Available online at www.sciencedirect.com
ScienceDirect
Behavior Therapy xxx (2023) xxx–xxx
Behavior Therapy
www.elsevier.com/locate/bt

An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children

Alexandria Meyer
Lyndsey Chong
Karl Wissemann
Lushna Mehra
Isaac Mirzadegan
Florida State University

In the current study, we utilize an experimental medicine approach to examine the extent to which a single-session, computerized intervention impacts a transdiagnostic neural marker of risk (i.e., the error-related negativity [ERN]) in 70 children between the ages of 6 and 9 years. The ERN is a deflection in the event-related potential occurring after an individual makes a mistake on a lab-based task and has been shown to be transdiagnostically associated with a variety of anxiety disorders (e.g., social anxiety, generalized anxiety), obsessive-compulsive disorder, and depressive disorders in over 60 studies to date. Building on these findings, work has been done to link an increased ERN to negative reactions to, and avoidance of, making mistakes (i.e., error sensitivity). In the current study, we capitalize on this previous work by examining the extent to which a single-session, computerized intervention may engage the target of "error sensitivity" (measured by the ERN, as well as self-report of error sensitivity). We examine the convergence of multiple measures of the construct of "error sensitivity" (i.e., child self-report, parent report on child, and child electroencephalogram [EEG]). We also examine relationships between these three measures of "error sensitivity" and child anxiety symptoms. Overall, results suggested that treatment condition predicted changes in self-reported error sensitivity but not changes in ERN. Based on the lack of previous work in this area, we view this study as a novel, preliminary, first step toward using an experimental medicine approach to examine our ability to engage the target of the ERN (i.e., error sensitivity) early in development.

Keywords: error-related negativity; ERN; child anxiety; computerized treatment; single-session treatment

It is widely known that poor health behaviors account for a large portion of disease burden in the United States. Thus, there is a critical need to translate insights from basic science to mechanistically informed, behavior change intervention development (Nielsen et al., 2018; Riddle & Science of Behavior Change Working Group, 2015). The National Institutes of Health (NIH) created the Science of Behavior Change (SOBC) Working Group in 2008 to address this issue. This team suggested that researchers identify transdisease mechanistic targets and utilize an experimental medicine approach to develop novel interventions (Nielsen et al., 2018). Target mechanisms should be malleable, play a role in the initiation or maintenance of a problematic behavior or clinical outcome, and must be able to be measured at different levels (Nielsen et al., 2018; Riddle & Science of Behavior Change Working Group, 2015). Moreover, this group suggested that neurobiological variables be included as assays or intermediate biomarkers for behavior change interventions (Nielsen et al., 2018).

The experimental medicine approach involves the development of interventions that engage puta-

The authors declare no conflicts of interest.
Address correspondence to Alexandria Meyer, Ph.D., Florida State University, Psychology Department. e-mail: Ammeyer3@gmail.com.

0005-7894/

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

tive mechanistic targets and includes specific tests of target engagement. This approach includes four steps: (a) identifying an intervention target, (b) developing measures or assays of the target, (c) engaging the target via an intervention, and (d) examining the degree to which target engagement produces behavior change (Riddle & Science of Behavior Change Working Group, 2015). Contrary to the standard approach of focusing on the efficacy of an intervention on a health outcome, this approach explicitly tests whether an intervention works *by engaging a specific target mechanism of change* (Nielsen et al., 2018). Importantly, this approach emphasizes multiple levels of measurement of the target mechanism, including neurobiological units of measurement.

In the current study, we utilize an experimental medicine approach in a pilot study to examine the extent to which a single-session, computerized intervention impacts a mechanistic neural target (i.e., the error-related negativity [ERN], a transdiagnostic neural marker of risk for anxiety). The ERN is an event-related potential–electrical activity measured via electroencephalography (EEG) and time locked to an event or response (in this case, when individuals make errors). The ERN is measured when an individual makes errors on a lab-based task and has been shown to be transdiagnostically associated with a variety of anxiety disorders—social anxiety, generalized anxiety disorder (GAD), and obsessive-compulsive disorder (OCD)—in over 60 studies to date (Cavanagh & Shackman, 2015; Hajcak, 2012; Meyer, 2017). This neural response is thought to be generated in the anterior cingulate cortex, an area of the brain associated with pain, punishment, negative affect, and response monitoring (Shackman et al., 2011).

Errors can be conceptualized as motivationally salient events that require attention and corrective action and sometimes may threaten an individual's safety (e.g., tripping or hitting one's hand with a tool). We view individual differences in the neural response to errors (i.e., the ERN) as partially reflecting variability in the extent to which an individual finds errors distressing, aversive, or threatening (i.e., "error sensitivity"; Chong & Meyer, 2018; Meyer, 2022; Weinberg et al., 2012). Consistent with this conceptualization, a wealth of evidence suggests that the ERN is increased in anxious individuals (Cavanagh & Shackman, 2015; Cavanagh et al., 2012; Meyer, 2016, 2017; Weinberg et al., 2015a, 2016). More specifically, the ERN is increased among individuals with disorders typically characterized by increased concern about performance, behavior, or mistakes—that is, social anxiety disorder (Endrass et al., 2014), GAD (Weinberg et al., 2010), and OCD (Riesel, 2019; Riesel et al., 2019b).

Consistent with findings in adults, an increased ERN has also been observed among clinically anxious children and adolescents in 10 studies to date (Meyer, 2017, 2022). An elevated ERN has been found in clinically anxious children as young as 6 years (Meyer et al., 2013) and also appears to index risk for future increases in anxiety—for example, an increased ERN in 6-year-old children predicted new onset anxiety disorders 3 years later, even when controlling for baseline symptoms (Meyer et al., 2015). This same pattern has also been observed in adolescents (Meyer et al., 2018)—that is, the ERN predicted new-onset GAD across 2 years. Similarly, other work has found that children who are high in behavioral inhibition and have an increased ERN, are particularly prone to anxiety disorders later in life (Lahat et al., 2014; McDermott et al., 2009; Meyer et al., 2015; Tang et al., 2020). Along these same lines, the ERN has also been shown to be a prognostic indicator, predicting increases in anxiety symptoms over 2 years among clinically anxious children and adolescents (Meyer et al., 2021).

Although much work has been done demonstrating that the ERN is increased among clinically anxious individuals, less is known about what specific psychological constructs underlie this association. A number of within-subject studies suggest that the ERN reflects the salience of errors—for example, the ERN is larger when errors are more costly (Ganushchak & Schiller, 2008; Hajcak et al., 2005), when performance is evaluated or observed (Barker et al., 2015, 2018; Hajcak et al., 2005; Kim et al., 2005; Meyer et al., 2019; Voegler et al., 2018), when accuracy is emphasized (Falkenstein et al., 2000; Gehring et al., 1993), and when errors are punished (Meyer & Gawlowska, 2017; Riesel et al., 2012, 2019a).

Additionally, some work has linked the ERN to perfectionism (Barke et al., 2017; Meyer & Wissemann, 2020; Perrone-McGovern et al., 2017; Schrijvers et al., 2010; Stahl et al., 2015). One core element of perfectionism is hypervigilance surrounding mistakes or one's own performance. Indeed, the ERN has been shown to be specifically related to maladaptive perfectionism (Perrone-McGovern et al., 2017), doubts about actions (i.e., the tendency to be dissatisfied with one's own performance; Stahl et al., 2015), and concern over mistakes (Meyer & Wissemann, 2020). Other work has linked the ERN to checking behavior (i.e., the tendency to monitor one's

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

own behavior to reduce anxiety; Weinberg et al., 2015b, 2016) and error sensitivity (i.e., the degree to which an individual finds mistakes aversive; Chong & Meyer, 2018). Moreover, some of this work suggests that it is these psychological constructs (i.e., error sensitivity, concern over one's own performance, perfectionism, etc.) that link the increased ERN to anxiety disorders (Chong & Meyer, 2018; Meyer & Klein, 2018; Meyer & Wissemann, 2020).

Thus far, four studies have examined the ERN before and after treatment for anxiety disorders (Hajcak et al., 2008; Kujawa et al., 2016; Ladouceur et al., 2018; Riesel et al., 2015). All four studies found that traditional cognitive-behavioral therapy (CBT) did not impact the ERN, despite decreases in anxiety symptoms—for example, children with OCD who participated in exposure therapy still displayed an increased ERN after the successful completion of therapy (Hajcak et al., 2008). Moreover, a recent study suggested that although CBT related to a decrease in anxiety symptoms, it was not related to either a decrease in the ERN or in *worry related to performance* (i.e., error sensitivity; Ladouceur et al., 2018). Considering the fact that an increased ERN is a prognostic indicator of risk among clinically anxious individuals (Meyer et al., 2021), an elevated ERN posttreatment may confer risk for future relapse or increases in anxiety.

Building on these findings, some have begun to develop intervention approaches that may directly target the psychological constructs that link the ERN to anxiety (i.e., error sensitivity or concern over mistakes). In a previous study, Meyer et al. (2020) tested the extent to which a 1-hour, computer-based tutorial covering topics such as perfectionism, fear of the social consequences of making a mistake, and overvaluation of the negative consequences of errors would impact the ERN in college-age participants. Results suggested that the intervention reduced the ERN compared to a control condition, and that the impact of this intervention was larger among individuals with an increased ERN at baseline. Although these results are promising, this study was limited insofar as the intervention was delivered to adults and we did not include measures of error sensitivity or anxiety symptoms. Considering the fact that an elevated ERN *early in development* appears to confer risk for anxiety (Meyer, 2017) and early intervention is more effective (Mancebo et al., 2014), it is especially important that this approach can be utilized in children.

In the current study, we build on this previous work and utilize an experimental medicine approach by conducting a pilot study to examine the extent to which a single-session, computerized intervention may engage the target of "error sensitivity" in young children (see Figure 1 for a conceptual diagram). Thus, we accomplish the first step of the experimental medicine approach by identifying a mechanistic target (i.e., error sensitivity) for intervention. Based on previous longitudinal work suggesting that an elevated ERN prospectively predicts risk for future increase in anxiety (Lahat et al., 2014; McDermott et al., 2009; Meyer et al., 2015, 2018; Tang et al., 2020), we hypothesize that it is by being hyperresponsive and hypervigilant toward one's own mistakes that an individual, over time, experiences an increase in anxiety symptoms. We accomplish the second step of the experimental medicine approach by developing and examining multiple assays of the target: We examine the convergence of multiple measures of the construct of error sensitivity (i.e., child self-report, parent report on child, and child EEG). We also examine the relationships between these three measures of error sensitivity and child anxiety symptoms. And, finally, we accomplish Step 3 of the experimental medicine approach by examining the extent to which we can engage the target of child error sensitivity via an adapted, short, computer-based intervention. Based on the lack of previous work in this area, we view this study as a novel, preliminary, first step toward using an experimental medicine approach to examine our ability to engage the mechanistic target of error sensitivity in young children.

Method

PARTICIPANTS

The current study included 70 children between the ages of 6 and 9 years, $M = 6.83$, $SD = 0.80$, who were recruited from the surrounding community of Tallahassee, Florida. A total of 31 females, 28 males, and 1 whose gender was identified as "other" participated in the study. Overall, 11% of the sample identified as Hispanic or Latino, 3% as Asian, 14% as Black or African American, 49% as White or Caucasian, and 4% as other. Moreover, for estimated annual family income, 2% of the sample reported less than $10,000, 5% reported $10,000–$25,000, 7% reported $25,000–$40,000, 24% reported $40,000–$75,000, and 31% reported more than $75,000.

Of these children, 61 had adequate EEG data for the current study. Reasons for missing EEG data include child refusal to complete the EEG task ($N = 1$), too much noise in EEG data

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

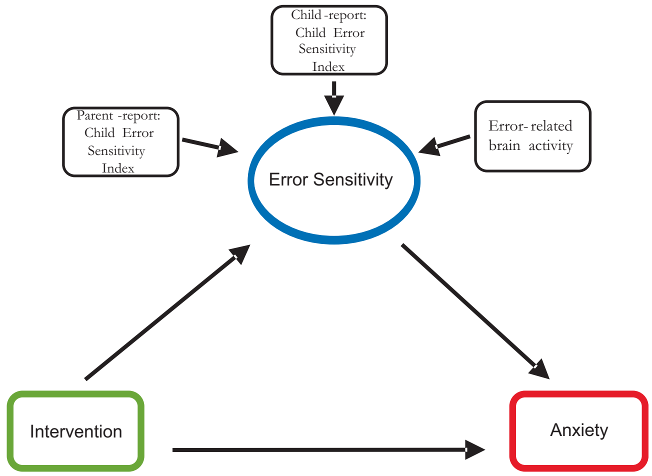

FIGURE 1 Conceptual diagram of proposed model wherein a targeted intervention will impact error sensitivity (as indexed by parent and child reports on the Child Error Sensitivity Index), and error-related brain activity, and by engaging this mechanism (i.e., error sensitivity), child anxiety symptoms will be reduced.

($N = 4$), computer or experimenter error ($N = 1$), or too few error responses ($N = 3$). Based on previous work, children were only included in the analyses if they made at least six errors per condition (Meyer et al., 2014; Olvet & Hajcak, 2009). A total of 25 females, 35 males, and 1 child who identified their gender as "other" were included in the final analyses. The average age of these participants was 6.82, $SD = 0.79$, range: 6–9 years. The children who were excluded based on the lack of EEG data did not differ from the total sample on any demographic or main study variable (including intervention vs. control group), all $ps > .10$. Overall, of the 35 participants assigned to each condition, 33 participants assigned to the intervention condition and 28 participants assigned to the control condition had adequate EEG data.

SELF-REPORT MEASURES

The Child Error Sensitivity Index was previously used in one study (Chong & Meyer, 2018). This is a nine-item questionnaire measuring children's reactions to making mistakes. The items on the Child Error Sensitivity Index were developed based on pervious work linking the ERN to performance-related concerns. Items include the following: "I feel upset when other people don't like something I have done"; "If I make a mistake, I always want to fix it"; "When I make a mistake, I feel anxious"; "I am afraid of making mistakes in front of other people"; "I like to do things perfectly"; "My stomach feels sick when I make a mistake"; "When someone notices I did something wrong, I feel upset"; "When I make a mistake, I start sweating or blushing"; and "When I notice a mistake I made, I feel upset." Children rated each item using the following scale: 1 (*not at all like me*), 2 (*somewhat like me*), and 3 (*a lot like me*). In previous work (Chong & Meyer, 2018), the Child Error Sensitivity Index demonstrated good internal reliability, as well as convergent and divergent validity with the Fear Survey Schedule for Children—Revised (FSSC-R; Ollendick, 1983) subscales (i.e., the Child Error Sensitivity Index related to the Fear of Failure or Criticism subscale, but not to the Fear of Minor Injury or Small Animals subscale). In the current study, to administer the questionnaire a research assistant played a board game with the child participants. The board game contained a start and finish, with square spaces in between. Children were given a game piece that they advanced after they answered a question. They were told that they would be able to pick out a prize when they completed the board game.

The Child Error Sensitivity Index was also administered to parents to report on their child's error sensitivity. The parent who attended the lab visit completed the questionnaire (82% mothers, 95% reported being the biological parent of the child, 69% reported being the primary caregiver of the child, and 30% reported sharing caregiving responsibilities with their partner). The same items were included in the parent-report version of this questionnaire as the child version—however, these items were reworded so the parent would answer them about their children (e.g., "My child feels upset when other people don't like something she or he has done"). There were nine

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

items that were rated 1 (*not at all like my child*), 2 (*somewhat like my child*), and 3 (*a lot like my child*).

To measure anxiety and attention symptoms, we utilized the Child Behavior Checklist (CBCL; Achenbach & Edelbrock, 1981). Parents rated items about their children for the past 6 months on a scale from 0 (*not true*) to 2 (*very or often true*). The CBCL is a widely used, empirically derived measure that assesses emotional and behavioral problems in children. This measure contains eight syndrome scales (e.g., Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints) and also contains scales that map onto *Diagnostic and Statistical Manual of Mental Disorders* (DSM) clinical disorders (e.g., anxiety, oppositional defiant disorder). For the purposes of the current study, we utilize the DSM Anxiety Problems scale because the anxiety-related syndrome scales do not dissociate anxiety from depression (an important consideration when examining the ERN; see Bress et al., 2015). Additionally, for the purposes of examining discriminative validity, we utilize the Attention Problem Syndrome scale, which indexes general issues with attention.

Go/No-Go Task

Children completed a go/no-go task while EEG was recorded. Children were instructed to "shoot" aliens by clicking the mouse button as soon as the aliens appeared on the screen and "save" astronauts by refraining from clicking the mouse button when astronauts appeared on the screen. Stimuli included an image of an alien or astronaut that appeared on the screen for 500 ms, with an intertrial interval (ITI) of 1,000–2,000 ms. A fixation cross appeared in the center of the screen during the ITI period. Children completed 400 trials in total, 200 trials before the intervention, and 200 trials after the intervention. Before beginning the task, children completed five practice trials.

Intervention and Control Videos

The intervention and control videos were 20-minute recorded PowerPoint presentations. A research coordinator helped children advance through the videos and complete the activities. The intervention video utilized cognitive-behavioral approaches to target error sensitivity. The video focused on concepts such as everybody makes mistakes, mistakes can be funny, and mistakes are a chance to learn. Children were asked to answer questions regarding a time they remember making a mistake, how they felt, and what they "told themselves" (i.e., what were their thoughts) when they made the mistake. Material was also presented regarding what "kids who have trouble with mistakes" might do (e.g., procrastinate, avoid trying things that might be hard, pay more attention to mistakes vs. successes, give up without trying). The concept of a "mistake bully" and a "mistake buddy" was introduced to help coach children through adaptive responding to mistakes (e.g., mistakes are a chance to learn, I can try again, everybody makes mistakes). The intervention video also contained information about emotional or bodily reactions to making mistakes (e.g., sweating, heart beating fast). A suggestion to notice how their body feels and to use their mistake buddy to challenge negative thoughts was given. Additionally, the concept of being in the "challenge zone" was presented to encourage children to try difficult things, even when they know they might make mistakes. The narrator of the video suggests that if you are not making mistakes, you may be in the "comfort zone" and not actually improving. The control video was created to match the intervention video in length and style—however, instead of focusing on error sensitivity, the control video focused on healthy behaviors (e.g., eating fruits and vegetables, sleeping, brushing teeth). Children were rewarded with small prizes throughout the completion of the videos.

PROCEDURE

Upon the family's arrival in the lab, the experimenter oriented them to the study procedure and informed consent was obtained from the parent and assent was obtained from the child. We used a simple randomization technique to assign the participants to a condition (intervention vs. control). The child completed self-report measures (with the assistance of a research coordinator) before and after the EEG tasks and intervention or control video. A research coordinator read the items from the self-report questionnaires to accommodate different reading abilities across this age range. The research coordinator was also instructed to reword, act out, give examples, or explain items to children when necessary. Handouts with pictures were provided so children could point to their answers for the self-report measures. In these handouts, each option was accompanied by an image depicting the concept of the answer (e.g., fingers close together to illustrate the concept of "a little bit"). We also utilized a board game to increase engagement with the completion of the self-report measures. After the completion of the baseline self-report measures, the EEG cap was set up, children completed the go/no-go task, and children watched either the intervention or control

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

video. After completion of the video, children completed the self-report measures and the go/no-go task again, and then the EEG cap was removed. Parents completed questionnaires in a separate room while children completed their portion of the lab visit. The Florida State University IRB approved the study protocol.

EEG Data Acquisition and Processing

Continuous EEG data at 34 electrode sites was recorded with an elastic cap and the BioSemi ActiveTwo system (BioSemi, Amsterdam, Netherlands). Electrooculogram (EOG) data produced by eye movements and blinks were collected using four facial electrodes: two approximately 1 cm outside of the outer edge of the right and left eyes (to record horizontal eye movements) and two approximately 1 cm above and below the right eye (to record vertical eye movements and blinks). The EEG signal was preamplified at the electrode to improve signal-to-noise ratio and amplified with a gain of 1 by a BioSemi ActiveTwo system. During data acquisition, all active electrodes were referenced to a common mode sense (CMS) active electrode producing a monopolar (nondifferential) channel. EEG was recorded with a low-pass fifth order sinc filter with a half-power cutoff of 204.8 Hz and digitized at a 2-bit resolution with a sampling rate of 1,024 Hz.

Offline, data were processed using Brain Vision Analyzer software. EEG data were rereferenced to the mean of the left and right mastoids and band-pass filtered between 0.1 and 30.0 Hz and the roll-off for the offline filter was 12 dB/oct for the low cutoff and 24 dB/oct for the high cutoff. The EEG was segmented –500–1,000 ms prior to and following response onset for each trial. We corrected for eye blinks and eye movements using the Gratton et al. (1983) method. Artifact rejection was done automatically in Brain Vision Analyzer on all EEG channels—maximal allowed voltage step: 50 μV; maximal allowed difference of values in intervals: 300 μV; lowest activity in intervals: 0.5 μV. Response-locked exposure and response prevention responses (ERPs) were averaged separately using an area measure for correct and error trials from 0 to 100 ms after the response, and baseline corrected using the interval from –500 to –300 ms. The trial rejection rates did not differ between the intervention and control group, all $ps > .32$. Mean trial rejection rate for the preassessment: control group = 20.6%, intervention group = 23.6%. Mean trial rejection rate for the postassessment: control group = 23.5%, intervention group = 26.8%. Additionally, accuracy did not differ across the groups, all $ps > .70$—preassessment: control group = 88.6%, intervention group = 88.6%; postassessment: control group = 88.3%, intervention group = 85.7%. Midline electrodes Fz and Cz were pooled, and to isolate error-related brain activity we created residualized difference scores (Meyer et al., 2017)—that is, saved the unstandardized residual scores from a regression equation wherein the correct-related brain activity was entered predicting the error-related brain activity for both the pre- and post-EEG measures. All analyses were conducted on these residualized difference scores. It should be noted that both the ERN and the residualized difference scores are a negativity (i.e., more negative values = more activity) and thus negative associations with other study variables indicate that as the ERN (and residualized scores) increases, so does the other study variable.

For statistical analyses, we utilized SPSS (Version 27) General Linear Model software. Split-half reliabilities were calculated to examine internal consistency for the ERPs. Cronbach's alpha was calculated as a measure of internal consistency for the Child Error Sensitivity Index. We examined convergent validity by examining the Pearson correlations between the parent and child report on the Child Error Sensitivity Index, as well as relationships with the ERN and child anxiety symptoms (as reported by parents on the CBCL). To examine discriminative validity, we examined the Pearson correlations between the error sensitivity measures and attention problems (as reported by parents on the CBCL).

To examine a mediation model wherein the relationship between the ERN and child anxiety symptoms was mediated by the Child Error Sensitivity Index, we utilized a nonparametric bootstrapping approach (MacKinnon et al., 2002, 2004). This approach has been shown to be more statistically powerful than other tests of mediation (MacKinnon et al., 2002). We used the SPSS macro (Preacher & Hayes, 2004), which provides a bootstrap estimate of the indirect effect between the independent and dependent variables, 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 5,000 bootstrap samples.

To examine the impact of the intervention on the child report on the Child Error Sensitivity Index and the ERN, we conducted separate regression analyses wherein the treatment condition (intervention vs. control) was entered as the

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

independent variable and the baseline measure (e.g., child error sensitivity pre or ERN pre) was entered as a covariate predicting the postmeasure (e.g., child error sensitivity post or ERN post). The effect size of the treatment was calculated using Cohen's *d*. Pair-samples *t* tests were also utilized to examine potential treatment-related changes. Based on previous work (Meyer et al., 2020), we also conducted exploratory analyses to examine whether the impact of the intervention on error-related brain activity would be larger among individuals with an elevated baseline ERN. To do so, we conducted the same analyses described above among individuals who had a baseline ERN at or above the median.

POWER ANALYSIS

Our final sample size, after excluding children who did not have adequate EEG data, was $N = 61$. Based on limited previous work suggesting that the ERN and child error sensitivity are moderately correlated (Chong & Meyer, 2018), the current study has approximately 80% power to detect this association. Moreover, based on previous work suggesting that the ERN and anxiety are moderately correlated (Meyer, 2017; Moser et al., 2013), the current study has approximately 80% power to detect this association. Based on a previous study in adults examining the impact of a brief, computerized intervention on the ERN (Cohen's *d* of .48; Meyer et al., 2020), the current study has approximately 80% to detect the impact of the intervention on the ERN.

Results

MEASURE RELIABILITY: ERROR SENSITIVITY

Our first aim was to examine the psychometric properties of the measures of error sensitivity included in the current study. These measures included the ERN (a neural measure), child report on the Child Error Sensitivity Index, and parent report on the Child Error Sensitivity Index.

Overall, the neural response to errors was more negative than the neural response to correct responses, $F(1, 50) = 105.56$, $p < .001$: ERN pre, $M = -9.51$, $SD = 25.17$; CRN pre, $M = 13.64$, $SD = 13.56$; ERN post, $M = -13.63$, $SD = 27.44$; CRN post, $M = 13.57$, $SD = 11.45$. Split-half reliabilities were the following: ERN pre = .36, CRN pre = .76, ERN post = .37, CRN post = .56. To isolate error-related brain activity, we created residualized difference scores (Meyer et al., 2017)—that is, saved the unstandardized residual scores from a regression equation wherein the CRN was entered predicting the ERN for both the pre- and post-EEG measures. All further analyses were conducted on these residualized difference scores.

The psychometric properties of the child report on the Child Error Sensitivity Index has previously been reported in one study to date (Chong & Meyer, 2018). Similar to previous findings, in the current study, the Cronbach's alpha for the nine total items included in this measure was .70. Additionally, the Cronbach's alpha for the nine total items included in the parent-report version of the Child Error Sensitivity Index measure was .86.

Convergent and Discriminant Validity of Error Sensitivity

To examine convergent validity of the measures of error sensitivity, we examined the bivariate correlations between error-related brain activity (i.e., the ERN) and parent and child report of error sensitivity on the Child Error Sensitivity Index (see Table 1). Results suggested that parent and child report on the Child Error Sensitivity Index were significantly correlated, $r(59) = .21$, $p < .05$. And, although the child report on the Child Error Sensitivity Index was not significantly correlated with the ERN, $r(48) = -.03$, $p = .43$, the parent report on the Child Error Sensitivity Index was significantly correlated with the ERN, $r(48) = -.27$, $p < .05$, such that children whose parents reported that their children were higher in error sensitivity displayed more neural activity to errors during the EEG task (see Figure 2).

We also examined convergent and discriminant validity of the error sensitivity measures in relation to clinical symptoms as reported by parents on the CBCL. Results suggested that both child and parent reports on the Child Error Sensitivity Index were significantly correlated with anxiety symptoms, $r(59) = .22$, $p < .05$ and $r(59) = .47$, $p < .01$, respectively. Additionally, error-related brain activity was increased among anxious children, $r(48) = -.29$, $p < .05$. To examine discriminant validity, we examined the relationships between the error sensitivity measures and attention problems as reported by parents on the CBCL. Results suggested that attention problems were not significantly related to the ERN nor the parent or child report on the Child Error Sensitivity Index, all *p*s > .10.

MEDIATION MODEL: THE ERN TO CHILD ANXIETY VIA CHILD ERROR SENSITIVITY

Our theoretical model suggests that the psychological construct that partially explains the association between the ERN and anxiety is error sensitivity (i.e., the degree to which an individual

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

Table 1
Bivariate Correlations Between All Main Study Variables

	1	2	3	4
1. Parent report: Child Error Sensitivity Index	–			
2. Child report: Child Error Sensitivity Index	.21*	–		
3. Error-related brain activity	−.27*	−.03	–	
4. CBCL: anxiety symptoms	.47**	.22*	−.29*	–
5. CBCL: attention symptoms	.02	−.15	−.05	.19

* $p < .05$.
** $p < .01$.

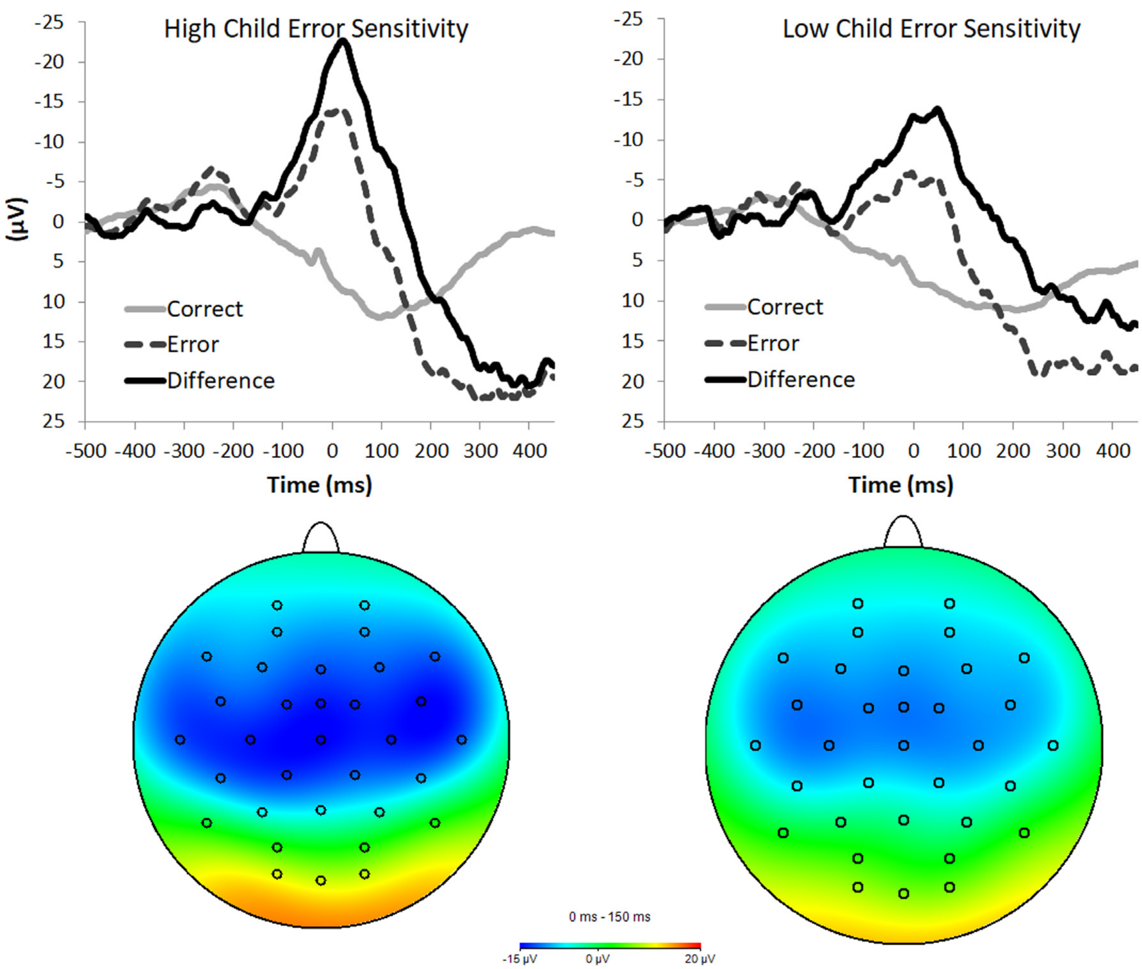

FIGURE 2 Depicts head maps (bottom: error minus correct) and waveforms (top) of error-related brain activity for children whose parents reported that they were high and low in error sensitivity on the Child Error Sensitivity Index (high and low quartiles).

finds mistakes distressing). In other words, we are suggesting that anxious individuals tend to find their mistakes more aversive and that this explains the enhanced ERN that has been observed in over 60 studies to date (Meyer, 2016, 2017; Moser et al., 2013). Because the development of the intervention approach used in the current study is based on this notion, it is important to examine this model. In one previous study, we have shown that the relationship between error-related brain activity and child anxiety is mediated by child error sensitivity (Chong & Meyer, 2018). We examine this same model in the current study (see Figure 3). Results from this model suggest that the pathway from the ERN to the parent report of child error sensitivity is significant, coeff = –0.09, t = –1.95, $p < .05$, 95% CI [–0.17, –0.02]. Moreover, the pathway from the parent report of child error sensitivity to child anxiety symptoms was significant, coeff = 0.17, t = 3.03, $p < .01$, 95%

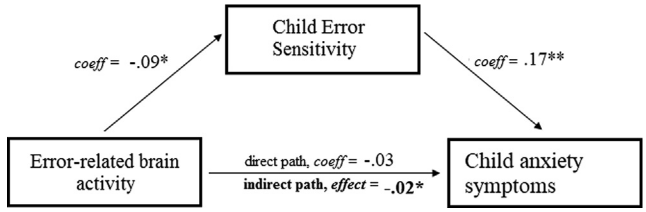

FIGURE 3 A graphical depiction of a mediation model examining the relationship between error-related brain activity (i.e., error-related negativity [ERN]) and child anxiety symptoms (parent report on the Child Behavior Checklist [CBCL]), mediated by child error sensitivity (i.e., parent report on the Child Error Sensitivity Index).

CI [0.07, 0.26]. Results supported the mediation model—the indirect path from the ERN to child anxiety symptoms (parent report on the CBCL) via child error sensitivity (parent report) reached significance, coeff = –0.02, 95% CI [–0.04, –0.01]. It should be noted that a mediation model wherein the child report on the Child Error Sensitivity Index was used as the mediator did not reach a significant, indirect path: coeff = –0.00, 95% CI [–0.01, 0.00].

INTERIM SUMMARY

To summarize, the psychometric properties of the neural measure, error-related brain activity (i.e., the ERN), were fair to good and both the child and parent reports on the Child Error Sensitivity Index displayed good internal reliability. Moreover, we found evidence of convergent validity: the child and parent reports on the Child Error Sensitivity Index were significantly related, the parent report of child error sensitivity related to error-related brain activity (ERN), and both the child and parent reports on the Child Error Sensitivity Index and the ERN related to child anxiety symptoms. Thus, results suggest that error sensitivity can be reliably measured via EEG and via parent or child self-report, and that enhanced error sensitivity is related to enhanced anxiety symptoms. Additionally, we examined discriminative validity and found that neither the ERN, nor child or parent report on the Child Error Sensitivity Index related to child attention symptoms on the CBCL. Furthermore, we replicated a previous finding, suggesting that the relationship between error-related brain activity and child anxiety was mediated by child error sensitivity (parent report), suggesting that targeting the psychological construct of error sensitivity may be an effective way of reducing the ERN and thus, anxiety, in children.

Pilot Intervention Effects

To examine the impact of this single-session, pilot, computerized intervention on error sensitivity, we used both the EEG measure (i.e., the ERN) and child report on the Child Error Sensitivity Index as measures of the target mechanism. As this was a pilot study, we did not focus on either the parent report on the Child Error Sensitivity Index or the outcome behavior (anxiety symptoms on the CBCL), due to the fact that we would not expect either of these to be impacted immediately after a single-session computerized intervention delivered to the child.

To examine the impact of the intervention on the child report on the Child Error Sensitivity Index, we conducted a regression wherein treatment condition (intervention was coded as 1; control condition was coded as 2), as well as the scores on the baseline Child Error Sensitivity Index were entered, predicting the scores on the post-Child Error Sensitivity Index. Results suggested that baseline child error sensitivity significantly predicted postchild error sensitivity, $B = 0.56$, $SE\ B = 0.12$, $\beta = .48$, $p < .001$. Moreover, treatment condition (intervention vs. control) predicted changes in the Child Error Sensitivity Index, $B = -0.94$, $SE\ B = 0.45$, $\beta = -.22$, $p < .05$. Paired-samples t tests suggested that although scores on the Child Error Sensitivity Index did not differ from pre to post among children in the control condition, $t(20) = 0.60$, $p = .56$, scores did decrease from pre to post among children in the intervention condition, $t(45) = 2.71$, $p < .01$ (see Table 2). The effect size estimate of the impact of the intervention on the Child Error Sensitivity Index was medium, Cohen's $d = .40$.

To examine the impact of the intervention on the ERN, we conducted a regression wherein treatment condition (intervention was coded as 1; control condition was coded as 2), as well as the baseline ERN was entered, predicting the post-ERN. Results suggested that the baseline ERN significantly predicted the post-ERN, $B = 0.30$, $SE\ B = 0.14$, $\beta = .32$, $p < .01$—however, treatment condition (intervention vs. control) did not predict changes in the ERN, $B = -0.13$, $SE\ B = 3.31$, $\beta = -.01$, $p = .97$. Paired-samples t tests confirmed this: scores on the pre- versus post-ERN did not differ in either the intervention group, $t(12) = 0.004$,

Table 2
Means and Standard Deviations for the Pre- and Postmeasures on the Child Error Sensitivity Index (Child Report) and the Error-Related Negativity (i.e., ΔERN Residual Score) for the Intervention and Control Groups

	Intervention		Control	
	Pre	Post	Pre	Post
Child Error Sensitivity Index (child report)	16.95 (3.47)*	15.65 (4.50)*	17.71 (3.49)	17.33 (4.50)
ΔERN	−.06 (10.84)	−.05 (10.84)	.16 (11.92)	.14 (9.91)

** $p < .01$, comparing pre- versus postmeasures.
* $p < .05$.

$p = .99$, nor the control group, $t(34) = -0.002$, $p = .99$ (see Table 2).

In this pilot study, we did not recruit participants based on elevations in error sensitivity or the ERN—however, based on the theoretical basis of the intervention (targeting above-average ERN/error sensitivity), as well as a previous study in adults suggesting that a similar intervention approach was more effective in reducing error-related brain activity among individuals characterized by an elevated ERN (Meyer et al., 2020), it is possible that the impact of the current pilot intervention would be larger among children with increased baseline error-related brain activity. To examine this possibility, we selected individuals with an ERN at or above the median at baseline and repeated the analyses described above. When only including individuals with a baseline ERN at or above the median at baseline ($N = 24$), results from a regression predicting the post-ERN scores suggested that treatment condition (intervention vs. control) did not predict changes in the ERN, $B = 7.57$, $SE\ B = 10.16$, $\beta = .15$, $p = .46$—however, paired-samples t tests suggested that although the ERN did not show evidence of change in the control group, ERN pre: $M = -17.12$, $SD = 10.41$, ERN post: $M = -10.77$, $SD = 28.10$, $t(4) = -0.53$, $p = .62$, the ERN did decrease from pre to post in the intervention group, ERN pre: $M = -15.18$, $SD = 12.20$, ERN post: $M = -1.87$, $SD = 12.20$, $t(18) = -3.18$, $p < .01$. The effect size estimate of the impact of the intervention on the ERN (among children with an elevated baseline ERN) was large, Cohen's $d = .73$.

Discussion

In the current study, we build on previous work and utilize an experimental medicine approach—conducting a pilot study to examine the extent to which a single-session, computerized intervention may engage the target of "error sensitivity" in young children (see Figure 1 for a conceptual diagram). We identify a mechanistic target (i.e., error sensitivity) and examine multiple levels of measurement of this target, finding that the child and parent report on the Child Error Sensitivity Index have good internal reliability and are moderately correlated. Additionally, the parent report on the Child Error Sensitivity Index was moderately correlated with the neural measure of error-related activation (i.e., the ERN), suggesting convergent validity between the self-report measures and the neural measure. Moreover, the parent and child reports on the Child Error Sensitivity Index, as well as the ERN, related to child anxiety symptoms, supporting the notion that error sensitivity may be a mechanistic target related to child anxiety. We also examined the impact of a brief, computer-based intervention on the child report of error sensitivity and the ERN. Results suggested that children in the intervention group displayed a greater decrease in self-reported error sensitivity from pre- to postintervention. And, although the impact of the intervention did not significantly relate to decreases in the ERN across the entire sample, exploratory analyses suggested that the intervention may have been related to a decrease in the ERN among individuals with a large baseline ERN.

Due to the limited previous work on this topic, it is especially important to examine the psychometric properties of the self and parent report on the Child Error Sensitivity Index, as well as the ERN, including their convergent validity. In the current study, we identified the mechanistic target of error sensitivity and proposed three levels of measurement of this target: parent and self-report and a neural measure. Results suggested that all three levels of measurement had good psychometric properties and were moderately convergent (i.e., parent and child reports on the Child Error Sensitivity Index were moderately correlated, and the parent report related to the child ERN. It should be noted that the internal reliability of the ERN that was observed in the current study was consistent with previous work in adults and children (Meyer et al., 2014; Riesel et al., 2013)—however, it should be noted that, contrary to previous findings (Chong & Meyer, 2018), child

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

report on the Child Error Sensitivity Index did not relate to the ERN. Furthermore, all three measures (parent and child reports of error sensitivity, and the ERN) related to child anxiety symptoms, suggesting that error sensitivity may be a viable target to reduce child anxiety. Although this was an important first step in the multilevel measurement of error sensitivity, future work could also examine additional levels of measurement: in-lab observational measures (e.g., coding children's reactivity to making mistakes), behavioral measures, multi-informants (e.g., fathers and teachers), and naturalistic observations (e.g., observing children in school).

We also examined a mediation model wherein the relationship between the ERN and child anxiety symptoms was mediated by child error sensitivity. Our theoretical model suggests that anxious individuals tend to find their mistakes more aversive and that this explains the enhanced ERN among anxious individuals that has been observed in over 60 studies to date (Meyer, 2016, 2017). Because the development of the intervention approach used in the current study is based on this notion, it is important to examine this model. Consistent with previous work (Chong & Meyer, 2018), results supported a mediation model wherein the relationship between the ERN and child anxiety symptoms was mediated by the parent report on the Child Error Sensitivity Index (although this same pattern was not significant using child report). These findings support the notion that the ERN is increased in anxious children *because they are more reactive to their mistakes* and that targeting the psychological construct of error sensitivity may be an effective way to reduce the ERN and thus anxiety in children.

Results suggested that a brief, computerized intervention, compared to a control condition, related to a decrease in child-reported error sensitivity (with a medium effect size). Although these preliminary results are promising, it remains unknown whether the impact of the intervention had any lasting impact on child error sensitivity or whether reducing child error sensitivity leads to significant reductions in child anxiety. We hypothesize that by engaging the target of error sensitivity during this brief intervention, we may expect reductions in anxiety over time (i.e., over the course of days, weeks, or months). Future longitudinal work is needed to further elucidate these issues. Moreover, the intervention was not related to a significant reduction in the ERN across the sample—however, exploratory analyses suggested that the intervention may have been more impactful among children with a larger baseline ERN. Although this is consistent with previous work in adults (Meyer et al., 2020), in the current study, we were not adequately powered to examine this question. Thus, these results should be interpreted with caution.

Although the results from the current study are promising insofar as the intervention seems to impact child error sensitivity (measured via child self-report), the impact of the intervention on the ERN was not significant across the sample. Thus, full target engagement was not achieved. In a previous study utilizing this approach in adults (Meyer et al., 2020), the intervention video was longer (1 hour) compared to the current study (20 minutes). Perhaps by lengthening the intervention, it may be more impactful. Also, the previous study was conducted in an adult population—children may require more interactive techniques (e.g., games, activities, cartoons). Additionally, the current intervention approach did not include any behavioral exposures to making mistakes on purpose. Considering that the avoidance of errors may be important in maintaining the fear of errors, this may be an important consideration. Other important considerations include the fact that the intervention video was delivered during a single session and may not have allowed children enough time and exposure to the materials to internalize them. We are currently collecting data for a large, NIH-funded, follow-up study, examining the impact of a computerized parent and child intervention targeting child error sensitivity, which includes behavioral exposures to making mistakes on purpose, as well as weekly booster sessions (5-minute videos) for 6 months. Results from this study will fill in the gaps from the current investigation (e.g., determining whether the intervention makes a lasting impact on error sensitivity and whether reductions in error sensitivity relate to changes in child anxiety).

The current study has several limitations. As mentioned above, we did not include a follow-up assessment to determine whether the intervention had a lasting impact on error sensitivity or the ERN. And, because there were no follow-up assessments, we could not utilize parent report of child error sensitivity or anxiety symptoms as a postmeasure. Additionally, in the current study, we did not recruit participants based on elevations in error sensitivity or the ERN. Thus, this may not have been an ideal sample for testing this intervention and the study may have been underpowered to detect intervention effects among children with a large baseline ERN. Additionally, although the research assistants who administered the question-

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

naires to child participants were unaware of the study purpose, design, and hypotheses, they could have heard the content of the intervention or control videos as the child was viewing them, and thus may have inadvertently influenced the responses of the child.

Overall, the results from the current study are an important extension of previous work suggesting that the ERN may be a malleable, neurobiological intervention target. Considering that an increased ERN early in life is a marker of risk for anxiety, combined with the fact that traditional CBT approaches do not appear to impact the ERN, this approach may aid the development of a novel prevention and intervention approach. Results from this preliminary pilot study were promising insofar as we observed good construct validity among multiple levels of measurement (i.e., child and parent reports of child error sensitivity and the ERN were related); we observed that child error sensitivity and the ERN related to child anxiety; and we observed that a brief, computerized intervention reduced child error sensitivity. Future work is needed to determine whether these effects are lasting and clinically meaningful.

References

Achenbach, T. M., & Edelbrock, C. (1981). *Child Behavior Checklist*. Erlbaum.

Barke, A., Bode, S., Dechent, P., Schmidt-Samoa, C., Van Heer, C., & Stahl, J. (2017). To err is (perfectly) human: Behavioural and neural correlates of error processing and perfectionism. *Social Cognitive and Affective Neuroscience, 12*(10), 1647–1657.

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, and 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, 55*(9), e13089.

Bress, J. N., Meyer, A., & Hajcak, G. (2015). Differentiating anxiety and depression in children and adolescents: Evidence from event-related brain potentials. *Journal of Clinical Child and Adolescent Psychology, 44*(2), 238–249.

Cavanagh, J. F., & Shackman, A. J. (2015). Frontal midline theta reflects anxiety and cognitive control: Meta-analytic evidence. *Journal of Physiology, Paris, 109*(1–3), 3–15.

Cavanagh, J. F., Zambrano-Vazquez, L., & Allen, J. J. (2012). Theta lingua franca: A common mid-frontal substrate for action monitoring processes. *Psychophysiology, 49*(2), 220–238.

Chong, L. J., & Meyer, A. (2018). Understanding the link between anxiety and a neural marker of anxiety (the error-related negativity) in 5 to 7 year-old children. *Developmental Neuropsychology*, 1–17.

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.

Falkenstein, M., Hoormann, J., Christ, S., & Hohnsbein, J. (2000). ERP components on reaction errors and their functional significance: A tutorial. *Biological Psychology, 51*(2–3), 87–107. https://doi.org/10.1016/s0301-0511(99)00031-9.

Ganushchak, L. Y., & Schiller, N. O. (2008). Motivation and semantic context affect brain error-monitoring activity: An event-related brain potentials study. *NeuroImage, 39*(1), 395–405.

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. H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology, 55*(4), 468–484. https://doi.org/10.1016/0013-4694(83)90135-9.

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

Hajcak, G., Franklin, M. E., Foa, E. B., & Simons, R. F. (2008). Increased error-related brain activity in pediatric obsessive-compulsive disorder before and after treatment. *American Journal of Psychiatry, 165*(1), 116–123. https://doi.org/10.1176/appi.ajp.2007.07010143.

Hajcak, G., Moser, J. S., Yeung, N., & Simons, R. F. (2005). On the ERN and the significance of errors. *Psychophysiology, 42*(2), 151–160.

Kim, E. Y., Iwaki, N., Uno, H., & Fujita, T. (2005). Error-related negativity in children: Effect of an observer. *Developmental Neuropsychology, 28*(3), 871–883.

Kujawa, A., Weinberg, A., Bunford, N., Fitzgerald, K. D., Hanna, G. L., Monk, C. S., Kennedy, A. E., Klumpp, H., Hajcak, G., & 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 and Biological Psychiatry, 71*, 162–168.

Ladouceur, Cecile D., Tan, Patricia Z., Sharma, Vinod, Bylsma, Lauren M., Silk, Jennifer S., Siegle, Greg J., & Forbes, Erika E. (2018). Error-related brain activity in pediatric anxiety disorders remains elevated following individual therapy: a randomized clinical trial. *Journal of Child Psychology and Psychiatry, 59*(11), 1152–1161.

Lahat, A., Lamm, C., Chronis-Tuscano, A., Pine, D. S., Henderson, H. A., & Fox, N. A. (2014). Early behavioral inhibition and increased error monitoring predict later social phobia symptoms in childhood. *Journal of the American Academy of Child and Adolescent Psychiatry, 53*(4), 447–455.

MacKinnon, D. P., Lockwood, C. M., Hoffman, J. M., West, S. G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods, 7*(1), 83–104.

MacKinnon, D. P., Lockwood, C. M., & Williams, J. (2004). Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate Behavioral Research, 39*(1), 99–128.

Mancebo, Maria C., Boisseau, Christina L., Garnaat, Sarah L., Eisen, Jane L., Greenberg, Benjamin D., Sibrava, Nicholas J., Stout, Robert L., & Rasmussen, Steven A. (2014). Long-term course of pediatric obsessive–compulsive disorder: 3 years of prospective follow-up. *Comprehensive Psychiatry, 55*(7), 1498–1504.

McDermott, J. M., Perez-Edgar, K., Henderson, H. A., Chronis-Tuscano, A., Pine, D. S., & Fox, N. A. (2009). A history of childhood behavioral inhibition and enhanced response monitoring in adolescence are linked to clinical

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

anxiety. *Biological Psychiatry, 65*(5), 445–448. https://doi.org/10.1016/j.biopsych.2008.10.043.

Meyer, A. (2016). Developing psychiatric biomarkers: A review focusing on the error-related negativity as a biomarker for anxiety. *Current Treatment Options in Psychiatry, 3*, 356–364.

Meyer, A. (2017). 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. (2022). On the relationship between the error-related negativity and anxiety in children and adolescents: From a neural marker to a novel target for intervention. *Psychophysiology, 59*(6), e14050.

Meyer, A., Bress, J., & Proudfit, G. H. (2014). Psychometric properties of the error-related negativity in children and adolescents. *Psychophysiology, 51*(7), 602–610.

Meyer, A., Carlton, C., Chong, L. J., & Wissemann, K. (2019). The presence of a controlling parent is related to an increase in the error-related negativity in 5–7 year-old children. *Journal of Abnormal Child Psychology, 47*(6), 935–945.

Meyer, A., & Gawlowska, M. (2017). Evidence for specificity of the impact of punishment on error-related brain activity in high versus low trait anxious individuals. *International Journal of Psychophysiology, 120*, 157–163.

Meyer, A., Gibby, B., Wissemann, K., Klawohn, J., Hajcak, G., & Schmidt, N. B. (2020). A brief, computerized intervention targeting error sensitivity reduces the error-related negativity. *Cognitive, Affective, and Behavioral Neuroscience, 20*(1), 172–180.

Meyer, Alexandria, Greg Hajcak, Dana C. Torpey, Autumn Kujawa, Jiyon Kim, Sara Bufferd, Gabrielle Carlson, and Daniel N. Klein. Increased error-related brain activity in six-year-old children with clinical anxiety. Journal of abnormal child psychology, (41) 2013:1257–1266.

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), 266–274.

Meyer, A., & Klein, D. N. (2018). Examining the relationships between error-related brain activity (the ERN) and anxiety disorders versus externalizing disorders in young children: Focusing on cognitive control, fear, and shyness. *Comprehensive Psychiatry, 87*, 112–119.

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., Mehra, L., & Hajcak, G. (2021). Error-related negativity predicts increases in anxiety in a sample of clinically anxious female children and adolescents over 2 years. *Journal of Psychiatry and Neuroscience, 46*(4), E472–E479.

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, 59*(11), 1162–1170.

Meyer, A., & Wissemann, K. (2020). Controlling parenting and perfectionism is associated with an increased error-related negativity (ERN) in young adults. *Social Cognitive and Affective Neuroscience, 15*(1), 87–95.

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*, 466.

Nielsen, Lisbeth, Riddle, Melissa, King, Jonathan W., Aklin, Will M., Chen, Wen, Clark, David, Collier, Elaine, et al. (2018). The NIH Science of Behavior Change Program: Transforming the science through a focus on mechanisms of change. *Behaviour research and therapy, 101*, 3–11.

Ollendick, T. H. (1983). Reliability and validity of the revised Fear Survey Schedule for Children (FSSC-R). *Behaviour Research and Therapy, 21*(6), 685–692.

Olvet, D. M., & Hajcak, G. (2009). Reliability of error-related brain activity. *Brain Research, 1284*, 89–99.

Perrone-McGovern, Kristin, Simon-Dack, Stephanie, Esche, Aaron, Thomas, Christopher, Beduna, Kerry, Rider, Katie, Spurling, Alyssa, & Matsen, Julie (2017). The influence of emotional intelligence and perfectionism on Error-Related Negativity: An event related potential study. *Personality and Individual Differences, 111*, 65–70.

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, and Computers, 36*(4), 717–731.

Riddle, M., & Science of Behavior Change Working Group (2015). News from the NIH: Using an experimental medicine approach to facilitate translational research. *Translational Behavioral Medicine, 5*(4), 486–488.

Riesel, A. (2019). The erring brain: Error-related negativity as an endophenotype for OCD—a review and meta-analysis. *Psychophysiology, 56*(4), e13348.

Riesel, A., Endrass, T., Auerbach, L. A., & Kathmann, N. (2015). Overactive performance monitoring as an endophenotype for obsessive-compulsive disorder: Evidence from a treatment study. *American Journal of Psychiatry, 172*(7), 665–673. https://doi.org/10.1176/appi.ajp.2014.14070886.

Riesel, A., Kathmann, N., Wüllhorst, V., Banica, I., & Weinberg, A. (2019a). Punishment has a persistent effect on error-related brain activity in highly anxious individuals twenty-four hours after conditioning. *International Journal of Psychophysiology, 146*, 63–72.

Riesel, Anja, Klawohn, Julia, Grützmann, Rosa, Kaufmann, Christian, Heinzel, Stephan, Bey, Katharina, Lennertz, Leonhard, Wagner, Michael, & Kathmann, Norbert (2019b). Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder. *Psychological medicine,, 49*(7), 1207–1217.

Riesel, A., Weinberg, A., Endrass, T., Kathmann, N., & Hajcak, G. (2012). Punishment has a lasting impact on error-related brain activity. *Psychophysiology, 49*(2), 239–247.

Riesel, A., Weinberg, A., Endrass, T., Meyer, A., & Hajcak, G. (2013). The ERN is the ERN is the ERN? Convergent validity of error-related brain activity across different tasks. *Biological Psychology, 93*(3), 377–385.

Schrijvers, D. L., De Bruijn, E. R., Destoop, M., Hulstijn, W., & Sabbe, B. G. (2010). The impact of perfectionism and anxiety traits on action monitoring in major depressive disorder. *Journal of Neural Transmission, 117*(7), 869–880.

Shackman, A. J., Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J., & Davidson, R. J. (2011). The integration of

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005

negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience, 12*(3), 154–167.

Stahl, J., Acharki, M., Kresimon, M., Völler, F., & Gibbons, H. (2015). Perfect error processing: Perfectionism-related variations in action monitoring and error processing mechanisms. *International Journal of Psychophysiology, 97*(2), 153–162.

Tang, A., Crawford, H., Morales, S., Degnan, K. A., Pine, D. S., & Fox, N. A. (2020). Infant behavioral inhibition predicts personality and social outcomes three decades later. *Proceedings of the National Academy of Sciences, 117*(18), 9800–9807.

Voegler, R., Peterburs, J., Lemke, H., Ocklenburg, S., Liepelt, R., & Straube, T. (2018). Electrophysiological correlates of performance monitoring under social observation in patients with social anxiety disorder and healthy controls. *Biological Psychology, 132*, 71–80.

Weinberg, A., Dieterich, R., & Riesel, A. (2015a). Error-related brain activity in the age of RDoC: A review of the literature. *International Journal of Psychophysiology, 98* (2), 276–299.

Weinberg, A., Kotov, R., & Proudfit, G. H. (2015b). Neural indicators of error processing in generalized anxiety disorder, obsessive-compulsive disorder, and major depressive disorder. *Journal of Abnormal Psychology, 124*(1), 172–185.

Weinberg, A., Meyer, A., Hale-Rude, E., Perlman, G., Kotov, R., Klein, D. N., & Hajcak, G. (2016). Error-related negativity (ERN) and sustained threat: Conceptual framework and empirical evaluation in an adolescent sample. *Psychophysiology, 53*(3), 372–385.

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., 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, 36*(1), 84–100.

Received: February 8, 2022
Revised: January 11, 2023
Accepted: January 19, 2023
Available online: xxxx

Please cite this article as: Meyer, Chong, Wissemann et al., An Experimental Therapeutics Approach to the Development of a Novel Computerized Treatment Targeting Error-Related Brain Activity in Young Children, Behavior Therapy, https://doi.org/10.1016/j.beth.2023.01.005