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Harsh parenting and serotonin transporter and BDNF Val66Met polymorphisms as predictors of adolescent depressive symptoms

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Abstract

Objective—Depressive symptoms are prevalent and rise during adolescence. The present study is a prospective investigation of environmental and genetic factors that contribute to the growth in depressive symptoms and the frequency of heightened symptoms during adolescence.

Method—Participants included 206 mother-father-adolescent triads (M age at T1 = 13.06 years, $SD = .51$, 52% female). Harsh parenting was observationally assessed during a family conflict paradigm. DNA was extracted from saliva samples and genotyped for the *5-HTTLPR* and *BDNF Val66Met* polymorphisms. Adolescents provide self-reports of depressive symptoms annually across early adolescence.

Results—The results reveal gene-by-environment (GxE) interactions as predictors of adolescent depressive symptom trajectories in the context of harsh parenting as an environmental risk factor. A *BDNF Val66Met* x harsh parenting interaction predicted the rise in depressive symptoms across a three-year period while a *5-HTTLPR* x harsh parenting interaction predicted greater frequency in elevated depressive symptoms.

Conclusions—The findings highlight the importance of unique genetic and environmental influences in the development and course of heightened depressive symptoms during adolescence.

¹Prior to fitting the full model with covariates, genetic variants, and interaction variables, harsh parenting was examined as the sole predictor in the LCS model. There was no main effect of harsh parenting on the intercept ($\beta = .09$, $p = .28$) or slope ($\beta = .01$, $p = .97$) of depressive symptoms.

²ZIP analyses were conducted examining harsh parenting as the sole predictor and harsh parenting was not associated with being in the zero group ($B = -.86$, $SE = .87$, $p = .32$) or the frequency of elevated depressive symptoms ($B = -.04$, $SE = .04$, $p = .29$).

Keywords

Depressive Symptoms; Adolescence; Harsh Parenting; *5-HTTLPR*; *BDNF Val66Met*

The prevalence of depressive symptoms rises steadily across adolescence. A nationally representative sample shows that approximately 1 in 10 sixth graders, 1 in 5 eighth graders, and 1 in 4 tenth graders report depressive symptoms (Saluja et al., 2004). Sub-threshold depression is highly prevalent during adolescence and places individuals at a greater risk for subsequently developing major depression (Bertha & Balázs, 2013). Lifetime prevalence for mood disorders is roughly 1 in 5 (Kessler et al., 2005) and many develop symptoms prior to adulthood highlighting the necessity to understand the environmental and genetic factors that are associated with the emergence of depressive symptoms during adolescence.

Harsh parenting is associated with increased rates of depressive symptoms and internalizing problems as well as a wider host of behavioral and health problems such as externalizing problems and poorer physical health (e.g., Barber, 1996; Kaslow, Deering, & Racusin, 1994; Repetti, Taylor, & Seeman, 2002). Harsh parenting encompasses a broad set of parenting behaviors including unsupportive, coercive, controlling, and insensitive parenting strategies. Despite evidence that harsh parenting and negative family climates increase the risk for depressive symptoms, not all youth exposed to these risky family environments develop problem behavior. Thus, identifying which youth are at increased risk is important for understanding change in symptoms and persistence in heightened symptoms during adolescence. There is mounting evidence for the role of different genetic variants as moderators in the family risk-adjustment difficulties association. In particular, both the serotonin transporter linked polymorphism (*5-HTTLPR*) and the brain-derived neurotrophic factor (*BDNF Val66Met*) polymorphism have been implicated in increased risk for depression and heightened depressive symptoms in the presence of environmental adversity. The present study is an investigation of the role of environmental and genetic contributions in the prediction of the growth in depressive symptoms and frequency of heightened symptoms across early adolescence.

The serotonin transporter is involved in the reuptake of serotonin in the synapse and variation in the promoter region of the *5-HTTLPR* polymorphism regulates transcription (Heils et al., 1996). Relative to the long allele, the short allele is associated with reduced transcriptional activity of the serotonin transporter and has been associated with greater risk for depression in interaction with environmental adversity. Caspi and colleagues (2003) found that presence of at least one short allele moderated the relation between life stress and depression in a prospective longitudinal study. Although GxE findings for the *5-HTTLPR* polymorphism and depression remain mixed, results of recent meta-analyses support the finding that individuals with the short allele are at increased risk (Karg, Burmeister, Shedden, & Sen, 2011; Sharpley, Palanisamy, Glyde, Dillingham, & Agnew, 2014). Research supports similar associations in the context of adolescent depression (see Dunn et al., 2011; Xia & Yao, 2015 for reviews of the GxE research, including the *5-HTTLPR* and *BDNF Val66Met* polymorphisms, in adolescent depression). For example, the presence of the short allele has also been found to moderate the environmental adversity-health

association in the context of harsh parenting for adolescents (Brody et al., 2014). Greater increases in adolescent depressive symptoms have been found among youth with the short allele in the context of heightened chronic family stressors (Jenness, Hankin, Abela, Young, & Smolen, 2011) and idiographic stressors (Hankin, Jenness, Abela, & Smolen, 2011) utilizing prospective research designs. In addition to differences in transcriptional activity due to fragment length, there is a single nucleotide A>G substitution in the long allele that is associated with transcriptional differences such that the transcriptional activity of the L_G allele is functionally similar to the short allele (Hu et al., 2005; 2006). The triallelic 5-*HTTLPR* polymorphism has been found to relate to differences in 5-HTT density (Praschak-Rieder et al., 2007) and in vivo mRNA expression (Wankerl et al., 2014). Given the functional differences of the L_A and L_G alleles that may contribute to the inconsistent finding of the role the serotonin transporter gene in predicting depression, the present study examined the triallelic 5-*HTTLPR* polymorphism.

BDNF is involved in neuronal growth and survival and synaptic plasticity and has been implicated in psychopathology. Decreased BDNF levels in the hippocampus are associated with depression-like behaviors in rats (Taliaz, Stall, Dar, & Zangen, 2010). Additionally, reduced serum BDNF concentrations are found among depressed patients compared to healthy controls and depressed patients receiving anti-depressants (Molendijk, Spinhoven, Polak, Buss, Penninx, & Elzinga, 2014). A single nucleotide polymorphism in the *BDNF* gene (*Val66Met*) results in a valine (Val) to methionine (Met) substitution; the Met allele is associated with reduced BDNF activity (Chen et al., 2004; Egan et al., 2003). Growing evidence supports the moderational role of *BDNF Val66Met* in the context of environmental adversity for depressive symptoms. A recent meta-analysis shows that the *BDNF Val66Met* polymorphism serves as a moderator of the life stress-depression association; individuals with the Met allele, in the presence of environmental risk, have higher rates of depression (Hosang, Shiles, Tansey, McGuffin, & Uher, 2014). Similar to adult research, the *BDNF Val66Met* has been found to interact with environmental stressors in the prediction of adolescent depressive symptoms; however, the particular allele (Val versus Met) associated with conferring greater risk varies across different investigations during adolescence (Carver, Johnson, Joormann, LeMoult, & Cuccaro, 2011; Chen, Li, McGue, 2012; 2013; Gottfredson, Foshee, Ennett, Haberstick, & Smolen, 2015). It has been posited that which allele of the *BDNF Val66Met* polymorphism that is associated with poorer phenotype outcomes may vary as a function of development (Casey et al., 2009).

While cross-sectional findings support the role of 5-*HTTLPR* and *BDNF Val66Met* polymorphisms in depression and heightened depressive symptoms, inconsistencies in the literature remain suggesting the need to expand examinations beyond cross-sectional and retrospective research designs to further our understanding of the role of GxE interactions in depression. In particular, Uher and colleagues (2011) note that the investigation of longitudinal phenotypes may reduce inconsistencies in GxE research. Researchers also posit that more nuanced investigations of the onset and course of depression may be necessary for replication of these GxE interaction effects (Brown & Harris, 2008). Brown and colleagues (2014) posit that the 5-*HTTLPR* and *BDNF Val66Met* polymorphisms, in interaction with environmental adversity, play distinct roles in the course of depression. Specifically, these authors hypothesize that the *BDNF Val66Met* polymorphism is implicated in the onset of

depression whereas the serotonin transporter polymorphism is involved in the chronicity of depression. In support of these hypotheses, Uher and colleagues (2011) reported that a *5-HTTLPR*-by-maltreatment interaction predicted persistence in depression (defined as meeting criteria at more than one time point across four longitudinal assessments). Additionally, Brown and colleagues (2013) found that the *5-HTTLPR* polymorphism interacted with childhood maltreatment to predict chronic depression but not the onset of depression. In a follow-up study, Brown and colleagues (2014) found that the Met allele of the *BDNF Val66Met* polymorphism interacted with recent life stress to predict the onset of new depressive episodes in adult women. However, little work has examined these relations during adolescence.

Depressive symptoms and the incidence of depression increase during adolescence making it an important developmental period for understanding individual differences in longitudinal trajectories of symptoms. Subclinical depressive symptoms during adolescence increase the risk for major depression during adulthood (Pine, Cohen, Cohen, & Brook, 1999) and adolescents evidencing stability in sub-threshold depressive disorder, defined as those meeting criteria across time points, are more likely to escalate to full-syndrome depression (Klein, Shankman, Lewinsohn, & Seeley, 2009). Both symptom severity and persistent course have been posited as important dimensions in depressive disorders that may differ in etiology (Klein, 2008). Thus investigation of both dimensions of depressive disorders is important. Furthermore, it is expected that the biological mechanisms that account for why GxE interactions relate to change in symptoms and persistence of heightened symptoms are likely to be the same when considering subclinical symptoms. Thus, the present investigation sought to examine the extent to which these same genes may play unique roles in longitudinal relations of depressive symptoms during adolescence.

The present study examined GxE interaction effects of harsh parenting and the *BDNF Val66Met* and *5-HTTLPR* polymorphisms predicting longitudinal trajectories of depressive symptoms and the frequency of elevated symptoms in a prospective study. This extended previous research by examining unique predictors of different aspects of adolescent depressive symptoms including both concurrent and longitudinal relations. First, predictors of initial levels (e.g., cross-sectional relations) and change in depressive symptoms were modeled. Second, utilizing cut-off scores on a depressive symptom measure, predictors of adolescents meeting or exceeding the threshold of potentially clinically-elevated levels of depressive symptoms as well as the number of time points in which adolescents exceeded the threshold (as a measure of the frequency of meaningfully elevated symptoms) were examined. Building on adult depression research, it was expected that the *BDNF Val66Met* and *5-HTTLPR* polymorphisms may play unique roles in increasing risk for the change and persistence in depressive symptoms during adolescence for those experiencing heightened environmental risk in the family context; such that in interaction with environmental adversity, the *BDNF Val66Met* polymorphism would increase the risk for changes in depressive symptoms whereas the *5-HTTLPR* polymorphism would increase the risk for frequency of elevated symptoms. Additionally, given the potential for adolescent behavior to evoke harsher parenting (Larsson, Viding, Rijksdijk, & Plomin, 1998; O'Connor, Deater-Deckard, Fulker, Rutter, & Plomin, 1998), adolescents' oppositional and irritable behaviors were investigated.

Method

Participants

Families included 206 mother-father-adolescent triads taking part in a larger longitudinal study on family risk and child adjustment. Families were representative of the communities from which they were drawn resulting in a predominantly Caucasian middle class sample (see Table 1 for complete participant demographics). Data for the current study were drawn from the longitudinal study during the early adolescent years when families participated in three annual assessments (T1 $M=13.06$ years, $SD=.51$; T1 median grade = 7; see Table 1 for adolescent ages at T2 and T3). The majority of mothers and fathers were the biological parent of the participating adolescent and reported being married at T1.

Adolescents participating in the genetic sample collection at T3 were included in the present analysis resulting in 206 adolescents (107 girls, 99 boys). Families with partial participation ($N=8$) across the three assessments were included. Of the 206 families, 2 did not participate at T1 or T2, 3 did not participate at T1, and 3 did not participate at T2. Families with partial participation did not differ on demographic variables and most study variables including child age and gender, family income, race and ethnicity, *BDNF Val66Met* and *5-HTTLPR* genotypes, harsh parenting, and T1 and T2 depressive symptoms. However, adolescents with partial participation did report higher depressive symptoms at T3 ($M=18.38$, $SD=13.11$) compared to adolescents participating at all three assessments ($M=10.68$, $SD=8.63$, $F(1,194)=5.83$, $p<.05$).

Families were recruited from a Midwestern and a Northeastern city through flyers distributed at local schools, churches, community events, and by ads placed in local newspapers. As a part of the larger longitudinal study, 295 families participated in at least one time point across the three adolescent assessments and 250 families participated at T3. Participants who attended a T3 laboratory session were eligible for participation in the DNA collection; the majority of families participating at T3 consented to the supplemental DNA collection (206/211). Families that participated in the DNA collection ($n=206$) were compared to several subsets of families without DNA samples including 1) families without DNA samples that participated at any point across T1-T3 ($n=89$), 2) families without DNA samples that participated at T3 ($n=44$), and 3) families without DNA samples that attended the T3 laboratory sample when the DNA samples were collected ($n=5$). Comparisons were made among study variables and demographic data including T1-T3 adolescent depressive symptoms, T1 harsh parenting, T1 adolescent behavior during the FPST, T1 family income, T1-T3 adolescent age, and adolescent gender. There was one significant difference when comparing to families with DNA samples to those without DNA samples that participated at any point across T1-T3 such that adolescents with DNA samples were slightly young at T1 ($F(1,252)=4.57$, $p<.05$; $M=13.06$, $SD=.51$) compared to those without ($M=13.22$, $SD=.58$). There were no differences among any of these variables when comparing to families with DNA samples to those that participated in some form at T3. Lastly, there was one difference among those with and without DNA samples that participated in the T3 laboratory session (e.g., declined DNA portion only) such that all 5 participants without DNA samples were adolescent males ($\chi^2(1)=5.27$, $p<.05$).

Procedure

Mothers, fathers, and adolescents participated in three annual laboratory assessments. Parents and adolescents provided consent and assent for participation in the larger longitudinal study at each of the assessments. Separate consent and assent were obtained for participation in the DNA collection. All procedures were approved by the universities' institutional review boards. Parents received monetary compensation for their participation and adolescents received a giftcard for their participation at each of the assessments.

Family Problem-Solving Task—At T1 mother-father-adolescent triads participated in a seven minute family problem-solving task (FPST). Each family member was asked to individually select one topic that was problematic among the three family members. Participants were provided with a list of common topics of disagreement among parents and adolescents to aid in their selection. Following their individual selections, families were asked to together choose one topic to discuss. Families were instructed to discuss their selected problematic topic for seven minutes with the goal of developing a solution or resolution to their selected topic. The FPST was videotaped and later coded for family and individual functioning. The FPST is consistent with other procedures for triadic interactions (e.g., Gordis, Margolin, & John, 2001; Lindahl & Malik, 1999).

DNA collection, extraction, and genotyping—Adolescents provided DNA samples through whole saliva collected using the Oragene DNA collection kits at T3. Adolescents rinsed their mouths prior to providing saliva samples in the Oragene vials. DNA was purified from .5ml of Oragene DNA solution using the DNeasy protocol for manual sample purification with prepIT-L2P. Sample concentrations were determined using the Quant-iT PicoGreen dsDNA Assay Kit (P7589, Invitrogen), after which genotyping was performed using established procedures. SNP genotyping was conducted using Applied Biosystems Custom Taqman SNP Genotyping Assays. The products of these analyses were analyzed using endpoint allelic discrimination. Human DNA from cell lines were purchased from Coriell Cell Repositories for each genotype and used as control samples. The genotype was confirmed using dye terminator cycle sequencing chemistry on an ABI 3130xl. All control samples were genotyped twice for quality control. Study samples that were not genotyped to a 95% confidence level were repeated under the same procedures for a maximum of four times.

Serotonin transporter genotype: The present study examined the triallelic *5-HTTLPR* polymorphism. Human genomic DNA was diluted to a working concentration and PCR amplified with HotStar Taq PCR Mix (Qiagen, Catalog 203205) and previous described primers (Gelernter, Kranzler, & Cubells, 1997), followed by fragment analysis using a CEQ8000 (Beckman-Coulter, Inc.). The SNP located within the *5-HTTLPR* L/S region, rs25531 (NC_000017.11:g. 30237328T.C), was genotyped using previously reported TaqMan probes (Lesch et al., 1996). Individual allele determinations were made using TaqMan Genotyping Master Mix (Life Technologies, Catalog 4371357) with amplification on a GeneAmp 9700 (Applied Biosystems) and analyzing the endpoint fluorescence using a Tecan M200 and data analyzed with JMP 10.0 (SAS, Inc.). Call rate in the present sample was 99.5% (205/206). An A>G substitution in a SNP upstream from the promoter region has

shown that the L_G allele functions similarly to the S allele. Thus, adolescents with the L_AL_A ($N=47$) genotype were compared to adolescents with at least one functional S allele ($N=158$; $SS\ N=37$, $L_GS\ N=17$, $L_AL_S\ N=84$, $L_GL_G\ N=1$, $L_AL_G\ N=19$). The genotype distribution was in Hardy-Weinberg equilibrium (HWE; $\chi^2(3)=.40$, ns). There were no differences in race/ethnicity by genotype $\chi^2(6)=4.19$, ns).

BDNF (rs6265) genotype: Saliva derived Human DNA samples were diluted to a working concentration and genotyped for the rs6265 (C_000011. 10:g.27658369C.T) SNP in the *BDNF* gene using TaqMan SNP genotyping assay C_115 92758_10 (Applied Biosystems). Individual allele determinations were made using TaqMan Genotyping Master Mix (Life Technologies, Catalog 4371357) with amplification on a GeneAmp 9700 (Applied Biosystems) and analyzing the endpoint fluorescence using a Tecan M200 and JMP 10.0 (SAS, Inc.). Call rate for the *BDNF Val66Met* genotype was 100% (206/206). The majority of adolescents had the Val/Val genotype ($N=152$), followed by the Val/Met genotype ($N=48$), and the Met/Met genotype ($N=6$). Consistent with other investigations of the *BDNF Val66Met* polymorphism (e.g., Gunnar et al., 2012; Hariri et al., 2003) and functional differences across genotypes (Soltész et al., 2014), the Met/Met and Val/Met genotypes were collapsed into an any Met allele group. The genotype distribution for the *BDNF Val66Met* polymorphism was in Hardy-Weinberg equilibrium ($\chi^2(1)=.83$, ns). There were no differences in race/ethnicity by genotype $\chi^2(6)=10.88$, ns).

Measures

Harsh Parenting—Mothers' and fathers' use of harsh parenting during the FPST was observationally coded using the System for Coding Interactions and Family Functioning (SCIFF; Lindahl & Malik, 2000). Separate codes were obtained for mothers and fathers using the *Parental Rejection and Invalidation* and the *Parental Coerciveness* scales. The parental rejection and invalidation code assesses the frequency and intensity of the parent's insensitive and critical statements as well as their use of condescending or dismissing emotional tone. The parental coerciveness code assesses the frequency of manipulative and threatening statements and behaviors the parent uses toward the child. Instances of general parental frustration that do not include rejection or coercion directed to the child are not captured in the parenting codes. Each code was assessed on a 5-point scale ranging from *very low* to *high*. A subset of 20% of FPST videotapes were coded by an independent coder to measure reliability. Intraclass correlation coefficients (ICCs) in the present sample for mothers were $ICC=.71$ (rejection and invalidation) and $ICC=.74$ (coerciveness) and for father were $ICC=.89$ (rejection and invalidation) and $ICC=.93$ (coerciveness). The sum of the four scales was computed as a measure of the level of harsh parenting present in the family. All four scales were significantly correlated with one another (r s range .15–.56, all p s<.05).

Adolescent Behavior—Adolescents' behavioral responses during the FPST were observationally coded using the SCIFF (Lindahl & Malik, 2000). Videotaped interactions were coded using the *Anger and Frustration* and *Opposition/Defiance* scales. The anger and frustration scale captures adolescents' expressions of frustration, irritation, and anger evident in their emotional tone, behavior, and statements. The opposition/defiance scale assesses

adolescents' noncompliant, disrespectful, and argumentative behaviors and statements. Each code was rated on a 5-point scale ranging from *very low* to *high*. A subset of 20% of FPST videotapes were coded to assess reliability; ICCs in the present sample were ICC=.82 (opposition/defiance) and ICC=.75 (anger and frustration). The two scales were significantly correlated ($r=.61$, $p<.001$). The sum of the two scales was used as a measure of adolescent behavioral responses during the FPST.

Adolescent Depressive Symptoms—At each of the annual assessments, adolescents completed the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The CES-D is a 20-item measure assessing depressive symptoms in the past week and has been found to be suitable for assessing depressive symptoms during adolescence (Radloff, 1991; Roberts, Andrews, Lewinsohn, & Hops, 1990). Adolescents rated how frequently they experienced each item on a 4-point likert scale with higher scores signifying elevations in depressive symptoms. Scores of 16 or greater indicate potentially clinical levels of depressive symptoms in adult populations. In the present study 19.5% (T1), 18.5% (T2), and 21.9% (T3) of adolescents reported scores of 16 or greater. The CES-D has adequate internal reliability (present sample α range: .86–.87). The number of assessments in which adolescents scored in the clinical range was used as a measure of the frequency of heightened symptoms (range 0-3).

Data Analytic Plan

Analyses were conducted in four parts. First, descriptive statistics, correlations, and gender differences were examined among study variables. Second, gene-environment correlations (rGE) were examined. One-way between-subjects analysis of variance (ANOVAs) were conducted to determine if harsh parenting or adolescent oppositional behavior during the FPST differed by adolescent genotype. Third, latent change score models were fit to examine predictors of change in depressive symptoms across the study period. Unconditional models were fit to determine the type of change in depressive symptoms. After the appropriate type of change was determined, predictors of both the latent intercept (e.g., T1 depressive symptoms) and slope (e.g., change in depressive symptoms from T1-T3) were added to the model including covariates, main effects of genotype and harsh parenting, and two-way GxE interactions. Lastly, regression analyses were conducted to examine predictors of the frequency in heightened symptoms. Frequency of heightened symptoms was assessed as the total number of time points in which adolescents' CES-D scores met or exceeded potentially clinical levels (scores greater than or equal to 16). Several models were considered to determine the appropriate model for the data including a poisson regression, negative binomial regression, zero-inflated poisson (ZIP) regression, and zero-inflated negative binomial (ZINB) regression. In particular, zero-inflated regression models were considered as they are appropriate analyses for data that contain a preponderance of zeros. This type of analysis fits two simultaneous models: 1) a logistic regression predicting the probability of being in the zero group (e.g., not meeting criteria for heightened depressive symptoms at any point of the study) and 2) a poisson or negative binomial regression predicting the number of time points criteria was met (e.g., frequency of heightened depressive symptoms). After the appropriate model was determined, predictors of the main effect of harsh parenting and genotype and the two-way GxE interactions were included. For

both the LCS models and count regression analyses, covariates included family income, T1 adolescent age, adolescent gender (0=male, 1=female), ethnicity (0=Caucasian/White, 1=all other racial/ethnic backgrounds), and adolescents' use of oppositional behaviors during the FPST.

Results

Descriptive Statistics

Means, standard deviations, and correlations among all study variables are displayed in Table 2. Adolescent depressive symptoms were significantly correlated across the three assessments. Harsh parenting was not significantly correlated with adolescent depressive symptoms in the sample as a whole. Greater family income was associated with fewer adolescent depressive symptoms at each time point. Approximately half of the parents (50.3%) displayed no instances of harsh parenting during the FPST. The remaining 49.7% of families had at least one observable instance of harsh parenting coded during the seven-minute FPST (the global coding scale does not provide specific frequencies beyond the absence/presence of harsh parenting distinction).

One-way between subjects ANOVAs and chi-square difference tests were conducted examining adolescent gender differences. There were no differences between boys and girls in study variables and demographics including, T1 family income, adolescent age, harsh parenting, adolescent behavior, adolescent ethnicity/race, T1 and T2 adolescent depressive symptoms, and *BDNF Val66Met* and *5-HTTLPR* gene frequencies. However, there was a statistical trend for differences in depressive symptoms at T3 ($F(1,195)=3.82, p=.052$); girls reported higher rates of T3 depressive symptoms ($M=12.15, SD=9.21$) compared to boys ($M=9.67, SD=8.49$). Thus, child gender was included as a covariate in subsequent analyses.

To examine the possibility of gene-environment correlations (rGE) in the present data, ANOVAs were conducted examining differences in harsh parenting and adolescent behavioral responses during the FPST by *BDNF Val66Met* and *5-HTTLPR* genotypes. There were no differences in harsh parenting by *BDNF Val66Met* genotype ($F(1,182)=.54, ns$; Val/Val $M=5.52, SD=2.43$; Any Met $M=5.24, SD=1.91$) or *5-HTTLPR* ($F(1,182)=.17, ns$; L_AL_A $M=5.31, SD=1.84$; functional short $M=5.48, SD=2.41$). Similarly, there were no differences in adolescent behavior by *BDNF Val66Met* ($F(1,182)=.00, ns$; Val/Val $M=3.70, SD=2.17$; Any Met $M=3.72, SD=2.28$) or *5-HTTLPR* genotype ($F(1,182)=1.24, ns$; L_AL_A $M=3.36, SD=2.08$; functional short $M=3.80, SD=2.22$).

Predictors of Change in Adolescent Depressive Symptoms

LCS models were fit to determine the type of change in adolescent symptoms. Changes in adolescent depressive symptoms were modeled using a univariate latent change score (LCS) model (McArdle & Hamagami, 2001). To determine the type of change in adolescent depressive symptoms, four unconditional models were fit including 1) a no change model, 2) a constant change model, 3) a proportional change model, and 4) a dual change model. The no change model assumes stability in symptoms. Change in depressive symptoms in the constant change model is fit as a constant rate of change (e.g., linear change). Change in

depressive symptoms in the proportional change model is a proportion based on an individual's previous score. The dual change model includes both the constant and proportional change components. Nested unconditional models were compared with a chi-square difference test using the Satorra-Bentler scaled chi-square (Satorra, 2000). Models were fit in the structural equation model framework in MPLUS (version 7; Múthen & Múthen, 1998-2012). Full-information maximum likelihood estimation with robust standard errors was used to estimate missing data. In the present study, the constant change model ($\chi^2(3)=1.69$, *ns*) fit the data significantly better than the no change model ($\chi^2(6)=16.22$, $p<.05$; χ^2 diff = 14.90, $df=3$, $p<.01$). The proportional change model ($\chi^2(5)=17.31$, $p<.01$) did not fit the data significantly better than the no change model (χ^2 diff = .53, $df=1$, *ns*). Lastly, the dual change model ($\chi^2(2)=.59$, *ns*) did not fit significantly better than the constant change model (χ^2 diff = 1.07, $df=1$, *ns*). Thus the constant change model was selected to model linear change in adolescent depressive symptoms and provided good fit to the data ($\chi^2(3)=1.69$, *ns*, RMSEA=.00, CFI=1.00).

To examine whether genetic polymorphisms moderated the impact of harsh parenting on depressive symptoms, a conditional constant change LCS model was fit¹. Predictors of initial symptoms and change in symptoms included the main effects of harsh parenting and the *BDNF Val66Met* (0=Any Met allele, 1=Val/Val allele) and *5-HTTLPR* (0=functional short allele, 1=long allele $L_A L_A$) polymorphisms, the two two-way interactions between harsh parenting and each of the polymorphisms (e.g., harsh parenting X *BDNF Val66Met*, harsh parenting X *5-HTTLPR*), and covariates. The conditional model provided good fit to the data ($\chi^2(13)=7.75$, *ns*; RMSEA=.00, CFI=1.00). Results are displayed in Table 3. The predictors and covariates accounted for a modest amount of the variance in initial symptoms ($R^2=.13$) and change in depressive symptoms ($R^2=.21$). Family income was the sole predictor of initial depressive symptoms ($\beta = -.30$, $p<.001$); higher annual family income at T1 was associated with lower initial depressive symptoms. There were no main effects of harsh parenting or genetic polymorphisms or GxE interactions predicting initial depressive symptoms. Additionally, there was no main effect or GxE interaction for the *5-HTTLPR* polymorphism in predicting change in depressive symptoms. However, there was a main effect of the *BDNF Val66Met* polymorphism ($\beta = -.27$, $p<.01$) and a main effect for harsh parenting ($\beta = .60$, $p<.05$) predicting change in adolescent depressive symptoms (in the context of a significant interaction). Furthermore, there was a significant two-way interaction ($\beta = -.54$, $p<.05$) between harsh parenting and *BDNF Val66Met* predicting change in adolescent depressive symptoms (See Figure 1). To probe the significant harsh parenting X *BDNF Val66Met* interaction, simple slope analyses were conducted. There was no effect of harsh parenting on the change in depressive symptoms among the Val/Val carriers ($t=.00$, *ns*). However, there was an effect of harsh parenting on the change in depressive symptoms among the Met carriers ($t=2.51$, $p<.05$) such that Met carriers had greater increases in depressive symptoms in the presence of harsh parenting. Lastly, there was a significant main effect of adolescent behavior during the FPST such that greater oppositional and irritable behaviors were associated with less change in depressive symptoms ($\beta = -.19$, $p<.05$).

Predictors of the Frequency of Elevated Depressive Symptoms

Consistent with a community sample, the majority of adolescents (60.3%; $N=123$) did not meet cut-off criteria on the CES-D at any point in the study. The remaining adolescents met cut-off criteria on the CES-D at least one of the three time points (26.0% 1 time point, 8.3% 2 time points, 5.4% 3 time points). A series of four models were fit to the data to determine the best-fitting model including, a poisson model, a negative binomial model, a ZIP model, and a ZINB model. The poisson and negative binomial models and the ZIP and ZINB models are nested models and were compared using a likelihood ratio test. Non-nested models were compared using the Vuong test (Greene, 1994). Maximum likelihood estimation with robust standard errors was used to estimate missing data in each of the models. First, comparisons of the nested models indicate that the poisson ($LL=-178.11$) and the ZIP models ($LL=-168.87$) fit the data better than the negative binomial ($LL=-177.02$) and ZINB models ($LL=-168.69$), respectively (poisson vs. negative binomial: LRT $\chi^2(1)=21.8$, ns ; ZIP vs. ZINB: LRT $\chi^2(1)=.004$, ns). Furthermore, the non-nested comparisons using the Vuong test indicated that the ZIP model fit the data better than both the poisson regression ($V=2.39$) and the negative binomial regression ($V=2.42$). Thus, the ZIP model was selected.

To examine whether the *BDNF Val66Met* and *5-HTTLPR* polymorphisms moderated the impact of harsh parenting on the frequency of elevated symptoms, predictors included the main effects of harsh parenting and the *BDNF Val66Met* and *5-HTTLPR* polymorphisms, the two-way interactions between harsh parenting and each of the polymorphisms (e.g., harsh parenting X *BDNF Val66Met*, harsh parenting X *5-HTTLPR*), and covariates². Results of the ZIP model with predictors are displayed in Table 4. Adolescent gender was the only predictor of the probability of being in the zero group (e.g., not meeting criteria during the study period). Girls were less likely to be in the group not meeting criteria ($\beta=-.45$, $p<.01$, $OR=.03$). Additionally, there were significant predictors of the poisson portion of the model representing predictors of the frequency of elevated symptoms. There was a significant interaction between harsh parenting and *5-HTTLPR* ($\beta=.32$, $p<.05$). Figure 2 depicts the interaction between harsh parenting and the *5-HTTLPR* polymorphism. Adolescents with at least one short allele had greater frequency of elevated symptoms regardless of the level of harsh parenting whereas adolescents with the long allele had greater frequency of elevated symptoms in the presence of higher harsh parenting. To examine the interaction between harsh parenting and the *5-HTTLPR* polymorphism, the incident rate ratios (IRR) were examined for individuals with the long and short alleles. For the long allele, adolescents had a 20.80% increase in the frequency of elevated depressive symptom for each unit change in observed harsh parenting ($IRR=1.21$). On the other hand, for individuals with the short allele, harsh parenting was not associated with frequency of elevated symptoms; individuals with the short allele had a 1.98% decrease in this measure for each unit of change in harsh parenting ($IRR=.98$). Lastly, family income and adolescent age were significant predictors such that greater family income was associated with lower frequency of elevated symptoms ($\beta=-.61$, $p<.01$, $IRR=.89$) and being older at T1 was associated with a higher frequency of heightened symptoms ($\beta=.65$, $p<.05$, $IRR=2.01$).

Discussion

The present study examined the moderational role of genetic polymorphisms in the context of harsh parenting to account for differences in adolescent depressive symptoms. In particular, this study moved beyond the prediction of cross-sectional symptom levels to account for trajectories of adolescent depressive symptoms as well as the frequency of elevated symptoms in a prospective study. Different genetic polymorphisms, in interaction with environmental risk, were implicated in these processes during adolescence. The *BDNF Val66Met* x harsh parenting interaction was associated with growth in adolescent depressive symptoms whereas the *5-HTTLPR* x harsh parenting interaction predicted greater frequency of elevated depressive symptoms. There were no main effects or GxE interactions predicting cross-sectional levels of depressive symptoms providing further evidence for the consideration of longitudinal phenotypes.

Harsh parenting was associated with greater increases in adolescent depressive symptoms among individuals with at least one Met allele. Brown and colleagues' (2014) research in adult samples provides support for the role of the *BDNF Val66Met* polymorphism in the onset of new depressive episodes highlighting its importance in the etiology of symptom severity. Building on this research, the present study demonstrates the role of *BDNF Val66Met* polymorphism in the rise in depressive symptoms during adolescence for those individuals experiencing adversity in the family context. The present study provides further support for the notion that the *BDNF Val66Met* and *5-HTTLPR* polymorphisms may have distinct roles in understanding change and persistence in depressive symptoms. This work extends previous research to examine these relations in a community sample of families representing a continuum of adolescent depressive symptoms. Furthermore, the findings of the present study highlight the notion that these same genes may contribute to individual differences in subthreshold depressive symptoms prior to adulthood during adolescence when individuals may be particularly susceptible to increases in symptoms.

Heightened harsh parenting also served as a risk factor for greater frequency of elevated symptoms for adolescents with the long allele of the *5-HTTLPR* polymorphism such that as levels of harsh parenting increased, greater frequency of heightened symptoms was evident. In contrast, adolescents with the functional short allele had more frequent heightened symptoms regardless of the level of harsh parenting. Previous research on parenting, serotonin levels, and adolescent health has found that serotonin may serve as a moderator of the family risk-adolescent mental health association. Crowell and colleagues (2008) found that peripheral serotonin moderated the relation between negativity in a mother-adolescent conflict task and self-injury. Adolescents with lower serotonin levels had higher rates of self-harm largely independent of negativity whereas level of negativity and self-harm behaviors were positively associated for adolescents with higher levels of serotonin. Furthermore, previous research has also found that the role of GxE interactions involving the serotonin transporter gene in depression may be more complex than elevating the risk for heightened levels of depressive symptoms at any one time point. Uher et al. (2011) found support for a *5-HTTLPR*-by-maltreatment interaction predicting persistence in depression (defined as meeting criteria at more than one time point across four longitudinal assessments). In this same study, the authors did not find support when examining differences in single time point

depression. Thus the lack of the *5-HTTLPR* x harsh parenting interaction in the logistic portion of the model, coupled with this GxE interaction contributing to the prediction of greater frequency of meeting criteria, is consistent with Uher and colleagues work with adult populations and provides further evidence that the serotonin transporter gene may be involved in the persistent or chronic dimension of depressive disorders.

Future research is needed to understand the biological pathways leading from individual differences in genetic variants to the behavioral manifestation of depressive symptoms. The short allele of the *5-HTTLPR* polymorphism is associated with reduced transcriptional activity of the serotonin transporter (Heils et al., 1996) and the Met allele of the *BDNF Val66Met* polymorphism is associated with decreased BDNF trafficking and attenuated activity-dependent secretion (Egan et al., 2006). However, how these differences lead to depression remains unknown. BDNF may serve as a mediator for synaptic plasticity and neurogenesis (Binder & Scharfman, 2004; Casey et al., 2009). The *5-HTTLPR* polymorphism has been found to be associated with differences in amygdala activation (Hariri et al., 2002) and stress reactivity of the hypothalamic-pituitary-adrenal axis (Gotlib, Joorman, Minor, & Hallmayer, 2008) highlighting their potential roles in the biological pathways to depression. The role for both serotonin and BDNF in the pathophysiology of depression remains an important line of inquiry.

The measures used in the present investigation are not akin to assessing the onset of new depressive episodes and chronicity outlined by Brown and Harris (2008) and prohibit a direct test. Nevertheless the inclusion of both variations in symptom levels and frequency of elevated symptoms allowed for examination of two distinct dimensions of depressive disorders (Klein, 2008) in a non-clinical population. The frequency of heightened symptoms does not allow for separation of chronicity versus separate reoccurrences of sub-threshold heightened symptoms. However, it has been posited that the latter may lie on a continuum of chronicity (Klein, 2008) and thus the measurement of the frequency of heightened symptoms across the study period may provide differentiation along this dimension. Clinical assessments of depression and more frequent assessments of participants would provide more clear measures of symptom severity and chronicity. Even so, findings converge with research in adult clinical populations suggesting that the biological mechanisms accounting for GxE findings in depression may extend to subclinical assessments of depressive symptoms.

Much of the previous work examining the role of the serotonin transporter gene in combination with environmental risk highlights to role of maltreatment. In a recent meta-analysis, Karg and colleagues (2011), found evidence for stronger relations between *5-HTTLPR* and maltreatment in the prediction of depression compared to more general reports of stressful life events. The present study finds additional support for GxE interactions with the serotonin transporter gene for environmental risk that may be more characteristic of parenting variation in a community sample population. Future work is necessary to understand the role of harsh parenting as a form of environmental risk in contributing to this literature separate from experiences of maltreatment and experiences of broader life stress. Additionally, the present study utilized a composite measure of harsh parenting employed during the family conflict task rather than an investigation of the unique effects of maternal

or paternal harsh parenting. Utilizing a composite measure allowed for capturing the degree to which the family system is characterized by harsh parenting strategies reflective of the overall level of family risk. In terms of adolescent mental health, the presence of harsh parenting, regardless of which parent utilizes these parenting behaviors, may be the important factor in predicting later health.

In the present study, adolescent oppositional behavior during the FPST was significantly correlated with harsh parenting during the FPST. Given the nature of the observational assessment in providing global measures of functioning during the task, we are unable to determine whether adolescents' behaviors elicited harsh parenting strategies from caregivers or whether these behaviors were in response to harsh parenting strategies. It has long been posited that parent and child behaviors are likely transactional in nature (Bell, 1968; Sameroff, 1975). Tests of the gene-environment correlations in the present study do not suggest that significant rGE between study variables account for the GxE interactions found. However, we can not rule out the possibility that passive and evocative rGE may operate among unmeasured genetic and environmental contributions. We focused on adolescents' oppositional behaviors during the conflict task due to research suggesting that children at risk for antisocial behavior have been found to evoke more negative control from caregivers and this association is partially mediated by children's own externalizing behaviors (O'Connor, Deater-Deckard, Fulker, Rutter, & Plomin, 1998). It may be that these behaviors elicit negative parenting and place youth at greater risk for other types of problems such as aggression and conduct problems rather than depressive symptoms which was the focus of the present investigation.

It is unclear why there was no support for a main effect of harsh parenting on adolescent depressive symptoms. The presence of significant moderators may mask a main effect. It is also possible that harsh parenting may be underrepresented in the present study as some parents may be able to withhold their use of harsher strategies in the laboratory setting with the knowledge that their interactions were being videotaped and discussions occurred for a short duration. It should be noted that the use of an observational measure of harsh parenting assessed during a conflict-specific paradigm may represent a smaller subset of the larger repertoire of behaviors that caregivers draw upon during broader parent-child interactions. Findings of the present study may not generalize to broader parenting strategies that caregivers utilized during parent-child interactions in other contexts. Nevertheless, parent-child conflict is a regular occurrence during adolescence so the assessment of parenting strategies during conflict represents an ecologically-valid context for assessing parenting. These findings suggest that even moderate parenting risk may heighten youth's risk for the development of and persistence in depressive symptoms during early adolescence in combination with genetic risk factors.

There was no support for a main effect of gender in the initial or change in depressive symptoms or the frequency of elevated symptoms. Cross-sectional differences in symptoms did not emerge in the present study until T3 suggesting that the impact of gender in symptom differences may emerge later in development than the initial window of time captured in the present investigation. However, gender was associated with the logistic

portion of the ZIP regression model and may reflect the developmental change in gender differences in depression disorders that emerge during adolescence (Hankin et al., 1998).

The present study is not without limitations. Adolescents and families in the present study represent a community sample of families exhibiting a range of parenting behaviors and mental health symptoms. Findings may not replicate and translate to clinical samples of distressed families. However, subclinical levels of depressive symptoms and family distress do contribute to the emergence of clinical disorders and provide evidence for the etiology of adolescent depression. Adolescents provided self-reports of depressive symptoms and categorizations of those meeting criteria for depression represent adolescents that exhibit potentially clinical levels of depression rather than those with a formal diagnosis of depression. Thus, there may be variation in the significance and impairment of those categorized as meeting criteria without the use of formal diagnostic measures.

The sample size in the present investigation is limited given criticisms raised in regards to sufficient sample size recommendations in GxE research (Duncan & Keller, 2011). As such there is the possibility for false positive discovery and further replication is warranted. However, it has been noted that latent variable modeling and longitudinal designs may increase power to detect GxE interactions (McArdle & Prescott, 2010); thus the study design may partially mitigate concerns regarding the sample size in the present investigation. The consistency of our findings with the adult clinical research is important in light of the relatively small sample; replication efforts remain an important endeavor in GxE research. The sample size impedes the examination of further moderation of the GxE interactions and main effects by important covariates beyond their contributions as main effects on adolescent depressive symptoms; interactions between main effects and covariates have been recommended in GxE interaction studies (Keller, 2014). The present sample was comprised of largely a Caucasian middle class sample and limits the generalizability of these findings. There were no main effects of race/ethnicity in these analyses and there were no differences in race/ethnicity by genotype. In the absence of ancestral genetic markers, it is unclear the extent to which parent-reported race/ethnicity reflect ancestral differences and findings should be interpreted with caution in light of the racial/ethnic heterogeneity in the present sample. Additionally, the *BDNF Val66Met* may vary by ethnicity (Chen et al., 2012; 2013) as well as across developmental time points (Casey et al., 2009). Thus additional research is needed examining whether findings extend beyond community samples of similar sociodemographics.

The sample size precludes further investigations of GxGxE interactions that may be involved in understanding variation in depressive symptoms. Previous research has found that the *BDNF Val66Met* and serotonin transporter polymorphisms interact with one another at varying levels of risk (e.g., GxGxE) to confer differential risk for depression (e.g., Cicchetti & Rogosch, 2014; Gutiérrez et al., 2014; Kaufman et al., 2006). Future work with larger samples sizes is necessary to examine the GxGxE effects in prospective research designs that allow for examining the longitudinal change in depressive symptoms throughout adolescence.

Nevertheless, the present study provides support for the role of different genetic polymorphisms that may contribute to the heterogeneity in adolescent depressive symptoms in the presence of similar exposure to environmental risk. The present study highlights the importance of examining GxE interactions in prospective longitudinal designs that allow for capturing both the change in symptoms and the frequency of elevated symptoms that may contribute to the inconsistent findings in the broader literature. For adolescents exposed to higher levels of harsh parenting, the *BDNF Val66Met* polymorphism conferred differential risk for change in symptoms whereas the *5-HTTLPR* polymorphism contributed to the persistence of elevated depressive symptoms. Results provide important advancements in understanding heterogeneity in depressive symptoms during adolescence in the context of family risk.

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Figure 1.

Trajectories of adolescent depressive symptoms.

Note. Figure depicts Any Met (Val/Met and Met/Met) and Val/Val carriers of the *BDNF* Val66Met genetic polymorphism. Low and high harsh parenting refer to ± 1 SD.

Figure 2.

The interaction of *5-HTTLPR* and harsh parenting predicting the frequency of elevated depressive symptoms.

Note. Figure depicts functional short and long alleles of the *5-HTTLPR* genetic polymorphism. Low and high harsh parenting refer to $-/+$ 1 SD.

Table 1**Participant Demographics**

Sample Total	<i>N</i>	206
Adolescent Gender	<i>N</i> female (%)	107 (51.9%)
T1 Adolescent Age	<i>M</i> (<i>SD</i>) years, [range]	13.06 (.51) [11.85 - 14.51]
T2 Adolescent Age	<i>M</i> (<i>SD</i>) years, [range]	14.23 (.55) [12.84 - 15.62]
T3 Adolescent Age	<i>M</i> (<i>SD</i>) years, [range]	15.40 (.64) [13.78 - 17.01]
T1 Adolescent Grade	Median grade (%), [range]	7 (81.3%) [6 - 8]
Adolescent Race/Ethnicity		
Caucasian/White	<i>N</i> (%)	137 (66.5%)
Black/African-American	<i>N</i> (%)	30 (14.6%)
Multiracial/Other	<i>N</i> (%)	21 (10.2%)
Hispanic/Latino	<i>N</i> (%)	18 (8.7%)
T1 Family Income	Median range (%), [range]	\$55,000 - 74,999 (24.4%) [\$6,000 - \$125,000]
T1 Marital Status	<i>N</i> married (%)	169 (84.1%)
Maternal Caregiver	<i>N</i> (at T1)	201
Relation to Adolescent	<i>N</i> biological mother (%)	191 (93.2%)
T1 Age	<i>M</i> (<i>SD</i>), [range]	41.44 (6.19) [25 - 71]
Education	Median level (%), [range]	Some college (26.8%)
Paternal Caregiver	<i>N</i> (at T1)	189
Relation to Adolescent	<i>N</i> biological father (%)	149 (78.8%)
T1 Age	<i>M</i> (<i>SD</i>), [range]	43.49 (6.78) [25 - 75]
Education	Median level (%)	Bachelor's degree (27.4%)

Table 2

Descriptive Statistics and Correlations

	1	2	3	4	5	6	7
1. T1 Harsh Parenting	1.00						
2. T1 Adolescent Depressive Symptoms	.09	1.00					
3. T2 Adolescent Depressive Symptoms	.03	.52***	1.00				
4. T3 Adolescent Depressive Symptoms	.10	.37***	.63***	1.00			
5. T1 Adolescent Behavior	.39***	.07	.05	-.01	1.00		
6. T1 Adolescent Age	.11	.10	-.04	.02	.05	1.00	
7. T1 Family Income	-.28***	-.23**	-.27***	-.14 [†]	-.12	.02	1.00
<i>M</i>	5.44	10.48	10.39	10.99	3.70	13.06	--
<i>SD</i>	2.30	8.72	8.41	8.94	2.19	.51	--

Note.

* $p < .05$,[†] $p < .10$,** $p < .01$,*** $p < .001$.

Table 3

Parameter estimates for predictors of latent change in adolescent depressive symptoms.

<i>Parameter Estimates</i>		<i>B(SE)</i>	<i>p</i>	<i>95% CI</i>	<i>R</i> ²
Intercept					.13
Mean		8.97 (1.33)	.000 ***	6.36, 11.58	
Variance		50.32 (10.34)	.000 ***	30.95, 70.60	
Linear Slope					.21
Mean		1.31 (.78)	.095 †	-.23, 2.84	
Variance		11.52 (3.88)	.003 **	3.91, 19.14	
<i>Predictors</i>					
T1 Harsh Parenting	→Intercept	-.50 (.57)	.38	-1.62, .63	
	→Linear Slope	1.00 (.40)	.01 *	.22, 1.79	
<i>5-HTTLPR</i>	→Intercept	.37 (1.43)	.80	-2.43, 3.17	
	→Linear Slope	-1.18 (.79)	.14	-2.73, .38	
<i>BDNF Val66Met</i>	→Intercept	2.08 (1.41)	.14	-.68, 4.83	
	→Linear Slope	-2.22 (.82)	.01 **	-3.84, -.61	
<i>5-HTTLPR</i> × Harsh Parenting	→Intercept	.98 (.60)	.10	-.20, 2.16	
	→Linear Slope	-.39 (.34)	.26	-1.05, .28	
<i>BDNF Val66Met</i> × Harsh Parenting	→Intercept	.28 (.60)	.64	-.90, 1.46	
	→Linear Slope	-1.00 (.44)	.02 *	-1.86, -.15	
Adolescent Gender	→Intercept	.24 (1.27)	.24	-2.24, 2.73	
	→Linear Slope	1.21 (.77)	.12	-.29, 2.71	
Adolescent T1 Age	→Intercept	1.42 (1.10)	.20	-.73, 3.58	
	→Linear Slope	-.19 (.70)	.78	-1.56, 1.17	
T1 Family Income	→Intercept	-.78 (.24)	.001 ***	-1.24, -.32	
	→Linear Slope	.19 (.14)	.18	-.09, .47	
T1 Adolescent Behavior	→Intercept	.26 (.34)	.44	-.40, .92	
	→Linear Slope	-.35 (.16)	.03 *	-.66, -.04	
Adolescent Race/Ethnicity	→Intercept	-.92 (1.58)	.56	-4.01, 2.17	
	→Linear Slope	.78 (.86)	.37	-.91, 2.47	

Note. Unstandardized parameter estimates reported. *5-HTTLPR* (0=Functional Short Allele, 1=L_AL_A). *BDNF Val66Met* (0=Any Met allele, 1=Val/Val).

†
p<.10,

*
p<.05,

**
p<.01,

***
p<.001.

Table 4

Parameter estimates for predictors of zero-inflated poisson regression analyses.

<i>Parameter Estimates</i>	<i>Logistic Regression</i>			<i>Poisson Regression</i>		
	<i>B(SE)</i>	<i>p</i>	<i>95% CI</i>	<i>B(SE)</i>	<i>p</i>	<i>95% CI</i>
T1 Harsh Parenting	-.49 (.45)	.28	-1.38, .40	-.02 (.07)	.78	-.16, .12
<i>5-HTTLPR</i>	-.26 (2.26)	.91	-4.67, 4.18	-.36 (.29)	.22	-.93, .21
<i>BDNF Val66Met</i>	-.58 (2.28)	.80	-5.05, 3.88	.03 (.39)	.94	-.74, .80
<i>5-HTTLPR</i> × Harsh Parenting	1.71 (1.50)	.25	-1.22, 4.64	.21 (.08)	.01*	.05, .37
<i>BDNF Val66Met</i> × Harsh Parenting	-.52 (.68)	.44	-1.84, .80	-.08 (.09)	.41	-.26, .11
Adolescent Gender	-3.36 (1.63)	.04*	-.655, -.17	-.31 (.36)	.38	-1.01, .39
Adolescent T1 Age	2.86 (4.28)	.50	-5.52, 11.25	.70 (.35)	>.05*	.002, 1.39
T1 Family Income	-.11 (.20)	.58	-.50, .28	-.12 (.04)	>.01**	-.20, -.03
T1 Adolescent Behavior	-.40 (.77)	.60	-1.19, 1.10	-.03 (.05)	.54	-.13, .07
Adolescent Ethnicity	.71 (2.36)	.76	-3.92, 5.34	.05 (.33)	.88	-.59, .69

Note. Unstandardized parameter estimates reported. *5-HTTLPR* (0=Functional Short Allele, 1=L_AL_A). *BDNF Val66Met* (0=Any Met allele, 1=Val/Val).

* $p < .05$,

** $p < .01$.