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A History of Childhood Behavioral Inhibition and Enhanced Response Monitoring in Adolescence Are Linked to Clinical Anxiety

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Abstract

Background—Behaviorally inhibited (BI) children who also exhibit enhanced response monitoring might be at particularly high risk for anxiety disorders. The current study tests the hypothesis that response monitoring, as manifest in the error-related negativity (ERN), moderates the association between BI and anxiety.

Methods—Participants (n = 113; 73 male) assessed for early-childhood BI were re-assessed as adolescents with a clinical interview and a flanker paradigm that generated behavioral data and event-related potentials (ERPs). Risk for anxiety disorders in adolescents was examined as a function of childhood-BI status and adolescent performance on the flanker paradigm.

Results—Adolescents with childhood BI displayed ERP evidence of enhanced response monitoring, manifest as large ERNs. The ERN moderated the relationship between early BI and later clinically significant disorders.

Conclusions—Physiological measures of response monitoring might moderate associations between early-childhood BI and risk for psychopathology. The subset of children with BI and enhanced response monitoring might face greater risk for later-life clinical anxiety than children with either BI or enhanced response monitoring alone.

Keywords

Anxiety; attention; behavioral inhibition; ERP; flanker; response monitoring

Early appearing behavioral inhibition (BI) predicts heightened emotional reactivity throughout childhood (see 1 for a review) and increased risk for clinically significant anxiety (2-5). Nevertheless, only a subset of BI children actually develops anxiety disorders. Little research to date has identified the mechanisms by which some children with BI develop anxiety disorders and others do not.

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Theories on moderators of the BI/anxiety association suggest that both biological attributes of the child (6) as well as parental traits (7,8) might influence initial temperamental dispositions, leading to increased vigilance toward threat particularly in novel or unfamiliar social situations. This heightened vigilance is thought to increase a child's monitoring of their interactions with the environment, which in turn might enhance the risk for anxiety in BI children (see 9).

Consistent with this possibility, data have demonstrated links between physiological measures of response monitoring, manifest as the error-related negativity (ERN) (10) and anxiety (11-13). These studies suggest that anxious individuals display enhanced response monitoring and heightened ERNs compared with non-anxious subjects. However, to date, there has been no examination of error monitoring in BI children. And most of the studies linking anxiety and response monitoring have used cross-sectional designs. The current, prospective, longitudinal study examines the degree to which response monitoring moderates the association between early-childhood BI and adolescent anxiety.

Methods and Materials

Participants

Participants (n = 153, 73 male) were assessed during infancy and early childhood for BI. The mean of children's BI scores at four time points (14 and 24 months, 4 and 7 years of age) indexed a BI composite. Participants were seen in adolescence (mean = 15.1 ± 1 years), at which time parents/adolescents provided written informed consent/assent, and the flanker task (14) was completed (n = 113, 50 male subjects). No significant demographic differences emerged between participants who did or did not complete the flanker task. Participants with only one BI assessment (n = 8) or with incomplete (n = 10) or inaccurate (n = 13) flanker data were excluded. Demographic and BI data were similar in the final included (n = 82, 37 male) and excluded subjects (Supplements 1).

Procedures

Flanker Task—Equal numbers of congruent (HHHHH or SSSSS) and incongruent (SSHSS or HHSHH) trials were presented, and participants were told to use a button-box to identify the middle letter (14). Hand-letter mappings were counterbalanced; participants were encouraged to respond quickly and accurately. A practice block (20 trials) was administered, followed by three test blocks (160 trials each) during which reaction time (RT) and accuracy were recorded. Trials with RTs ≤ 200 msec were excluded.

Electroencephalogram Data—Electroencephalogram was recorded from 15 sites (F3, Fz, F4, F7, F8, Fz, C3, C4, P3, P4, Pz, O1, O2, T7, and T8; Cz reference, AFz ground). Impedance was 10 kΩ or below. Electroencephalogram was time-locked to participant response to create ERPs for both correct and incorrect trials. Only errors of commission (average number of trials = 47 ± 34.2) were classified as incorrect and were used to generate the ERN, scored as the negative most deflection in a −20–120 msec window. The Pe was scored as the positive most peak 100 – 400 msec after response. Both the ERN and Pe were scored for minimal and maximal amplitudes, and mean amplitudes, respectively, as well as mean amplitude at Fz, Cz, and Pz (12). Results did not differ between approaches; thus only peak amplitude data are presented.

Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version Diagnostic Interview—Adolescents and parents completed semi-structured diagnostic interviews, conducted by advanced clinical psychology doctoral students under the supervision of diagnostic experts, all of whom were blind to BI data (15). Final diagnoses were discussed by the clinical team and made by expert consensus. Audio-taped interviews (n = 59) also were reviewed by experts to maintain reliability ($\kappa > .80$

for all diagnostic categories). The current study focused on the lifetime presence or absence of any clinically significant anxiety disorder (including generalized anxiety, separation anxiety, and social phobia).

Data Analysis

Flanker performance was examined with two separate repeated-measures analyses of variance (ANOVAs) with trial type (congruent vs. incongruent) and accuracy (correct or incorrect) as within-subjects variables and BI (median split to create high vs. low groups) served as the between-subjects factor. Gender and age served as covariates. Response monitoring was first investigated with separate repeated-measures ANOVAs for the ERN and Pe, with site as a within-subjects factor, BI group as the between-subjects factor, and gender and age as covariates. Of note, correct-trial-amplitude (CRN) did not differ as a function of BI, verifying that group differences did not reflect general task responding. Response monitoring was then further examined in relation to anxiety outcomes, with ANOVAs and logistic regression.

Results

Behavioral Performance

The main effects for trial type indicated that all participants were more accurate [$F(1,78) = 76.03$, $p < .01$] and had faster reaction times [$F(1,78) = 144.86$, $p < .01$] on congruent as compared with incongruent trials (see Table 1). These findings demonstrate the expected pattern of behavioral performance on the flanker task.

Response Monitoring

For the ERN, a two-way interaction emerged between BI Group and Site [$F(2,156) = 3.15$, $p < .05$]. Specifically, adolescents high in childhood BI exhibited greater ERN amplitude at site Fz than low childhood BI adolescents [$t(80) = 2.84$, $p < .05$; see Figure 1]. No effects with group emerged for the Pe.

BI, Response Monitoring, and Anxiety

The two-way interaction between frontal ERN and BI predicted anxiety diagnosis (odds ratio = 1.3; 95% confidence interval = 1.02–1.6; Wald $\chi^2 = 4.4$; $p < .05$; see Figure 2). This interaction reflected the fact that the relations between ERN and anxiety varied by BI classification. In the high BI group, smaller ERN responses were related to lower risk for anxiety diagnosis at a trend level (odds ratio = .82; 95% CI = .66 –1.01; Wald $\chi^2 = 3.39$, $p = .06$). For the low BI group, there was no relation between ERN response and anxiety diagnosis (odds ratio = 1.2; 95% CI = .92–1.5; Wald $\chi^2 = 1.7$, $p = .19$).

Discussion

Two main findings emerged from this study. First, children with BI exhibited an enhanced ERN response as adolescents. Second, those BI children with enhanced ERN responses were at particularly high risk for clinically significant anxiety. These findings correspond to work with BI adults (16), which suggests that an enhanced cholinergic system in highly inhibited individuals contributes to enhanced ERNs by initiating phasic decreases in the dopaminergic system. According to Gray (17,18), the cholinergic system is also involved in the expression of heightened anxiety via inhibited behavior.

Although previous work links early childhood BI and anxiety disorders, major questions have remained concerning which BI children face particularly high risk for anxiety. The current study provides evidence within a longitudinal framework that variability in the ERN response moderates individual differences in vulnerability to anxiety disorders among BI and non-BI

children. Due to the sample sizes and trend-level significance of the key post hoc test (ERN-by-anxiety relation in the high anxiety group) as well as the use of concurrent measures of anxiety and response monitoring, replication of these relations is needed.

Interestingly, there were no significant findings for the Pe despite the appearance of a large group difference at Fz. This result is similar to the work of Ladouceur *et al.* (13) in which Pe amplitude was visibly distinct but not significantly different among clinically anxious and non-anxious adolescents. Although a number of functions have been ascribed to the Pe (19,20), this component is not well-studied yet, especially within populations at-risk for clinical issues (16). Thus, future work should extend the investigation of this sample of children and aim to further clarify the basic neural processes within the frontal region that are linked to heightened response monitoring and self-evaluation at the level of regional specification and function.

In sum, this study highlights the role of individual differences in response monitoring patterns among adolescents and implicates monitoring as an important cognitive process involved in modulating outcomes associated with anxious behavior. Whereas other studies have found that adults exhibiting negative affect or anxiety disorders show heightened self-monitoring, this is the first study to demonstrate these associations in a sample of children selected as at-risk for anxiety disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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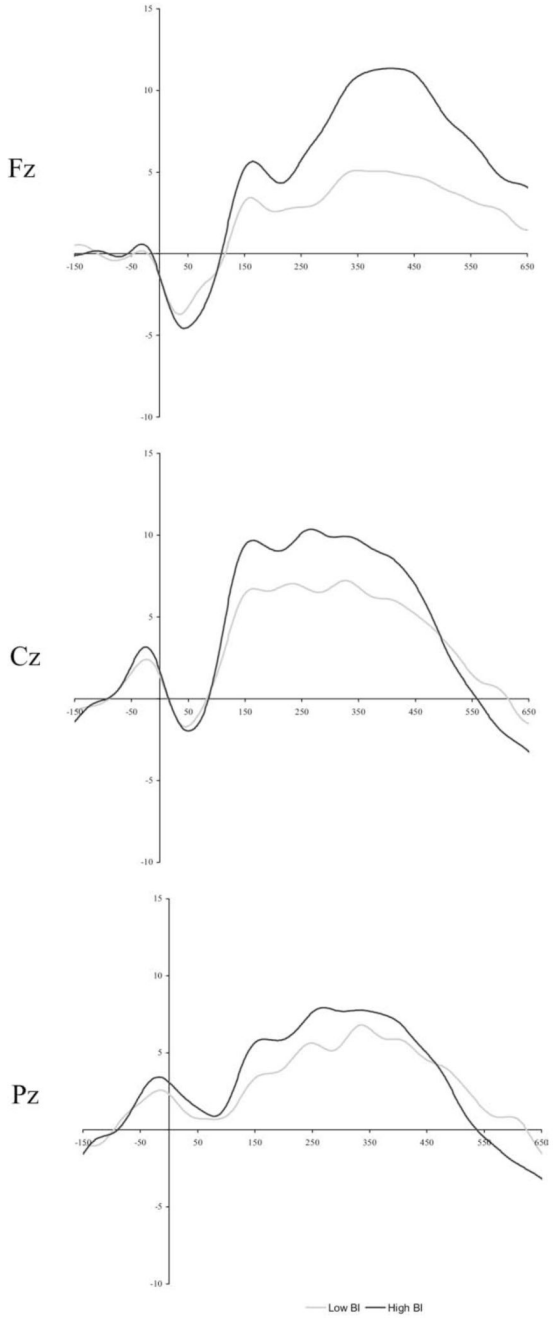

Figure 1.

Average event related potential amplitudes for incorrect trials across the midline sites of Fz, Cz, and Pz. Low and high behaviorally inhibited (BI) groups are represented by gray and black lines, respectively. The window for the error-related negativity response is −20–120 msec, whereas the positivity window is from 100 to 400 msec.

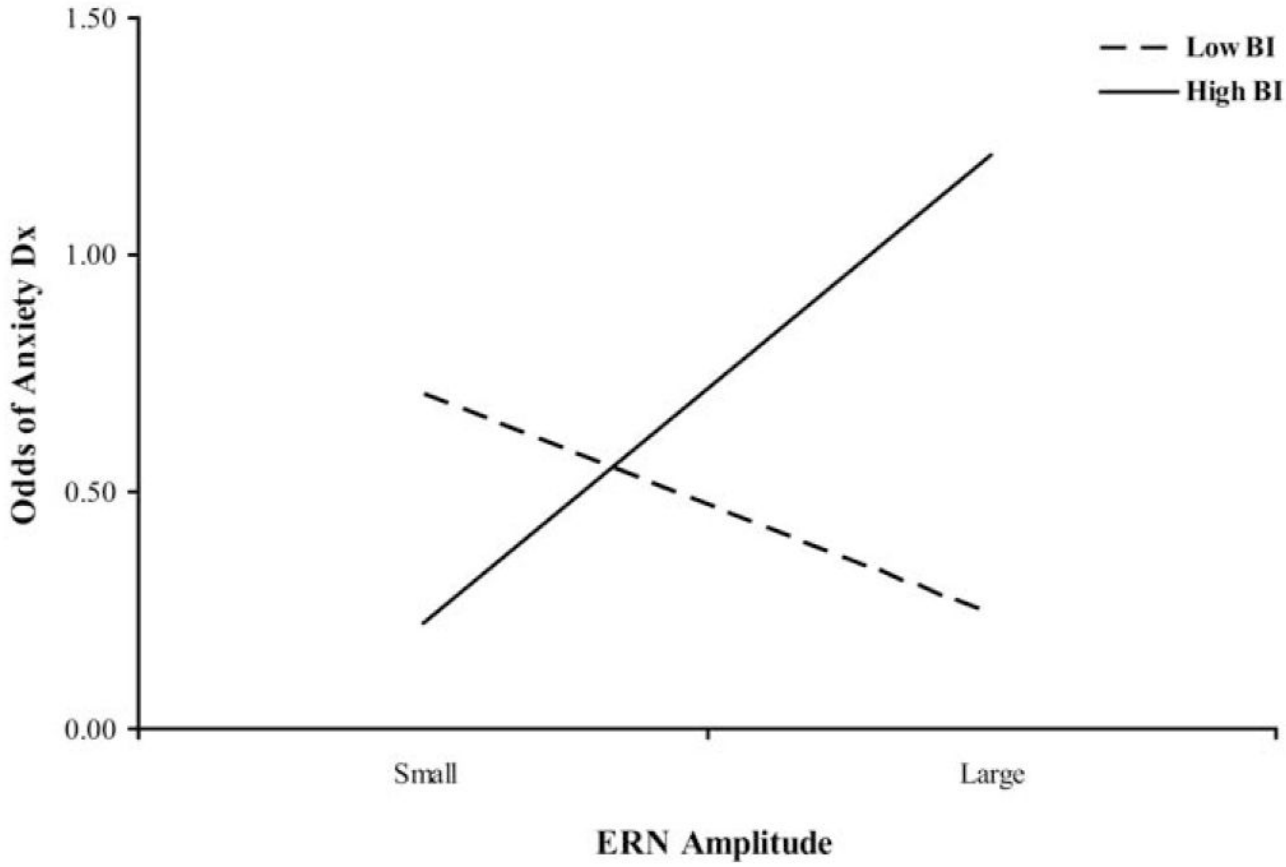

Figure 2.
The relation between behavioral inhibition (BI) and frontal error-related negativity (ERN) with respect to risk of anxiety diagnosis. High BI children with large ERN responses are at greater risk of an anxiety diagnosis, as are low BI children with small ERN responses.

Table 1

Flanker Interference Effects as Assessed by Accuracy Rate and Average Reaction Time

	% Accuracy Rate (SD)	Average RT in msec (SD)
Congruent Trials		
Total sample	95.7 (7.8)[a]	448 (65)[b]
Low BI	94.6 (9.5)	453 (57)
High BI	96.9 (5.3)	442 (72)
Incongruent Trials		
Total sample	87.2 (10.5)[a]	492 (71)[b]
Low BI	86.3 (12.1)	500 (69)
High BI	88.2 (8.7)	484 (73)

Typical flanker effects were present across all participants regardless of behaviorally inhibited (BI) group, such that faster and more accurate responses emerged for congruent as compared with incongruent trials. Note: matching superscripts indicate significant differences (p values < .01).