiety disorders (Kujawa et al., 2016; Meyer, 2017a, 2017b; Weinberg, Klein et al., 2012; Weinberg, Olvet, & Hajcak, 2010; Weinberg, Klein et al., 2012; Weinberg, Riesel et al., 2012) and thereby may be a useful diagnostic marker.

The results from the current study are a first step in elucidating the development of a neural biomarker of risk for anxiety. Future work should establish norms for the ERN that can be used to identify who is most at risk for anxiety during different stages of development. Additionally, future studies should examine what factors may influence or shape the ERN during specific developmental periods – for example, some work suggests harsh parenting styles may increase the ERN in offspring (Brooker & Buss, 2014; Meyer, Proudfit et al., 2015). Moreover, given that the ERN indexes risk for anxiety, future work should examine whether the ERN may be a viable target for treatment and prevention efforts.

References

Agler, R., & De Boeck, P. (2017). On the interpretation and use of mediation: Multiple perspectives on mediation analysis. *Frontiers in Psychology*, 8, 1984.

Ball, T. M., Stein, M. B., & Paulus, M. P. (2014). Toward the application of functional neuroimaging to individualized treatment for anxiety and depression. *Depression and Anxiety*, 31(11), 920–933.

Barker, T. V., Troller-Renfree, S., Pine, D. S., & Fox, N. A. (2015). Individual differences in social anxiety affect the salience of errors in social contexts. *Cognitive, Affective & Behavioral Neuroscience*, 15(4), 723–735.

Barker, T. V., Troller-Renfree, S. V., Bowman, L. C., Pine, D. S., & Fox, N. A. (2018). Social influences of error monitoring in adolescent girls. *Psychophysiology*, 13089.

Beesdo, P. D. S. L. R. W. H. (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Archives of General Psychiatry*, 67(1), 47–57. <https://doi.org/10.1001/archgenpsychiatry.2009.177>.

Beesdo, K., Knappe, S., & Pine, D. S. (2009). Anxiety and anxiety disorders in children and adolescents: Developmental issues and implications for DSM-V. *The Psychiatric Clinics of North America*, 32(3), 483–524. <https://doi.org/10.1016/j.psc.2009.06.002>.

Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., ... Neer, S. M. (1997). The screen for child anxiety related emotional disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child and Adolescent Psychiatry*, 36(4), 545–553.

Brooker, R. J., & Buss, K. A. (2014). Harsh parenting and fearfulness in toddlerhood interact to predict amplitudes of preschool error-related negativity. *Developmental Cognitive Neuroscience*, 9, 148–159.

Bunford, N., Kujawa, A., Fitzgerald, K. D., Swain, J. E., Hanna, G. L., Koschmann, E., ...

Phan, K. L. (2017). Neural reactivity to angry faces predicts treatment response in pediatric anxiety. *Journal of Abnormal Child Psychology*, 45(2), 385–395.

Cavanagh, J. F., & Shackman, A. J. (2014). Frontal midline theta reflects anxiety and cognitive control: Meta-analytic evidence. *Journal of Physiology-Paris*.

Colburn, W., DeGruttola, V. G., DeMets, D. L., Downing, G. J., Hoth, D. F., Oates, J. A., ... Biomarkers Definitions Working Group (2001). Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework. *Clinical Pharmacology & Therapeutics*, 69, 89–95.

Copeland, W. E., Angold, A., Shanahan, L., & Costello, E. J. (2014). Longitudinal patterns of anxiety from childhood to adulthood: The great smoky mountains study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 53(1), 21–33.

Crozier, W. R., & Burnham, M. (1990). Age-related differences in children's understanding of shyness. *The British Journal of Developmental Psychology*, 8(2), 179–185. <https://doi.org/10.1111/j.2044-835X.1990.tb00832.x>.

Davies, P. L., Segalowitz, S. J., & Gavin, W. J. (2004). Development of response-monitoring ERPs in 7- to 25-year-olds. *Developmental Neuropsychology*, 25(3), 355–376.

Endrass, T., Riesel, A., Kathmann, N., & Buhlmann, U. (2014). Performance monitoring in obsessive-compulsive disorder and social anxiety disorder. *Journal of Abnormal Psychology*, 123(4), 705.

Eriksen, B., & Eriksen, C. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Attention, Perception & Psychophysics*, 16(1), 143–149. <https://doi.org/10.3758/bf03203267>.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. *Electroencephalography and Clinical Neurophysiology*, 78(6), 447–455. [https://doi.org/10.1016/0013-4694\(91\)90062-9](https://doi.org/10.1016/0013-4694(91)90062-9).

Gabrieli, J. D., Ghosh, S. S., & Whitfield-Gabrieli, S. (2015). Prediction as a humanitarian and pragmatic contribution from human cognitive neuroscience. *Neuron*, 85(1), 11–26.

Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science*, 4(6), 385–390.

Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, 55(4), 468–484.

Gullone, E. (2000). The development of normal fear: A century of research. *Clinical Psychology Review*, 20(4), 429–451.

Hajcak, G. (2012). What we've learned from mistakes. *Current Directions in Psychological Science*, 21(2), 101–106. <https://doi.org/10.1177/0963721412436809>.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, 62(6), 593–602.

Kessler, R. C., DuPont, R. L., Berglund, P., & Wittchen, H.-U. (1999). Impairment in pure and comorbid generalized anxiety disorder and major depression at 12 months in two national surveys. *The American Journal of Psychiatry*, 156(12), 1915–1923.

Kujawa, A., Weinberg, A., Bunford, N., Fitzgerald, K. D., Hanna, G. L., Monk, C. S., ... Phan, K. L. (2016). Error-related brain activity in youth and young adults before and after treatment for generalized or social anxiety disorder. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, 71, 162–168.

La Greca, A. M., & Lopez, N. (1998). Social anxiety among adolescents: Linkages with peer relations and friendships. *Journal of Abnormal Child Psychology*, 26(2), 83–94.

Last, C. G., Perrin, S., Hersen, M., & Kazdin, A. E. (1996). A prospective study of childhood anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, 35(11), 1502–1510.

Meyer, A. (2016). Developing psychiatric biomarkers: A review focusing on the error-related negativity as a biomarker for anxiety. *Current Treatment Options in Psychiatry*, 1–9.

Meyer, A. (2017a). A biomarker of anxiety in children and adolescents: A review focusing on the error-related negativity (ERN) and anxiety across development. *Developmental Cognitive Neuroscience*, 27, 58–68.

Meyer, A. (2017b). *Developing psychiatric biomarkers: A review focusing on the error-related negativity (ERN) as a biomarker for anxiety*. Springer Nature.

Meyer, A., Hajcak, G., Torpey-Newman, D. C., Kujawa, A., & Klein, D. N. (2015). Enhanced error-related brain activity in children predicts the onset of anxiety disorders between the ages of 6 and 9. *Journal of Abnormal Psychology*, 124(2), 266.

Meyer, A., Hajcak, G., Torpey, D. C., Kujawa, A., Kim, J., Bufferd, S., ... Klein, D. N. (2013). Increased error-related brain activity in six-year-old children with clinical anxiety. *Journal of Abnormal Child Psychology*, 41(8), 1257–1266.

Meyer, A., Lerner, M. D., De Los Reyes, A., Laird, R. D., & Hajcak, G. (2017). Considering ERP difference scores as individual difference measures: Issues with subtraction and alternative approaches. *Psychophysiology*, 54(1), 114–122.

Meyer, A., Nelson, B., Perlman, G., Klein, D. N., & Kotov, R. (2018). A neural biomarker, the error-related negativity, predicts the first onset of generalized anxiety disorder in a large sample of adolescent females. *Journal of Child Psychology and Psychiatry*.

Meyer, A., Proudfit, G. H., Bufferd, S. J., Kujawa, A. J., Laptook, R. S., Torpey, D. C., et al. (2015). Self-reported and observed punitive parenting prospectively predicts increased error-related brain activity in six-year-old children. *Journal of Abnormal Child Psychology*, 43(5), 821–829.

Meyer, A., Weinberg, A., Klein, D. N., & Hajcak, G. (2012). The development of the error-related negativity (ERN) and its relationship with anxiety: Evidence from 8 to 13 year-olds. *Developmental Cognitive Neuroscience*, 2(1), 152–161. <https://doi.org/10.1016/j.dcn.2011.09.005>.

Moser, J. S., Hajcak, G., & Simons, R. F. (2005). The effects of fear on performance monitoring and attentional allocation. *Psychophysiology*, 42(3), 261–268.

Moser, J. S., Moran, T. P., Schroder, H. S., Donnellan, M. B., & Yeung, N. (2013). On the relationship between anxiety and error monitoring: A meta-analysis and conceptual framework. *Frontiers in Human Neuroscience*, 7.

- Muris, P., Merckelbach, H., Van Brakel, A., Mayer, & Birgit (1999). The revised version of the screen for child anxiety related emotional disorders (SCARED-R): Further evidence for its reliability and validity. *Anxiety, Stress, and Coping*, 12(4), 411–425.
- Olvet, D., & Hajcak, G. (2009). The effect of trial-to-trial feedback on the error-related negativity and its relationship with anxiety. *Cognitive, Affective & Behavioral Neuroscience*, 9(4), 427–433. <https://doi.org/10.3758/cabn.9.4.427>.
- Pine, D. S., Cohen, P., Gurley, D., Brook, J., & Ma, Y. (1998). The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Archives of General Psychiatry*, 55(1), 56–64.
- Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods Instruments & Computers*, 36(4), 717–731.
- Rabinak, C. A., Holman, A., Angstadt, M., Kennedy, A. E., Hajcak, G., & Phan, K. L. (2013). Neural response to errors in combat-exposed returning veterans with and without post-traumatic stress disorder: A preliminary event-related potential study. *Psychiatry Research Neuroimaging*, 213(1), 71–78.
- Riesel, A., Endrass, T., Kaufmann, C., & Kathmann, N. (2011). Overactive error-related brain activity as a candidate endophenotype for obsessive-compulsive disorder: Evidence from unaffected first-degree relatives. *The American Journal of Psychiatry*, 168(3), 317–324. <https://doi.org/10.1176/appi.ajp.2010.10030416>.
- Riesel, A., Kathmann, N., & Endrass, T. (2014). Overactive performance monitoring in obsessive-compulsive disorder is independent of symptom expression. *European Archives of Psychiatry and Clinical Neuroscience*, 1–11.
- Rothman, K. J. (1990). No adjustments are needed for multiple comparisons. *Epidemiology*, 43–46.
- Saville, D. J. (1990). Multiple comparison procedures: The practical solution. *The American Statistician*, 44(2), 174–180.
- Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience*, 12(3), 154–167.
- Spence, S. H., Rapee, R., McDonald, C., & Ingram, M. (2001). The structure of anxiety symptoms among preschoolers. *Behaviour Research and Therapy*, 39(11), 1293–1316. [https://doi.org/10.1016/s0005-7967\(00\)00098-x](https://doi.org/10.1016/s0005-7967(00)00098-x).
- Tamnes, C. K., Walhovd, K. B., Torstveit, M., Sells, V. T., & Fjell, A. M. (2013). Performance monitoring in children and adolescents: A review of developmental changes in the error-related negativity and brain maturation. *Developmental Cognitive Neuroscience*, 6(0), 1–13. <https://doi.org/10.1016/j.dcn.2013.05.001>.
- Vasey, M., Crnic, K., & Carter, W. (1994). Worry in childhood: A developmental perspective. *Cognitive Therapy and Research*, 18(6), 529–549. <https://doi.org/10.1007/bf02355667>.
- Weinberg, A., Olvet, D. M., & Hajcak, G. (2010). Increased error-related brain activity in generalized anxiety disorder. *Biological Psychology*, 85(3), 472–480. <https://doi.org/10.1016/j.biopsycho.2010.09.011>.
- Weinberg, A., Klein, D. N., & Hajcak, G. (2012). Increased error-related brain activity distinguishes Generalized Anxiety Disorder with and without comorbid Major Depressive Disorder. *Journal of Abnormal Psychology*, 121(4), 885. <https://doi.org/10.1037/a0028270>.
- Weinberg, A., Riesel, A., & Hajcak, G. (2012). Integrating multiple perspectives on error-related brain activity: The ERN as a neural indicator of trait defensive reactivity. *Motivation and Emotion*, 1–17.
- Whitfield-Gabrieli, S., Ghosh, S., Nieto-Castanon, A., Saygin, Z., Doehrmann, O., Chai, X., ... Gabrieli, J. (2016). Brain connectomics predict response to treatment in social anxiety disorder. *Molecular Psychiatry*, 21(5), 680.
- Wittchen, H.-U., Nelson, C. B., & Lachner, G. (1998). Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. *Psychological Medicine*, 28(01), 109–126.
- Wittchen, H.-U., Stein, M. B., & Kessler, R. C. (1999). Social fears and social phobia in a community sample of adolescents and young adults: Prevalence, risk factors and comorbidity. *Psychological Medicine*, 29(2), 309–323.