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Early behavioral inhibition and increased error monitoring predict later social phobia symptoms in childhood

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Abstract

Objective—Behavioral inhibition (BI) is an early childhood temperament characterized by fearful responses to novelty and avoidance of social interactions. During adolescence, a subset of children with stable childhood BI develop social anxiety disorder and concurrently exhibit increased error monitoring. The current study examines whether increased error monitoring in seven-year-old behaviorally inhibited children prospectively predicts risk for symptoms of social phobia at age 9.

Method—Two hundred and ninety one children were characterized on BI at 24 and 36 months of age. Children were seen again at 7 years of age, where they performed a Flanker task, and event-related-potential (ERP) indices of response monitoring were generated. At age 9, self- and maternal-report of social phobia symptoms were obtained.

Results—Children high in BI, compared to those low in BI, displayed increased error monitoring at age 7, as indexed by larger (i.e., more negative) error-related negativity (ERN) amplitudes. Additionally, early BI was related to later childhood social phobia symptoms at age 9 among

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children with a large difference in amplitude between ERN and correct-response negativity (CRN) at age 7.

Conclusions—Heightened error monitoring predicts risk for later social phobia symptoms in children with high BI. Research assessing response monitoring in children with BI may refine our understanding of the mechanisms underlying risk for later anxiety disorders and inform prevention efforts.

Keywords

Behavioral inhibition; error monitoring; ERN; anxiety; longitudinal

Behavioral inhibition (BI) is an early childhood temperament characterized by fearful responses to novelty and avoidance of social interactions¹⁻⁴. Adolescents characterized with BI in childhood face increased risk for anxiety^{1, 5-7}, particularly social phobia⁸. Nevertheless, only about 40% of children with BI develop anxiety⁸. Behaviorally inhibited children who show enhanced vigilance face particularly high risk for anxiety⁹, possibly through increased response monitoring¹⁰. Thus, neural correlates associated with this underlying mechanism may identify a subset of behaviorally inhibited children facing particularly high risk¹. Prior studies collected data concurrently rather than prospectively in adolescence or adulthood^{1,11-13}. The current prospective study examines response-monitoring data at age 7 to predict anxiety at age 9, in order to understand why some, but not all, behaviorally inhibited children develop anxiety.

Event-related-potentials (ERPs) associated with response monitoring have been linked to anxiety¹¹⁻¹⁶. These include the error related negativity (ERN), correct response negativity (CRN), and error positivity (Pe). The ERN has a medial-frontal scalp distribution, typically peaking 50-to-100 ms following an erroneous response¹⁷. Developmental studies suggest that this component is expressed in an earlier time window and with smaller amplitude in young children than in adolescents and adults¹⁸. Furthermore, the ERN often precedes an erroneous response, potentially occurring precisely when errors are initiated¹⁹. In contrast, the CRN occurs after correct responses and is considered an index of response control²⁰. Trials following this component are characterized by increased accuracy and reduced reaction time interference²¹. Furthermore, the CRN reflects a comparison between the actual response and desired response²² and is frequently used as a comparison condition to the ERN (ERN-CRN)²³⁻²⁵. The Pe is also associated with response monitoring, and is usually observed between 200-to-500 ms following an error and its functional significance has been debated²⁶. Some consider it to reflect conscious awareness of errors²⁷, while others argue that it is associated with affective processing²² or the motivational significance of the error²⁸.

Studies on response monitoring and anxiety consistently find increased ERNs in adults with anxiety relative to healthy adults^{12,13,15,16}. Similar findings emerge in children and adolescents^{14,29,30}. For example, anxious 6-year-olds were characterized by a larger (i.e., more negative) ERN³¹. Additionally, among older children (age 11-13), elevated anxiety symptoms were associated with a larger ERN, whereas among younger children (age 8-10), the ERN-anxiety relation was not significant¹¹. Furthermore, a smaller Pe was associated

with greater anxiety, but only among older children¹¹. Thus, although the ERN is linked to anxiety, developmental questions remain that can be clarified through a longitudinal study of BI.

In prior research, adolescents high in childhood BI displayed increased ERNs compared to those with low childhood BI, linking early BI to increased error monitoring in adolescence. Importantly, only among adolescents with a history of childhood BI did larger ERN amplitudes relate to higher levels of anxiety¹. This prior study assessed ERN in adolescence concurrently with anxiety. As a result, it is unclear whether error monitoring moderates the link between early BI and later anxiety, and whether this pattern is present earlier in development, prior to the onset of anxiety.

The present longitudinal study examined response monitoring amongst 7-year-old children, characterized by BI during early childhood. We focused on social phobia symptoms, the most common class of anxiety linked to BI^{5,7,8,32,33}. We expected increased error monitoring in high, relative to low, behaviorally inhibited children. Furthermore, we expected that error monitoring would moderate the link between early BI and later social phobia symptoms during childhood.

Method

Participants and procedure

Infants (N=779) were seen at 4 months of age, during which positive and negative affect and motor reactivity to novel stimuli were assessed (for a complete description see³⁴). Of this sample, 291 infants (135 males, 156 females) representing the full range of reactivity were selected for a longitudinal study, with 64% Caucasian, 14% African-American, and 22% from other backgrounds. When children were 24 and 36 months of age, observations were conducted on 268 participants, and maternal report of temperament was collected. At age 7, 173 children completed an ERP Flanker task³⁵. Reasons for missing data included difficulty scheduling visits (n = 87), refusal to wear the EEG net or complete the task (n = 4), and technical errors (n = 4). An additional 47 children were excluded because they completed a version of the task that did not yield enough errors. Of the 126 who completed the task, children with less than 30% accuracy or fewer than 10 artifact-free trials were excluded, yielding behavioral data on 113 participants, CRN data on 106 participants, and ERN, ERN-CRN, and Pe data on 67 participants. No significant differences were found on BI, all $ps > .09$, or gender, all $ps > .22$, for participants who were included or excluded. At age 7, we obtained maternal-report on the Child Behavior Checklist (CBCL; n = 188)³⁶. Participants were re-assessed at 9 years using maternal- and child-report on the Screen for Child Anxiety Related Emotional Disorders-Revised (SCARED-R) (n=125),^{37,38} and the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)³⁹ (n=116). Hierarchical regression examined ERP moderation of the BI-social phobia symptoms relations in n=67 (CRN), n=46 (ERN-CRN), or n=47(ERN, Pe) participants. Consent was obtained in an IRB-approved protocol.

Measures

Behavioral inhibition.—BI was observed at 24 and 36 months of age during three episodes (stranger, robot, tunnel) involving unfamiliar people and objects^{2,40}. Observations were coded for each episode and inter-rater reliability (Intraclass correlations) ranged from .72 to .98 ($M = .87$; 19% overlap; two coders) for 2-year coding and .93 to 1.00 ($M = .98$; 10% overlap; two coders) for 3-year coding. Maternal report of social fear was obtained using the Toddler Behavior Assessment Questionnaire (TBAQ;⁴¹). As in previous work, measures were standardized and averaged to create a BI composite^{42,43}. Combining data from different contexts, informants, and ages better reflects the child's temperament than one single measure alone. The BI composite was created based on theory and confirmed through principal components analysis (eigenvalue = 2.04; loadings = .62–.81).

Flanker task—The Flanker task was administered at 7 years of age³⁵. Participants completed 24 practice trials. For 4 errors or less, they completed a faster version of the task; for 5 to 11 errors they completed a slower version; for 12 to 24 errors they repeated the practice until they had 11 errors or less. A total of 11 children were administered the fast version (5 high BI; 6 low BI). Similar results were obtained when removing these children from the analyses. The task was then administered, comprising 200 trials (64 congruent and 136 incongruent) presented across four blocks, using proportionately more incongruent trials to increase errors⁴⁴ and to elicit ERN in this young sample of children¹⁸.

In each trial, a fixation appeared for 190 ms, followed by a 40 ms black screen, and then a 250 ms (fast version) or 300 ms (slow version) target (five fish presented horizontally). Fish-targets were either pointing left or right (divided equally across each block), with the central fish being either congruent or incongruent with the flanking fish. Participants made right-button pushes for central fish-targets pointing right, and left-button pushes for central fish-targets pointing left. Participants were asked to respond as quickly and as accurately as possible. Following the fish, a black response window screen appeared for 500 ms (fast) or 600 ms (slow). Participants were allowed to respond either during the fish stimulus or the response window. The response window was followed by a 640 ms black screen. Next, feedback appeared for 1000 ms (positive feedback) or 690 ms (negative feedback). The feedback consisted of a smiley face for correct responses, and a sad face for incorrect or no responses. Feedback was followed by a 90 ms black screen. The purpose of the feedback was to keep children engaged. As well, positive feedback was longer than negative feedback in order to make it more salient and engaging. Feedback ERPs were not examined.

CBCL—At age 7, mothers completed the CBCL³⁶, a standardized, reliable measure of emotional and behavioral problems. We used the anxiety problems subscale raw score to index anxiety during the age of ERP assessments.

SCARED-R—At age 9, both children and mothers completed the SCARED-R^{37,38}, also a standardized, reliable measure⁴⁵. Based on prior work^{5,8}, our main focus was on the social phobia symptoms scale. However, other SCARED-R scales were used as well. To reduce statistical tests and generate cross-informant indices, scales were standardized and averaged

across informants (cross-informant correlation, $r = .26$; $p < .01$)^{46,47}. This averaging creates a multi-perspective measure.

K-SADS-PL—At age 9, children and their mothers completed the K-SADS-PL, conducted by a clinical psychologist supervised by diagnostic experts blind to BI data³⁹. Procedures were identical to those from prior work⁵. Reliability was monitored by random expert review of audio-recordings in approximately 50% of cases; this generated acceptable reliability ($\kappa > 0.75$) for a clinical anxiety disorder diagnosis. Children with any current, $t(88) = -3.69$, $p < .0001$, or lifetime, $t(88) = -3.43$, $p < .001$, anxiety disorder scored significantly higher on the social phobia symptoms composite of the SCARED-R, (Any current $M = .10$, $SD = .92$; Any lifetime $M = .62$, $SD = .10$) as compared to children without anxiety (Any current $M = -.01$, $SD = .72$; Any lifetime $M = -.06$, $SD = .67$). These results demonstrate clinical relevance of data obtained with the SCARED-R. However, because only ten (5 High BI; 5 Low BI) of 126 children completing the Flanker had any anxiety disorder, K-SADS-PL data were not analyzed further.

ERP data collection and analysis—EEG was recorded using a 64-channel Hydrocel net and sampled at 250 Hz, using EGI software (Net Station; Electrical Geodesic, Inc., Eugene, OR), with impedance values below 50 k Ω . All channels were referenced to Cz and after acquisition, data were re-referenced using an average reference. Data were filtered using a FIR bandpass filter with a low pass frequency of 50 Hz and a high pass frequency of .3 Hz. Eye-blink artifact thresholds were set to a peak-to-peak difference of 140 μ V. Trials in which blinks were identified were removed. Electrodes with signal activation change exceeding a peak-to-peak difference of 190 μ V across the entire trial were marked as bad and interpolated. Response-locked waveforms for correct and incorrect congruent and incongruent trials were segmented into epochs from 250 ms before to 650 ms after the response and baseline corrected from -250 to -50 ms preceding the response. Mediofrontal scalp ERN and CRN activation at FCz was maximal between -20 and 20 ms. Pe activation was maximal at Cz between 190 and 270 ms. Thus, peak activation for error (ERN, Pe) and correct (CRN) trials was exported for these time windows. Additionally, mean activation during these time periods was also exported. Mean activation results were similar to peak activation results, thus, to avoid redundancy, only results corresponding to peak activation are reported.

Results

To maintain consistency with prior research^{1,48,49}, high and low BI groups were created via median split (see Table 1 for characteristics). The two BI groups did not differ on age, $t(111) = .43$, $p = .67$, sex, $\chi^2(1, n = 113) = .19$, $p = .66$, ethnicity, $\chi^2(11, n = 113) = 11.25$, $p = .42$, CBCL anxiety $t(100.47) = -1.53$, $p = .13$, or social phobia symptoms, $t(76) = -.50$, $p = .62$.

Flanker behavioral results

Since preliminary behavioral analysis revealed sex differences, sex was entered as a factor in all Flanker analyses. Separate repeated measures analyses of variance (ANOVA) were

conducted for accuracy, reaction times (RTs), and post-error slowing with BI group (high, low) and sex (male, female) as between subjects factors, and condition (congruent, incongruent) as a repeated measure. The ANOVA for accuracy revealed a main effect for condition, $F(1, 109) = 126.37, p < .0001, \eta_p^2 = .51$, with higher accuracy on congruent than incongruent trials (Table 1), and a main effect for sex, $F(1, 109) = 6.93, p < .01, \eta_p^2 = .06$, with females ($M = .72, SE = .02$) performing better than males ($M = .63, SE = .03$). The ANOVA for RTs revealed a main effect for condition, $F(1, 109) = 49.40, p < .0001, \eta_p^2 = .31$, with faster RTs on congruent than incongruent trials (Table 1), and a main effect for sex, $F(1, 109) = 8.78, p < .01, \eta_p^2 = .08$, with males ($M = 472.27, SE = 11.73$) having faster RTs than females ($M = 519.64, SE = 10.87$). The ANOVA for post-error slowing revealed a main effect for sex, $F(1, 109) = 11.04, p < .001, \eta_p^2 = .09$, with females ($M = 26.60, SE = 6.32$) slowing down more than males ($M = -4.28, SE = 6.82$) after erroneous responses. No behavioral effects emerged with BI.

Flanker ERP results

An examination of the response-locked topographical plots of the grand-averaged data revealed fronto-central ERN and CRN components, as well as a central Pe component. Based on topographical maps, ERP data were analyzed at FCz for ERN and CRN and at Cz for Pe. Because few participants had at least 10 artifact free error trials in the congruent condition, only incongruent trials were analyzed (error trial counts $M = 25.21, SD = 12.94$; correct trial counts $M = 46.18, SD = 22.94$). This is consistent with the notion that the incongruent condition is the main condition of interest, as it is associated with increased conflict and error monitoring⁵⁰. Figure 1 presents grand averaged waveforms for each BI group. Because the number of trials comprising an ERP can affect ERP activation, trial counts were entered as covariates in all ERP analyses. ANCOVAs were conducted on ERN, CRN, ERN-CRN, and Pe amplitudes with BI group (high, low) and sex (male, female) as between-subjects factors.

ERN results indicated a main effect for BI group, $F(1, 62) = 8.12, p < .01, \eta_p^2 = .12$, with high behaviorally inhibited ($M = -2.46, SD = 3.63$) children showing a larger (i.e., more negative) ERN amplitude than low behaviorally inhibited children ($M = -.57, SD = 2.39$). No other significant main effects or interactions were found. No significant main effects or interactions were found for the ANCOVA with CRN. Next, consistent with prior research using these components (e.g.,^{23,24,25}), we calculated a difference score between amplitudes on incongruent ERN and incongruent CRN trials (i.e., ERN-CRN), thereby creating a more pure measure of error monitoring. No significant main effects or interactions were found for the ANCOVA with ERN-CRN. Finally, the results for Pe indicated a main effect for sex, $F(1, 62) = 4.65, p < .05, \eta_p^2 = .07$, with males ($M = 3.09, SD = 4.88$) showing a larger Pe amplitude than females ($M = .53, SD = 4.81$).

Pearson correlations examined the association between task performance and ERP amplitudes. ERN-CRN difference score on incongruent trials negatively correlated with RTs on incongruent trials, $r = -.31, p < .01$, suggesting that as ERN-CRN difference increases (i.e., becomes more negative), RTs become slower. Additionally, CRN on incongruent trials

positively correlated with RTs on incongruent trials, $r = .22, p < .05$, suggesting that as CRN amplitude decreases (i.e., becomes more positive) RTs become slower.

ERP moderation of BI-anxiety association

We examined whether ERP amplitudes moderated the early-BI/age-9-social phobia symptoms relation. We also examined other age-9 SCARED-R scores and CBCL anxiety at age 7. Separate hierarchical multiple regression analyses were conducted with either ERN, CRN, ERN-CRN, or Pe as moderators. To reduce multi-collinearity and aid in interpretation, mean centered predictors were used. Next, the interaction terms were computed as the product between BI group and the mean-centered ERP measure (amplitudes for negative ERP components were multiplied by -1 in order to aid in interpretation). The first step of each regression included the effects of sex, trial counts, BI, and ERP amplitude. For age-9 SCARED-R, we also entered CBCL anxiety at age 7 to control for anxiety during the time of the ERP assessment. To test for significant moderation effects of ERP amplitude on the link between BI and anxiety, the interaction product term between BI group and ERP amplitude was entered in the second step of each regression analysis. Although all of the regression models were examined, the moderation hypotheses were tested in the second step for whether they significantly increased the variance explained by the models. Interactions were probed and plotted according to the guidelines by Aiken and West⁵¹. High and low levels of ERP amplitudes were computed as ± 1 SD. Follow-up regressions from these probes are reported below.

Significant results were found only for the interaction between BI group and ERN-CRN in predicting social phobia symptoms. This interaction significantly improved the model, $R^2 = .10, F(1,38) = 4.85, p < .05$. The full model with the interaction term predicted 26% of the variance in social phobia symptoms (Table 2, Figure 2). To decompose this interaction, follow-up regressions were conducted. The findings indicate that among participants who had a relatively large ERN-CRN, BI group was positively related to later social phobia symptoms, $\beta = .45, t(38) = 2.30, p < .05$. However, no such relation emerged in participants with a small ERNCRN, $\beta = -.18, t(38) = -.88, p = .38$.

When examining other SCARED-R scales, a significant interaction was found between BI group and ERN-CRN in predicting generalized anxiety symptoms, $R^2 = .10, F(1,34) = 5.57, p < .05$. However, follow-up regressions for generalized anxiety symptoms were not significant. Additionally, a trend was found for the interaction between BI group and ERN-CRN in predicting total anxiety symptoms, $R^2 = .09, F(1,31) = 3.91, p = .06$. No significant findings were obtained when examining CBCL anxiety at age 7.

Discussion

In this prospective study, 7-year-old children, characterized with BI at ages 2 and 3 participated in a Flanker task. When these children were 9-years-old, self- and maternal-report measures of social phobia symptoms were obtained. Two main findings emerged. First, high behaviorally inhibited children exhibited increased ERN amplitudes, as compared to low behaviorally inhibited children. Second, the ERN-CRN difference in amplitude moderated the relations between early BI, as quantified four years *before* the ERP

assessment, and social phobia symptoms, as quantified two years *after* the ERP assessment. Specifically, BI was positively related to social phobia symptoms at age 9 only among children with large ERN-CRN at age 7. This study is the first to demonstrate associations between error monitoring and social phobia symptoms prospectively in a non-clinical but high risk sample.

Our ERP findings are consistent with prior studies suggesting that high behaviorally inhibited children show heightened response monitoring and increased performance concerns^{1,48,49}. This may contribute to increased vigilance and fear of negative evaluation when monitoring their internal and external environments. The findings are also consistent with research indicating that anxious individuals are characterized by increased error monitoring, e.g.,^{11,12,13,31}. Children with increased error monitoring who are also highly behaviorally inhibited may not flexibly engage their control processes, and this can result in a pattern of hyper-vigilance, as well as rigid, inflexible, and over controlled behaviors in social situations⁵². In turn, this could lead to maladaptive social-emotional behaviors, including social phobia symptoms.

Our findings suggest that the *combination* of early BI and increased error monitoring predict social phobia symptoms later in childhood. BI alone did not predict social phobia symptoms, rather those children who were both highly behaviorally inhibited *and* showed increased error monitoring, also showed increased social phobia symptoms. These data are consistent with other studies which demonstrated that not all behaviorally inhibited children are at risk for anxiety^{1,53} and provide insight for a mechanism linking childhood temperament and anxiety symptoms. As such it may have potential implications for early intervention and prevention.

Significant findings were observed particularly for social phobia symptoms. These findings are consistent with previous research showing that social anxiety is most prevalent among behaviorally inhibited children and adolescents^{5,7,8,32}. We also found a significant interaction between BI and ERN-CRN for the generalized anxiety (albeit follow-up analyses were not significant) and a trend for the total anxiety scale. These findings are consistent with studies showing relations between BI and other types of anxiety^{5,6}. It is important to note, that no BI group differences in anxiety were found at age 7 during the time of the ERP assessment. In addition, the interaction between BI and ERPs did not predict anxiety at age 7, but did predict social phobia symptoms at age 9 when controlling for age 7 anxiety.

Our results are line with prior research showing increased ERN amplitudes among 6-year-old anxious children³¹. However, other work found that the relation between ERN and anxiety is moderated by age: only for older children (age 11-13) was a large ERN related to increased anxiety, while the relation was not significant for younger children (age 8-10)¹¹. Although the ERN-anxiety relation is becoming clearer, our work extends prior research and points to the importance of considering individual differences related to temperament, which may account for some of these discrepancies between studies.

Despite the ERP BI group differences, we did not find group differences on behavioral measures of the Flanker task. This suggests that children high and low in BI maintained

comparable levels of task performance despite differences in physiological responses. These findings also point to the greater sensitivity of neurophysiological data than behavioral data alone. Nonetheless, we found correlations between ERPs and RTs. Thus, overall, behavior during this task appears to be related to ERP activation.

Of note, our ERP findings were observed with ERN, and not ERN-CRN, while the moderation of social phobia symptoms was observed with ERN-CRN, and not ERN. The CRN reflects a comparison between the actual response and desired response²². The ERN may involve this comparison process along with error detection, whereas the CRN does not involve error detection. If so, subtracting the CRN from ERN provides a purer measure of error detection. It is possible that in our sample, ERN-CRN is related more to social phobia symptoms than the combination of the error signal with the comparison process, or the comparison process alone. Also, BI and ERN were related to one another and this could limit power to detect an interaction between them. Additionally, we did not observe significant BI group or moderation findings with Pe. This is not at odds with prior research on BI¹, as well as work with anxious adolescents²⁹, and the Pe has not been consistently associated with anxiety^{14,16}.

Our results predicting social phobia symptoms were obtained with the SCARED-R, a measure of subthreshold anxiety symptoms and not a clinical diagnosis of anxiety. However, the reliability and validity of the SCARED-R have been established with children diagnosed with anxiety disorders⁴⁵. Moreover, our SCARED-R data were related to anxiety diagnoses using the K-SADS-PL. Our findings are important in light of the notion that childhood anxiety symptoms predict risk for adolescent anxiety disorders⁵⁴. Early identification may allow clinicians to target children in need for prevention and early intervention.

Finally, the attrition rate in the present study should be acknowledged. Although this is a limitation, attrition in longitudinal designs with young children is expected. Additional loss of data in the present study is related to ERP methodology and the difficulty to collect usable ERP data with young children.

In sum, our findings suggest increased error monitoring among high behaviorally inhibited children as compared to low behaviorally inhibited children. Furthermore, error monitoring plays a role in the relation between BI and social phobia symptoms during childhood. These findings during childhood extend previous work with behaviorally inhibited adolescents¹. Taken together, this line of work demonstrates that error-monitoring may be an important mechanism that plays a role in the relation between early BI and later anxiety problems. Given that childhood anxiety symptoms predict risk for adolescent anxiety⁵⁴, future research should follow children with BI through adolescence in order to better understand risk for adolescent anxiety disorders.

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References

1. McDermott JM, Perez-Edgar K, Henderson HA, Chronis-Tuscano A, Pine DS, Fox NA. A history of childhood behavioral inhibition and enhanced response monitoring in adolescence are linked to clinical anxiety. *Biological Psychiatry*. 2009; 65(5):445–448. [PubMed: 19108817]
2. Fox NA, Henderson HA, Rubin KH, Calkins SD, Schmidt LA. Continuity and discontinuity of behavioral inhibition and exuberance: Psychophysiological and behavioral influences across the first four years of life. *Child Development*. 2001; 72(1):1–21. [PubMed: 11280472]
3. Kagan J, Snidman N. Temperamental factors in human development. *American Psychologist*. 1991; 46(8):856–862. [PubMed: 1928938]
4. Fox NA, Henderson HA, Marshall PJ, Nichols KE, Ghera MM. Behavioral inhibition: linking biology and behavior within a developmental framework. *Annu. Rev. Psychol.* 2005; 56:235–262. [PubMed: 15709935]
5. Chronis-Tuscano A, Degnan KA, Pine DS, et al. Stable early maternal report of behavioral inhibition predicts lifetime social anxiety disorder in adolescence. *J Am Acad Child Adolesc Psychiatry*. Sep; 2009 48(9):928–935. [PubMed: 19625982]
6. Biederman, J.; Rosenbaum, JF.; Chaloff, J.; Kagan, J. Behavioral inhibition as a risk factor for anxiety disorders.. In: March, JS., editor. *Anxiety disorders in children and adolescents*. Guilford Press; New York, NY: 1995. p. 61-81.
7. Biederman J, Hirshfeld-Becker DR, Rosenbaum JF, et al. Further evidence of association between behavioral inhibition and social anxiety in children. *American journal of Psychiatry*. 2001; 158(10): 1673–1679. [PubMed: 11579001]
8. Clauss JA, Blackford JU. Behavioral Inhibition and Risk for Developing Social Anxiety Disorder: A Meta-Analytic Study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2012; 51(10):1066–1075. [PubMed: 23021481]
9. Reeb-Sutherland BC, Vanderwert RE, Degnan KA, et al. Attention to novelty in behaviorally inhibited adolescents moderates risk for anxiety. *J Child Psychol Psychiatry*. Nov; 2009 50(11): 1365–1372. [PubMed: 19788588]
10. Rapee RM, Heimberg RG. A cognitive-behavioral model of anxiety in social phobia. *Behaviour Research and Therapy*. 1997; 35(8):741–756. [PubMed: 9256517]
11. Meyer A, Weinberg A, Klein DN, Hajcak G. The development of the error-related negativity (ERN) and its relationship with anxiety: Evidence from 8 to 13 year-olds. *Developmental Cognitive Neuroscience*. 2012; 2:152–161. [PubMed: 22308177]
12. Weinberg A, Olvet DM, Hajcak G. Increased error-related brain activity in generalized anxiety disorder. *Biological psychology*. 2010; 85(3):472–480. [PubMed: 20883743]
13. Gehring WJ, Himle J, Nisenson LG. Action-monitoring dysfunction in obsessive-compulsive disorder. *Psychological science*. 2000; 11(1):1–6. [PubMed: 11228836]
14. Hajcak G, Franklin M, Foa E, Simons R. Increased error-related brain activity in pediatric obsessive-compulsive disorder before and after treatment. *American journal of Psychiatry*. 2008; 165(1):116–123. [PubMed: 17986681]
15. Hajcak G, Simons RF. Error-related brain activity in obsessive-compulsive undergraduates. *Psychiatry Research*. 2002; 110(1):63–72. [PubMed: 12007594]
16. Endrass T, Klawohn J, Schuster F, Kathmann N. Overactive performance monitoring in obsessive-compulsive disorder: ERP evidence from correct and erroneous reactions. *Neuropsychologia*. 2008; 46(7):1877–1887. [PubMed: 18514679]
17. Gehring WJ, Goss B, Coles MGH, Meyer DE, Donchin E. A neural system for error detection and compensation. *Psychological science*. 1993; 4(6):385–390.
18. Davies PL, Segalowitz SJ, Gavin WJ. Development of Response-Monitoring ERPs in 7-to 25-Year-Olds. *Developmental neuropsychology*. 2004; 25(3):355–376. [PubMed: 15148003]
19. Holroyd, CB.; Nieuwenhuis, S.; Mars, RB.; Coles, MG. Anterior cingulate cortex, selection for action, and error processing.. In: Posner, MI., editor. *Cognitive Neuroscience of Attention*. Guilford Press; New York: 2004. p. 219-231.
20. Falkenstein M, Hielcher H, Dziobek I, et al. Action monitoring, error detection, and the basal ganglia: an ERP study. *Neuroreport*. 2001; 12(1):157–161. [PubMed: 11201078]

21. Ridderinkhof, KR.; Nieuwenhuis, S.; Hajcak, G.; van den Wildenberg, W.; Burle, B. Suboptimal action monitoring in mediofrontal cortex results in performance declines.. Poster presented at the 11th annual meeting of the Cognitive Neuroscience Society; San Francisco. 2004;
22. Falkenstein M, Hoormann J, Christ S, Hohnsbein J. ERP components on reaction errors and their functional significance: a tutorial. *Biological psychology*. 2000; 51(2–3):87–107. 23. [PubMed: 10686361]
23. Bates AT, Kiehl KA, Laurens KR, Liddle PF. Error-related negativity and correct response negativity in schizophrenia. *Clinical Neurophysiology*. 2002; 113(9):1454–1463. [PubMed: 12169328]
24. Mathalon DH, Whitfield SL, Ford JM. Anatomy of an error: ERP and fMRI. *Biological psychology*. 2003; 64(1):119–141. [PubMed: 14602358]
25. Olvet DM, Hajcak G. Reliability of error-related brain activity. *Brain research*. 2009; 1284:89–99. [PubMed: 19501071]
26. Rubin KH, Krasnor LR. Age and gender differences in solutions to hypothetical social problems. *Journal of Applied Developmental Psychology*. 1983; 4:263–275.
27. Nieuwenhuis S, Ridderinkhof KR, Blom J, Band GPH, Kok A. Error-related brain potentials are differentially related to awareness of response errors: Evidence from an antisaccade task. *Psychophysiology*. 2001; 38(5):752–760. [PubMed: 11577898]
28. Overbeek TJM, Nieuwenhuis S, Ridderinkhof KR. Dissociable components of error processing: On the functional significance of the Pe vis-a' -vis the ERN/Ne. *Journal of Psychophysiology*. 2005; 19:319–329.
29. Ladouceur CD, Dahl RE, Birmaher B, Axelson DA, Ryan ND. Increased error-related negativity (ERN) in childhood anxiety disorders: ERP and source localization. *Journal of Child Psychology and Psychiatry*. 2006; 47(10):1073–1082. [PubMed: 17073986]
30. Santesso DL, Segalowitz SJ, Schmidt LA. Error-related electrocortical responses are enhanced in children with obsessive–compulsive behaviors. *Developmental neuropsychology*. 2006; 29(3): 431–445. [PubMed: 16671860]
31. Meyer A, Hajcak G, Torpey D, et al. Increased error-related brain activity in six-year-old children with clinical anxiety. *Journal of Abnormal Child Psychology*. 2013; (41):1257–1266. 2013/05/23. [PubMed: 23700171]
32. Hirshfeld-Becker DR, Biederman J, Henin A, et al. Behavioral Inhibition in Preschool Children At Risk Is a Specific Predictor of Middle Childhood Social Anxiety: A Five-Year Follow-up. *Journal of Developmental and Behavioral Pediatrics*. 2007; 28(3):225–233. [PubMed: 17565290]
33. Mick MA, Telch MJ. Social anxiety and history of behavioral inhibition in young adults. *Journal of Anxiety Disorders*. 1998; 12(1):1–20. [PubMed: 9549606]
34. Hane AA, Fox NA, Henderson HA, Marshall PJ. Behavioral reactivity and approach-withdrawal bias in infancy. *Developmental psychology*. 2008; 44(5):1491–1496. [PubMed: 18793079]
35. Eriksen BA, Eriksen CW. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception and Psychophysics*. 1974; 16:143–149.
36. Achenbach, TM.; Rescorla, LA. Manual for the ASEBA school-age forms and profiles. University of Vermont, Research Center for Children, Youth, and Families; Burlington, VT: 2001.
37. Muris P, Merckelbach H, Schmidt H, Mayer B. The revised version of the Screen for Child Anxiety Related Emotional Disorders (SCARED-R): Factor structure in normal children. *Personality and Individual Differences*. 1998; 26(1):99–112.
38. Muris P, Dreessen L, Bögels S, Weckx M, Melick M. A questionnaire for screening a broad range of DSM-defined anxiety disorder symptoms in clinically referred children and adolescents. *Journal of Child Psychology and Psychiatry*. 2004; 45(4):813–820. [PubMed: 15056312]
39. Kaufman J, Birmaher B, Brent D, Rao U. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:980–988. [PubMed: 9204677]
40. Calkins SD, Fox NA, Marshall TR. Behavioral and physiological antecedents of inhibited and uninhibited behavior. *Child Development*. 1996; 67(2):523–540. [PubMed: 8625726]

41. Goldsmith H. Studying temperament via construction of the Toddler Behavior Assessment Questionnaire. *Child Development*. 1996; 67(1):218–235. [PubMed: 8605830]
42. Walker OL, Henderson HA, Degnan KA, Penela EC, Fox NA. Associations between behavioral inhibition and children's social problem-solving behavior during social exclusion. *Social Development*. DOI: 10.1111/sode.12053.
43. Lamm C, Walker OL, Degnan KA, et al. Cognitive control moderates early childhood temperament in predicting social behavior in seven year old children: An ERP study. *Developmental Science*. in press.
44. Santesso DL, Segalowitz SJ. The error-related negativity is related to risk taking and empathy in young men. *Psychophysiology*. 2008; 46(1):143–152. [PubMed: 18803599]
45. Muris P, Steerneman P. The Revised version of the Screen for Child Anxiety Related Emotional Disorders (SCARED-R): First evidence for its reliability and validity in a clinical sample. *British Journal of Clinical Psychology*. 2001; 40(1):35–44. [PubMed: 11317947]
46. Guyer AE, Lau JY, McClure-Tone EB, et al. Amygdala and ventrolateral prefrontal cortex function during anticipated peer evaluation in pediatric social anxiety. *Archives of General Psychiatry*. 2008; 65(11):1303. [PubMed: 18981342]
47. Roy AK, Fudge JL, Kelly C, et al. Intrinsic Functional Connectivity of Amygdala-Based Networks in Adolescent Generalized Anxiety Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2013; 52(3):290–299. [PubMed: 23452685]
48. Guyer AE, Nelson EE, Perez-Edgar K, et al. Striatal functional alteration in adolescents characterized by early childhood behavioral inhibition. *J Neurosci*. Jun 14; 2006 26(24):6399–6405. [PubMed: 16775126]
49. Bar-Haim Y, Fox NA, Benson B, et al. Neural correlates of reward processing in adolescents with a history of inhibited temperament. *Psychol Sci*. Aug; 2009 20(8):1009–1018. [PubMed: 19594857]
50. van Noordt SJR, Segalowitz SJ. Performance monitoring and the medial prefrontal cortex: a review of individual differences and context effects as a window on self-regulation. *Frontiers in Human Neuroscience*. 2012;6. [PubMed: 22375109]
51. Aiken, LS.; West, GM. Multiple regression: Testing and interpreting interactions. Sage; Newbury Park, CA: 1991.
52. Derryberry D, Rothbart MK. Reactive and effortful processes in the organization of temperament. *Development and Psychopathology*. 1997; 9:633–652. [PubMed: 9448999]
53. White LK, McDermott JM, Degnan KA, Henderson HA, Fox NA. Behavioral inhibition and anxiety: the moderating roles of inhibitory control and attention shifting. *Journal of Abnormal Child Psychology*. 2011; 39(5):735–747. [PubMed: 21301953]
54. Pine DS. Research review: a neuroscience framework for pediatric anxiety disorders. *Journal of Child Psychology and Psychiatry*. 2007; 48(7):631–648. [PubMed: 17593144]

Figure 1. Response-locked grand-averaged error related negativity waveform at FCz on incongruent trials for high and low behaviorally inhibited (BI) children

Figure 2.
Joint effect of behavioral inhibition (BI) and error related negativity-correct response negativity (ERN-CRN) on social phobia symptoms

Table 1

Demographics and descriptive statistics by behavioral inhibition (BI) group

	Total sample	Low BI	High BI
n	113	59	54
Mean age in months (and SD)	91.94 (2.99)	92.06 (2.82)	91.81 (3.18)
Gender			
Males, n	52	26	26
Females, n	61	33	28
Ethnicity			
Caucasian, n	77	43	34
African American, n	15	8	7
Other, n	21	8	13
Mean proportion of correct responses (SD)			
Congruent trials	.73 (.19) ^a	.74 (.19)	.71 (.20)
Incongruent trials	.63 (.19) ^a	.64 (.17)	.63 (.20)
Mean RT in ms (SD)			
Congruent trials	486.86 (81.46) ^b	482.67 (77.33)	491.45 (86.25)
Incongruent trials	507.90 (94.73) ^b	504.60 (89.81)	511.51 (100.56)
CBCL anxiety raw score	1.32 (1.49)	1.11 (1.33)	1.55 (1.62)
Social phobia symptoms composite Z-score (SD)	-.03 (.80)	-.08 (.84)	.01 (.78)

Note: Matching superscripts indicate significant differences. All p 's < .0001. RT = Reaction time; CBCL = Child Behavior Checklist.

Table 2

Hierarchical multiple regression analysis predicting social phobia symptoms

Variables by step	R ²	β (t)
Step 1 (df 6/39)	.16	
Sex		-.04 (-.21)
Incongruent correct trial counts		-.06 (-.40)
Incongruent error trial counts		.01 (.05)
CBCL anxiety		.33 (2.19)
BI		.15 (1.02)
ERN-CRN		.17 (1.13)
Step 2 (df 7/38)	.26	
Sex		-.02 (-.10)
Incongruent correct trial counts		-.10 (-.67)
Incongruent error trial counts		.01 (.06)
CBCL anxiety		.33 (2.32)
BI		.15 (1.07)
ERN-CRN		-.18 (-.85)
BI $\times$ ERN-CRN		.47 (2.20) *

Note: BI = Behavioral inhibition; CBCL= Child Behavior Checklist; CRN = Correct response negativity; ERN= Error-related negativity.

*
 $p < .05$