Early Childhood Behavioral Inhibition Predicts Cortical Thickness in Adulthood

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Objective: Behavioral inhibition (BI) during early childhood predicts risk for anxiety disorders and altered cognitive control in adolescence. Although BI has been linked to variation in brain function through adulthood, few studies have examined relations between early childhood BI and adult brain structure.

Method: The relation between early childhood BI and cortical thickness in adulthood was examined in a cohort of individuals followed since early childhood (N = 53, mean age 20.5 years). Analyses tested whether anxiety and/or cognitive control during adolescence moderated relations between BI and cortical thickness. Cognitive control was measured with the Eriksen Flanker Task. Initial analyses examined cortical thickness in regions of interest previously implicated in BI, anxiety disorders, and cognitive control: dorsal anterior cingulate (dACC), anterior insula (al), and subgenual anterior cingulate (sgACC); and volumes of the amygdala and hippocampus. Exploratory analyses examined relations across the prefrontal cortex.


Conclusion: Temperament in early childhood and the interaction between temperament and later anxiety relate to adult brain structure. These results are consistent with prior work associating BI and anxiety with functional brain variability in the dACC and VLPFC.

Key words: behavioral inhibition, anxiety, cortical thickness, structural MRI, cingulate

BI relates to behaviors or experiences associated with atypical brain development. In either case, linking adult brain structure to early childhood BI biologically connects early childhood BI to an adult measure that could inform outcome prediction and early intervention in children with high BI.

Prior research provides initial evidence for a link between individual differences in BI and brain structure. Schwartz et al.28 used a longitudinal design and compared cortical thickness in young adults with or without histories of high reactivity at 4 months of age, an early marker of BI. Adults with high reactivity at 4 months of age had thinner left orbitofrontal cortex and thicker right ventromedial prefrontal cortex compared to adults with low reactivity at 4 months of age. Another study examining relations between brain structure during adulthood and retrospective report of BI during childhood noted increased amygdala and caudate volumes associated with BI.29 The current study examines adult brain structure in relation to a stable measure of BI acquired prospectively over 4 assessments from 14 months to 7 years of age. Given that prospectively acquired measures of stable BI more consistently relate to later-life psychopathology than measures collected at a single time point,5 the current study uses a phenotype relevant to functioning in adolescence and young adulthood.

The current study tests the hypothesis that BI measured during early childhood predicts cortical thickness measured during adulthood. This study further tests whether relations between early childhood BI and cortical thickness in adulthood are moderated by anxiety and/or altered cognitive control occurring during adolescence. Such moderation is expected, given that both of these conditions have been linked to BI and have been associated with an overlapping set of brain regions. To address these questions, the study uses a well-characterized, rigorously ascertained cohort containing individuals followed since 4 months of age through early adulthood.3,30 This unique longitudinal cohort permits a rare opportunity to test prospective relations. Initial analyses test whether childhood BI predicts adult cortical thickness in regions commonly associated with BI, anxiety, and cognitive control: dACC, aI, or sgACC; or volume of the amygdala or hippocampus. These analyses test whether anxiety and/or cognitive control measured at intervening time points (in adolescence) moderate any relations detected between early childhood BI and cortical thickness in adulthood. Parallel exploratory vertexwise analyses examine these same relations across all of the prefrontal cortex.

**METHOD**

**Participants**

Participants were derived from an ongoing longitudinal study of BI in which behavioral data were available beginning at 4 months of age.3,30 Participants were originally recruited from the suburban Washington, DC area through commercially available mailing lists. Potential participants were screened over the telephone and excluded on the basis of prematurity, low birth weight, or perinatal complications. A home or laboratory visit was then scheduled for 433 infants (from 2 separate cohorts) within 2 weeks of their 4-month birthday, and infants were assessed for motor reactivity and emotional reaction to novel stimuli. Infants at the extreme ends of these measures were invited to participate in the full longitudinal study on the basis of selecting infants at high and low risk for developing behaviorally inhibited temperament.3,31 A small number of participants (5 in the sample used in the current study) were added to the study in early childhood to serve as unfamiliar peers in a social laboratory assessment (4 or 7 years of age).

A total of 163 were potential participants for the current study on the basis of having participated in BI assessments during childhood as well as anxiety assessments during adolescence or young adulthood. Of these 163 participants, 25 refused participation in the young adult study, and an additional 105 were either excluded or not approached on the basis of the following: contraindication to magnetic resonance imaging (MRI), psychotropic medication use, psychopathology requiring immediate clinical attention, recent completion of other studies, and/or participant request not to be contacted for a period of time after which the current study was completed.12 Acceptable neuroimaging data were therefore available for a subset of participants (n = 53, mean age 20.5 years, 29 male and 24 female). Table 1 lists demographics for this subset and participation rates for the 7 time points where data were acquired (ages 4 months, 14 months, 24 months, 4 years, 7 years, early adolescence [mean age 14.7 years], and young adulthood [mean age 19.8 years]).

Children were observed for an assessment of BI at 14 and 24 months of age and for an assessment of social reticence at 4 and 7 years of age.1,2,28 BI at 14 and 24 months was assessed by measuring infants’ reactions to novel objects and people.3 Mothers also reported their child’s social fear at 14 and 24 months using the Toddler Behavior Assessment Questionnaire.34 Social reticence is considered a marker of BI during the early school-age years. For the assessments of social reticence at ages 4 and 7 years, children’s

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Demographic Characteristics and Assessment Participation Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>24 (45.3)</td>
</tr>
<tr>
<td>Age, y, mean (SD)</td>
<td>20.5 (1.62)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>53 (100)</td>
</tr>
<tr>
<td>Maternal education</td>
<td></td>
</tr>
<tr>
<td>High school graduate</td>
<td>3 (5.7)</td>
</tr>
<tr>
<td>Some college or technical school</td>
<td>6 (11.3)</td>
</tr>
<tr>
<td>College graduate</td>
<td>26 (49.1)</td>
</tr>
<tr>
<td>Graduate professional training</td>
<td>15 (28.3)</td>
</tr>
<tr>
<td>Other/no information</td>
<td>3 (5.7)</td>
</tr>
<tr>
<td>IQ, m (SD)</td>
<td>114.1 (10.5)</td>
</tr>
<tr>
<td>Data available for assessment</td>
<td></td>
</tr>
<tr>
<td>Age 4 mo visit</td>
<td>43 (81.1)</td>
</tr>
<tr>
<td>Age 14 mo visit&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44 (83.0)</td>
</tr>
<tr>
<td>Age 24 mo visit&lt;sup&gt;a&lt;/sup&gt;</td>
<td>45 (84.9)</td>
</tr>
<tr>
<td>Age 4 y visit&lt;sup&gt;a&lt;/sup&gt;</td>
<td>45 (84.9)</td>
</tr>
<tr>
<td>Age 7 y visit&lt;sup&gt;a&lt;/sup&gt;</td>
<td>44 (83.0)</td>
</tr>
<tr>
<td>Adolescent visit (mean age 14.7 y)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>49 (92.5)</td>
</tr>
<tr>
<td>Young adult visit (mean age 19.8 y)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>52 (98.1)</td>
</tr>
<tr>
<td>Conflict task visit (mean age 14.8 y)</td>
<td>29 (54.7)</td>
</tr>
</tbody>
</table>

Note: Data are expressed as n (%) except where noted.

<sup>a</sup>Indicates assessments that were used to compute the behavioral inhibition score.

<sup>b</sup>Indicates assessments that were used to calculate the anxiety score.
reticent behavior with 3 unfamiliar peers was measured with Rubin’s Play Observation Scale.38 Mothers also rated their child’s social fear at 4 and 7 years using the shyness subscale of the Colorado Child Temperament Inventory.39 For each of the 4 time points, observed behavioral and maternal report measures were standardized in the full cohort and then averaged to create a single measure of early childhood BI.36,37 For our primary analyses, we used this continuous composite measure of early childhood BI and social reticence. This composite provides a stable measure of early childhood BI and has been used extensively in prior work.11,12,36,37 For a secondary analysis to compare results with other studies, we categorized participants on the basis of their reactivity profiles at 4 months of age. This analysis attempts to replicate findings from the only other longitudinal structural brain study of young adults with histories of BI in infancy.28 All 53 participants had the primary composite measure of BI available. For the secondary analysis, 43 had complete data for the 4-month reactivity phenotype available (of which 19 were classified as high negative reactive and 11 as low reactive).

In addition to examining the influence of early childhood BI, we wished to test whether anxiety and/or cognitive control during adolescence moderated the relation between early childhood BI and brain structure in young adulthood. This analysis minimized the number of statistical comparisons and derived a measure of anxiety incorporating as much data from the current study as possible. Accordingly, a single composite measure of anxiety over adolescence and young adulthood was created for each participant. This composite measure was created on the basis of 3 measures obtained during adolescence (mean age 14.7 years): parent report from Screen for Child Anxiety Related Disorders (SCARED), child report from SCARED38; the Anxious/Depressed raw score on the Youth Self-Report (YSR39); and 3 measures obtained during young adulthood (mean age 19.8 years): Beck Anxiety Inventory,40 Liebowitz Social Anxiety Scale,41 and the Anxious/Depressed raw score on the YSR. Standardized scores were created for each measure for each participant on the basis of all participants with available data on these anxiety measures (n = 163), not just the subset imaged for this current study. The use of standardized scores allows an equal weighting of each measure in the composite. The composite anxiety measure was an average over these 6 standardized measures (Cronbach’s alpha = 0.71). The adolescent and young adult composite were correlated (Spearman’s rho = 0.48, p < .001), suggesting traitlike features. Data were available in more than 80% of the imaged participants for each individual scale; 92.5% of participants had at least 1 measure from adolescence, and 98.1% had at least 1 measure from adulthood. All participants had at least 2 of the 6 measures available.

The Eriksen Flanker Task was used to measure cognitive control in the current sample. A subset of the cohort with imaging data in young adulthood had completed the Eriksen Flanker Task in adolescence (n = 25, mean age 14.8 years, 9 female and 16 male). The Eriksen Flanker Task consisted of equal numbers of congruent (HHHHH and SSSSS) and incongruent (HHSSH and SSHSS) trials in which participants had to indicate the central letter with a button press.42 Cognitive control was measured with the congruency effect, computed as the difference in reaction time for incongruent versus congruent trials, divided by the reaction time on congruent trials. Higher scores indicate poorer cognitive control.

Neuroimaging

All MRI data were acquired on the same scanner, a GE Healthcare MR750 3.0 Tesla scanner with a 32-channel head coil. Each scanning session included a single high-resolution, T1-weighted structural imaging sequence (MPRAGE; sagittal acquisition; 176 slices; 1 mm³ isotropic voxels; 256 × 256 matrix; flip angle = 7°; repetition time [TR] = 7.7 milliseconds; echo time [TE] = 3.42 milliseconds; inversion time [TI] = 425 milliseconds).

Image Processing

FreeSurfer 5.3 (http://surfer.nmr.mgh.harvard.edu/) was used to generate subcortical segmentations,43,44 cortical parcellations using the Destrieux et al. atlas,45 and pial and white matter surfaces from the T1-weighted images.46-48 After the parcellations and surfaces were generated, they were visually reviewed by trained research assistants and, where necessary, manually edited and regenerated. Regional volumes and cortical thicknesses were obtained from the edited parcellations and surfaces.45,48

Regional A Priori Analyses

Three bilateral regions of interest (ROIs) from the Destrieux et al. atlas45 were selected a priori for initial cortical thickness analyses: the middle anterior part of the cingulate gyrus and sulcus (dACC), the short insular gyrus (ai), and the subcallosal gyrus (sgACC). These ROIs are depicted in Figure 1A. Bilateral volumes of the amygdalae and hippocampi were examined in a priori analyses as well. In an effort to replicate findings by Schwartz et al.,28 2 additional ROIs were explored exclusively in the secondary analysis when examining the relations between 4-month temperament and cortical thickness: left orbitofrontal and right ventromedial regions were hand-drawn on an average FreeSurfer volume based on Figures 1 and 2 from Schwartz et al.28 These regions were then projected to individual participants to generate thickness values for the left orbitofrontal and right ventromedial regions for each participant.

Prefrontal Cortex Exploratory Analyses

We additionally performed exploratory analyses in the prefrontal cortex.28 General linear modeling programs available through FreeSurfer (Qdec) were used for these vertexwise analyses. A prefrontal cortex mask was generated by combining the following parcellations from the Desikan atlas46: superior frontal, rostral, and caudal middle frontal, pars opercularis, pars triangularis, pars orbitals, lateral and medial orbitofrontal, frontal pole, and rostral and caudal anterior cingulate cortices. To correct for multiple comparisons, Monte Carlo simulations available in the FreeSurfer software were used to determine that an area of cortex 68.1 mm² with each individual vertex p < .001 was required to meet prefrontal cortex-wide clusterwise significance of p < .05. Clusters meeting multiple comparison correction are reported in Montreal Neurological Institute (MNI) coordinates.

Statistical Analyses

All statistical tests were performed using SPSS version 20 (IBM, Armonk, NY) with the exception of the prefrontal cortex vertexwise analyses, which were carried out using FreeSurfer. We used t tests to compare BI and anxiety in the subset of participants that provided versus did not provide imaging data, and χ² tests to test for potential group differences in sex. Analogous tests compared participants in the current study that did versus did not provide Eriksen Flanker Task data in adolescence.

The relations among temperament, anxiety, and cortical thickness were examined with repeated measures analyses of variance predicting thickness. Specifically, for each a priori region, cortical thickness values from left and right hemispheres were included in a single model, with hemisphere treated as a repeated measure. Additional factors for the primary models comprised childhood BI, anxiety in adolescence/young adulthood, the interaction between...
BI and anxiety, sex, and whole-brain average cortical thickness. Variables were mean centered before computing interactions for all analyses. When significant effects emerged in primary models, secondary models added IQ and maternal education as covariates. Three participants each were missing IQ and maternal education data, and these missing values were replaced with group means; excluding these participants did not change the significance of results. Only results from secondary models are reported; primary models were included to ensure that results were not driven exclusively because of the addition of multiple covariates. For amygdala and hippocampus analyses, volumes were used instead of thicknesses, and whole-brain volume was used as a covariate instead of whole-brain average thickness. Bonferroni correction was used to protect against false-positive results for the 5 models based on the a priori regions.

Prefrontal cortex vertexwise analyses were conducted separately for each hemisphere using the primary model with FreeSurfer. One participant’s composite BI measure was 3 standard deviations from the mean, and another participant’s composite anxiety measure was 3 standard deviations from the mean. These outliers were handled by Winsorizing for all analyses; no outliers were detected in other measures.

Analyses examining the relations between cognitive control and cortical thickness of dACC were based on Westlye et al. The congruency effect on the Eriksen Flanker Task for each participant was computed as the difference in reaction time for incongruent versus congruent trials divided by the reaction time on congruent trials. Higher scores indicate poorer cognitive control, and the mean score across the sample was 0.10 with a standard deviation of 0.051. To attempt replication, the relation between congruency and cortical thickness was examined with a repeated-measures analysis of variance with hemisphere as a repeated measure and congruency, sex, and IQ as covariates. This model was followed up by additionally controlling for whole-hemisphere thickness. Finally, we included congruency, early childhood BI, and the interaction between BI and congruency in a single model to determine whether congruency moderated the relation between BI and cortical thickness.

Power analyses were computed using G*Power 3.1. Using a single predictor in a regression model to detect a moderate effect size (partial $\eta^2 = 0.15$), power in the full sample of 53 was 0.84, power in the sample using just the 4-month phenotype ($n = 30$) was 0.59, and power in the sample using the Eriksen Flanker Task data ($n = 25$) was 0.51. The power to detect a larger effect size (partial $\eta^2 = 0.25$, on the order of the effect size of the main result in this study) was 0.98 in the full sample, 0.86 for the 4-month phenotype data, and 0.79 for the Eriksen Flanker Task data.

RESULTS

Participants

Compared to participants from the larger longitudinal study who did not undergo imaging, participants who did undergo imaging for the current study had significantly lower anxiety scores over adolescence/young adulthood ($-0.18, SD = 0.57$, versus $0.16, SD = 0.91$, $t = 2.5$, $p = .012$, $d = 0.45$), but there were no differences in early childhood BI scores ($-0.06, SD = 0.73$, versus $0.012, SD = 0.60$, $t = 0.71$, $p = .48$, $d = 0.11$) or sex ($\chi^2 = 1.5$, $p = .22$). Follow-up analyses revealed that imaged participants had significantly lower levels of anxiety compared to excluded participants ($-0.18$ versus $0.17$, $t = 2.6$, $p = .012$). There was no difference in anxiety scores between the imaged participants and participants who refused participation ($-0.18$ versus $-0.07$, $t = 0.7$, $p = .49$). It should be noted, however, that the absolute difference in anxiety between imaged participants and the total cohort was less than 0.2 SDs from the cohort mean, and the imaged participants were representative of the original longitudinal cohort in terms of BI scores. Within the current study sample, there were no significant differences in anxiety, BI, or sex ($t = 1.39$, $p = .17$, $d = 0.38$; $t = 0.24$, $p = .81$, $d = 0.07$; $\chi^2 = 0.23$, $p = .63$, respectively) between the subset of individuals who participated versus

![Image](https://jaacap.org/announcements/125/FIGURE_1.png)

**FIGURE 1** Early childhood behavioral inhibition predicts cortical thickness in the dorsal anterior cingulate (dACC) in young adulthood. Note: Panel A illustrates the 3 cortical a priori regions of interest, derived from the Destrieux atlas. Panel B depicts the significant relation between early childhood behavioral inhibition (BI) and cortical thickness in the dACC in adulthood. Each dot represents a single participant, and thickness values are averaged across left (L) and right (R) dACC. The encircled participant’s BI value was Winsorized because BI > 3 SD from the mean. sgACC = subgenual anterior cingulate.
the subset of those who did not participate in the Eriksen Flanker Task in adolescence. Early childhood BI and anxiety in adolescence/young adulthood were not significantly related in the sample used in this study ($r = -0.043, p = .76$).

**Behavioral Inhibition, Anxiety, and Cortical Thickness: Regional Analysis**

The relations among BI during early childhood, anxiety in adolescence/young adulthood, and cortical thickness in young adulthood were examined in 3 bilateral a priori cortical regions of interest: the dorsal anterior cingulate (dACC), anterior insula (aI), and subgenual anterior cingulate (sgACC). These regions are depicted in Figure 1A. Parallel analyses examined relations with hippocampus and amygdala volumes. As depicted in Figure 1B, early childhood BI predicted thinner cortex in the dACC with a large effect size ($F_{1,45} = 16.2, p < .001$ uncorrected, partial $\eta^2 = 0.26$, survived Bonferroni correction for 5 a priori regions). This analysis controlled for multiple potential confounding factors, including sex, maternal education, IQ, whole-brain average cortical thickness, anxiety in adolescence/young adulthood, and the interaction between BI and anxiety. Of note, similar results emerged in bivariate analyses examining only the relations between BI and dACC thickness. Early childhood BI similarly predicted thinner cortex in the sgACC ($F_{1,45} = 5.2, p = .027$ uncorrected, partial $\eta^2 = 0.10$), although with a smaller effect size. Unlike findings for the dACC, this result did not survive Bonferroni correction for 5 comparisons. Neither anxiety nor the interaction between BI and anxiety was significantly related to dACC or sgACC cortical thickness, suggesting that anxiety did not moderate the relation between early childhood BI and thickness of the dACC in adulthood. There were no significant relations among childhood BI, anxiety in adolescence/young adulthood, or the interaction between BI and anxiety with anterior insula thickness or hippocampus or amygdala volumes.

**Behavioral Inhibition, Anxiety, and Cortical Thickness: Prefrontal Cortex Exploratory Analysis**

To complement the a priori ROI analysis, a parallel analysis examined the relations among BI during early childhood, anxiety in adolescence/young adulthood, and cortical thickness in young adulthood in an exploratory fashion across prefrontal cortex. In contrast to the regional analysis, the prefrontal cortex vertexwise analysis did not detect any regions surviving multiple comparison correction that were related to early childhood BI alone. A whole-brain vertexwise map, uncorrected at $p < .05$, demonstrating the relation between early childhood BI and cortical thickness in young adulthood, is provided in Figure S1, available online. This map is consistent with the regional analysis, as the thickness of a large swath of cortex near the dACC was related to early childhood BI; as above, however, this cluster likewise did not detect any regions surviving multiple-comparison correction that were related to anxiety in adolescence/young adulthood.

The prefrontal cortex vertexwise analysis did, however, detect a region in which thickness in young adulthood was related to the interaction between early childhood BI and anxiety in adolescence/young adulthood. As illustrated in Figure 2, cortical thickness in an 83 mm$^2$ patch of the right ventrolateral prefrontal cortex (VLPFC; centered at $+48.2 +10.0 +13.9$ in MNI coordinates, within the pars triangularis) was predicted by an interaction between childhood BI and anxiety in adolescence/young adulthood, controlling for sex and whole-hemisphere thickness ($p = .024$, corrected for multiple comparisons across prefrontal cortex). To explore the source of this interaction, a median split divided participants into those with low versus high levels of early childhood BI, and a similar median split was performed for anxiety. Note that effect sizes for this median split analysis are biased by the circular...
nature of the analysis, which computes statistics on a region initially identified in an exploratory test. Effect sizes are reported solely to interpret the interaction. In participants with low early childhood BI, a high level of anxiety during adolescence/young adulthood predicted thicker VLPFC compared to a low level of anxiety ($d = 1.56$). In participants with high early childhood BI, however, anxiety during adolescence/young adulthood was unrelated to VLPFC thickness in young adulthood ($d = -0.46$).

**DISCUSSION**

The primary goal of the current study was to test the hypothesis that BI in early childhood predicts thickness in specific cortical regions, as well as volume of amygdala and hippocampus, during adulthood. Consistent with this hypothesis, BI during early childhood predicted thinner dACC in adulthood, although no differences as a function of BI were detected in anterior insula, sgACC (after correction for multiple comparisons), amygdala, or hippocampus. Neither anxiety nor cognitive control during adolescence moderated the relation between early childhood BI and dACC thickness in adulthood, although a higher congruency effect on the Eriksen Flanker Task during adolescence was independently related to thinner dACC in adulthood. High anxiety during adolescence and young adulthood was related to thicker cortex in the right VLPFC in young adulthood, but only among those who had low BI as children.

These results are consistent with prior literature linking BI to the dACC. The dACC is part of a network of brain regions involved in identifying and signaling the need for increased cognitive control. A series of studies in the current and other samples use event-related potentials and functional MRI (fMRI) to measure brain activity during tasks that require trial-by-trial changes in levels of cognitive control. This series of studies demonstrates consistently larger increases in neuronal activity in or near the dACC among children and adolescents with high BI relative to those with low BI.

These data are consistent with a model in which the dACC of individuals high in BI is highly sensitive to conflict, signaling the need for cognitive control. Notably, research has shown this BI-related pattern of brain function does not generate behavioral benefits but, rather, relates to risk for anxiety. In light of this model, the current findings of thinner dACC among individuals with higher BI suggests the hypotheses that either a thinner dACC generates a larger neural signal or that repeatedly high activity in the dACC over development results in thinner cortex. Longitudinal studies incorporating neuroimaging early in life are needed to adjudicate these possibilities. In either case, these data may provide a biological explanation for the link between early childhood BI and adult outcomes. Moreover, by linking early temperament to adult brain structure, the current findings raise questions about the types of impairing behaviors expressed in adulthood that could relate to both early childhood temperament and dACC structure. For example, adults with a childhood history of high BI may have subtle abnormalities of cognitive control associated with decreased dACC thickness. If so, interventions targeting impairment in children with high BI could influence these or other behaviors in adulthood.

Importantly, variation in neither adolescent anxiety nor cognitive control on the Eriksen Flanker Task moderated the relation between early childhood BI and adult dACC thickness. These results suggest that the association between early childhood BI and adult dACC thickness manifests independently of anxiety and/or this 1 particular measure of cognitive control. One possibility is that although thinner dACC in individuals with a history of BI may increase risk for pathological anxiety and alterations in cognitive control, some individuals compensate for this risk. Further studies could test whether this compensation occurs functionally within the dACC (i.e., activity is normal even though structure is abnormal) or through functional and/or structural changes in other brain areas.

In the current study, adolescent/young adult anxiety moderated the relations between early childhood BI and cortical thickness in a portion of the right VLPFC. High anxiety in adolescence and adulthood related to increased VLPFC thickness in young adults with a history of low BI in
In summary, the current study demonstrates that variation in early childhood temperament is related to adult brain structure. These data reinforce the hypothesis that the dACC is a key brain structure in the physiology of BI, and provide a candidate biological basis for the associations between early childhood BI and adult functional outcomes. Future studies following cohorts incorporating longitudinal neuroimaging that begin earlier in childhood are needed to determine whether alterations are present early in childhood or emerge later in the course of development. In addition, future studies are required to determine the functional implications of the cortical thickness differences detected in this study. Regardless of the outcome of these additional studies, data from the current study highlight the importance of early intervention for children who are functionally impaired from high BI because of the potential for enduring effects on brain structure that occur into adulthood.

REFERENCES


FIGURE S1  Whole-brain, vertexwise map demonstrating the relation between early childhood behavioral inhibition (BI) and cortical thickness in young adulthood. Note: Results are adjusted for anxiety during adolescence/young adulthood, the interaction between BI and anxiety, sex, and whole-hemisphere mean cortical thickness. Maps are thresholded at $p < .05$, uncorrected. Warmer colors indicate a positive relation between BI and cortical thickness, and cooler colors indicate a negative relation. Although no patches of cortex were significant after correcting for multiple comparisons across the prefrontal cortex, the highest peak in these maps is centered near the dorsal anterior cingulate cortex, consistent with the regional analyses.