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Differential Susceptibility in Spillover Between Interparental Conflict and Maternal Parenting Practices: Evidence for OXTR and 5-HTT Genes

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Abstract

Guided by the affective spillover hypothesis and the differential susceptibility to environmental influence frameworks, the present study examined how associations between interparental conflict and mothers' parenting practices were moderated by serotonin transporter (5-HTT) and oxytocin receptor (OXTR) genes. A sample of 201 mothers and their two-year old child participated in a laboratory-based research assessment. Results supported differential susceptibility hypotheses within spillover frameworks. With respect to OXTR rs53576, mothers with the GG genotype showed greater differential maternal sensitivity across varying levels of interparental conflict. Mothers with one or two copies of the 5-HTTLPR S allele demonstrated differential susceptibility for both sensitive and harsh/punitive caregiving behaviors. Finally, analyses examined whether maternal depressive symptoms and emotional closeness to their child mediated the moderating effects. Findings suggest that maternal emotional closeness with their child indirectly linked OXTR with maternal sensitivity. The results highlight how molecular genetics may explain heterogeneity in spillover models with differential implications for specific parenting behaviors. Implications for clinicians and therapists working with maritally distressed parents are discussed.

Keywords

Interparental Conflict; Parenting; Differential Susceptibility; Oxytocin; Serotonin

Research has shown that interparental relationships characterized by conflict, anger, and aggression have substantial negative implications for caregiving behaviors (e.g., Erel & Burman, 1995; Krishnakumar & Buehler, 2000; Sturge-Apple, Davies, Cicchetti, & Cummings, 2009). To account for this association, theoretically driven process models of interparental discord have focused on understanding how affect and emotion arising from interparental conflict “spills-over” or sets in motion processes that ultimately influence interactions within the parent-child system (Easterbrooks & Emde, 1988, Grych, 2002). Existing studies testing spillover models in process pathways linking interparental conflict and parenting have generally found support for the presence of parenting disturbances (e.g.,

Benson, Buehler, & Gerard, 2008; Levendosky, Leahy, Bogat, Davidson, von Eye, 2006; Margolin & John, 1997; Owen, Thompson, & Kaslow, 2006; Sturge-Apple, Davies, & Cummings, 2006). However, others have reported that interparental conflict is associated with more effective parenting practices (Casaneva, Martin, Runyan, Barth, & Bradley, 2008; Letourneau, Fedick, & Willms, 2007; Levendosky, Huth-Bocks, Shapiro, & Semel, 2003). The presence of these complex and counterintuitive results in the spillover literature raises a central question: Why do parents evince substantial differences in their parenting behaviors within the context of interparental relationship dynamics?

Consideration of the interplay between genetic variation and the environmental context of interparental relationships, or GxE, may help inform our understanding. Prior research in molecular genetics has shown that individuals who carry “risk” alleles are more vulnerable to negative outcomes in the context of high adversity such as child maltreatment (Caspi et al., 2002). More recently, however, researchers have begun to focus on the unique adaptive fitness of individuals carrying specific alleles, renamed “plasticity” alleles, in differing environments (Belsky et al., 2009). These conceptualizations strongly suggest that a model of differential sensitivity to environmental cues might better account for contextually-dependent outcomes (Belsky, 1997, 2005; Belsky & Pluess, 2009; Ellis, Jackson, & Boyce, 2006). Translated to spillover frameworks, differential susceptibility models offer promising conceptual blueprints for identifying sources of heterogeneity in the nature and magnitude of associations between interparental conflict and parenting behavior.

Recent work has highlighted the power of this approach for enhancing our understanding of other family process models (e.g., Belsky & Beaver, 2011; Beach, et al., in press). However, to our knowledge, no study has examined the presence of genetic susceptibility in associations between interparental conflict and parenting perturbations. The potential significance of genetically informed research in this area is further highlighted by the high prevalence of homes characterized by interparental hostility and aggression (see, e.g., National Survey of Children’s Health, 2005) and the prominent clinical aim of understanding the etiology of parenting difficulties (Emery, Fincham, & Cummings, 1992). Toward this end, the present study tested whether differential susceptibility models of molecular genetics may pinpoint sources of heterogeneity in spillover between interparental conflict and aggression and parenting behaviors. To guide our research, we identified two genes which have conceptual linkages to caregiving behaviors and have demonstrated direct associations with parenting in prior work with human samples – namely, the oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes (Bakermans-Kranenburg & van IJzendoorn, 2008; Mileva-Seitz, et al., 2011).

The serotonergic system has been long believed to be associated with regulation of aggressive, impulsive, and dangerous behaviors (e.g., Gollan, et al., 2005; Higley, 2003), as well as increased risk for depression and anxiety, particularly in the context of environmental adversity (e.g., Caspi et al., 2003; Cicchetti & Toth, 1995; Murphy, et al., 2001). Considering the regulatory aspects of the serotonin system, it is surprising that very little research has been conducted examining the relationship between serotonergic system activity and human maternal care. Investigations of serotonin and maternal behavior in primates suggest that reduced serotonergic function is associated with higher rates of maternal rejection in rhesus macaque mothers (Maestripieri, Lindell, & Higley, 2007).

The serotonin transporter gene (5-HTT) in human populations has been implicated in serotonergic transmission. In particular, efforts have focused on variants of the promoter-linked polymorphic region (5-HTTLPR). The gene linked polymorphic region is typically defined by a short (s) allele comprising 14 copies of a 20-23 base pair repeat unit and a long (l) allele comprising 16 copies. Investigations with human subjects and nonhuman primates

have demonstrated that individuals who possess the s/s and s/l allelic variants have lower levels of serotonergic activity than do individuals with the l/l variant (Heinz et al., 2000; Smith, et al., 2004). Genetic variants of the 5-HTTLPR are known to be sensitive to the beneficence of the social environment (Caspi et al., 2003; Caspi et al., 2010; Taylor et al., 2006).

In human populations, two studies examining the role of the serotonin transporter gene in maternal sensitivity have produced conflicting results. Bakermans-Kranenburg and van IJzendoorn's (2008) seminal study exploring the relationship between a functional variant of the 5-HTT gene and mother-child interactions, 5-HTTLPR SCL6A4, was the first to indicate that differences in allelic functioning may be associated with insensitive parenting practices. In their sample of 159 Caucasian middle-class mothers and their 2-year old child, mothers possessing the s/s allelic combination were less sensitive during parent-child interactions compared to mothers possessing the s/l or l/l combination. In contrast, a recent study conducted by Mileva-Seitz and colleagues (2011) in a sample of 204 mothers and their 6-month old infant using the tri-allelic 5-HTTLPR, found that mothers with an s/Lg allele across the 5-HTTLPR SCL6A4 and rs25531 genotypes displayed greater sensitivity during parent-infant interactions. The discrepancies between these two studies may lay in the level of adversity and risk experienced by the mothers, with higher levels of risk reported in the Mileva-Seitz et al., sample. Supporting this, Mileva-Seitz report an interaction between 5-HTTLPR genotype and early quality of care such that mothers with the s/Lg alleles evidenced higher relationship quality with their infant as early reported care quality increased. This GxE finding lends support for the current study's examination of whether the association between the interparental conflict and maternal caregiving may be moderated by 5-HTTLPR genotype.

Over the past several decades, oxytocin has been implicated in influencing maternal sensitivity as well as other social behaviors across animal and human species (Bakermans-Kranenburg & van IJzendoorn, 2008; Champagne & Meaney, 2006; Mileva-Seitz, 2011; Saphire-Bernstein, Way, Kim, Sherman, & Taylor, 2011). First, extensive research has repeatedly shown that the oxytocin hormone is a critical mediator of many complex emotional and social behaviors including attachment (e.g., Buchheim et al., 2009), emotional cues (Kirsch et al., 2005; Petrovic et al., 2008; Savaskan et al., 2008), and social cognition (Unkelbach, Guastella, & Forgas, 2008; Kosfeld, Heinrichs, Zak, Fishbacher, & Fehr, 2005). With respect to parenting, rodent studies have demonstrated that oxytocin antagonists and lesions of the paraventricular nucleus block the onset of maternal behavior (Insel & Harbaugh, 1989; van Leengoed, Kerker, & Swanson, 1987). Research in human populations has shown that higher plasma oxytocin levels are associated with trust and positive parenting styles (Feldman et al., 2010; Kosfield et al., 2005).

The human OXTR gene is located on chromosome 3p25, containing four exons and three introns. A single nucleotide polymorphism (SNP) in the third intron of OXTR, rs53576 (G/A), has been identified as a candidate gene underlying social behavior in humans (Inoue et al., 1994). Through neuroimaging and psychiatric genetic studies, investigators have tried to establish the functionality of OXTR allelic variants. In a college sample, Rodrigues et al. (2009) found that the OXTR rs53576 genes were associated with empathy and stress reactivity. In particular, individuals with GG alleles performed better than those with the AA or AG alleles on emotional state and empathy recognition tasks. Despite associations between oxytocin and caregiving, there has been a lack of research that has concentrated on OXTR rs53576's role in parental sensitivity. Bakermans-Kranenburg and van IJzendoorn's (2008) seminal study, cited previously, also examined the relationship between the functional variants of the OXTR rs53576 receptor gene and mother-child interactions and

found that those with oxytonegic AA/AG genes showed lower levels of maternal sensitivity.

Although Bakermans-Kranenburg and van IJzendoorn found that the GG variant was associated with better parenting, some divergent findings have indicated that OXTR rs53576 GG alleles may confer less positive outcomes. For example, Bradley, Western and Mercer's (2011) study of the interaction between child maltreatment and OXTR rs53576 in an African American sample, found that GG carriers were at increased risk for emotion dysregulation when exposed to three or more categories of child abuse than AG and AA carriers. These discrepancies in the literature are highlighted by Bartz and colleagues (2011), who argue that consideration of the moderating impact of context may be essential for determining heightened susceptibility for particular OXTR alleles. In line with these recommendations, the present study examined how associations between interparental conflict and parenting may vary as a function of the OXTR alleles.

The present study also examined differential susceptibility with respect to two different classes of parenting behaviors including maternal sensitivity/responsiveness and maternal harsh/punitive caregiving. Historically, the quality of parenting has been measured dimensionally across two primary axes including sensitivity/warmth and behavioral control (Baumrind, 1966; Maccoby & Martin, 1983). Primate studies with free-ranging rhesus macaques have suggested specificity in genetic associations with parental warmth/sensitivity. Particularly, research has shown that variation in maternal rejection may be associated primarily with serotonin activity, while variation in indicators of maternal warmth (e.g., nursing and grooming behaviors) may be associated with maternal plasma oxytocin levels (Maestriperi, Hoffman, Anderson, Carter, & Higley, 2009). However no research in humans has explored how the oxytocin and serotonin systems may be implicated across these two primary dimensions of parenting. Thus, it may be expected that genetic susceptibility may operate differently depending upon the dimension of parenting under consideration and simultaneous comparison across different dimensions of parenting may yield new insights into the generality or specificity of genetic susceptibility in spillover conceptualizations.

Finally, models of family process underscore the value of identifying the mechanisms underlying susceptibility to family relationships. Thus, a final goal of the present study was to examine whether the moderating role of genotype in associations between interparental conflict and parenting was explained by two underlying mechanisms: maternal depressive symptoms and positive parent-child relationship appraisals. In humans, the 5-HTT gene has been associated with elevated levels of depression and mood disorders (e.g., Caspi et al., 2010; Lee et al., 2009). Furthermore, maternal depressive symptomatology also has been unequivocally associated with perturbations in parenting behaviors. Numerous studies to date across a wide range of samples and methodologies have detailed associations between depressive symptoms and parental insensitivity, increased hostility and rejection, as well as disengagement (Goodman & Brumley, 1990; Goodman & Gotlib, 2002). In support of the maternal perceptions of psychological closeness with their children as an explanatory mechanism, oxytocin has been associated with a greater affiliative tendencies and emotion understanding (e.g. Domes et al., 2007). Empirical research with humans has shown that maternal affiliation and empathy toward her child is associated with responsive parenting practices (e.g., Kochanska, Friesenborg, Lange, & Martel, 2004; Trentacosta & Shaw, 2008). Thus, one of the critical ways in which OXTR may have an influence on parenting behaviors is through the facilitation of maternal affiliation and emotional cohesiveness with their child.

In summary, the goal of the present study was to test whether incorporating genetic variation in associations between interparental conflict and parenting may offer greater precision in delineating differential susceptibility in spillover models. We hypothesized that the ss/sl carriers of the 5-HTTLPR and the GG carriers of the OXTR would evidence differential susceptibility to marital conflict. We further hypothesized that OXTR would evidence greater spillover between interparental conflict and maternal insensitivity, whereas 5-HTTLPR variants would be primarily associated in spillover with maternal harsh/punitive parenting. Finally, we hypothesized that maternal depressive symptoms and emotional closeness would mediate these moderating effects.

Methods

Participants

Participants included 201 two-year-old children and their mothers in a moderately-sized metropolitan area in the Northeastern United States. A two-step recruitment process was implemented to enroll a high-risk sample of families experiencing elevated levels of interparental aggression and sociodemographic adversity. In the first step, we recruited participants through agencies serving disadvantaged children and families, including Women, Infants, and Children and Temporary Assistance to Needy Families rosters from the Department of Human and Health Services, and the county family court system. In the second step, we administered the abbreviated version of the Physical Assault Scale of the Conflict Tactics Scale 2 (CTS2; Straus et al., 1996) to obtain roughly equal proportions of participating mothers who experienced (a) no physical violence (i.e., 40%), (b) mild/moderate physical violence (i.e., 24%), and (c) severe physical violence (i.e., 36%) in the interpartner relationship. Additional inclusionary criteria for the study consisted of: (a) the adult female participant is the biological mother and primary caregiver of the target child; (b) the child participant is 27-months old (± 5 months); and (c) the child has no serious cognitive, sensory, or motor impairments.

Average annual income for the family household was \$20,807 (US; $SD = 12,278$) per year and a substantial minority of mothers (33%) and their partners (22%) did not complete high school. The mean age of the children was 25.4 months ($SD = 1.55$), with 56% of the sample consisting of boys ($n = 110$) and 44% consisting of girls ($n = 91$). Mothers, fathers, and children lived in the same household for an average of 6.4 years ($SD = 1.09$). The majority of the sample of mothers and children were African-American (56%), followed by smaller proportions of family members who identified as European-American (25%), Multi-Racial (8%), Latino (7%), and "Other" (4%).

Procedures

Mothers and their toddlers made three visits to our laboratory within a one- to two-week time period to obtain the primary measures. The research procedures were approved by the Institutional Review Board at the research site prior to conducting the study. Mothers completed questionnaires across the three visits. Procedures were standardized across participants.

Mother-Child Problem Solving Task—Mothers and their children participated in a 20 minute problem-solving task which was videotaped for later coding. During the task, dyads were given a series of four puzzles that were too difficult for the child to solve on their own. Mothers were instructed to help their child in the way that they usually did at home.

Mother-Child Free Play/Compliance Task—Mothers and their children participated in an observational free-play/compliance task which was videotaped for later coding. The

mothers were instructed to play with their child as they would at home after the dyad was escorted into a room containing several developmentally appropriate toys. After seven minutes, an experimenter knocked on the door. Mothers were then instructed to ask their children to stop playing and clean up the toys without providing assistance. The experimenter continued to knock on the door at one-minute intervals, up to three minutes, if the child appeared to be off-task. By the third knock mothers were told that they could provide assistance to their child with picking up the toys. The compliance portion of the task was recorded for six minutes.

Measures

Interpartner Conflict—First, maternal report on the psychological and physical aggression subscales of the Revised Conflict Tactics Scale (CTS2; Straus et al., 1996) were used to assess interparental conflict in the home. Following scoring guidelines, prevalence scores were calculated based on the sum of whether (1 = act occurred one or more times) or not (0 = specific act did not occur) the specific act in each of the items occurred in the past year. The Psychological Aggression Subscale is comprised of 14 items that assess maternal and partner verbal and psychological forms of hostility directed toward one another (e.g., “insulted or swore at my partner,” “I shouted or yelled at my partner”). The Physical Aggression subscale contains 24 items designed to assess maternal and partner acts of aggression toward each other in the interpartner relationship. Items vary from relatively mild (e.g., “I pushed or shoved my partner.”) to severe (e.g., “I used a knife or gun on my partner”).

Second, maternal reports on the Conflict and Problem-Solving Scale (CPS; Kerig, 1996) were used. Specifically, mothers reported on negative escalation behaviors which were derived from a factor analysis of the resolution items on the CPS. Although the original scale contains thirteen items, the majority of the statements reflect unsuccessful or destructive ways of ending conflict that are reverse scored (e.g., “We feel worse about one another than before the fight,” “We stay mad at one another for a while”). To determine whether the thirteen items yield a single factor, all the items were subjected to a principal components analysis with varimax rotation. The results supported a two-factor solution that discriminated between the four constructive items (e.g., “We feel that we’ve resolved it, or come to an understanding”) and nine destructive items reflecting gridlock and escalation of conflict. Therefore, to obtain an uncontaminated assessment of escalation, the nine destructive items were summed together to form a conflict escalation scale. Reliability was satisfactory for both the CTS2 and CPS scales in this sample (α s ranged from .87 - .92 for each subscale) and prior research supports the validity of the measures (Davies, Martin, & Cicchetti, in press; Kerig, 1996).

Maternal Parenting—Observer ratings of maternal caregiving behaviors were completed using subscales adapted from the Iowa Family Interaction Rating Scales (IFIRS; Melby & Conger, 2001). Ratings were assessed on nine-point Likert-type scales ranging from 1 (not characteristic at all) to 9 (mainly characteristic). Indices of Maternal Sensitivity were obtained from the Problem Solving task and the Free Play task. The *Warmth* scale was assessed across both tasks, and indicated the extent to which mothers demonstrated appreciation, care, or praise during the interactions. Examples include smiling at or hugging the child and giving positive reinforcement. The *Disengagement* scale was assessed in the free play tasks and taps into maternal behaviors that passively encouraged emotional or physical distance between the mother and child. Examples include ignoring the child or responding in an apathetic manner. Indices of Maternal Harsh/Punitive parenting were obtained from ratings on the Compliance Task. The *Harsh* subscale assessed critical, rejecting, or hostile behavior directed toward the child. Examples of harsh parenting include

belittling or critical statements, signs of anger, or hitting or slapping the child. The *Verbal Aggression* subscale assessed mothers' curt, abrupt, and demeaning verbalizations with the child. *Harsh Discipline* assessed mothers' critical, hostile, aggressive behaviors used when disciplining the child for misbehavior or failure to complete requests. Two teams of independent coders were trained for each task. To determine inter-rater reliability within task, coders rated 25% of the interactions within each task. The intraclass correlation coefficients of shared ratings, ranged from .84 to .94 across the interactions. To form the maternal sensitivity construct, ratings for maternal warmth and disengagement (reverse scored) were combined. Supporting the consolidation of these scales, correlations on ratings of maternal sensitivity scales ranged from .55 to .76 ($p < .05$). To form maternal harsh/punitive parenting, ratings for harsh, verbal aggression, and harsh discipline were combined. The correlation across scales ranged from .68 to .83 ($p < .05$) across the two tasks. Scales were subjected to a principal components analysis with a varimax rotation. Results indicated two distinct components which explained 75% of the variance with subscales loading independently onto their purported factor (range .61 - .91). Given indication of the distinction in the subscales, ratings for maternal sensitivity and harsh/punitive parenting were summed to form composite scores.

Maternal Emotional Closeness—Emotional closeness was assessed through two maternal questionnaires. First, mothers completed the Empathetic Awareness Toward Children's Needs scales from the Adult-Adolescent Parenting Inventory (AAPI; Bavolek, 1984). The scale indexes parental sensitivity to the developmental needs of young children (e.g., 8 items; "Young children who feel secure often grow up expecting too much."). Second, mothers completed the Nurturance scale of the Parenting Dimensions Inventory (PDI; Power, 2003). This six-item scale is rated on a six-point format (1=not at all descriptive of me, 6 = highly descriptive of me) and assesses maternal perceptions of love and care towards her child. The measures had good internal reliability in our sample, with α s of .82 for Empathetic Awareness and .87 for Nurturance in our sample. Scales were standardized and combined.

Maternal Depressive Symptoms—Trained experimenters administered the Computerized Diagnostic Interview Schedule IV (C DIS IV; Robins et al., 2000) to mothers to obtain assessments of maternal symptomatology. The DIS is a structured psychiatric interview originally designed for lay interviewers in the Epidemiological Catchment Area (ECA) studies. The interview consists of a computer-generated series of structured interviewed questions with "yes" or "no" response alternatives. Consistent with established procedures (Toth, Rogosch, Sturge-Apple, & Cicchetti, 2009), all interviewers were trained to criterion reliability in the administering the DIS. A measure of maternal depressive difficulties was derived from a sum of symptom counts from the dysthymia disorder module. Mothers indicated either the presence or absence of symptoms including, "hopelessness", "sleeping poorly", "fatigue".

DNA Collection, Extraction, and Genotyping

Of the 201 participants, 8 mothers did not provide DNA samples and thus were excluded from analyses. Therefore, our final sample for genotyping was reduced to 193 mothers. Using an established protocol, trained research assistants obtained DNA samples from mothers by collecting buccal cells with the Epicentre Catch-All Collection Swabs. Subsequently, using the conventional method, DNA was extracted with the Epicentre Buccal Amp DNA Extraction Kit, in order to prepare DNA for polymerase chain reaction (PCR) amplification. Genotyping was conducted following previously published protocols for OXTR and 5-HTT.

DNA was whole-genome amplified using the Repli-g kit (Qiagen, Chatsworth, CA., Catalog No. 150043) per the kit instructions to ensure the availability of data over the long term for this valuable sample. Amplified samples were then diluted to a working concentration. The OXTR rs53576 SNP was genotyped using a TaqMan SNP assay from Applied Biosystems, Inc. Individual allele determinations were made using TaqMan Genotyping Master Mix (Applied Biosystems, Catalog No. 4371357) with amplification on an ABI 9700 thermal cycler and analyzing the endpoint fluorescence using a Tecan M200 with JMP 8.0 (SAS, Inc.). 5-HTTLPR samples were genotyped for fragment length polymorphisms of 5-HTTLPR with Hot Star Taq PCR Mix (Qiagen, Catalog No. 203205), and previously described primers (Gelernter, Kranzler, & Cubells, 1997), followed by fragment analysis using a CEQ8000 (Beckman-Coulter, Inc., Fullerton, CA). Although genotypes with one or two short (S) alleles of the 5-HTTLPR gene are generally associated with lower transcription and function of 5-HTT protein in vitro (Bevilacqua & Goldman, 2011) than genotypes with two long (L) alleles, research identifying an A>G substitution in a SNP upstream (rs25531) from the promoter region has shown that L_G functions more similarly to the S allele than the L_A in its expression and binding potential (Praschak-Rieder et al., 2007; Reimold et al., 2007). Therefore, following established procedures to maximize power to identify genetic differences in 5-HTT (Mileva-Seitz et al., 2011), we used a triallelic approach to contrasting the genotypes with a least one copy of S or L_G with genotypes with two copies of L_A . Consequently, the $L_A L_A$ genotype (30%) was contrasted with an aggregated grouping of genotypes (70%) with a least one functional copy of the S allele (20% $L_A L_G$, 10% $L_G S$, 3% $L_G L_G$, 27% $L_A S$, 10% SS).

If a genotype for either gene could not be determined after the first run, then it was repeated up to four times. If the null result persisted, then a genotype was not assigned to that individual. The call rate for OXTR was 100% (193/193). The call rate for 5-HTTLPR was 99.48% (192/193). Thus, there were 193 mother-child dyads available for OXTR analyses and 192 dyads for 5-HTTLPR analyses.

The genotype distribution for OXTR ($n = 11$ AA, $n = 64$ AG, $n = 118$ GG) was in Hardy-Weinberg equilibrium $\chi^2(1, N = 193) = .38, ns$. In order to examine differences between mothers with the less efficient variants of the oxytonergic system, we combined mothers with AA and AG genotypes in model analyses. The genotype distribution for the Effective Triallelic 5-HTTLPR ($n = 59$ ss, $n = 89$ sl, $n = 44$ ll) was in Hardy-Weinberg equilibrium $\chi^2(3, N = 192) = .53, ns$. For purposes of quantification in analyses, the homozygote L and functional heterozygote S carriers were assigned values of 0 and 1, respectively.

All DNA samples were genotyped in duplicate for quality control. Additionally, human DNA from cell lines was purchased from Coriell Cell Repositories for all representative genotypes in duplicate, and genotypes were confirmed by sequencing using DTCS chemistry on an ABI 3130x1. These and a no template control were run alongside study samples representing 9% of the total data output. Any samples that were not able to be genotyped to a 95% or greater confidence level were repeated under the same conditions.

Analysis Plan

To chart the moderating effect of genotype on pathways between interparental conflict and parenting variables, a series of path models were specified with child gender, ethnicity, and maternal income concerns as covariates. For study analyses involving ethnicity, mothers were identified as either European-American (23%) or Non-European-American (77%). A conceptual model outlining our tests for moderating effects is presented in Figure 1 with all possible pathways included. Prior to running analyses, all covariates and predictor variables were centered to avoid problems with multicollinearity (Aiken & West, 1991). Models were run in stepwise fashion with main effects of interparental conflict, genotype, and covariates

entered first. The next model included the interaction effect. This was done to examine the influence of both genetic variables and interparental conflict at each step of the model. Significant interactions were clarified through post hoc statistical tests (e.g., simple slope analyses) to examine whether the regression slopes representing associations between interparental conflict and parenting were significantly different from 0 for different genotypes (Preacher, Curran, & Bauer, 2006). Upon the establishment of significant moderating effects, we next tested whether maternal depressive as well as maternal emotional closeness mediated the moderator pathways. This represents a first stage mediated moderation model (e.g., Edwards & Lambert, 2007). Within this framework, mediated moderation is supported when the moderator similarly influences the pathway between interparental conflict and mediating variables, and in turn these mediating variables are associated with the parenting outcome variables. Analyses proceeded in similar fashion with main effects entered first, followed by interaction effects.

Results

Table 1 shows the means, standard deviations, and correlations for the main variables in the study. In examining the table, we can first test for the presence of a gene-environment correlation (rGE) between 5-HTTLPR and OXTR. Bivariate correlations for both genotypes with interparental conflict were non-significant. The lack of an association suggests that any GxE effects are not a function of rGE, specifically evocative, passive or active effects.

Main Analyses

All path model analyses were performed using AMOS software (SPSS Inc., Chicago, 2007). Approximately 6% of the mother-child dyads were missing data on various assessments. To maximize our sample size, we utilized Full Information Maximum Likelihood estimation available in AMOS (e.g., FIML; Enders, 2001), this method is appropriate when the data are missing at random (e.g., no identifiable pattern exists in the missing data) and the amount of missing data is as high as 50% (Schlomer, Bauman, & Card, 2010). To evaluate whether data were missing completely at random (MCAR), we examined the patterns of missing data using Little's MCAR test (Little, 1988). Results showed that the data were indeed MCAR [$\chi^2 = 216.59$ (208), $p = .33$]. Finally in order to conserve space, model fit is not reported for each analysis; however, all of the path models fit the data well according to alternative indices of fit (*RMSEA* range = .00 to .07, *CFI* range = .96 to 1.00).

Moderation Analyses

OXTR—We first examined the association between covariates, oxytocin, and interparental conflict on maternal sensitivity and harsh/punitive parenting. Results are presented in Table 2. Supporting the presence of spillover effects, path model analyses revealed that there were significant associations between interparental conflict and maternal sensitivity and harsh/punitive caregiving. In addition, there were no main effects of OXTR on parenting variables. Our next model specified the pathway between the GxE interaction and both parenting constructs. There was a significant OXTR x Interparental Conflict effect on maternal sensitivity. The graph of this interaction is presented in Figure 3a. Post hoc simple slope analyses revealed that the simple slope for the GG genotype was significantly different from zero ($\beta = -.47$, $p < .001$), while the slope for the AA/AG genotype was not different than zero ($\beta = .25$, $p = .27$). The plot shows that the GG alleles demonstrated plasticity across levels of interparental conflict. Under levels of low conflict, these mothers were high in sensitivity; however, as interparental conflict increased their sensitivity significantly decreased. In addition, the simple slopes for the AA/AG and GG mothers were significantly different from one another ($t = 3.12$, $p < .01$). There was not a significant interaction effect

for maternal harsh/punitive parenting. Thus, the OXTR genotype interacted with interparental conflict to specifically predict maternal sensitivity.

5-HTTLPR—Our next analysis examined the GxE interaction between interparental conflict, 5-HTTLPR, and parenting variables (see Table 2). Path model analyses testing of main effects, again, revealed significant associations between interparental conflict and maternal sensitivity and harsh/punitive caregiving. In addition, there was no main effect of 5-HTTLPR on parenting variables. Our next model specified the pathway between the GxE interaction and both parenting constructs. There was a significant 5-HTTLPR x Interparental Conflict effect on both maternal sensitivity and harsh/punitive parenting. First, we explored the GxE interaction on maternal sensitivity. The graph of the interaction for maternal sensitivity is presented in Figure 3b. Post hoc simple slope analyses revealed that the simple slope for the ss/sl genotype was significantly different from zero ($\beta = -.45, p < .01$), while the slope for the ll genotype was no different than zero ($\beta = .06, p = .65$). The plot details that the ss/sl genotype demonstrated plasticity across levels of interparental conflict. In addition, the simple slopes for the ss/sl and ll mothers were significantly different from one another ($t = 2.63, p < .01$). Second, we explored the interaction for maternal harsh/punitive parenting. Similar to the findings for harsh parenting, post hoc simple slope analyses revealed that the simple slope for the ss/sl genotypes was significantly different from zero ($\beta = .59, p < .001$), while the slope for the ll genotype was not different than zero ($\beta = -.23, p = .36$). Inspection of the plot of the interaction (Figure 3c), shows that the ss/sl alleles demonstrated plasticity across levels of interparental conflict. Under levels of low conflict, these mothers were low in harsh/punitive parenting; however, as interparental conflict increased their harsh parenting significantly increased. Mothers with the ll genotype were not impacted by levels of interparental conflict in their use of harsh/punitive parenting. Finally, the simple slopes for the ss/sl and ll mothers were significantly different from one another ($t = 2.882, p < .001$). Thus, across both maternal sensitivity and harsh/punitive parenting practices, results support greater plasticity in mothers with an s allele.

Mediated Moderation Analyses

Our next set of analyses followed up significant GxE findings by testing for the presence of mediated moderation through a series of path models outlined in Figure 2.

OXTR—With respect to the OXTR findings, we first specified a path model in which maternal depressive symptomatology and emotional closeness were regressed onto the interaction predictor variables. Analyses revealed that interaction between interparental conflict and the OXTR genotype was significantly associated with maternal emotional closeness ($\beta = -.14, SE = .10, p < .05$). The graph of this interaction is presented in Figure 3d. Post hoc simple slope analyses revealed that the simple slope for the GG genotype was significantly different from zero ($\beta = -.17, p < .001$), while the slope for the AA/AG genotype was not different than zero ($\beta = .03, p = .75$). The plot shows that the GG alleles demonstrated plasticity across levels of interparental conflict. Under levels of low conflict, these mothers were high in emotional closeness; however, as interparental conflict increased this significantly decreased. In addition, the simple slopes for the AA/AG and GG mothers were significantly different from one another ($t = 2.13, p < .05$). The pathway between the Interparental Conflict x OXTR interaction and maternal depressive symptomatology was not significant ($\beta = .01, SE = .10, p = .90$). Given that the interaction effect on maternal emotional closeness was in the same direction as the effect on maternal sensitivity, we re-ran the model specifying the path between maternal emotional closeness and maternal sensitivity. The path was significant ($\beta = .27, SE = .19, p < .001$). In addition, the direct pathway between the Interparental Conflict x OXTR interaction and maternal sensitivity was reduced to non-significance ($\beta = -.13, SE = .29, p = .07$). Bootstrapping tests utilizing the

PRODCLIN software program indicated that the indirect path involving the interaction, maternal emotional closeness, and maternal sensitivity variables was significantly different from 0, 95% CI = $-.32$ to $-.01$ (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; Preacher & Hayes, 2008). This finding suggested that mother's perceptions of cohesion and closeness to her child may mediate the association between interparental conflict and sensitive caregiving practices for the GG genotype.

5-HTTLPR—Our final analysis examined whether maternal depressive symptomatology and emotional closeness mediated the significant IPCx5-HTTLPR interaction effect on maternal harsh/punitive and sensitive parenting. Path model analyses revealed that there were no significant associations between IPCx5-HTTLPR and depressive symptoms ($\beta = .11$, $SE = .10$, $p = .12$) and emotional closeness ($\beta = -.02$, $SE = .11$, $p = .74$). Taken together, these findings suggested that mediated moderation for 5-HTT was not evident in the sample.

Finally, although race was included as a covariate in model analyses, several race by gene interaction effects have been reported previously in the literature (Propper et al., 2007; Widom & Brzustowicz, 2006; Williams et al., 2003). Thus, we re-ran all of the process model analyses to test if there were any RxGxE effects. We tested all possible combinations of race including the 3-way and lower level 2-way interactions independently. None of the interactions involving race were significant in predicting either mediators or parenting practices.

Discussion

Spillover conceptualizations stress the primacy of the interparental relationship towards shaping parenting. Within these models, a main assumption is that frustration, anger, and emotional distress stemming from interparental conflicts disrupt parent's ability to care for their children (e.g., Erel & Burman, 1995). However, heterogeneity in research findings exists, hindering the ability to form firm conclusions regarding the nature of effects. Towards adopting a process-oriented, epistatic approach to family research, the present study represents the first attempt to examine how models of molecular genetics may influence pathways between interparental relationships and maternal caregiving behaviors. Our findings highlight the potential for genetic susceptibility frameworks in research on interparental conflict and parenting models. In addition, the findings chart how the oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes may be differentially implicated in spillover models.

First, our findings with respect to the serotonin transporter gene concur with emerging viewpoints that suggest the *s* allele may operate as a plasticity gene, conferring advantage within low-risk environments and evidencing greater difficulties under conditions of heightened adversity (Belsky & Beaver, 2011; Taylor, et al., 2006). Within our sample, mothers with at least one copy of the *s* allele evidenced greater sensitivity and lower harsh/punitive parenting under low interparental conflict yet also showed greater parenting difficulties under high interparental conflict. These results corroborate earlier findings reported by Mileva-Seitz and colleagues who also demonstrated the *s*-carrying mothers demonstrated greater plasticity in maternal sensitivity as a function of variations in exposure to adversity during childhood. However, we extend this research by demonstrating that 5-HTT may be also implicated in spillover models and may have implications for a broad array of parenting behaviors. The generality of effects for the serotonin system for caregiving behaviors in the present study is in contrast to animal research suggesting specificity (e.g., Maestripieri, et al., 2009). However the versatility of the serotonin system in terms of evidencing a broader range of influence on psychological and behavioral

functioning and has become increasingly noted within the human literature (Carver, Johnson, & Joormann, 2008).

In an attempt to explicate underlying processes which may serve to explain the differential susceptibility to interparental conflict exhibited by the mothers carrying an *s* allele, we further examined two possible mediating mechanisms. Despite empirical evidence suggesting linkages between individuals with an *s* allele and mood disorders, our tests of maternal depressive symptoms in model pathways did not emerge as explanatory variables underlying the GxE effects on parenting. This result was surprising, particularly with respect to documented linkages between both the 5-HTT and parenting behaviors with maternal depressive symptoms. Thus, the processes underlying the GxE finding for the 5-HTTLPR in spillover models remain unknown. Although we were not able to examine this within the present study, research in the area of social cognition may provide some insight and promising future avenues for explicating how 5-HTT may be implicated in spillover models. Specifically, it has been argued that carriers of the *s* allele of 5-HTTLPR show greater amygdala reactivity to emotional stimuli (Hariri, et al., 2002), and improved social cognition (Canli & Lesch, 2007). Thus, associations between 5-HTT and the amplification of detection of environmental cues may serve to facilitate sensitivity in maternal care within benign/low risk environments, but confer higher risk for overreactive/harsh and insensitive care within threatening environments.

As for OXTR genotype, our findings suggest some specificity with parenting practices. Within our sample the GxE was primarily associated with maternal sensitivity. Furthermore, findings also revealed that plasticity resides with the mothers carrying the GG alleles in the current sample. When interparental conflict was low, these mothers evidenced higher sensitivity. These findings for OXTR converge with those reported by Bakermans-Kranenburg and van IJzendoorn (2008), who demonstrated within a low-risk sample, mothers carrying the GG genotype showed higher levels of sensitive caregiving. However, with increasing levels of conflict present in the current sample, maternal sensitivity sharply declined within mothers carrying the GG allelic variant. There is some empirical support for the differential susceptibility of the GG carriers in human populations. Reim et al. (2011) found that females with OXTR GG alleles were more reactive to the sound of an infant crying than those with the AG or AA allele with low depressive symptoms. However, when the females with the homozygous G genotype had higher depressive symptoms, these differences between genetic profiles failed to reach significance. Furthermore, in a study of the interaction between adult retrospective reports of child maltreatment and OXTR rs53576 in an African American sample, Bradley, Western and Mercer's (2011) found that G/G carriers were at increased risk for emotion dysregulation when exposed to three or more categories of child abuse than A/G and A/A/ carriers. The research on OXTR and human parenting is very limited, and the present findings suggest that it may be worthwhile to explore whether allelic variants express themselves in a "better or for worse manner"—evincing optimal responsiveness in both directions to match the valence of the stimuli.

As a further indicator of the differential susceptibility of the GG genotype, we also uncovered a GxE pathway through maternal emotional closeness with their child. Over the past several decades oxytocin has been implicated in influencing prosocial behaviors, social bonding, and psychological closeness across animal and human species (Champagne & Meaney, 2006; MacDonald & MacDonald, 2010). Our findings demonstrate that the moderating role of OXTR in the pathway between interparental conflict and maternal sensitivity may be explained by individual differences in the maternal psychological bond with their child. Recent work exploring mechanisms underlying genetic effects for the OXTR gene also support psychological mediators in process pathways (e.g., Saphire-Bernstein, Way, Kim, Sherman, & Taylor, 2011). In line with this evidence, other findings

have also indicated that G allele carriers might show a higher sensitivity to social distress (Kim et al. 2010; Tost et al, 2010).

Fully interpreting the results of this study also requires consideration of limitations. First, process model pathways would be bolstered by the examination of parenting practices over time in order to better define the nature of predictive pathways within our theoretical model. Second, our sample was recruited to obtain higher levels of adversity in interparental relationships. Our focus on challenging environments provided a wider variation in stressful socialization contexts, however this precludes us from examining differential susceptibility to the entire range of interparental relationship functioning, including supportive and cohesive relationships. Third, our examination of underlying mechanisms of the associations explored in our process model was limited. Future progress on molecular genetic models of spillover hinges upon identifying mechanisms by which interparental violence negatively impacts diminished parenting.

In conclusion, our multi-method study represents the first attempt to examine how genetic moderation may operate in spillover models of interparental conflict and multiple dimensions of maternal parenting. Findings from the present study call for increased precision of molecular genetic conceptualizations within differential susceptibility to environmental influence models of parenting. Furthermore they serve to highlight the potential value of utilizing genetically-informed evolutionary models in research on parenting within stressful family environments (Belsky & Pluess, 2010; Ellis et al., 2011). However, forward progress in charting the pathways by which genetic moderation of family dynamics influences functioning ultimately hinges on uncovering the underlying physiological, psychological, and neurobiological mechanisms explaining these effects.

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Figure 1. Conceptual model outlining all possible pathways examined in testing Gene x Interparental Conflict effects on maternal parenting practices.

Figure 2. Conceptual model outlining mediated moderation by maternal depressive symptomatology and emotional closeness in Gene x Interparental Conflict effects and covariates on maternal parenting practices.

Figure 3a.
Plot of significant OXTR x Interparental Conflict interaction on Maternal Sensitivity.

Figure 3b.
Plot of significant 5-HTTLPR x Interparental Conflict interaction on Maternal Sensitivity.

Figure 3c.
Plot of significant 5-HTTLPR x Interparental Conflict interaction on Maternal Harsh/
Punitive Parenting.

Figure 3d.
Plot of significant OXTR x Interparental Conflict interaction on Emotional Closeness.

Table 1

Means, standard deviations, and intercorrelations of the primary variables in the study

Variables	1	2	3	4	5	6	7	8	9	10
1. Oxytocin Polymorphism	--									
2. Serotonin Polymorphism	-.09	--								
3. Interparental Conflict	.06	.04	--							
4. Maternal Sensitivity	-.06	-.09	-.15*	--						
5. Maternal Harsh/Punitive	.13	.12	-.16*	-.49*	--					
6. Depressive Symptoms	.08	-.04	-.04	-.06	-.04	--				
7. Emotional Closeness	-.06	-.12	-.15*	.31*	-.21*	.02	--			
8. Income	.03	-.06	.06	.06	-.07	.08	.16*	--		
9. Ethnicity	-.04	.03	.03	.39*	-.24*	-.04	.24*	.00	--	
10. Child Gender	-.06	.06	.08	.16*	-.11	.02	.04	.09	.00	--
<i>M</i>	0.60	0.31	0.00	18.77	6.58	0.41	0.00	2.81	0.27	0.46
<i>SD</i>	0.49	0.46	2.40	4.30	4.57	1.44	1.67	0.76	0.44	0.50

Table 2

Path Model Coefficients Testing the Moderating Role of Genotype on Associations Between Interparental Conflict and Parenting Behaviors

	Maternal Insensitivity			Dependent Variables		
	β	SE	p-value	Maternal Harsh/Punitive	SE	p-value
<u>OXTR:</u>						
1. IPC	-.15	.13	.03*	.16	.14	.03*
OXTR	-.03	.61	.66	.11	.23	.14
Income	.03	.40	.67	-.02	.44	.77
Child Gender	.17	.60	.02*	-.12	.67	.09
Race	.38	.68	.01*	-.23	.75	.01*
2. IPC	-.11	.13	.12	.16	.18	.03*
OXTR	-.04	.60	.58	.10	.85	.15
OXTRxIPC	-.19	.28	.01*	.09	.38	.19
<u>5-HTTLPR:</u>						
1. IPC	-.15	.13	.03*	.16	.14	.02*
5-HTTLPR	-.09	.65	.19	.12	.72	.09
Income	.02	.40	.79	-.01	.44	.94
Child Gender	.18	.60	.01*	-.14	.67	.06
Race	.38	.67	.01*	-.24	.76	.01*
2. IPC	-.16	.12	.02*	.18	.14	.01*
5-HTTLPR	-.10	.64	.15	.14	.71	.06
5-HTTLPRxIPC	.14	.25	.04*	-.20	.29	.01*

Note: IPC = Interparental Conflict,

* = $p < .05$.