Further evidence of the limited role of candidate genes in relation to infant–mother attachment outcomes

By: Esther M. Leerkes, Lindsey R. Gedaly, Nan Zhou, Susan Calkins, Vincent C. Henrich, and Andrew Smolen

Leerkes, E.M., *Gedaly, L.R., *Zhou, N., Calkins, S.D., Henrich, V. & Smolen, A. (2017). Further evidence of the limited role of candidate genes in relation to infant- mother attachment outcomes. *Attachment & Human Development, 19, 76-105.*

This is an Accepted Manuscript of an article published by Taylor & Francis in *Attachment & Human Development* on 16 November 2016, available online: http://www.tandfonline.com/10.1080/14616734.2016.1253759

Abstract:

In this paper, we examine the associations between specific candidate genes (DRD2, DRD4, COMT, biallelic and tri-allelic 5HTTLPR, and OXTR) and infant attachment outcomes as main effects and in conjunction with maternal sensitivity. The sample included 200 infants (97 European American, 94 African-American, and 9 biracial) and their mothers. Maternal sensitivity and overtly negative maternal behavior were observed when infants were 6 months and 1 year old in distress-eliciting contexts, attachment was assessed via the Strange Situation at age 1, and DNA samples were collected when children were 2 years old. Consistent with recent research in large samples, there was little evidence that these genes are associated with attachment security, disorganization, or distress as main effects (in additive, dominant, and homozygous models) or in conjunction with maternal sensitivity or overtly negative behavior (primarily dominance models). Furthermore, there was little evidence that associations vary as a function of race.

Keywords: Attachment | candidate genes | molecular genetics | maternal sensitivity | G X E

Article:

A good deal of research demonstrates that infants with insecure or disorganized attachments are at a heightened risk for psychopathology relative to securely attached/organized infants (Fearon, Bakermans-Kranenburg, van IJzendoorn, Lapsley, & Roisman, 2010; Madigan, Atkinson, Laurin, & Benoit, 2013). Thus, identifying the factors that predict infant attachment classifications is a significant endeavor for both basic and applied science. Beginning with Ainsworth's seminal work (Ainsworth, Blehar, Waters, & Wall, 1978), the quality of maternal behavior has been identified as one important antecedent of infant attachment outcomes. Generally, infants are more likely to form a secure attachment if their mothers are consistently,

promptly, and appropriately responsive to their cues; such mothers are described as sensitive. However, the association between maternal sensitivity and infant attachment outcomes is moderate (mean r = .35; Verhage et al., 2016), prompting researchers to consider other factors that may predict attachment quality. Recently, specific genotypes have been identified as potential contributing factors to whether infants will develop insecure or disorganized attachments, but the results have been quite inconsistent across studies, and most studies have focused on primarily or exclusively white participants (see Chen, Barth, Johnson, Gotlib, & Johnson, 2011; Cicchetti, Rogosch, & Toth, 2011 as exceptions). Thus, the primary goal of this paper is to determine if prior findings associating specific genes to attachment security and disorganization as main effects or by moderating associations between maternal sensitivity and attachment outcomes can be replicated in an independent sample composed of African-American and European American dyads.

Prior investigators examining the molecular genetic underpinnings of attachment have focused on candidate genes in the dopaminergic, serotonergic, and oxytonergic systems because such genes have been associated with functional differences in attention, motivation, affect, and social cognition that may affect social relationships, as reviewed below. Additionally, these candidate genes have often been characterized as susceptibility genes, such that individuals who carry certain alleles appear to be more susceptible to the effects of the environment, in this case maternal sensitivity, on developmental outcomes (Belsky & Beaver, 2011). Next, we briefly review the function of the genes under consideration, and prior research examining their associations with attachment outcomes. We particularly highlight the findings from two large-scale studies addressing these questions. Specifically, Luijk et al. (2011) presented data from two large-scale datasets, the NICHD Study of Early Child Care and Youth Development (SECCYD) (n = 478–522 for various genotypes) and the Generation R study (n = 506–547 for various genotypes). This report focused exclusively on white participants. Subsequently, Roisman, Booth-Laforce, Belsky, Burt, and Groh (2013), reanalyzed the data from the NICHD SECCYD (employing more stringent quality control for genotyping and testing additional outcomes), and included results for nonwhite participants (n = 144 nonwhite, n = 530 white).

Dopamine genes

The dopaminergic system is related to the prefrontal cortex, which plays a role in cognition and emotional processes (Wang, Zhong, Gu, & Yan, 2003), and is involved in the attentional, motivation, and reward mechanisms (Robbins & Everitt, 1999). In previous studies, the T (also known as A1) allele of the dopamine receptor D2 gene (DRD2 rs1800497), has been associated with reduced dopamine binding (Jönsson et al., 1999) and reduced D2 expression in the striatum (Noble, Blum, Ritchie, Montgomery, & Sheridan, 1991). The dopamine D4 receptor gene (DRD4) contains a 48 bp variable number tandem Repeat (VNTR) polymorphism in the third exon, which results in 10 allelic products comprising 2–11 repeat units, with 2, 4, and 7 repeats being the most common variants (Van Tol et al., 1992). The 7 repeat (7R) allele of DRD4 has been associated with a blunted intracellular response to dopamine *in vitro* as compared with shorter alleles (Asghari et al., 1995). Likewise, Catechol-O-methyltransferase, or COMT (rs4680) is a gene associated with dopamine activity such that the Val allele (also known as G) is associated with a fourfold reduction in the activity of the enzyme that metabolizes dopamine (Akil et al., 2003). And, COMT Val is associated with less limbic and prefrontal activation in

response to negative stimuli (Smolka et al., 2005). Thus, the general expectation is that carriers of DRD4 7+ repeats, DRD2 T, or COMT Val alleles are at heightened risk of insecurity and disorganization and will evidence stronger negative associations between maternal sensitivity and negative attachment outcomes.

In fact, the empirical evidence to date in support of this view is scant and inconsistent. To date, no statistically significant associations between DRD2 and attachment outcomes have been reported as main effects or in conjunction with maternal sensitivity (Luijk et al., 2011; Roisman et al., 2013). In contrast, some research has identified associations between DRD4 and attachment outcomes. Specifically, infants who carried the DRD4 7+ (i.e., seven or higher) repeat were more likely to be *disorganized* in one small sample (Lakatos et al., 2000), but this main effect did not replicate in several other studies (Bakermans-Kranenburg & Van IJzendoorn, 2004; Cicchetti et al., 2011; Spangler, Johann, Ronai, & Zimmermann,) including the larger n study conducted by Luijk et al. (2011). Although the finding appeared to be somewhat replicated among nonwhite infants in the SECCYD for whom carrying more 7+ repeats of DRD4 (additive model) or being homozygous for DRD4 was associated with higher *disorganization*, these effects were not statistically significant following an alpha correction for multiple analyses nor when Lakatos et al.'s (2000) specific approach to coding risk (i.e., grouping individuals with repeats higher than seven in the low-risk group rather than a 7+ group) was used (Roisman et al., 2013). Evidence of significant interactions between sensitivity and DRD4 has also been mixed. In the SECCYD, white sample, sensitivity was only associated with *security* among infants who did not carry the 7+ repeat, but this effect was not replicated in the Generation R sample (Luijk et al., 2011), the nonwhite SECCYD sample (Roisman et al., 2013), nor another small primarily nonwhite sample (Cicchetti et al., 2011). In terms of *disorganization*, non-maltreated children carrying the DRD4 7+ allele were more likely to be disorganized, but this was not the case among maltreated children suggestive of an interaction between parenting quality and DRD4 (Cicchetti et al., 2011). However, when interactions between sensitivity/parenting and DRD4 have been directly tested in relation to disorganization, they have not been statistically significant (Luijk et al., 2011; Roisman et al., 2013; Spangler et al., 2009; van IJzendoorn & Bakermans-Kranenburg, 2006).

COMT has only been examined in relation to attachment outcomes in two published studies. Luijk et al. (2011) reported that white heterozygotes were more likely to be *disorganized* in both the SECCYD and Generation R samples. Roisman et al. (2013) confirmed this, and further demonstrated that carrying the COMT Val allele was modestly associated with disorganization among white infants, and reported no significant effects of COMT among nonwhites across all three models (additive, dominance, and homozygosity). Furthermore, Luijk et al. (2011) reported that COMT heterozygosity and maternal sensitivity interacted such that sensitivity was only associated with disorganization for heterozygotes in the Generation R sample but not the SECCYD sample, as later confirmed by Roisman et al. (2013).

Serotonin genes

The serotonin transporter, 5HTTLPR, (Locus Symbol SLC6A4) contains a 43 bp insertion/deletion polymorphism in the 5′ regulatory region of the gene (Heils et al., 1996). The short (S) allele of 5HTTLPR (typically 14 repeats) is associated with lower expression of the 5-

HTT gene (Ebstein, 2006), and has been found to be associated with increased fear and anxiety-related behaviors (Hariri et al., 2002) in comparison with the long (L) allele which consists of 16 or more repeats. Generally, infants carrying the S allele have been viewed as at higher risk for negative outcomes, and as being more susceptible to the negative effects of maternal insensitivity. Once again, the empirical evidence is not particularly consistent with this perspective in relation to attachment outcomes.

In one small study, carriers of the 5HTTLPR L allele were more *secure* than carriers of the S allele (Barry, Kochanska, & Philibert, 2008), but this effect was not replicated in other small and large sample studies (Cicchetti et al., 2011; Luijk et al., 2011; Roisman et al., 2013; Spangler et al., 2009). Likewise, in another small study, children with the S allele were more likely to be *disorganized* than carriers of the L allele (Spangler et al., 2009), but this main effect was not replicated in other studies (Cicchetti et al., 2011; Luijk et al., 2011; Roisman et al., 2013). Further, both of the significant main effects were qualified by interactions with maternal sensitivity (Barry et al., 2008; Spangler et al., 2009).

In terms of interactions between 5HTTLPR and sensitivity, only one study has reported a statistically significant interaction in relation to *security* such that maternal responsiveness was positively associated with security only among infants with the S allele (Barry et al., 2008). This interaction effect was not replicated in three other studies (Luijk et al., 2011; Roisman et al., 2013; Spangler et al., 2009). In contrast, statistically significant interactions (or the like) between 5HTTLPR and sensitivity predicting *disorganization* have been reported in three studies, but the nature of the interaction has varied. That is, Spangler et al. (2009) reported that differences in disorganization as a function of 5HTTLPR were only apparent among infants whose mothers were low on responsiveness, such that carrying more S alleles was associated with greater odds of being disorganized in this context. In contrast, Cicchetti et al. (2011) reported that differences in disorganization as a function of 5HTTLPR were only apparent among infants who were not maltreated, for whom the S allele was associated with disorganization. Finally, Roisman et al. (2013) reported that maternal sensitivity was marginally positively associated with disorganization among S carriers, and marginally negatively associated with disorganization among infants homozygous for L in the white subsample of the SECCYD, a counterintuitive pattern. No such interaction effect was apparent in the Generation R sample (Luijk et al., 2011).

Notably, each of these studies relied on the biallelic characterization of 5HTTLPR. However, it has been noted that a SNP (rs25531, A/G) in the L form of 5HTTLPR may alter the function of the L allele (Hu et al., 2005). That is, the more common L_A allele is associated with higher basal activity, whereas the less common L_G allele has transcriptional activity no greater than the S allele. As such, a tri-allelic approach has been suggested in which individuals with the $L_G$alleles should be grouped with individuals with the S alleles (Hu et al., 2006). This is important because inconsistent results across prior studies could be due to unmeasured differences in the nature and hence function of the L alleles. To our knowledge, only one prior study has examined variation in tri-allelic 5HTTLPR in relation to attachment outcomes. Raby et al. (2012) reported no differences in attachment security versus insecurity as a function of tri-allelic 5HTTLPR, but infants who carried more S/L_G alleles were more likely to be classified in the high distress attachment groups (i.e., secure subgroups B_3/B_4 or resistant) than the low distress attachment

groups (i.e., secure subgroups B_1/B_2 or avoidant). This effect was not replicated in the SECCYD sample using the biallelic approach (Roisman et al., 2013).

Oxytocin genes

Finally, the oxytonergic system is related to bonding, affiliation, and empathy (Carter, 1998; Feldman, Weller, Zagoory-Sharon, & Levine, 2007). Although the function of oxytocin receptor genes is somewhat less certain than other genes, the A allele of the oxytocin receptor gene, OXTR rs53576, has been associated with a decrease in the functional response of the amygdala (Tost et al., 2010), which plays a role in mediating fear responses (Adolphs et al., 2005). Likewise, the A allele of *OXTR* rs2254298, has been associated with a larger amygdala volume (Furman, Chen, & Gotlib, 2011; Inoue et al., 2010). Thus, carrying the A allele of either is generally considered a risk factor. However, the GG allele of OXTR is related to better social cognition and prosocial behaviors (Bartz, Zaki, Bolger, & Ochsner, 2011); thus, it has been argued and demonstrated that carriers of the GG allele may be more sensitive to their social environment and therefore more strongly affected by it (Sturge-Apple, Cicchetti, Davies, & Suor, 2012). Of the selected genes, this is the only case in which the risk allele (A) and the susceptibility allele (G) are not the same.

In prior research, carrying the A allele of *OXTR* rs2254298 was associated with attachment security among nonwhite infants, but not among white infants (Chen et al., 2011), a result that was not replicated by Roisman et al. (2013) among nonwhite participants of the SECCYD. In the current report, we focus only on OXTR rs53576, as we did not assay OXTR rs2254298. Prior research with OXTR rs53576 has not yielded statistically significant main effects or interactions with maternal sensitivity in relation to attachment security or disorganization (Chen et al., 2011; Luijk et al., 2011; Roisman et al., 2013).

Criticism of this approach and the current study

As noted by Luijk et al. (2011) and Roisman et al. (2013), there is little consistent evidence for the role of these variants of these candidate genes in predicting attachment outcomes as main effects or in conjunction with maternal sensitivity. Furthermore, the few statistically significant results may be due to chance (i.e., false positives) given the number of analyses run, and small frequencies for certain genotypes. On the other hand, conducting attachment research in single samples that are sufficiently large to detect very small genetic effects is somewhat unlikely given the cost. As such, continued reporting of observed effects in small samples is likely useful for replication purposes, to avoid the file drawer problem, and to stimulate meta-analyses or subsequent integrative data analyses combining multiple studies. Integrative data analyses, which involve pooling data across multiple samples (Curran & Hussong, 2009), are particularly appealing because they would increase the sample size and hence statistical power. Genetic measures and measures of attachment outcomes are fairly standard, which is ideal for this approach. Although measures of sensitivity/behavior vary across studies, a large international group, The Collaboration on Attachment Transmission Synthesis, is currently working to identify appropriate approaches to address this in integrative data analysis (Verhage et al., 2015). In an effort to facilitate such efforts, we attempt to directly replicate the results reported in the

papers by Luijk et al. (2011) and Roisman et al. (2013) by following their procedures and analytic plan as closely as possible.

Four features of the current study are particularly notable in the context of prior research on this topic. First, our sample is half European American and half African-American presenting an important opportunity to add to the literature among nonwhite dyads without grouping multiple nonwhite racial/ethnic groups together. Following Roisman et al. (2013), we not only present all results separately for African-American and European American dyads but also present the results for the entire sample and formally test race as a moderator of all effects. Formally testing race as a moderator is important given associations between specific genes and attachment outcomes may be significant in one group but not the other even if the associations do not vary between the groups lending the impression that genes function differently in different racial groups when this may not in fact be the case. Second, we present the results for both tri-allelic and biallelic 5HTTLPR, and to our knowledge are the first to examine tri-allelic variation in relation to attachment disorganization. Third, in contrast to prior research that focused on maternal sensitivity during play and/or feeding interactions (e.g., Luijk et al., 2011; Raby et al., 2012; Spangler et al., 2009) or aggregated across a variety of potentially stressful and non-stressful tasks (Barry et al., 2008), we observed maternal sensitivity in contexts designed to elicit infant distress. Prior research has demonstrated that sensitivity to infant distress cues or in distressing situations is more predictive of attachment security than is maternal sensitivity to non-distress cues or in non-distressing contexts (Leerkes, 2011; McElwain & Booth-LaForce, 2006). Thus, it may be the case that candidate genes moderate the association between sensitivity to distress and attachment outcomes differently than between sensitivity to non-distress and attachment outcomes. Finally, we test the extent to which associations between specific egregious, overtly negative maternal behaviors (e.g., negativity toward the infant, intrusiveness, and laughing when the infant cries) and attachment outcomes are moderated by genes. This is important because in prior research, including with this sample, such behaviors have been more predictive of attachment disorganization than global measures of maternal sensitivity (e.g., Beebe et al., 2012; Gedaly & Leerkes, 2016; Madigan et al., 2006; Wang, Cox, Mills-Koonce, & Snyder, 2015).

Based on the literature to date, we anticipated few if any statistically significant main or moderating effects of these candidate genes on infant attachment security, disorganization, or distress groups. We further anticipated that the average of such effects would be near zero, consistent with Roisman et al. (2013). Additionally, we did not anticipate significant moderation by race given limited evidence of different patterns of results for white and nonwhite infants in prior research (Roisman et al., 2013).

Method

Participants

The current sample was drawn from a larger study examining the antecedents of maternal sensitivity and its links with child adjustment over time. The original sample included 259 primiparous mothers (128 European American, 131 African-American). Mothers in the sample ranged from 18 to 44 years old (Mean = 25.1). Approximately 65% had at least some college-

level schooling, and annual family income ranged from poverty to over $100,000, Median = $35,000. The majority (71%) of mothers were married or living with their child's father, 11% were in a relationship but not living with their child's father, and 18% were single. All infants were full term and healthy; 125 (49%) were male and 129 (51%) were female.

The current sample included dyads who participated in the Strange Situation Procedure at the 1-year time point or provided DNA at the 2-year time point. This resulted in an analytic sample of 200. Key reasons for attrition, missing data, or being withdrawn from the study include infant mortality (2 cases), moving from the area and an inability to return for behavioral observations (19 cases), withdrawing from the study (9 cases), declining to provide DNA (4 cases), providing insufficient or questionable DNA (3 cases), and failure to schedule or complete data collection after multiple attempts to schedule (22 cases).

Participants in the analytic sample did not significantly differ from those not in the analytic sample on race, child gender, marital status, or income level. However, participants in the analytic sample were significantly older ($M = 25.50$, $SD = 5.27$) and higher educated ($M = 3.96$, $SD = 1.79$) than those not in the analytic sample ($M = 23.54$, $SD = 5.64$, $t(256) = 2.46$, $p < .05$ for maternal age; $M = 3.27$, $SD = 1.72$, $t(255) = 2.64$, $p < .01$ for maternal education).

Infant race was defined by the combination of mother-reported mother and father race. As such, 97 children were European American, 94 children were African-American, and 9 children were mixed race. Mixed race children were not considered in analyses involving racial differences but were included in the full sample analyses.

Procedures

Expectant mothers were recruited from childbirth classes, obstetric practices, and prenatal breastfeeding classes offered by the Special Supplemental Nutrition Program for Women Infants and Children (WIC), via flyers and presentations given by research staff members. Upon enrolling in the study, women were mailed their consent forms and a packet of questionnaires, including a demographic form. Mothers were contacted by phone and visits were scheduled in our laboratory within 2 weeks of the child's 6-month birthday ($M = 6.39$ months old, $SD = .72$) and 1 month of the child's 13-month birthday ($M = 13.9$ months old, $SD = .98$). At the 6-month and 1-year visits, mothers and infants participated in a series of videotaped interactive tasks designed to elicit infant distress and to assess maternal sensitivity. During the 1 year visit, dyads participated in the Strange Situation Procedure to assess infant–mother attachment security. DNA was collected via saliva samples from children during a subsequent 2-year laboratory visit. Twelve mothers who had moved from the area provided their infants' saliva samples via the mail. Mothers received $50, $100, and $120, respectively, at the conclusion of each visit, and infants received a small toy. All procedures were approved by the internal review board.

Measures

Observed maternal behavior and sensitivity at 6 months and 1 year

Mothers and infants participated in a series of brief distress-eliciting tasks during the 6-month (arm restraint, novel toy approach, and still face) and 1-year (attractive toy in a jar and novel character approach) laboratory visits as described in Gedaly and Leerkes (2016). Mothers were seated near the infants and within reach of a toy basket at the start of each task. They were instructed to interact with their infants as they liked. Infant affect and maternal behavior were continuously rated/coded from digital media files using INTERACT 9 (Mangold, Arnstorf, Germany) by different teams of coders. Infant affect was rated on a 7-point scale ranging from (1) high positive affect (intense smile, laughing, or squealing) to (7) high negative affect (screams, wails, sobs intensely). Inter-rater reliability was good at 6 months and 1 year: weighted kappa = .76 and .75 based on 34 and 30 double-coded cases, respectively. At 6 months, 96% of infants became distressed, and the average duration of distress across the tasks was 2 min (range = 0–7.75 min). At 1 year, 91% percent of infants became distressed, and the average duration of distress was 1 min (range = 0–4.45 min).

Maternal behaviors were continuously coded using 12 mutually exclusive categories (negative, intrusive, mismatched affect, withdraw, distracted, persistent ineffective, monitor, task focused, calming, supportive, non-task-focused engagement, and routine care) described in Leerkes (2010). About 30 cases and 27 cases were double-coded for reliability at 6 months (kappa = .77) and 1 year (kappa = .80), respectively. Given the goals of the current report, we focused on the most overtly negative maternal behaviors in our coding scheme that most closely map onto behaviors found to predict attachment disorganization in other studies (Beebe et al., 2012; Madigan et al., 2006; Wang et al., 2015). These were negative (directs negative affect toward the infant), intrusive (forces own agenda on the infant), and mismatched affect (primarily, laughing or smiling in response to infant's distress). Scores reflecting the percentage of time mothers engaged in each of these three interactive behaviors across tasks were computed for both the 6-month (arm restraint task, novelty task, and still face) and 1-year time points (limitations task and novel character approach) and then averaged over time to yield measures of the percentage of observation time in which mothers engaged in these overtly negative parenting behaviors.

Then, the infant affect and maternal behavior code files were merged and mothers were assigned an a priori sensitivity rating for each second of the tasks based on the appropriateness of the maternal behavior in the light of the infant's affective state at that moment on a 3-point scale (1 = *insensitive*, 2 = *moderately sensitive*; 3 = *sensitive*). For example, monitoring a neutral infant is rated as sensitive because the infant is not signaling a need. Monitoring when an infant is distressed is rated as insensitive because the infant is signaling a clear need to which the mother does not respond. Sensitivity ratings for each discrete maternal behavior during infant positive, neutral and negative affect are described in Leerkes (2010). Mothers' average sensitivity rating during each task was then calculated. These ratings were then averaged across tasks and the two time points yielding a single measure of maternal sensitivity during distress-eliciting tasks; Cronbach's alpha = .78.

The Strange Situation Procedure

Infant–mother attachment security was assessed at 1 year using the Strange Situation Procedure (Ainsworth et al., 1978). The Strange Situation was administered and coded (by E. Carlson) according to standard procedures. Thirty cases were double coded by a staff member to establish

inter-rater reliability. The distribution of attachment classifications was as follows: 71.4% secure among the full sample (69.6% among European Americans, 71.1% among African-Americans), 3.3% avoidant among the full sample (3.3% among European Americans, 3.6% among African-Americans), 3.3% resistant among the full sample (3.3% among European Americans, 3.6% among African-Americans), and 22.0% disorganized among the full sample (23.8% among European Americans, 21.7% among African-Americans).

Following Luijk et al. (2011) and Roisman et al. (2013), we calculated Van IJzendoorn and Kroonenberg (1990) adaptation of the continuous attachment security score first described by Richters, Waters, and Vaughn (1988), and we used the 9-point continuous rating of disorganized behavior (Main & Solomon, 1990) as the measure of disorganization. Inter-rater reliability (assessed via intraclass correlation coefficients) for the items used to construct the security score ranged from .78 to .92 and was .60 for disorganization. Additionally, we classified B1/B2 and avoidant infants as low distress (58.8% among the full sample, 57.6% among European Americans and 61.4% among African-Americans) and B3/B4 and resistant infant as high distress (41.2% among the full sample, 42.4% among European Americans and 38.6% among African-Americans) following Raby et al. (2012) and Roisman et al. (2013). Reliability for this distinction was $\kappa = .81$ (90% agreement).

DNA collection and genotyping

Children's DNA was collected via buccal samples during the 2-year visit (or at the child's home in rare instances in which samples were mailed) using the Oragene Collection Kit 500OrageneTM, DNAgenotek, Ottawa, Ontario, Canada, www.DNAgenotek.com). Children's samples were collected by using a q tip-like swab (the Oragene swab format; #OG-575) to collect the saliva and twist it into a tube that when capped releases a stabilizing lysis buffer. All samples were given a bar-coded label linked only to the research records maintained by the PI before sending the tubes for DNA processing. The DNA was prepared at the Molecular/Cellular Biology Core Laboratory at the University of North Carolina at Greensboro using the methodologies described by Oragene. Then, DNA was quantified by spectrophotometry (Nanodrop Spectrophotometer) and standardized to a working concentration of 20 ng/µl. Genotyping was then conducted at the Institute for Behavioral Genetics at the University of Colorado under the supervision of Andrew Smolen. Two individuals scored genotypes independently, and inconsistencies were reviewed and rerun when necessary.

The assay of the dopamine D2 receptor gene, (DRD2 rs1800497) was done using a fluorogenic 5′nuclease (Taqman®, ABI, Foster City, CA) method (Haberstick & Smolen, 2004) on an ABI Prism® 7000 Sequence Detection System using the allelic discrimination mode (Livak, 1999). Primer and probe sequences were forward: 5′-GTGCAGCTCACTCCATCCT-3′ and reverse: 5′-GCAACACAGCCATCCTCAAAG-3′; with A1 Probe: 5′-VIC-CCTGCCTTGACCAGC-NFQMGB-3′; and A2 Probe: 5′-FAM-CTGCCTCGACCAGC-NFQMGB-3′.

The assay of the dopamine D4 receptor gene, (DRD4; Anchordoquy, McGeary, Liu, Krauter, & Smolen, 2003) was a modification of an extant method (Lerman et al., 1998). The primer sequences were forward: 5′-VIC-GCT CAT GCT GCT GCT CTA CTG GGC-3′ and reverse: 5′-

CTG CGG GTC TGC GGT GGA GTC TGG-3′, which yielded PCR products from 279 (2R) to 663 bp (10R).

The assay of the Catechol-O-methyltransferase (COMT rs4680) gene was performed using a fluorogenic 5′nuclease (Taqman®, Applied Biosystems, Foster City, CA) method (Haberstick & Smolen, 2004). Primer and probe sequences were forward: 5′-TCGAGATCAACCCCGACTGT-3′ and reverse: 5′-AACGGGTCAGGCATGCA-3′; with Val Probe: 5′-FAM-CCTTGTCCTTCACGCCAGCGA-NFQMGB-3′; and Met Probe: 5′-VIC-ACCTTGTCCTTCATGCCAGCGAAAT-NFQMGB-3′ (Mattay et al., 2003).

The *biallelic* assay of the serotonin transporter polymorphism gene, 5HTTLPR rs25531 is a modification (Anchordoquy et al., 2003) of the method of Lesch et al. (1996) using the primer sequences from Gelernter, Cubells, Kidd, Pakstis, and Kidd (1999). The primer sequences were forward: 5′-NED-ATG CCA GCA CCT AAC CCC TAA TGT-3′ and reverse: 5′-GGA CCG CAA GGT GGG CGG GA-3′ which yield PCR products of 376 (S) and 419 bp (L). The classic short allele has 14 repeats and the classic long allele has 16 repeats, but extra-long alleles (in our case, 20 and 26 repeats) were classified as long as is common practice.

The *tri-allelic* assay and scoring for 5HTTLPR was performed using Hu et al.'s (2005, 2006) procedure. The 5HTT SNP (rs25531, A/G) was assayed using the primer sequences of Hu et al. (2005). The primer sequences were forward: 5′-6FAM-GCA ACC TCC CAG CAA CTC CCT GTA-3′ and reverse: 5′-GAG GTG CAG GGG GAT GCT GGA A-3′ which yield PCR products of 138 (S) and 181 bp (L). The low-expressing S (genotyping described above) and L_G alleles were grouped together and the higher expressing L_A allele was designated as long.

The assay of the oxytocin receptor gene, OXTR rs53576 was performed using a fluorogenic 5′nuclease (Taqman®, LifeTechnologies, Grand Island, NY) method using the 40x primer-probe reagents obtained from the company (assay number C___3290335_10_M). Reactions were performed in an ABI Prism® 7000 Sequence Detection System using the allelic discrimination mode (Livak, 1999). Reactions containing 5–20 ng of DNA were performed in 15 µl reactions with Taqman® Universal PCR Master Mix using the standard cycling conditions.

The Hardy–Weinberg equilibrium (HWE) test was run separately by race to see if the gene frequencies in the sample are similar to gene frequencies in the general population. Frequency distributions conformed to the HWE, except for OXTR rs53576 for white participants ($p = .0029$).

Results

Preliminary analyses

Preliminary analysis of variance (ANOVA) and correlational analyses evaluated whether demographic variables were related to genotype and attachment security to identify potential covariates. None of the demographic variables in Table 1 was simultaneously associated with attachment quality, genotype, and maternal sensitivity in the overall sample. Thus, no covariates

were included in primary analyses. A summary of the specific candidate genes under consideration and their minor alleles is presented in Table 2.

Table 1. Sample characteristics, descriptive statistics, and group comparisons.

	Overall sample (*N* = 200)		**European American (*N* = 97)**		**African-American (*N* = 94)**		χ^2/t
	***M* (*SD*)**	***%***	***M* (*SD*)**	***%***	***M* (*SD*)**	***%***	
Child characteristics							
Child gender (female)		51.5		48.5		53.2	.43
Birth weight (g)	3109.10(522.54)		3212.19(511.46)		3004.75(515.46)		2.71**
Birth length (inch)	20.04 (1.87)		20.33 (1.00)		19.74 (2.49)		2.07*
Gestational age (weeks)	39.60 (1.24)		39.66 (1.27)		39.57 (1.17)		.49
Vaginal birth		69.0		67.0		71.3	.30
Maternal characteristics							
Age at intake	25.5 (5.27)		27.06 (5.14)		23.84 (5.00)		4.38**
2 years college or less		53.0		33.3		74.2	44.20**
Married/living together		71.0		92.8		51.1	71.22**
No employment 6 months		39.0		33.0		47.9	
Breastfed 6 months		42.9		56.8		29.8	14.08**
Key variables							
Maternal sensitivity	5.25 (1.43)		5.97 (1.27)		4.51 (1.22)		8.11**
Negative behavior	2.37 (3.01)		1.98 (2.86)		2.76 (2.98)		−1.78
Security	.88 (2.24)		.55 (2.14)		1.08 (2.30)		−1.56
Disorganization	3.06 (1.83)		3.17 (1.76)		3.01 (1.92)		.58

* $p < .05$, ** $p < .01$.

Table 2. Overview of genes under consideration.

Gene	Marker	Minor allele	MAF (%)
Dopaminergic system			
DRD2	rs1800497	T (A1)	38.7
DRD4	48 bp VNTR	7+	37.2
COMT	rs4680	G (val)	84.8
Serotonergic system			
Bi_5HTTLPR	43 bp VNTR	S	57.6
Tri_5HTTLPR	rs25531	S/L_G	75.9
Oxytonergic system			
OXTR	rs53576	A	44.0

Distribution of attachment scores and correlations with sensitivity

Mean scores for maternal sensitivity, overtly negative maternal behavior, attachment security, and disorganization for the full sample and separately for European American and African-American infants are presented in Table 1, along with *t*-tests or chi-square results comparing values between race groups. Table 3 presents means and standard deviations of security and disorganization scores by genotype for the full sample and across European American and African-American infants. The correlation between sensitivity and security was .06, $p = .40$ for the full sample, .10, $p = .17$ for European American infants, and .19, $p = .09$ for African-American infants. The correlation between sensitivity and disorganization was −.16, $p = .03$ for the full sample, −.15, $p = .17$ for European American infants and −.27, $p = .02$ for African-

American infants. The correlation between negative behavior and security was −.17, $p = .03$ for the full sample, −.18, $p = .10$ for European American infants, and −.17, $p = .12$ for African-American infants. The correlation between negative behavior and disorganization was .18, $p = .02$ for the full sample, .16, $p = .14$ for European American infants and .18, $p = .11$ for African-American infants.

Table 3. Means and standard deviations for attachment security and disorganization across various genotypes.

Gene	*Full sample*			*European American*			*African-American*		
	aa M (SD) n	***Aa M (SD) n***	***AA M (SD) n***	***aa M (SD) n***	***Aa M (SD) n***	***AA M (SD) n***	***aa M (SD) n***	***Aa M (SD) n***	***AA M (SD) n***
Security									
DRD2	0.86 (2.39)	0.62 (1.95)	2.07 (2.07)	0.57 (2.21)	0.39 (1.96)	3.09 (– –)	1.00 (2.56)	0.81 (1.99)	2.15 (2.05)
	108	54	14	64	24	1	40	29	11
DRD4	0.96 (2.25)	0.73 (2.27)	0.87 (2.29)	0.74 (2.03)	0.04 (2.46)	0.56 (2.03)	1.09 (2.49)	1.03 (1.95)	1.50 (2.98)
	112	53	12	59	22	8	49	28	4
COMT	0.82 (2.36)	0.99 (2.20)	0.77 (2.28)	0.47 (2.46)	0.90 (1.94)	−0.19 (2.15)	1.95 (1.70)	0.90 (2.52)	1.10 (2.20)
	26	86	66	20	48	21	6	34	42
Bi5HTTLPR	0.71 (2.24)	0.94 (2.18)	1.14 (2.48)	0.84 (2.31)	0.45 (2.07)	0.35 (2.12)	0.64 (2.22)	1.56 (2.22)	1.74 (2.81)
	70	78	29	27	45	17	43	29	9
Tri5HTTLPR	0.50 (2.18)	0.83 (2.26)	1.25 (2.25)	0.57 (2.14)	0.49 (2.26)	0.63 (2.00)	0.41 (2.30)	1.07 (2.24)	1.60 (2.41)
	38	88	51	21	44	24	17	41	23
OXTR	1.01 (2.39)	0.66 (2.13)	0.89 (1.87)	0.40 (2.29)	0.66 (2.08)	0.76 (1.88)	1.35 (2.38)	0.53 (2.28)	1.13 (1.98)
	97	56	23	43	31	15	49	23	8
Disorganization									
DRD2	3.16 (1.84)	3.10 (1.81)	2.14 (1.70)	3.34 (1.77)	2.85 (1.69)	1.00 (– –)	3.02 (1.94)	3.41 (1.88)	2.00 (1.79)
	110	56	14	65	26	1	41	29	11
DRD4	3.04 (1.77)	3.11 (1.92)	2.92 (2.10)	3.17 (1.71)	3.39 (1.85)	2.63 (1.92)	2.96 (1.87)	3.00 (2.00)	3.40 (2.51)
	114	54	13	61	23	8	49	28	5
COMT	3.00 (1.92)	3.13 (1.83)	3.00 (1.81)	3.04 (1.94)	3.08 (1.70)	3.50 (1.74)	2.83 (2.04)	3.29 (2.04)	2.81 (1.83)
	26	86	68	22	48	22	6	34	43
Bi5HTTLPR	3.24 (1.83)	3.00 (1.91)	2.76 (1.62)	3.11 (1.69)	3.28 (1.92)	3.00 (1.46)	3.32 (1.93)	2.66 (1.91)	2.56 (1.94)
	72	80	29	28	47	17	44	29	9
Tri5HTTLPR	3.02 (1.85)	3.13 (1.93)	2.94 (1.65)	1.63 (0.36)	3.26 (1.96)	3.00 (1.50)	2.82 (2.13)	3.10 (1.94)	2.96 (1.85)
	38	91	52	21	46	25	17	42	23
OXTR	2.87 (1.93)	3.55 (1.62)	2.70 (1.69)	3.14 (1.84)	3.55 (1.64)	2.47 (1.64)	2.76 (2.03)	3.57 (1.70)	3.13 (1.81)
	99	58	23	44	33	15	50	23	8

aa, homozygous for the typical ("wild-type") allele; Aa, heterozygous; AA, homozygous for minor allele. Higher security scores indicate more security; higher disorganization scores indicate more disorganization. " – –" indicates not applicable.

Main effects candidate gene associations and tests of racial differences

Following Roisman et al. (2013), associations between the pertinent gene polymorphisms and attachment security and disorganization were tested using correlation analyses applying additive genetic models (sum of number of "risk alleles" ranging from 0 to 2), genetic dominance models (1 or 2 risk allele(s) versus 0 risk alleles), and heterozygous versus homozygous genetic

association models (aA versus AA or aa). For each approach, interactions between candidate genes and child race were examined to test whether associations between candidate genes and attachment security and disorganization varied significantly across racial groups. Given space constraints, complete results of the interaction analyses are presented in supplemental tables in the Appendix and described in the text below.

Additive genetic models

Correlations (r_{add}) and exact p-values (p_{add}) based on additive genetic models are reported in Table 2 for the full sample as well as by race for security (top panel) and disorganization (bottom panel). Consistent with prior research, none of the genetic associations for attachment security and disorganization reached significance in the overall sample or in the European American/African-American subsamples. The average effect of the polymorphisms on security or disorganization was around zero. Interactions between candidate genes and child race did not reach significance (Appendix, Supplementary Table 1).

Table 4. Main effects of candidate genes on attachment security and disorganization by racial group R.

Gene	*Full sample*						*European American*						*African-American*					
	r_{add}	p_{add}	r_{dom}	p_{dom}	r_{hom}	p_{hom}	r_{add}	p_{add}	r_{dom}	p_{dom}	r_{hom}	p_{hom}	r_{add}	p_{add}	r_{dom}	p_{dom}	r_{hom}	p_{hom}
Security																		
DRD2	.08	.32	.01	.86	−.08	.31	.01	.89	−.02	.89	−.05	.67	.12	.31	.04	.74	−.09	.42
DRD4	−.03	.65	−.04	.57	−.05	.56	−.09	.41	−.12	.25	−.14	.20	.02	.90	.00	.99	−.02	.87
COMT	−.02	.78	.01	.87	.05	.54	−.11	.31	.02	.86	.18	.09	−.04	.74	−.11	.34	−.07	.56
Bi_5HTTLPR	.07	.36	.06	.41	.02	.76	−.09	.43	−.09	.41	−.05	.66	.20	.07	.21	.06	.15	.17
Tri_5HTTLPR	.12	.11	.09	.24	−.02	.77	.01	.92	−.01	.96	−.03	.81	.18	.11	.15	.18	−.01	.96
OXTR	−.04	.58	−.06	.42	−.07	.38	.07	.52	.07	.52	.04	.73	−.10	.38	−.14	.21	−.16	.17
Mean *r*	.03		.01		.02		−.03		−.03		−.01		.06		.03		−.03	
Disorganization																		
DRD2	−.11	.13	−.07	.37	.02	.84	−.17	.12	−.15	.17	−.12	.26	−.10	.37	.00	.99	.15	.18
DRD4	−.00	.98	.01	.91	.02	.79	−.04	.73	.01	.94	.07	.50	.04	.71	.03	.82	.00	1.00
COMT	−.01	.89	.01	.85	.04	.64	.09	.39	.04	.70	−.05	.61	−.08	.50	.03	.82	.12	.27
Bi_5HTTLPR	−.09	.22	−.08	.28	−.03	.72	−.01	.93	.03	.81	.06	.57	−.17	.13	−.18	.11	−.13	.23
Tri_5HTTLPR	−.02	.78	.01	.91	.04	.57	−.04	.70	−.01	.96	.05	.64	.02	.87	.05	.68	.05	.65
OXTR	.05	.53	.12	.11	**.18**	**.01**	−.08	.47	.02	.85	.16	.13	.14	.23	.18	.12	.18	.11
Mean *r*	−.03		.00		.05		−.04		−.01		.03		−.03		.02		.06	

Genetic dominance models

Results for genetic dominance models are presented in Table 4 (r_{dom} and p_{dom}). Similarly, none of the main effects of genetic associations on attachment security and attachment disorganization reached significance in the overall sample or in the European American/African-American samples. The average correlation between the polymorphisms and security or disorganization was trivial. One interaction between candidate genes and race reached statistical significance in the dominance models (Appendix, Supplementary Table 2). Biallelic 5HTTLPR interacted with child race to significantly predict attachment security scores ($\beta = .26$, $p = .05$). Specifically,

among European American infants, biallelic 5HTTLPR was unrelated to security (β = −.09, p = .41), whereas among African-American infants, carrying the S allele was marginally positively associated with security (β = .21, p = .06).

Heterozygous versus homozygous genetic association models

Results for associations between being homozygous on all polymorphisms and security and disorganization are presented in Table 4 (r_{hom} and p_{hom}). OXTR heterozygotes were significantly more likely to be disorganized in the full sample; this effect was not moderated by race (Appendix, Supplementary Table 3), and the coefficients were comparable, albeit not statistically significant either European American or African-American dyads. The average effect of being homozygous for the candidate genes was approximately zero for security and disorganization. No interactions between candidate genes and race reached statistical significance in the homozygosity models.

Table 5. Main and interaction effects between candidate genes and sensitivity on *attachment security*, genetic dominance models.

	Full sample				**European American**				**African-American**			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2												
DRD2	.09	.35	.02	.80	−.06	.51	−.01	.91	.13	.52	.03	.80
Sensitivity	.09	.12	.06	.43	.16	.18	.10	.38	.32	.21	.18	.12
DRD2 X Sens	−.09	.24	−.04	.71	.23	.38	.08	.56	−.50	.41	−.21	.23
DRD4												
DRD4	−.17	.35	−.04	.64	−.54	.48	−.12	.26	.14	.53	.03	.80
Sensitivity	.09	.12	.06	.43	.15	.18	.09	.39	.37	.21	.20	.08
DRD4 X Sens	−.46	.24	−.19	**.05**	−.55	.36	−.22	.14	−.36	.42	−.14	.40
COMT												
COMT	.08	.48	.01	.87	.04	.55	.01	.95	−1.16	.97	−.13	.24
Sensitivity	.10	.12	.06	.40	.16	.18	.10	.38	.38	.20	.21	.07
COMT X Sens	.13	.31	.08	.68	−.03	.40	−.01	.95	.03	.72	.02	.96
Bi_5HTTLPR												
Bi_5HTTLPR	.24	.35	.05	.50	−.47	.50	−.10	.35	.92	.50	.20	.07
Sensitivity	.09	.12	.06	.47	.18	.18	.11	.32	.34	.20	.18	.10
Bi_5HTT X Sens	−.19	.25	−.10	.44	−.40	.39	−.21	.30	.55	.40	.23	.18
Tri_5HTTLPR												
Tri_5HTTLPR	.46	.41	.09	.26	−.09	.54	−.02	.87	.74	.63	.13	.24
Sensitivity	.09	.12	.06	.45	.16	.18	.10	.37	.32	.20	.18	.12
Tri_5HTT X Sens	−.06	.29	−.03	.85	−.15	.43	−.08	.73	.49	.57	.25	.39
OXTR												
OXTR	−.28	.34	−.06	.41	.37	.46	.09	.43	−.73	.52	−.16	.17
Sensitivity	.09	.12	.06	.44	.18	.18	.11	.31	.35	.21	.19	.09
OXTR X Sens	−.19	.24	−.08	.43	−.20	.37	−.10	.59	−.86	.43	−.29	**.05**

Bold coefficients indicate significant at p < .05. Sen: maternal sensitivity across 6 months and age 1.

Maternal sensitivity × genotype interactions

Consistent with Luijk et al. (2011) and Roisman et al. (2013), we focused on genetic dominance models to examine interactions between candidate genes and maternal sensitivity predicting security (Table 5) and disorganization (Table 6). Maternal sensitivity was centered prior to analyses. Finally, three-way interactions among candidate genes, maternal sensitivity, and race were examined in the full sample (excluding nine mixed race children) to test whether interactions between candidate genes and maternal sensitivity were different across racial groups in the genetic dominance models (Appendix, Supplementary Table 4).

Table 6. Main and interaction effects between candidate genes and sensitivity on *attachment disorganization*, genetic dominance models.

	Full sample				**European American**				**African-American**			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2												
DRD2	−.30	.28	−.08	.28	−.57	.40	−.15	.15	.07	.42	.02	.87
Sensitivity	−.20	.09	−.16	**.03**	−.21	.14	−.15	.15	−.39	.17	−.26	**.02**
DRD2 X Sens	.01	.19	.01	.96	.24	.31	.11	.44	.19	.34	.09	.57
DRD4												
DRD4	−.04	.28	−.01	.88	.02	.39	.004	.97	−.08	.43	−.02	.86
Sensitivity	−.20	.09	−.16	**.03**	−.20	.14	−.15	.17	−.42	.17	−.28	**.01**
DRD4 X Sens	.03	.19	.02	.86	.19	.30	.09	.53	−.20	.34	−.10	.56
COMT												
COMT	.04	.37	.01	.92	.22	.43	.05	.61	.42	.80	.06	.60
Sensitivity	−.20	.09	−.16	**.03**	−.21	.14	−.15	.16	−.41	.17	−.27	**.01**
COMT X Sens	−.18	.24	−.13	.44	−.15	.32	−.10	.63	−.39	.59	−.24	.52
Bi_5HTTLPR												
Bi_5HTTLPR	−.19	.28	−.05	.49	.17	.40	.04	.68	−.61	.41	−.16	.14
Sensitivity	−.19	.09	−.15	**.05**	−.21	.15	−.15	.16	−.40	.16	−.26	**.02**
Bi_5HTT X Sens	.32	.19	.20	.09	.45	.31	.29	.16	.03	.33	.02	.92
Tri_5HTTLPR												
Tri_5HTTLPR	.10	.33	.02	.78	.05	.44	.01	.90	.36	.51	.08	.48
Sensitivity	−.20	.09	−.16	**.03**	−.20	.15	−.15	.17	−.42	.17	−.28	**.01**
Tri_5HTT X Sens	.20	.24	.14	.83	.31	.35	.21	.37	.51	.47	.31	.28
OXTR												
OXTR	.45	.27	.12	.10	−.004	.37	−.001	.99	.78	.43	.20	.07
Sensitivity	−.20	.09	−.16	**.03**	−.20	.15	−.15	.17	−.41	.16	−.27	**.01**
OXTR X Sens	.10	.19	.05	.58	.22	.30	.13	.48	.42	.35	.17	.24

Bold coefficients indicate significant at $p < .05$. Sen: maternal sensitivity across 6 month and age 1.

For the full sample, one significant two-way interaction between a candidate gene (DRD4) and maternal sensitivity was identified when predicting attachment security, $\beta = -.19$, $p = .05$. Specifically, maternal sensitivity was associated marginally with higher attachment security for infants without the DRD4 risk allele ($\beta = .18$, $p = .06$) but was not associated with attachment scores for infants with the DRD4 risk allele ($\beta = .12$, $p = .32$). No significant interactions between candidate genes and sensitivity were apparent among European American infants. However, there was a significant interaction between OXTR and maternal sensitivity in relation

to security among African-American infants, β = −.29, p = .05. Specifically, maternal sensitivity was associated with higher attachment security for African-American infants without OXTR risk allele (β = .35, p < .05) but was not associated with attachment security for African-American infants with the OXTR risk allele (β = −.12, p = .51).

No significant two-way interactions between candidate genes and maternal sensitivity were identified when predicting disorganization. No significant three-way interactions among candidate genes, maternal sensitivity, and race were identified when predicting either attachment security or disorganization, indicating the above two-way interaction between OXTR and sensitivity for African-American infants should be interpreted cautiously.

We also examined whether COMT homozygosity interacted with sensitivity in the prediction of security and disorganization as in Luijk et al. (2011) and Roisman et al. (2013). This interaction was not statistically significant in the full sample or among European American or African-American infants nor was there a significant three-way interaction between $COMT_{hom}$, sensitivity, and race (Appendix, bottom of Supplementary Table 4).

Table 7. Main and interaction effects between candidate genes and overtly negative maternal behavior on *attachment security*, genetic dominance models.

	Full sample				European American				African-American			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2												
DRD2	.12	.35	.03	.74	−.09	.50	−.02	.86	.22	.52	.05	.67
Overtly negative maternal behavior	−.13	.06	−.16	**.03**	−.13	.08	−.18	.10	−.13	.09	−.16	.17
DRD2 X Maternal behavior	.07	.12	.06	.56	.02	.22	.01	.92	.02	.19	.02	.92
DRD4												
DRD4	−.13	.35	−.03	.71	−.44	.48	−.10	.36	−.04	.52	−.01	.95
Overtly negative maternal behavior	−.12	.06	−.17	**.03**	−.12	.08	−.16	.14	−.14	.09	−.18	.12
DRD4 X Maternal behavior	.14	.11	.12	.22	.18	.16	.18	.26	.18	.20	.12	.37
COMT												
COMT	.03	.47	.00	.96	.04	.54	.01	.95	−1.16	.97	−.13	.24
Overtly negative maternal behavior	−.12	.06	−.17	**.03**	−.13	.08	−.18	.10	−.15	.09	−.19	.09
COMT X Maternal behavior	.21	.11	.21	.06	.22	.16	.21	.16	.24	.17	.24	.16
Bi_5-HTT												
Bi_5-HTT	.21	.34	.05	.55	−.46	.49	−.10	.35	.89	.51	.19	.08
Overtly negative maternal behavior	−.12	.06	−.17	**.03**	−.14	.08	−.18	.09	−.12	.09	−.16	.16
Bi_5-HTT X Maternal behavior	−.11	.11	−.12	.32	−.07	.17	−.08	.68	−.22	.18	−.17	.21
Tri_5-HTT												
Tri_5-HTT	.38	.41	.07	.35	−.16	.54	−.03	.76	.75	.63	.13	.24
Overtly negative maternal behavior	−.12	.06	−.16	**.03**	−.13	.08	−.18	.10	−.13	.09	−.16	.16
Tri_5-HTT X Maternal behavior	−.08	.13	−.09	.55	−.13	.18	−.14	.49	−.07	.19	−.07	.73
OXTR												
OXTR	−.23	.34	−.05	.51	.33	.45	.08	.47	−.55	.54	−.12	.31
Overtly negative maternal behavior	−.12	.06	−.16	**.04**	−.13	.08	−.18	.09	−.11	.09	−.13	.25
OXTR X Maternal behavior	.18	.11	.17	.13	.23	.16	.23	.14	.17	.19	.16	.37

Bold coefficients indicate significant at p < .05. Maternal behavior: Overtly negative maternal behavior across 6 months and age 1.

Overtly negative maternal behavior × genotype interactions

We also examined interactions between candidate genes and overtly negative maternal behavior predicting security (Table 7) and disorganization (Table 8). Overtly negative maternal behavior was centered prior to analyses. Three-way interactions among candidate genes, overtly negative maternal behavior, and race were examined in the full sample (excluding nine mixed race children) to test whether interactions between candidate genes and overtly negative maternal behavior were different across racial groups in the genetic dominance models (Appendix, Supplementary Table 5).

Table 8. Main and interaction effects between candidate genes and overtly negative maternal behavior on *attachment disorganization*, genetic dominance models.

	Full sample				**European American**				**African-American**			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2												
DRD2	−.30	.28	−.08	.28	−.55	.40	−.14	.17	−.05	.43	−.01	.91
Overtly negative maternal behavior	.12	.05	.18	**.01**	.10	.06	.15	.14	.12	.08	.18	.11
DRD2 X Maternal behavior	−.00	.09	−.00	.99	−.19	.18	−.12	.29	.09	.16	.10	.56
DRD4												
DRD4	−.02	.28	−.01	.93	−.06	.39	−.02	.88	.14	.43	.04	.75
Overtly negative maternal behavior	.11	.05	.18	**.02**	.10	.07	.16	.14	.12	.07	.19	.10
DRD4 X Maternal behavior	−.06	.09	−.07	.51	.00	.13	.00	.99	−.19	.16	−.15	.25
COMT												
COMT	.11	.37	.02	.77	.20	.43	.05	.64	.37	.81	.05	.65
Overtly negative maternal behavior	.11	.05	.18	**.02**	.10	.06	.16	.13	.12	.07	.19	.10
COMT X Maternal behavior	−.09	.09	−.11	.32	−.14	.13	−.17	.26	−.04	.15	−.05	.77
Bi_5-HTT												
Bi_5-HTT	−.24	.28	−.06	.39	.13	.40	.04	.74	−.62	.42	−.16	.14
Overtly negative maternal behavior	.11	.05	.17	**.02**	.10	.07	.16	.13	.10	.07	.17	.13
Bi_5-HTT X Maternal behavior	.05	.09	.06	.60	.15	.14	.20	.30	−.01	.15	−.01	.96
Tri_5-HTT												
Tri_5-HTT	.14	.33	.03	.69	.08	.44	.02	.86	.33	.53	.07	.53
Overtly negative maternal behavior	.11	.05	.18	**.02**	.10	.07	.16	.13	.12	.07	.18	.11
Tri_5-HTT X Maternal behavior	.03	.11	.04	.77	.17	.15	.24	.25	−.12	.16	−.15	.46
OXTR												
OXTR	.40	.27	.11	.14	.06	.37	.02	.88	.58	.44	.15	.20
Overtly negative maternal behavior	.11	.05	.18	**.02**	.10	.06	.16	.14	.11	.08	.15	.18
OXTR X Maternal behavior	−.06	.09	−.07	.53	−.16	.13	−.19	.23	.06	.16	.07	.71

Bold coefficients indicate significant at $p < .05$. Maternal behavior: Overtly negative maternal behavior across 6 month and age 1.

No significant interactions between candidate genes and overtly negative maternal behavior were identified when predicting attachment security or disorganization among the full sample, European American infants, or African-American infants. No significant three-way interactions among candidate genes, overtly negative maternal behavior, and race were identified when predicting either attachment security or disorganization, either.

We also examined whether COMT homozygosity interacted with overtly negative maternal behavior in the prediction of security and disorganization as in Luijk et al. (2011) and Roisman et al. (2013). This interaction was significant in the full sample such that overtly negative maternal behavior was associated with lower attachment security for COMT homozygous infants ($\beta = -.31$, $p < .01$) but was not for COMT heterozygous infants ($\beta = -.01$, $p > .05$). This interaction was not statistically significant among European American or African-American infants, nor was there a significant three-way interaction between $COMT_{hom}$, overtly negative maternal behavior, and race (Appendix, Supplementary Table 5).

Predicting emotion distress following Raby et al. (2012)

Finally, we examined the association between being grouped as a low versus high distress infant in the Strange Situation and candidate genes using genetic dominance models following Raby et al. (2012) and Roisman et al. (2013). No significant correlations were found between either biallelic or tri-allelic 5HTTLPR and being a low versus high distress infant (Supplementary Table 6). We also examined the interactions between polymorphisms in the candidate genes and race predicting distress classifications and no significant interaction effects emerged (Appendix, Supplementary Table 7).

Discussion

Consistent with recent larger sample studies, there was limited evidence of main effects of candidate genes related to dopamine, serotonin, and oxytocin on attachment security or disorganization whether additive, dominant, or homozygous models were employed (Luijk et al., 2011; Roisman et al., 2013). Consistent with Roisman et al. (2013), the average correlation between these genes and attachment outcomes was near zero across all models. Likewise, there was limited evidence that these candidate genes moderate associations between maternal sensitivity in distressing contexts and attachment outcomes. Notably, we formally tested race as a moderator, and very few of the tested two-way and three-way interactions involving race were statistically significant, consistent with our view that observed associations would be more similar than different between European American and African-American dyads. We elaborate on specific findings below.

The single main effect, out of 108 tested in relation to security or disorganization, was between $OXTR_{hom}$ and disorganization. In the full sample, heterozygotes were rated significantly higher on disorganization than homozygotes. The association was comparable in magnitude in the separate analyses for European American and African-American dyads but was not statistically significant given the small samples. The full sample association, although significant, was small in magnitude, and is not consistent with prior null findings for $OXTR_{hom}$and attachment outcomes (Roisman et al., 2013). Moreover, in most prior research, OXTR risk has primarily operated in dominant fashion (e.g., Smearman, Winiarski, Brennan, Najman, & Johnson, 2015); thus, in the absence of replication, this result should be interpreted with caution. Additionally, consistent with Roisman et al. (2013), none of the candidate genes distinguished between infants classified in the high versus low distress attachment groups. Thus, we did not replicate Raby et

al.'s (2012) finding that infants with tri-allelic 5HTTLPR S alleles are more likely to be classified in the high distress groups (i.e., B3/B4 or resistant).

The single two-way interaction between a candidate genes and race, out of 14 tested, involved biallelic 5HTTLPR and security. Biallelic 5HTTLPR was unrelated to security among European American infants; but among African-American infants, carrying the S allele was marginally associated with higher security. This is a counterintuitive finding given the S allele is typically considered an indicator of risk for maladaptive outcomes of this type (Yildirim & Derksen, 2013). Moreover, in other primarily nonwhite samples, carrying the S allele was either unrelated to attachment outcomes (Roisman et al., 2013) or associated with attachment disorganization (Cicchetti et al., 2011, among the non-maltreated group only). Of note, we did not replicate Roisman et al.'s (2013) finding that $DRD4_{add}$ and $DRD4_{hom}$were associated with disorganization among nonwhite infants, reiterating their point that such associations should be viewed skeptically, unless replicated, particularly when observed in such small samples.

Only 2 of 39 tested interactions (36 dominance models and 3 $COMT_{hom}$ models) between candidate genes and maternal sensitivity during distressing contexts were statistically significant. First, DRD4 and maternal sensitivity interacted to predict attachment security in the full sample, and this effect was not qualified by race. Specifically, maternal sensitivity in distressing contexts was marginally positively associated with attachment security among infants without the DRD4 risk allele (7+), but not among infants with the risk allele. This finding replicates a pattern first observed in the white subsample of the SECCYD (Luijk et al., 2011). However, it is important to note that the difference in the beta for those with and without the risk allele was very modest in this sample (.18 versus .12), and this finding has not been observed in other samples (Cicchetti et al., 2011; Luijk et al., 2011; Generation R sample; Roisman et al., 2013). Second, OXTR and sensitivity interacted in relation to attachment security among African-American infants only. Specifically, maternal sensitivity was associated with higher attachment security among African-American infants without the risk allele (GG), but not among risk allele carriers (A). This finding is inconsistent with Roisman et al.'s (2013) null finding in the non-white subsample, but is consistent with the view that the G allele is a susceptibility allele such that those infants with the GG allele are more strongly affected by the environment. However, there is no reason to expect this to be the case for African-American infants more so than European American infants. That the interaction is not significant in the full sample and the three-way interaction between OXTR, sensitivity and race was not statistically significant calls into question the appropriateness of interpreting this two-way interaction among African-American infants. When considering main effects, it is notable that maternal sensitivity was associated with lower attachment disorganization in the full sample (as a simple correlation and in the regression models), but not with higher attachment security. This is in contrast to prior research in which sensitivity has tended to predict attachment security more so than disorganization (Gedaly & Leerkes, 2016).

One of the 39 tested interactions between genes and overtly negative maternal behavior was statistically significant in relation to attachment outcomes. That is, COMT homozygosity moderated the association between overtly negative maternal behavior and attachment security such that negative maternal behavior was associated with lower security among COMT homozygotes only. This finding is in contrast to those reported by Luijk et al. (2011), who reported that sensitivity was only associated with lower disorganization among COMT

heterozygotes, and only in the Generation R sample. Furthermore, in our sample, the interaction was only significant in the full sample, and only if race was a covariate suggesting some type of suppressor effect. Thus, evidence that COMT plays an important role in the developing attachment relationship remains inconsistent. That we considered overtly negative maternal behavior, the type of behavior more frequently found to be associated with attachment disorganization, in conjunction with these candidate genes was a novel feature of this study. Although there was limited evidence of genetic moderation, overtly negative maternal behavior was associated with lower security and higher disorganization in the full sample as a simple correlation and in the regression models underscoring the importance of egregious forms of insensitivity characterized by negativity for the developing attachment relationship.

In sum, out of the many analyses conducted, extremely few were statistically significant. Moreover, we generally did not replicate significant effects of candidate genes reported in other small sample studies focused on the same variants, and the few significant effects we observed are generally inconsistent with prior research. Thus, these results add to accumulating evidence that these particular variants of these candidate genes play little if any direct role in infant–mother attachment. This is not entirely surprising given this phenotype is far removed from the biological function of these genes. Perhaps if there is any effect of these genes on attachment, they may be indirect via genetically linked individual differences in affect, cognition, and in particular social cognition that may play a role in shaping parent–child interaction, and perhaps the child's interpretation and representation of such interactions. Additionally, given genetic heterogeneity, it is not particularly surprising that a small set of well-studied polymorphisms of candidate genes are unrelated to this phenotype. In particular, relatively rare variants that may be *de novo* (i.e., new/recent mutations) and occur at low base rates in the general population, could be of interest. Thus, alternative design approaches may be useful in future exploration of the role of genetics in attachment. For example, in a recent study using genome wide gene-based analyses (i.e., multiple single-nucleotide polymorphisms (SNPs) within a gene are considered rather than just a single SNP), three novel genes were statistically significant in relation to attachment disorganization and one novel gene was statistically significant in relation to attachment security post-Bonferroni correction (Pappa et al., 2015). Alternatively, participants (parents and their children) may be selected for whole genome scans based on whether a family has no, one or multiple insecure/disorganized children (and perhaps parents) to determine if specific variants distinguish between insecure/disorganized versus secure/organized individuals within a family or in the sample as whole as has been done in the study of autism (Sebat et al., 2007). Such an approach has the advantage of requiring a smaller sample than traditional genome-wide association studies. Finally, considering joint effects of maternal and infant genotypes on attachment outcomes would be a novel approach. It is possible that infants are more likely to be insecure or disorganized if both members of the dyad carry specific "risk" alleles than if one or no members of the dyad carry specific risk alleles. However, this approach would still require large samples assuming small effect sizes.

An important limitation of this study is the small sample size, particularly in the subgroup analyses. As such, our analyses are underpowered to detect small effects as noted by Roisman et al. (2013). Moreover, our full sample is composed equally of two different racial groups, when homogenous samples are preferred in molecular genetic work (Cardon & Palmer, 2003). That said, we took great care to examine the possibility of race differences, and found extremely little

evidence that such differences exist in relation to infant attachment outcomes. Despite these concerns, we believe that presenting the results from small sample candidate gene studies is valuable to facilitate meta-analyses and integrative data analyses in the future. We took great care to replicate the analytic approach of prior studies, particularly Roisman et al. (2013) to facilitate these efforts.

Strengths of this study include the careful observation of maternal sensitivity and overtly negative maternal behavior in distressing contexts aggregated across two time points, which likely yields more reliable measures. This approach is novel in that we are the first to specifically test these genes as moderators of maternal sensitivity and overtly negative maternal behavior during distress-eliciting tasks in relation to attachment outcomes. Such an approach is useful given evidence that sensitivity to distress is a stronger predictor of attachment security than are other measures of sensitivity (Leerkes, 2011; McElwain & Booth-LaForce, 2006) and that more anomalous/egregious forms of insensitivity may be particularly relevant for the development of attachment disorganization (Madigan et al., 2006). In this regard, our results suggest these specific polymorphisms of dopamine, serotonin, and oxytocin candidate genes do not moderate the associations between sensitivity to distress or overtly negative maternal behavior and attachment outcomes any more or differently than they do between sensitivity to non-distress and attachment outcomes. Additionally, this is the second study to examine tri-allelic 5HTTLPR in relation to attachment security (Raby et al., 2012) and the first in relation to attachment disorganization and demonstrates no main effect or interactive effects with sensitivity to distress in relation to infant attachment outcomes.

In conclusion, the results of this study add to accumulating evidence that these specific polymorphisms in candidate genes related to dopamine, serotonin, and oxytocin play little role in the formation of early infant–mother attachment relationships.

Acknowledgments
This work was supported by the Eunice Kennedy Shriver National Institute for Child Health and Human Development (NICHD) under R01HD058578 and R21HD073594. The contents of this article are the sole responsibility of the authors and do not necessarily reflect the views of NICHD. We are grateful to the participants for their time and Dr. Regan Burney and project staff for their dedication.

Disclosure statement
No potential conflict of interest was reported by the authors.

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APPENDIX

Table 1A. Interaction effects between candidate genes and race for additive risk models for attachment security and disorganization scores, additive genetic models

	Security				Disorganization			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2								
DRD2	.06	.49	.02	.90	–.60	.40	–.20	.13
Race	.47	.36	.11	.20	–.004	.29	–.001	.99
DRD2 X Race	.31	.61	.07	.61	.32	.49	.09	.51
DRD4								
DRD4	–.29	.36	–.08	.43	–.10	.30	–.03	.74
Race	.54	.34	.12	.11	–.18	.28	–.05	.54
DRD4 X Race	.35	.56	.06	.63	.23	.45	.05	.61
COMT								
COMT	–.34	.35	–.11	.33	.23	.28	.09	.41
Race	.63	.36	.14	.08	–.16	.30	–.04	.58
COMT X Race	.21	.52	.04	.69	–.46	.43	–.11	.29
Di_5-HTT								
Di_5-HTT	–.26	.34	–.08	.45	–.03	.28	–.01	.93
Race	.61	.35	.14	.08	–.26	.29	–.07	.37
Di_5-HTT X Race	.93	.49	.20	.06	–.45	.41	–.12	.27
Tri_5-HTT								
Tri_5-HTT	.03	.33	.01	.92	–.10	.27	–.04	.71
Race	.51	.34	.12	.14	–.18	.28	–.05	.53
Tri_5-HTT X Race	.56	.48	.12	.25	.15	.40	.04	.70
OXTR								
OXTR	.20	.32	.06	.54	–.18	.26	–.07	.49

	Security				Disorganization			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
Race	.53	.35	.12	.13	–.13	.28	–.04	.65
OXTR X Race	–.54	.49	–.11	.27	.57	.40	.14	.16

Note. Additive models are presented. *B*, changes in security and disorganization scores per unit change in the predictor.

Table 2A. Interaction effects between candidate genes and race on attachment security and disorganization scores, genetic dominance models

Gene X Race	**Security**				**Disorganization**			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2								
DRD2	–.07	.53	–.02	.90	–.56	.42	–.15	.19
Race	.43	.45	.10	.96	–.31	.37	–.09	.39
DRD2 X Race	.24	.73	.05	.74	.56	.59	.13	.34
DRD4								
DRD4	–.56	.50	–.12	.27	.03	.41	.01	.94
Race	.35	.43	.08	.41	–.21	.36	–.06	.57
DRD4 X Race	.55	.71	.10	.44	.07	.58	.02	.90
COMT								
COMT	–.18	.48	–.03	.72	.18	.39	.04	.66
Race	.56	.35	.13	.11	–.19	.29	–.05	.51
COMT X Race	–1.04	1.10	–.23	.35	.02	.90	.01	.98
Di_5-HTT								
Di_5-HTT	–.41	.51	–.09	.42	.10	.42	.03	.82
Race	–.20	.54	–.05	.71	.21	.44	.06	.64
Di_5-HTT X Race	1.38	.71	.26	**.05**	–.78	.58	–.18	.18
Tri_5-HTT								
Tri_5-HTT	–.03	.56	–.01	.96	–.02	.46	–.01	.96
Race	–.17	.73	–.04	.82	–.37	.60	–.10	.54
Tri_5-HTT X Race	.89	.82	.19	.28	.24	.68	.06	.72
OXTR								
OXTR	.29	.47	.07	.54	.07	.38	.02	.85
Race	.95	.46	.21	.04	–.38	.38	–.10	.32
OXTR X Race	–.96	.69	–.17	.17	.62	.57	.13	.28

Note. Bold coefficients indicate significant at $p < .05$.

Table 3A. Interaction effects between candidate genes and race on attachment security and disorganization scores, heterozygous vs. homozygous genetic association models

Gene X Race	**Security**				**Disorganization**			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD2								
DRD2	–.33	.37	–.07	.37	.07	.30	.02	.81
Race	.57	.34	.13	.10	–.16	.28	–.04	.58
DRD2 X Race	–.23	.74	–.04	.76	1.06	.60	.22	.08
DRD4								

Gene X Race	Security				Disorganization			
Gene	***B***	***SE***	**β**	***p***	***B***	***SE***	**β**	***p***
DRD4	–.37	.38	–.08	.33	.14	.31	.04	.65
Race	.58	.34	.13	.10	–.19	.28	–.05	.51
DRD4 X Race	.58	.76	.10	.44	–.29	.62	–.06	.64
COMT								
COMT	.26	.34	.06	.45	.12	.28	.03	.67
Race	.56	.34	.13	.10	–.15	.28	–.04	.60
COMT X Race	–1.08	.68	–.19	.12	.67	.56	.14	.24
Di_5-HTT								
Di_5-HTT	.23	.35	.05	.52	–.12	.29	–.03	.67
Race	.57	.35	.13	.10	–.19	.28	–.05	.50
Di_5-HTT X Race	.93	.70	.16	.18	–.74	.57	–.15	.20
Tri_5-HTT								
Tri_5-HTT	–.07	.34	–.02	.84	.18	.28	.05	.51
Race	.54	.34	.12	.12	–.18	.28	–.05	.53
Tri_5-HTT X Race	.09	.69	.02	.90	.02	.56	.01	.97
OXTR								
OXTR	–.26	.37	–.06	.48	.66	.30	.17	**.03**
Race	.52	.34	.12	.13	–.10	.28	–.03	.72
OXTR X Race	–.96	.74	–.15	.20	.18	.60	.03	.77

Note. Bold coefficients indicate significant at $p < .05$.

Table 4A. Interaction effects of candidate genes, sensitivity, and race on attachment security and disorganization scores, genetic dominance models

		Security					Disorganization				
Gene		**ΔR^2**	***B***	***SE***	**β**	***p***	**ΔR^2**	***B***	***SE***	**β**	***p***
DRD2											
Step 1	DRD2	.03	.05	.36	.01	.89	**.05**	–.25	.29	–.07	.38
	Sensitivity		.24	.14	.15	.08		–.29	.11	–.23	**.01**
	Race		.87	.40	.19	**.03**		–.52	.33	–.14	.11
Step 2	DRD2 X Sens	.004	–.13	.28	–.05	.63	.02	.22	.23	.11	.34
	DRD2 X Race		–.002	.83	.00	.99		.96	.67	.22	.15
	Sense X Race		.19	.28	.08	.50		–.22	.22	–.11	.32
Step 3	DRD2 X Sens X Race	.01	–.72	.56	–.22	.20	.00	–.05	.45	–.02	.92
DRD4											
Step 1	DRD4	.04	–.22	.35	–.05	.53	**.05**	–.01	.43	.003	.98
	Sensitivity		.24	.14	.16	.07		–.30	.11	–.24	**.01**
	Race		.91	.39	.20	**.02**		–.63	.32	–.17	**.05**
Step 2	DRD4 X Sens	.02	–.46	.28	–.19	.10	.01	.01	.22	.003	.98
	DRD4 X Race		–.01	.82	–.002	.99		–.08	.68	–.02	.91
	Sense X Race		.23	.27	.10	.40		–.22	.22	–.11	.32
Step 3	DRD4 X Sens X Race	.001	.19	.55	.06	.73	.004	–.39	.45	–.14	.39
COMT											
Step 1	COMT	.04	–.29	.48	–.05	.55	**.05**	.27	.38	.05	.48
	Sensitivity		.26	.13	.17	.06		–.30	.11	–.24	**.01**
	Race		.95	.40	.21	**.02**		–.66	.33	–.18	**.05**

		Security					Disorganization				
Gene		**ΔR^2**	***B***	***SE***	**β**	***p***	**ΔR^2**	***B***	***SE***	**β**	***p***
Step 2	COMT X Sens	.01	–.01	.35	–.01	.97	.01	–.21	.28	–.15	.46
	COMT X Race		–1.22	1.26	–.27	.34		–.18	1.04	–.05	.86
	Sense X Race		.22	.28	.09	.43		–.16	.23	–.08	.48
Step 3	COMT X Sens X Race	.00	.06	.81	.02	.94	.001	–.23	.66	–.11	.73
Di_5-HTT											
Step 1	Di_5-HTT	.04	.24	.36	.05	.49	**.05**	–.23	.29	–.06	.43
	Sensitivity		.24	.13	.16	.07		–.29	.11	–.23	**.01**
	Race		.95	.40	.21	**.02**		–.67	.32	–.18	**.04**
	Sense X Race		.17	.27	.07	.78		–.15	.22	–.08	.30
Step 2	Di_5-HTT X Sens	.03	.08	.28	.04	.07	.02	.24	.23	.15	.49
	Di_5-HTT X Race		1.49	.80	.28	.54		–.45	.65	–.10	.50
Step 3	Di_5-HTT X Sens X Race	.02	.95	.56	.29	.09	.01	–.42	.46	–.16	.36
Tri_5-HTT											
Step 1	Tri_5-HTT	.04	.29	.41	.05	.48	**.05**	.20	.34	.05	.56
	Sensitivity		.24	.14	.16	.08		–.31	.11	–.25	**.01**
	Race		.87	.39	.20	**.03**		–.64	.32	–.17	**.05**
	Sense X Race		.15	.27	.06	.77		–.25	.22	–.13	.17
Step 2	Tri_5-HTT X Sens	.01	.10	.34	.06	.32	.02	.39	.28	.28	.26
	Tri_5-HTT X Race		.98	.97	.21	.58		.89	.79	.24	.25
Step 3	Tri_5-HTT X Sens X Race	.01	.64	.71	.25	.37	.001	–.25	.22	–.13	.74
OXTR											
Step 1	OXTR	.03	–.12	.35	–.03	.73	**.05**	.32	.28	.09	.25
	Sensitivity		.23	.14	.15	.09		–.28	.11	–.23	**.01**
	Race		.86	.40	.19	**.03**		–.52	.32	–.14	.11
Step 2	OXTR X Sens	.04	–.50	.28	–.21	.08	.03	.31	.23	.16	.19
	OXTR X Race		–1.81	.80	–.31	**.03**		1.24	.65	.26	.06
	Sense X Race		.02	.28	.01	.96		–.12	.23	–.06	.61
Step 3	OXTR X Sens X Race	.01	–.65	.57	–.16	.25	.001	.20	.46	.06	.66
Step 1	$COMT_{homo}$	.04	.23	.34	.05	.50	**.05**	.15	.28	.04	.59
	Sensitivity		.24	.13	.16	.07		–.30	.11	–.24	**.01**
	Race		.91	.39	.21	**.02**		–.59	.32	–.16	.07
Step 2	$COMT_{homo}$ X Sens	.02	.20	.27	.09	.46	.01	–.01	.22	–.01	.95
	$COMT_{homo}$ X Race		–.71	.79	–.13	.37		.57	.65	.12	.38
	Sense X Race		.23	.27	.10	.39		–.21	.22	–.11	.35
Step 3	$COMT_{homo}$ X Sens X Race	.00	.35	.54	.10	.52	.001	.47	.44	.16	.29

Note. Bold coefficients indicate significant at $p < .05$. Sen: maternal sensitivity across 6 months and age 1.

Table 5A. Interaction effects of candidate genes, overtly negative behavior, and race on attachment security and disorganization scores, genetic dominance models

		Security					Disorganization				
Gene		**ΔR^2**	***B***	***SE***	**β**	***p***	**ΔR^2**	***B***	***SE***	**β**	***p***
DRD2											
Step 1	DRD2	.04	.07	.36	.02	.84	.04	–.29	.29	–.08	.32
	Overtly negative maternal behavior		–.13	.06	–.17	**.03**		.11	.05	.17	**.03**

		Security					Disorganization				
Gene		**ΔR^2**	***B***	***SE***	**β**	***p***	**ΔR^2**	***B***	***SE***	**β**	***p***
	Race		.61	.35	.14	.09		–.16	.29	–.04	.57
Step 2	DRD2 X Maternal behavior	.00	.02	.14	.02	.89	.01	–.02	.12	–.02	.88
	DRD2 X Race		.30	.73	.06	.69		.51	.59	.12	.39
	Maternal behavior X Race		–.01	.14	–.01	.95		.04	.11	.04	.74
Step 3	DRD2 X Maternal behavior X Race	.00	–.00	.29	–.00	.99	.00	.28	.24	.23	.24
DRD4											
Step 1	DRD4	.05	–.23	.35	–.05	.51	.03	.03	.29	.01	.91
	Overtly negative maternal behavior		–.13	.06	–.17	**.02**		.11	.05	.17	**.03**
	Race		.66	.34	.15	.06		–.26	.28	–.07	.35
Step 2	DRD4 X Maternal behavior	.01	.18	.12	.15	.15	.01	–.08	.10	–.08	.43
	DRD4 X Race		.30	.71	.05	.68		.25	.59	.05	.68
	Maternal behavior X Race		.03	.12	.03	.80		.00	.10	.00	.99
Step 3	DRD4 X Maternal behavior X Race	.00	–.00	.25	–.00	.99	.01	–.19	.21	–.11	.37
COMT											
Step 1	COMT	.05	–.28	.48	–.05	.57	.03	.25	.39	.05	.53
	Overtly negative maternal behavior		–.14	.06	–.18	**.02**		.11	.05	.17	**.02**
	Race		.68	.35	.15	**.05**		–.29	.29	–.08	.32
Step 2	COMT X Maternal behavior	.02	.22	.12	.21	.06	.01	–.10	.10	–.12	.30
	COMT X Race		–.30	.50	–.05	.55		.43	.41	.09	.30
	Maternal behavior X Race		–.01	.12	–.01	.94		.02	.10	.02	.86
Step 3	COMT X Maternal behavior X Race	.00	.00	.23	.00	.99	.00	.09	.19	.07	.64
Step 1	Di_5-HTT	.05	.23	.35	.05	.51	.04	–.25	.29	–.07	.38
	Overtly negative maternal behavior		–.13	.06	–.17	**.03**		.10	.05	.17	**.03**
	Race		.70	.35	.16	**.05**		–.32	.29	–.09	.27
Step 2	Di_5-HTT X Maternal behavior	.03	–.15	.12	–.15	.22	.01	.07	.10	.08	.51
	Di_5-HTT X Race		1.44	.71	.27	**.04**		–.79	.58	–.18	.18
	Maternal behavior X Race		–.04	.12	–.04	.76		.03	.10	.04	.74
Step 3	Di_5-HTT X Maternal behavior X Race	.00	–.15	.25	–.09	.54	.00	–.16	.21	–.10	.45
Tri_5-HTT											
Step 1	Tri_5-HTT	.05	.25	.41	.05	.54	.03	.19	.34	.04	.57
	Overtly negative maternal behavior		–.13	.06	–.17	**.03**		.11	.05	.17	**.03**
	Race		.62	.34	.14	.07		–.26	.28	–.07	.36
Step 2	Tri_5-HTT X Maternal behavior	.01	–.10	.13	–.11	.47	.00	.03	.11	.03	.82
	Tri_5-HTT X Race		.97	.83	.21	.24		.24	.69	.06	.73
	Maternal behavior X Race		.01	.12	.01	.97		.02	.10	.02	.83
Step 3	Tri_5-HTT X Maternal behavior X Race	.00	.06	.26	.04	.83	.01	–.29	.22	–.27	.18
OXTR											
Step 1	OXTR	.04	–.07	.35	–.02	.84	.04	.29	.28	.08	.30
	Overtly negative maternal behavior		–.13	.06	–.16	**.04**		.10	.05	.16	**.04**
	Race		.61	.35	.14	.08		–.18	.28	–.05	.54
Step 2	OXTR X Maternal behavior	.03	.21	.12	.20	.09	.01	–.06	.10	–.07	.55
	OXTR X Race		–1.01	.70	–.18	.15		.57	.58	.12	.33
	Maternal behavior X Race		.01	.12	.01	.92		.01	.10	.01	.92
Step 3	OXTR X Maternal behavior X Race	.00	–.06	.25	–.04	.81	.01	.22	.20	.17	.29
Step 1	$COMT_{hom}$	**.05**	.28	.34	.06	.41	.03	.10	.28	.03	.72

		Security					Disorganization				
Gene		**ΔR^2**	***B***	***SE***	**β**	***p***	**ΔR^2**	***B***	***SE***	**β**	***p***
	Overtly negative maternal behavior		–.13	.06	–.17	**.02**		.11	.05	.17	**.03**
	Race		.67	.34	.15	**.05**		–.23	.28	–.06	.41
Step 2	$COMT_{hom}$ X Maternal behavior	.04	.23	.11	.22	**.05**[1]	.01	–.10	.10	–.12	.28
	$COMT_{hom}$ X Race		–1.17	.68	–.21	.09		.68	.56	.15	.23
	Maternal behavior X Race		–.01	.11	–.01	.92		.02	.10	.02	.86
Step 3	$COMT_{hom}$ X Maternal behavior X Race	.00	–.04	.23	–.03*	.85	.00	.11	.19	.09	.58

Note. Bold coefficients indicate significant at $p < .05$. Maternal behavior: Overtly negative maternal behavior across 6 months and age 1.

[1]The interaction between $COMT_{hom}$ and negative maternal behavior was not statistically significant in a model that did not include race suggesting this may be a suppressor effect. Nevertheless, we interpreted the interaction. Overtly negative maternal behavior was associated with lower attachment security for COMT homozygous infants ($\beta = –.31$, $p < .01$) but was not for COMT heterozygous infants ($\beta = –.01$, $p > .05$).

Table 6A. Main effects of candidate genes on emotional distress by group, genetic dominance models

	Full Sample		***European American***		***African American***	
Gene	**r_{dom}**	**p_{dom}**	**r_{dom}**	**p_{dom}**	**r_{dom}**	**p_{dom}**
DRD2	–.004	.96	–.07	.51	.06	.59
DRD4	.08	.31	.09	.41	.01	.96
COMT	.05	.52	.02	.87	.13	.26
Di_5-HTT	.09	.24	.09	.40	.06	.60
Tri_5-HTT	.02	.78	.10	.34	–.08	.45
OXTR	–.09	.26	–.15	.16	.04	.73
Mean *r*	.02		.01		.04	

Table 7A. Interaction effects between candidate genes and race on emotional distress, genetic dominance models

Gene X Race	**Emotional distress**		
Gene	***B***	***SE***	***p***
DRD2			
DRD2	–.03	.33	.94
Race	–.11	.32	.72
DRD2 X Race	–.21	.25	.81
DRD4			
DRD4	.20	.32	.53
Race	–.15	.31	.62
DRD4 X Race	–.43	.26	.10
COMT			
COMT	.31	.44	.48
Race	–.21	.32	.51
COMT X Race	1.14	1.23	.35
Di_5-HTT			
Di_5-HTT	.32	.33	.33

Gene X Race	Emotional distress		
Gene	***B***	***SE***	***p***
Race	–.07	.32	.84
Di_5-HTT X Race	–.16	.65	.81
Tri_5-HTT			
Tri_5-HTT	.08	.38	.84
Race	–.14	.31	.65
Tri_5-HTT X Race	–.91	.75	.23
OXTR			
OXTR	–.26	.32	.42
Race	–.16	.31	.62
OXTR X Race	.77	.63	.23