J Abnorm Child Psychol (2011) 39:783–790
DOI 10.1007/s10802-011-9526-2

Serotonin Transporter Genotype Moderates the Link Between Children's Reports of Overprotective Parenting and Their Behavioral Inhibition

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Published online: 3 June 2011

Abstract The goal of the current study was to examine environmental and genetic correlates of children's levels of behavioral inhibition (BI). Participants were 100 mother child pairs drawn from the community who were part of a larger study of the intergenerational transmission of depression. Results indicated that higher levels of maternal overprotection, as reported by the child, were associated with elevations in BI among children carrying two copies of the lower expressing 5-HTTLPR alleles (S or L_G), but not among those carrying only one copy or those homozygous for the L_A allele. In addition, this interaction was specific for the social component of BI, not the nonsocial component. This relation was maintained even after statistically controlling for children's and mother's psychopathology. Together, these findings add to emerging research demonstrating that G × E interactions predict variation in BI during childhood.

Keywords Behavioral inhibition · 5-HTTLPR · Parenting · G × E

This project was supported by National Institute of Child Health and Human Development grants HD048664 and HD057066 and by funding from the Center for Developmental Psychobiology, Binghamton University, awarded to B.E. Gibb as well as 1S10RR023457-01A1 and Shared equipment grants (ShEEP) from the Medical Research Service of the Department of Veteran Affairs, awarded to J. E. McGeary.

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Behavioral inhibition (BI) is a temperament style characterized by the tendency to react to novel and unfamiliar situations with reticence and withdrawal (Garcia-Coll et al. 1984). Several studies have found that BI may represent a common vulnerability for multiple internalizing disorders. Specifically, studies have demonstrated the role of BI in the development of social anxiety disorder (Biederman et al. 2001; Hirshfeld-Becker et al. 2008; Coles et al. 2006; Gladstone et al. 2005), panic disorder (Rosenbaum et al. 1991), obsessive–compulsive disorder (Coles et al. 2006; Van Ameringen et al. 1998), and depression (Caspi et al. 1996; Jaffee et al. 2002).

Although early studies examined BI broadly defined, more recent research has suggested that there may be two distinct components of BI–BI in social versus nonsocial situations (Kochanska 1991; Reznick et al. 1992). The social component of BI is characterized by reticence to interact with strangers and unfamiliar people, whereas the nonsocial component is characterized by reticence to explore unfamiliar surroundings and fearfulness when faced with novel situations. These two components of BI appear to be differentially related to the presence of, or risk for, psychopathology. Specifically, although studies have shown that both social and nonsocial BI are related to the presence of multiple forms of anxiety disorders as well as depression (Coles et al. 2006; Mick and Telch 1998; Neal et al. 2002; Schofield et al. 2009; Van Ameringen et al. 1998), there is

evidence that BI in social, compared to nonsocial, situations is more strongly associated with social anxiety (Mick and Telch 1998; Neal et al. 2002; Schofield et al. 2009). To the extent that BI in social versus nonsocial situations may contribute differential risk to various forms of psychopathology, it is important to determine whether they may have similar versus distinct developmental antecedents. Given that children who are consistently inhibited are at heightened risk for developing psychopathology (Biederman et al. 1990, 1993; Hayward et al. 1998; Hirshfeld-Becker et al. 2007; Schwartz et al. 1999), it is essential to examine factors contributing to the development of BI (both social and nonsocial BI), to facilitate the development of more targeted prevention and early intervention efforts.

Although research has suggested that BI is thought to be relatively stable over time (Kagan et al. 1984), there is some evidence for the impact of maternal behavior on children's levels of BI. These studies have focused on oversolicitous parenting and "overprotectiveness", defined as parental behavioral to protect the child from harm (Rapee 1997) and there is evidence that overprotective parenting is associated with toddler inhibition and preschool reticence (Rubin et al. 1997; 2001; 2002). In addition, during interactions in which there is little or no contextual structure, the mothers of BI children are more prone to exhibit overprotective behavior (Rubin et al. 2001). Despite this evidence for the influence of maternal overprotective behavior on children's levels of behavioral inhibition, there are also clear individual differences in that not all children of overprotective parents exhibit high levels of BI (Kagan et al. 1994).

More recent research, therefore, has examined the potential role of genetic influences on children's levels of BI. Twin studies have demonstrated clear genetic influences on BI (e.g., Dilalla et al. 1994). In terms of specific genetic influences, there is growing interest in the potential role played by a functional polymorphism in the serotonin transporter gene (5-HTTLPR). There are two common variants in 5-HTTLPR, a short (S) and long (L) allele, with the short allele exhibiting less transcriptional efficiency than the long allele (Lesch et al. 1996). Carriers of the 5-HTTLPR short allele have been shown to exhibit stronger amygdala reactivity to emotional stimuli (Munafò et al. 2008) and greater cortisol reactivity to a laboratory stressor (Gotlib et al. 2008). In addition, research on adults suggests that the short allele is associated with predispositions to anxiety and negative emotionality (Munafo et al. 2003). More recently, researchers have found evidence of triallelic variation (S, L_G, L_A) in 5-HTTLPR, with the L_G allele exhibiting functional equivalence with the S allele (Hu et al. 2005). This refined view of 5-HTTLPR genotype may be particularly relevant with regard to studies investigating G × E interactions, which have yielded some inconsistent results (for reviews, see Caspi et al. 2010; Karg et al. 2011; Risch et al. 2009). To the extent that carriers of the L_G allele were grouped with L_A homozygotes in these earlier studies, this may have contributed to the mixed findings. In the current study, therefore, we focused on triallelic variation in 5-HTTLPR.

Although one initial association study failed to find evidence for a link between 5-HTTLPR and BI (e.g., Schmidt et al. 2002), more recent research has suggested that 5-HTTLPR genotype may moderate the impact of environmental influences rather than exerting a main effect on BI. Specifically, Fox et al. (2005) found that children with low social support had increased risk of BI, but only if they carried at least one copy of the 5-HTTLPR short allele. What remains unclear, however, is whether a similar gene × environment (G × E) effect may be observed for other environmental influences linked to children's BI (i.e., maternal overprotection) and whether similar effects would be observed for both forms of BI—social and nonsocial.

The primary aim of the current study was to examine environmental and genetic correlates of children's BI. Consistent with a G × E model of risk, we predicted that maternal overprotectiveness would be related to children's BI and that this relation would be stronger among children carrying the lower expressing 5-HTTLPR genotypes (S or L_G allele). In examining children's BI, we focused on levels of social and nonsocial BI separately. Exploratory analyses were then conducted to determine whether the G × E influence would be stronger for one form of BI than another. In each of these analyses, we examined whether these relations would be at least partially independent of mother and child psychopathology (lifetime diagnoses and current symptoms of depression and anxiety). Finally, although this study focuses primarily on G × E interactions, we recognize that genetic influences could also be present in terms of active or passive rGE (gene–environment correlations) with children's or mother's 5-HTTLPR genotype. To evaluate the possibility of rGE effects, therefore, we also examined correlations between children's and mothers' genotypes and each of the parenting, as well as the BI variables.

Method

Participants

Participants were 100 mother child pairs drawn from the community who were participating in a larger study of the intergenerational transmission of depression (Gibb et al. 2009). Mothers were required to either meet criteria for a DSM-IV (American Psychiatric Association 1994) major depressive disorder (MDD) during the participating child's

lifetime (n=52) or have no lifetime diagnosis of any DSM-IV mood disorder (n=48). Exclusion criteria for both groups included symptoms of schizophrenia, organic mental disorder, or history of bipolar I disorder. To be included in the study, children had to be between the ages of 8 and 12 at the initial assessment, and no more than one child per family could participate. The average age of mothers in our sample was 39.56 years (SD=6.66, Range=26–53). In terms of race, 88% of the mothers were Caucasian, 6% were African American, 5% were Asian American, and one mother (1%) was multiracial. The median annual family income was $55,000–60,000. For the children in our sample, the average age was 9.97 years (SD=1.32, Range=8–12) and 59% were girls. In terms of child race, 82% of the children were Caucasian, 5% were African American, 2% were Asian American, and 11% were multiracial.

Measures

The Schedule for Affective Disorders and Schizophrenia—Lifetime Version (SADS-L; Endicott and Spitzer 1978) and the Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version (K-SADS-PL; Kaufman et al. 1997) were used to assess for current DSM-IV Axis I disorders in mothers and their children, respectively. Both measures are widely used diagnostic interviews with well-established psychometric properties (Angold 1989; Endicott and Spitzer 1978; Kaufman et al. 1997). The SADS-L and K-SADS-PL were administered by separate interviewers. For the K-SADS-PL, mothers and children were interviewed separately. Of the 52 women meeting criteria for at least one lifetime episode of MDD, eight met criteria for current MDD and 15 met criteria for at least one lifetime anxiety disorder, of whom 13 met criteria for one or more current anxiety disorders (social phobia = 7; posttraumatic stress disorder = 3; generalized anxiety disorder = 3). Of the 48 women who had no lifetime diagnosis of MDD, nine women met criteria for at least one lifetime anxiety disorder. In terms of children's diagnoses, 11 met criteria for a lifetime episode of MDD (ten children of depressed mothers), of whom six met criteria for current MDD (5 of depressed mothers). Sixteen children met criteria for at least one lifetime anxiety disorder (13 of depressed mothers), of whom eight met criteria for one or more current anxiety disorders (social phobia = 6; separation anxiety disorder = 1; generalized anxiety disorder = 1). A subset of 20 SADS-L and 20 K-SADS-PL interviews from this project were coded by a second interviewer and kappa coefficients for current diagnoses were: mother MDD (κ=1.00), mother any anxiety disorder (κ=0.83), child MDD (κ=1.00), and child any anxiety disorder (κ=0.83).

Mothers' and children's symptoms of depression were assessed using the Beck Depression Inventory-II (BDI-II; Beck et al. 1996) and Children's Depression Inventory (CDI; Kovacs 1981), respectively. Numerous studies have supported the reliability and validity of both measures (e.g., Beck et al. 1996; Kovacs 1981; Smucker et al. 1986). In the current study, both the BDI-II and the CDI exhibited good internal consistency (αs=0.93 and 0.86, respectively).

Mothers' and children's symptoms of anxiety were assessed using the Beck Anxiety Inventory (BAI; Beck et al. 1988) and the Revised version of the Screen for Child Anxiety Related Emotional Disorders (SCARED-R; Muris and Steerneman 2001), respectively. Previous studies have supported the reliability and validity of both questionnaires (e.g., Beck et al. 1988; Creamer et al. 1995; Muris and Steerneman 2001; Muris et al. 2004). In the current study, both the BAI and the SCARED-R exhibited good internal consistency (αs=0.90 and 0.94, respectively).

Children's levels of behavioral inhibition were assessed using the Retrospective Self-Report of Inhibition (RSRI; Reznick et al. 1992). Youth completed the RSRI, a retrospective self report questionnaire used to assess levels of behavioral inhibition exhibited during childhood (i.e., grades 1–6). The RSRI consists of 30 items rated on a Likert-type scale from 1 to 5 with 5 representing extreme inhibition. The RSRI consists of two factors, consistent with the social and nonsocial components of behavioral inhibition: (1) school and social situations (12 items), and (2) fear and illness (12 items). Both of these factors have been supported in several studies (Coles et al. 2006; Neal et al. 2002; Reznick et al. 1992; Schofield et al. 2009; Van Ameringen et al. 1998). Although the RSRI has been primarily used as a retrospective measure of BI among adult populations, it has also demonstrated good psychometric properties in pediatric samples (e.g., Beesdo et al. 2010; Hayward et al. 1998; Hirshfeld-Becker et al. 2010). In the current study, the internal consistency alpha coefficients of the RSRI social and the nonsocial components were 0.62 and 0.73, respectively.

Parenting behaviors were assessed using the shortened form of the Parental Bonding Instrument (PBI; Kendler 1996). The original PBI was designed to assess two dimensions of parenting: care and overprotection (Parker et al. 1979). However, more recent research has supported the reliability and validity of a 16-item shortened form which consists of three factors reflecting care/warmth, overprotection, and control/authoritarianism (Kendler 1996; Lizardi and Klein 2002; Murphy et al. 1997). Both the mother and the child completed the shortened form of the PBI. In the current study, internal consistency coefficients were calculated for each factor of the PBI for both child (warmth α=0.64, overprotection α=0.73, authoritar-

ianism α=0.56) and mother report (warmth α=0.70, overprotection α=0.73, authoritarianism α=0.52).

Finally, children provided buccal cells by rubbing swabs along their cheeks and gums and then rinsing their mouth with 10 ml of distilled water. DNA was collected and isolated using published procedures (Freeman et al. 1997; Lench et al. 1988). The 5-HTTLPR S alleles were assayed using previously reported methods (Pooley et al. 2003) and the rs25531 SNP genotypes (L_A vs. L_G) were obtained using a combination of published methods. Specifically, the primers used for PCR were those reported in Hu et al. (2005) and the MspI restriction site protocol follows Wendland et al. (2006). Samples were analyzed on an ABI PRISM® 3130xl Sequencer. Consistent with previous research (e.g., Zalsman et al. 2006), children's 5-HTTLPR genotype was coded to reflect the number of lower expressing alleles (S or L_G) present: children with two copies of the S or L_G allele (S′S′; n=25), children with 1 copy of the S or L_G allele and one copy of the L_A allele (S′L′; n=53), and those homozygous for the higher expressing L_A allele (L′L′; n=22). Results of an exact test for Hardy Weinberg proportions using Markov chain–Monte Carlo implementation (Guo and Thompson 1992) indicate that our observed genotype frequencies do not differ from Hardy Weinberg equilibrium (p=0.97).

Procedure

Potential participants were recruited from the community through a variety of means (e.g., newspaper and bus advertisements, flyers). Mothers responding to the recruitment advertisements were initially screened over the phone to determine potential eligibility. Those reporting either significant depressive symptoms during the child's life or no significant lifetime symptoms of depression were invited to participate in the study. Upon arrival at the laboratory, mothers were asked to provide informed consent and children were asked to provide assent to be in the study. Next, the mother was administered the K-SADS-PL interview by a research assistant. During this time, the child completed questionnaires, including the CDI, PBI, RSRI, and the SCARED-R in a separate room, and provided buccal cells for DNA analysis. After completing the K-SADS-PL with the mother, the same interviewer then administered the K-SADS-PL to the child. While children were being administered the K-SADS-PL, the mother provided buccal cells for DNA assessment, completed a series of questionnaires including the BDI-II, BAI, and the PBI, and was then administered the SADS-L by a separate interviewer. Participation in this initial assessment took approximately 3 h, which included frequent breaks for children to minimize fatigue effects. Families were compensated $50 for their participation. All study procedures were approved by the University's International Review Board.

Results

Preliminary analyses were conducted to determine whether any of the study variables were significantly related to children's age or gender. Children's age was negatively correlated with children's reports of authoritative (r=−0.25, p=0.01) and overprotective (r=−0.24, p=0.02) parenting, with younger children reporting higher levels than older children. In terms of gender differences, we found that girls reported significantly higher levels of BI related to fear and illness than boys, $t(98)$=2.38, p=0.02, $r_{\text{effect size}}$=0.28. Given these findings, age was entered as a covariate in all of the regression analyses, and gender was entered as a covariate in all of the regression analyses for which BI fear and illness served as the criterion variable. A significant gender difference was also found for the 5-HTTLPR genotype, χ^2=(1, N=100)=6.81, p=0.03. Comparing the three genotype groups, this difference was due to boys being more likely than girls to carry the S′S′ genotype (75% were boys) than the L′L′ genotype (25% were boys), χ^2=(1, N=47)=6.65, p=0.01, $r_{\text{effect size}}$=0.38. The proportion of boys with the S′L′ genotype did not differ significantly from those with the S′S′, χ^2=(1, N=78)=2.84, p=0.09, $r_{\text{effect size}}$=0.19, or the L′L′genotype, χ^2=(1, N=75)= 1.96, p=0.17, $r_{\text{effect size}}$=0.16. Finally, as a means of investigating potential rGE effects, we examined whether children's or mothers' 5-HTTLPR genotype was significantly related to any of the parenting and BI variables. None of these analyses were significant.

Next, hierarchical regression analyses were used to test our hypothesis that children's 5-HTTLPR genotype would moderate the link between overprotective parenting and behavioral inhibition. Because children were chosen for inclusion in the study based on mothers' history of MDD during their lifetime (yes vs no), the potential influence of mother MDD was statistically controlled for in all analyses. As noted above, child age was also included as a covariate in all of the analyses and child gender was included as a covariate in all analyses for which BI fear and illness was the criterion variable. Child and mother reports of parenting were examined in separate analyses. Focusing first on RSRI school and social situations scores as the criterion variable, mother MDD history (yes vs. no) and child age were entered in the first step of a hierarchical regression. Reports of maternal overprotection and child's 5-HTTLPR genotype were entered into the second step of the equation and the overprotection × 5-HTTLPR interaction was entered into the third step of the equation. Details of these analyses are provided in Table 1. As predicted, we found that children's 5-HTTLPR genotype moderated the link between children's reports of overprotective parenting and children's levels of BI in school and social situations, $t(95)$=2.26, p=0.02, pr= 0.24. In contrast, the overprotection × 5-HTTLPR interaction

Table 1 Summary of regression analyses predicting children's behavioral inhibition levels in school and social situations

Predictor	Child report			Mom report		
	β	t	pr	β	t	pr
Step 1						
Mom MDD	0.16	1.55	0.16	0.16	1.55	0.16
Child age	0.11	1.05	0.11	0.11	1.05	0.11
Step 2						
Overprotectiveness	0.14	1.37	0.14	0.15	1.52	0.15
Child 5-HTTLPR	0.05	0.44	0.05	0.03	0.26	0.03
Step 3						
Overprotectiveness × 5-HTTLPR	0.23	2.26*	0.24	0.07	0.51	0.15

MDD = major depressive disorder; Overprotectiveness = maternal overprotectiveness; Child 5-HTTLPR = child serotonin transporter genotype (number of lower expressing [S or L_G] alleles)

*$p<0.05$

was not significant when focusing on mothers' reports of her overprotectiveness, $t(95)=0.51$, $p=0.16$, $pr=0.15$. To determine the form of the significant child report of maternal overprotection × 5-HTTLPR genotype interaction, we examined the main effect of maternal overprotection in each of the three genotype groups separately. We found that children's reports of higher maternal overprotection were associated with elevations in BI in school/social situations among children carrying two copies of the lower expressing 5-HTTLPR alleles, $t(22)=2.24$, $p=0.04$, $pr=0.43$, but not among those homozygous for the L_A allele, $t(19)=0.93.$, $p=0.37$, $pr=0.21$. A nonsignificant trend was found for those with only one copy of the lower expressing 5-HTTLPR alleles, $t(50)=1.73$, $p=0.09$, $pr=0.24$, consistent with a dose dependent effect of child 5-HTTLPR genotype.

To test the robustness of these results, we examined this interaction statistically controlling for (a) children's and mothers' lifetime diagnoses of MDD and any anxiety disorder, and (b) children's and mothers' current symptoms of depression and anxiety. In each of these analyses, the G × E Interaction remained significant in predicting children's levels of BI in school and social situations (highest $p=0.03$). Supporting the specificity of this finding, the G × E interaction was not significant for children's reports of mothers' authoritative parenting, $t(95)=0.33$, $p=0.75$, $pr=-0.03$, or warmth, $t(95)=0.86$, $p=0.39$, $pr=-0.09$, in predicting levels of BI in school/social situations.

Finally, none of the G × E interactions predicted levels of BI for fear and illness and none of the G × E interactions were significant when focusing on mothers' reports of her own parenting styles (lowest $p=0.16$).[1]

Discussion

The primary goal of this study was to examine environmental and genetic correlates of children's levels of BI. Specifically, we examined whether 5-HTTLPR genotype moderates the link between maternal overprotectiveness and children's levels of BI. Consistent with our hypothesis, we found a significant genotype-by-parenting interaction in predicting levels of BI. Specifically, higher levels of child-reported maternal overprotection were associated with elevations in BI among children carrying two copies of the lower expressing 5-HTTLPR alleles (S or L_G), but not among those homozygous for the L_A allele. Further, this G × E interaction was specific to the school and social situations subscale, but not the fear and illness subscale. As previously noted, given that the social component of BI may be particularly important in the development of social phobia (Mick and Telch 1998; Neal et al. 2002; Schofield et al. 2009), this finding could have important implications. Specifically, the development of behavioral inhibition in social situations among children of overprotective mothers, particularly those children who also carry two of the lower expressing 5-HTTLPR alleles, may serve as an important mechanism of risk for the development of social phobia. Future research is needed to specifically examine prospective changes in children's level of behavioral inhibition in social situations and to determine whether this mediates the impact of the 5-HTTLPR × overprotective parenting interaction on risk for social phobia.

We should also highlight the fact that we did not find a significant G × E interaction when using mother's rating of maternal overprotectiveness. Although the reason for this pattern of findings is not clear, there are a number of potential explanations. First, it is possible that it is due to shared method variance in children's reports of parenting and BI, which may have inflated their relations. To the extent that this was the sole cause, however, one would have expected significant results for children's reports of all three forms of parenting and both forms of BI. A second potential reason for the mixed findings between child and mother report of overprotectiveness in this study is that children may be better reporters of mothers' parenting behavior than are mothers. Specifically, research has shown that it is common for different informants to disagree with one another (De Los Reyes and Kazdin 2005; Edelbrock et

[1] Details of these analyses are available from the first author.

al. 1986; Weissman et al. 1980). Supporting our focus on children's reports, researchers have found that parents' self-report of parenting may be systematically biased, and are overly positive compared to children, observers, and partners (Gaylord et al. 2003; Noller and Callan 1988; Schwarz et al. 1985). A third possibility is that it is the children's perceptions of parenting that are of greatest importance in this effect, given that they are the ones that are at risk for psychopathology. Additional research is needed to determine which of these explanations is most strongly supported.

This study had a number of strengths, including its use of two separate components of BI. In addition, this is the first study to provide evidence that a specific type of parenting (overprotective) is associated with a specific type of behavioral inhibition (for social situations) among children exhibiting a specific genetic risk factor (5-HTTLPR S or L_G allele). Despite these strengths, however, limitations of the current study should be noted as they may provide directions for future research. First, we used a retrospective, cross-sectional design for our constructs which does not allow us to draw causal relationship findings. Future research is needed, therefore, to determine whether overprotective parenting predicts prospective changes in children's levels of behavioral inhibition in school/social domains among children carrying two copies of the lower expressing 5-HTTLPR alleles.

Second, we relied primarily on children's reports of behavioral inhibition, which may have inflated links with children's reports of overprotective parenting. To the extent that this influenced our results, however, it is not clear why the results would be specific to children's reports of maternal overprotection and not the two other aspects of parenting assessed, nor is it clear why this differential would have occurred for children based on their 5-HTTLPR genotype. With regard our self-report measures, we should also note that the internal consistency of the RSRI was fairly low in our sample, though previous research has supported the psychometric properties of the RSRI in pediatric populations (Beesdo et al. 2010; Hayward et al. 1998; Hirshfeld-Becker et al. 2010). A potential contributor to this could be the fact that the RSRI is designed to measure BI levels in Grades 1–6 and some of the children in our sample have not yet reached grade 6. Because of this low internal consistency, the current results may reflect an underestimate of the true relations between overprotective parenting and behavioral inhibition. Future research, therefore, should employ multi-method assessments of BI using assessments with greater reliability.

A third caveat regards the nature of our sample. Specifically, children were chosen for inclusion based on their mothers' lifetime histories of major depression, which may limit the generalizability of our results to other samples. Importantly, we were able to show that the results were maintained even after statistically controlling for the influence of mother and child psychopathology. This said, future research would benefit from either more representative samples or samples that have no lifetime history of psychopathology to rule out this potential confound. Fourth, there is always the possibility in any genetic association study of an unmeasured genetic or nongenetic third variable accounting for the associations reported (e.g., population stratification or linkage disequilibrium between measured variant and actual functional variant). Future studies, therefore, would benefit from the inclusion of a genomic control. Fifth, we focused exclusively on self-report assessments of parenting behavior and behavioral inhibition, which may have been subject to recall or response bias. Therefore, future studies would benefit from multi-method assessments of each construct (i.e., interview-based report, including multiple informants (i.e., father) of parenting behaviors or observational methods for BI) and possibly prospective longitudinal studies. As noted earlier, Fox et al. (2005) found a G × E interaction in predicting prospective levels of BI, using social support as the environmental risk factor. Future research, therefore, should focus on prospective designs using overprotective parenting as the environmental factor in the G × E interaction in predicting levels of BI to determine if this finding can be replicated. Finally, research has suggested that fathers make separate contributions to the development of childhood psychopathology (i.e., anxiety) than mothers (Bogels and Phares 2008). Given that our study focused solely on mother's effects of BI levels, future research studies should include father data to get a more thorough understanding of the development of BI.

In summary, these findings add to emerging research illustrating that G × E interactions predict variation in BI during childhood. In terms of clinical implications, the identification of early risk factors (i.e., the presence of 5-HTTLPR S or L_G alleles and an overprotective parent) can facilitate the development of more targeted prevention efforts. Understanding how behavioral inhibition emerges will help clinicians better identify children at risk for developing other internalizing disorders (i.e., depression and anxiety). Future research studies are needed to replicate these findings using longitudinal, prospective designs.

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