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Associations of the Oxytocin Receptor Gene (OXTR) and Emotional Reactions to Betrayal in an Iterated Prisoner's Dilemma

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ASSOCIATIONS OF THE OXYTOCIN RECEPTOR GENE (OXTR) AND EMOTIONAL REACTIONS TO BETRAYAL IN AN ITERATED PRISONER'S DILEMMA

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Recent research has shown that variation in the gene encoding for the oxytocin receptor (OXTR) contributes to individual differences in social-cognitive and emotional functioning in both clinical and non-clinical populations. OXTR has been associated with prosocial behavior, positive and negative emotionality, empathy, maternal sensitivity, and stress reactivity. To date, no study has investigated OXTR in the context of behavioral and emotional reactions to betrayals in trust. The present study examined how variation in 10 SNPs on OXTR may contribute to individual differences in behavior, emotional reactions, and perceptions following a betrayal in trust in an iterated prisoner's dilemma game. Following correction for multiple testing, one SNP (rs237887) and two haplotypes (A-rs237887, C-rs2268490; G-rs237887, C-rs2268490) were significantly associated with positive emotional reactions to betrayal. In addition, one haplotype (C-rs9840864, T-rs2268490) was significantly associated with negative emotional reactions to betrayal. The present findings suggest that variation on OXTR may contribute to individual differences in emotional reactions to betrayals in trust.

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CHAPTER ONE: INTRODUCTION:

The neurohypophysial peptide oxytocin has a pervasive role in mammalian parturition, lactation, maternal care, pair bonding, social approach and motivation, and social recognition (for reviews see, Bartz & Hollander, 2006; Donaldson & Young, 2008; Lee, Macbeth, Pagani, & Young, 2009; Lim & Young, 2006). Research in humans has associated endogenous oxytocin with maternal attachment (Levine, Zagoory-Sharon, Feldman, & Welller, 2007; Strathearn, Fonagy, Amico, & Montague, 2009), bonding behaviors (Feldman, Weller, Zagoory-Sharon, & Levine, 2007), and decreased response to stress following affiliative contact (Light, Grewen, & Amico, 2005). Intranasal administration of oxytocin appears to increase trust (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), the perceived trustworthiness of strangers (Theodoridou, Rowe, Penton-Voak, & Rogers, 2009), generosity (Zak, Stanton, & Ahmadi, 2007), the ability to infer others' mental states by interpreting subtle social cues (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007), visual attention to the eye regions of human faces (Guastella, Mitchell, & Dadds, 2008), and constructive communication in couples (Ditzen, et al., 2009). Oxytocin also appears to alleviate physiological stress responses when combined with social support (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003). Furthermore, recent fMRI research suggests that the administration of oxytocin may dampen neural systems associated with social fear (Kirsch, et al., 2005; Petrovic, Kalisch, Singer, & Dolan, 2008), which may increase perceived sympathy (Petrovic, et al., 2008), and decrease aversion to betrayal (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008).

The social effects of oxytocin have significant implications for understanding the biological mechanisms underlying social processes in humans, as well as for identifying risk and protective factors associated with social deficit disorders or disorders characterized by social withdrawal such as Autism Spectrum Disorders (ASDs; Bartz & Hollander, 2008; Carter, 2007; Insel, O'Brien, & Leckman, 1999) and major depression (e.g., Cyranowski, et al., 2008; Ozsoy, Esel, & Kula, 2009). For example, studies suggest that people with ASDs may have lower levels of endogenous oxytocin than controls (Green, et al., 2001; Modahl, et al., 1998), and intranasal administration of oxytocin has decreased repetitive behaviors (Hollander, et al., 2003) and increased the processing and retention of social information in people with ASDs (Hollander, et al., 2007). Similarly, research has found lower levels of endogenous oxytocin (Ozsoy, et al., 2009) and dysregulation in oxytocin secretion (Cyranowski, et al., 2008) among females with major depression in comparison to controls.

Although research has demonstrated the influence of oxytocin on many aspects of social behavior, studies of endogenous oxytocin may not reflect levels of central oxytocin (Neumann, 2008), and recent evidence suggests that there are significant limitations associated with commonly used methods to measure oxytocin (Szeto, et al., in press). In addition, exogenously administered levels of oxytocin may not represent normative physiological levels (Donaldson & Young, 2008; Neumann, 2008) or socially relevant changes in natural levels of oxytocin (Taylor, 2008). For these reasons, studying genetic differences in OXTR provides unique advantages to endogenous measurement or exogenous administration studies.

The Oxytocin Receptor Gene (OXTR) and Social Behavior

Oxytocin gene expression occurs predominantly in the magnocellular neurons of the hypothalamic paraventricular and supraoptic nuclei, and oxytocin is stored and released into the peripheral blood stream via the posterior pituitary (Amico, 2008; Gimpl & Fahrenholz, 2001; Lee, et al., 2009). Unlike vasopressin, which differs from oxytocin on two amino acids and which has three different receptors, oxytocin has only one identified receptor (Lee, et al., 2009). This receptor, known as OXTR, is distributed throughout the brain of many species (for review see, Lee, et al., 2009), primarily in the amygdala, hippocampus, olfactory lobe, and hypothalamus (Amico, 2008; Gimpl & Fahrenholz, 2001), and is expressed in a variety of tissues including the heart, kidney, brain, and uterus (Gimpl & Fahrenholz, 2001). Different patterns of brain oxytocin receptor expression have been found in monogamous vole species in comparison to polygamous voles (Insel & Shapiro, 1992), and recent evidence indicates that these differences in receptor expression have an impact on social behavior. For example, overexpression of OXTR in the nucleus accumbens accelerates partner preference formation in monogamous prairie voles, but not in polygamous meadow voles (Ross, et al., 2009). In addition, OXTR density in the nucleus accumbens of female prairie voles plays a role in the facilitation of maternal behavior such as licking and grooming pups (a behavior uncharacteristic of polygamous species; Olazábal & Young, 2006).

Oxytocin is regulated by steroid hormones such as estrogen and testosterone (for reviews see, Gimpl & Fahrenholz, 2001; Lee, et al., 2009), which also contribute to sex differences in the expression of OXTR (Carter, 2007; Carter, Boone, Pournajafi-Nazarloo, & Bales, 2009; Shepard, Michopoulos, Toufexis, & Wilson, 2009). For

example, in a study of maternal care in rats, Francis, Young, Meaney, and Insel (2002) found that higher levels of maternal licking and grooming were associated with increased OXTR binding in several brain regions (i.e., the central nucleus of the amygdala and the bed nucleus of the stria terminalis) in female but not male offspring. Thus, epigenetic effects of OXTR expression appear to be sexually dimorphic.

OXTR, Social Cognition and Behavior

Following the identification of the 3p24-25 regions, which includes OXTR, as potential linkage sites involved in the etiology of ASDs (Lauritsen, et al., 2006; McCauley, et al., 2005; Ylisaukko-oja, et al., 2006), several studies have found associations among markers on OXTR and clinical disorders including ASDs (Gregory, et al., 2009; Jacob, et al., 2007; Lerer, et al., 2008; Liu, et al., 2010; Wu, et al., 2005; Yrigollen, et al., 2008) and major depression (B. Costa, et al., 2009; Riem, et al., in press; Thompson, et al., 2011). Building on this evidence, research has indicated that the role of OXTR in social-cognitive and emotional processes may extend beyond clinical disorders. As discussed by Taylor (2008), the study of oxytocin in non-clinical populations may increase our understanding of the range of phenotypic variation in social behavior. In a single-marker study, Kim et al. (2010) examined the association of rs53576 and cross-cultural differences in emotional support seeking among Americans and Koreans. The authors found that distressed Americans who carried the G allele (GG/AG) of rs53576 reported increased emotional social support seeking relative to those with the AA genotype. Furthermore, the authors found that this relationship did not exist among Koreans, providing additional support for the potential moderating role of cultural and environmental factors on the association of OXTR and social behavior. In a racially

admixed sample, Rodrigues, Saslow, Garcia, John, and Keltner (2009) also investigated rs53576 and showed that individuals with the A allele (AG/AA) demonstrated significantly lower empathy both behaviorally and via self-report. In addition, Rodrigues et al. (2009) found that the same individuals (AG/AA) demonstrated increased behavioral and self-reported stress reactivity.

Based in part on research identifying OXTR as a potential susceptibility gene for the development of ASDs, and studies associating endogenous oxytocin with maternal attachment and bonding (Feldman, et al., 2007; Levine, et al., 2007; Strathearn, et al., 2009), a recent study by Bakersmans-Kranenburg and van Ijzendoorn (2008) investigated the role of rs53576 in parenting behavior. Results indicated that Caucasian mothers carrying A allele variants (AA/AG) demonstrated less maternal sensitivity in comparison to mothers who were homozygous for the G allele.

The finding that OXTR is associated with maternal sensitivity suggests that genetic differences in OXTR may play a role in attachment formation. Additional evidence has suggested that endogenous levels of oxytocin are indeed associated with adult attachment (Gordon, et al., 2008; Tops, van Peer, Korf, Wijers, & Tucker, 2007). To address this potential link, Gillath, Shaver, Baek, and Chun (2008) examined rs53576 and adult attachment style in an racially admixed sample and did not find a significant association. Similarly, Costa et al. (2009) found no relationships between rs53576 and rs2254298 and attachment styles in a sample of Caucasian control participants. Although currently no significant associations between attachment style and OXTR have been found in a nonclinical sample, it should be noted that both studies examined only one or

two SNPs on OXTR. It is possible that future research examining additional polymorphisms may enhance the ability to locate relevant markers on OXTR that are related to attachment.

The impact of exogenous administration of oxytocin on prosocial behavior (e.g., Kosfeld, et al., 2005; Zak, et al., 2007) led Israel and colleagues (2009) to examine associations of OXTR and altruism in an Israeli sample. To do so, the authors used two economic games: the Dictator Game and the Social Value Orientations task. The Dictator Game is a one-shot game typically requiring two people (or the perception that one is playing against another). Player A is assigned the role of the "Dictator," given a sum of money, and asked to transfer as much as they would like to Player B (the "Recipient"). Unlike the Ultimatum Game in which Player B would be able to accept or reject the offer, Player B must accept any amount that is transferred to them by Player A. In the experiment, all participants were assigned the role of "Dictator" and remained anonymous. Israel et al. (2009) divided participants into high and low givers based on the modal amount of money transferred to their "partner." The Social Value Orientations task (Van Lange, 1999; Van Lange, De Bruin, Otten, & Joireman, 1997) categorizes people into selfless (prosocial), and selfish (individualistic, competitive) groups on the basis of their responses to a series of questions that involve three different types of payoffs for the player and a "partner." Those who maximize joint outcomes are labeled "prosocial," players who typically maximize personal gains are referred to as "individualistic," and players who are interested in maximizing the difference in outcomes between themselves and their partners are categorized as "competitive."

Using the dominant model, Israel et al. (2009) showed that eight htSNPs (rs237897, rs13316193, rs2254298, rs9840864, rs2268490, rs237887, rs237885, rs1042778) across OXTR were in nominal association (uncorrected for multiple testing) with prosocial behavior in the Dictator Game, the Social Value Orientation task, or both. Two of the SNPs examined (rs237897 and rs9840864) appeared to contribute to sex-specific effects based on nominal associations. Following multiple test correction, rs1042778 was significantly associated with both the Dictator Game and the Social Value Orientations task, and results from the Dictator Game including rs1042778 were confirmed in a second sample. Haplotype analysis found significant omnibus associations (i.e., the authors reported the tests for overall haplotype blocks, but not for individual haplotypes) of 2-5 locus haplotypes with both generosity in the Dictator Game and the Social Value Orientation task following correction for multiple testing.

Spurred by the findings of Israel and colleagues (2009), Apicella et al. (2010) examined associations among nine SNPS on OXTR and social preferences in a Swedish sample. Apicella and colleagues (2010) used the Dictator Game as well as the Trust game to measure social preferences. The authors used a variation of the Dictator Game in which the Dictator was asked to give a portion of his or her endowment to a charity rather than to another person. Similar to the Dictator Game, the Trust Game requires two people (or the perception that one is playing against another). Following the receipt of a certain amount of points or money, Player A is assigned the role of the "Trustor," and informed that he or she can send Player B (the "Trustee") any portion of his or her endowment with the knowledge that the amount transferred will be tripled before Player B is then asked to send back to Player A any portion of the newly tripled amount. Participants first played

the role of the Trustor and then played the role of the Trustee with anonymous partners. Trust was measured by the amount of money transferred when participants were in the Trustor's role, and trustworthiness was measured by taking the average percentage of money returned by the Trustee. Apicella et al. (2010) conducted principal components analysis with all three variables (charitable giving, trust, and trustworthiness) and used the first factor as a combined measure of social preferences. Analyses examined additive and dominant models, as well as sex-specific effects. No associations remained significant following correction for multiple testing. The authors suggested several potential explanations for the lack of agreement between their findings and those of Israel et al. (2009) including the winner's curse effect (i.e., i.e., when studies with low power tend to inflate estimated effect sizes; Zollner & Pritchard, 2007) and potential genetic and environmental differences associated with a Swedish versus an Israeli population. Although findings to date are mixed, these studies suggest that genetic variation on OXTR may contribute to social- cognitive and behavioral processes in non-clinical populations.

OXTR, Emotionality, and Brain Structure and Function

Building on evidence from Israel and colleagues (2009) suggesting a link between OXTR and prosocial behavior, as well as evidence associating oxytocin with specific brain areas related to social-cognitive and emotional functioning (Lee, et al., 2009; Gimpl & Fahrenholz, 2001), Tost et al. (2010) examined how variation on rs53576 was associated with individual differences in prosocial temperament (i.e., reward dependence) as well as structural and functional aspects of hypothalamic-limbic brain regions (i.e., the hypothalamus, amygdala, and dorsal anterior cingulate gyrus). The authors found that

lower levels of reward dependence (i.e., a personality dimension characterized by increased sociability; Tost, et al., 2010) was associated with individuals who carried the A allele (AG/AA) compared to individuals who carried the GG genotype. Tost and colleagues (2010) also showed that decreased gray matter volume in the hypothalamus (which itself was predictive of decreased self-reported reward dependence in males) and increased gray matter volume in the right amygdala were also associated with individuals who carried the A allele (AG/AA). Last, in a functional imaging study involving emotional face matching (i.e., images depicted angry and fearful faces), lower task-related activation in the amygdala was associated with individuals with the AA genotype on rs53576, whereas high activation was associated with individuals with the GG genotype. These findings provided additional evidence for increased connectivity of the hypothalamus and amygdala in carriers of the rs53576 A allele. Thus, Tost and colleagues (2010) demonstrated that variation on rs53576 was associated with individual differences in social and emotional functioning (via structural and functional aspects of hypothalamic-limbic brain circuits as well as self-reported reward dependence). Importantly, the results presented by the authors were largely sex-specific, suggesting the importance of examining gene by sex interactions in OXTR.

Inoue et al. (2010) examined associations among seven SNPs and one haplotype block on OXTR and global brain volume, amygdala volume, and hippocampal volume in Japanese adults. Individuals with the A allele (AA/AG) on rs2254298 showed significantly greater amygdala volume compared to individuals with the GG genotype. In addition, two haplotypes (rs918316, rs2268493, rs2254298) that included the rs2254298 SNP were significantly associated with bilateral amygdala volume wherein individuals

carrying the G allele on rs2254298 evidenced smaller bilateral amygdala volume. No significant associations were found among single or multi-markers on OXTR and global brain volume or hippocampal volumes. In contrast to the results of Inoue et al. (2010), Furman, Chen, and Gotlieb (in press) examined rs2254298 on OXTR in a sample of Caucasian adolescent females and found that individuals with the GG genotype had significantly smaller total amygdala volume compared to individuals with the AG genotype. In addition, the authors found an association between individuals with the GG genotype and greater overall gray matter volume. Exploratory analyses demonstrated additional significant differences in the volume of the posterior brain stem and dorsomedial anterior cingulate cortex in individuals with the GG genotype compared to those with the AG genotype. In sum, greater gray matter volume in the amygdala has been associated with carriers of the A allele on rs53576 in Caucasians (Tost, et al., 2010), and although greater amygdala volume has also been associated with individuals who carried the A allele on rs2254298 in Japanese populations (Inoue, et al., 2010), smaller amygdala volume has been associated with Caucasian female adolescents carrying the A allele of rs2254298 (Furman, et al., 2011). Thus, these studies demonstrate how variation on OXTR contributes to individual differences in brain structure and function in regions involved in social-cognitive and emotional processes (Lee, et al., 2009; Rilling & Sanfey, 2011), and also highlight the potentially moderating role of race on these relationships.

In addition to the role of OXTR in emotional support seeking, empathy, stress reactivity, and prosocial behavior, several studies have linked OXTR to positive and negative emotionality. In a study of German adults and adolescents, Lucht and colleagues (2009) found that males with the AA genotype on rs53576 showed lower positive affect

scores, and adolescents showed reduced non-verbal intelligence respectively. A 3-locus haplotype (rs53576, rs2254298, rs2228485) was also associated with both positive and negative affect and emotional loneliness. Importantly, results were based on nominal associations as the authors did not correct for multiple hypothesis testing. Kawamura et al. (2010) also found a relationship between haplotypes on OXTR and affective temperament in a Japanese population. Out of the 15 SNPs examined on OXTR, one haplotype (G-rs1131149, G-rs2243370, G-rs2243369, T-rs11316193, G-rs2254298, T-rs2268493, C-rs2268491) was significantly associated with depressive temperament. This relationship maintained significance following correction for multiple testing. In addition, in a large Caucasian sample, Montag, Fiebach, Kirsch, and Reuter (2011) found that the interaction between individuals with the two "long" alleles (LL) on the serotonin transporter polymorphism (5-HTTLPR) and the TT genotype of OXTR rs2268498 was associated with significantly lower scores on dispositional fear and sadness (i.e., aspects of negative emotionality). This association remained significant following correction for multiple testing.

The Present Investigation

Based on the recent finding that variation on OXTR contributes to individual differences in prosocial behavior (Israel, et al., 2009) and the effects of exogenous oxytocin on perceived trust (Kosfeld, et al., 2005; Theodoridou, et al., 2009), sympathy (Petrovic, et al., 2008), and decreased aversion to betrayal (Baumgartner, et al., 2008), it was hypothesized that variation on OXTR may influence individual differences in baseline levels of cooperation and reactions to betrayals in trust. Research linking single and multi-markers on OXTR to dispositional emotionality or temperament (Kawamura,

et al., 2010; Lucht, et al., 2009; Montag, et al., 2010; Tost, et al., 2010), emotional reactivity (Tost, et al., 2010), and stress reactivity (Rodrigues, et al., 2009), also suggest that variants of OXTR may contribute to emotional reactions and perceptions of betrayers, which could influence subsequent behavior (Singer, et al., 2006). Therefore, participants' emotional reactions to their "partners" were assessed through self-report ratings of different positive and negative emotions. To examine perceptions of betrayers, the focus of the present study was on the agreeableness dimension of the "Big Five" personality taxonomy (John, 1990). Agreeableness was chosen because perceiving transgressors as having a high level of agreeableness appears to increase forgiveness (Tabak & McCullough, in press; Tabak, McCullough, Luna, Bono, & Berry, in press) and reduce biological stress reactivity following interpersonal conflict (Tabak & McCullough, in press). In the present investigation, 10 SNPs on OXTR were chosen based on previous research demonstrating associations of these SNPs and various aspects of social cognition and behavior (for review see, Ebstein, et al., 2009; Tost, et al., 2010).

CHAPTER TWO: METHODS

Participants

The present study was conducted in two phases due to room availability. [1] Participants were 186 undergraduate psychology students at the University of Miami. During the post-task debriefing, 10 participants stated that they did not believe that they had been playing against another person, and were therefore removed from all analyses. Four participants cooperated between 0-8% during the first twelve rounds of the PDG, and were also removed from all analyses. In addition, seven participants were removed because they did not have 75% or more complete genotype data (i.e., the default criteria in Haploview version 4.2 (Barrett, Fry, Maller, & Daly, 2005; http://www.broadinstitute.org/mpg/haploview). The resulting sample included 165 (82 female, 83 male) participants (mean age = 19.21 years, SD = 1.79, range = 17-37) who self-reported their race as non-Hispanic White. All participants received course credit and were paid between $7 and $10 depending on their performance in the PDG.

Procedure

At the beginning of each session participants learned that they would be playing a computerized decision-making game that would consist of 20-40 rounds with a networked partner (randomly assigned). In actuality, all participants played against the same preprogrammed computer strategy described below. For the purpose of increasing effort, participants were informed that they would be financially compensated for 1/10 of

[1] In phase I, participants were 161 undergraduate students at the University of Miami. In this phase, 78 participants self-reported their race as non-Hispanic White and were therefore retained in the present study. All other participants were not examined. In phase II, recruitment efforts focused on undergraduate students who self-identified as non-Hispanic White by stating that only these students were eligible to participate (however, all participants were accepted). Among the 123 students who participated, 108 participants self-reported their race as non-Hispanic White and were retained in the present study.

their total points at the completion of the game. A 10-minute tutorial that provided instructions on how to play the PDG (modified from Rilling, et al., 2002) was read aloud by a research assistant while participants read along. During the tutorial, participants were encouraged to let the research assistant know if any part of the instructions required additional clarification, and the research assistant did not begin the PDG until receiving verbal confirmation from all group members that they understood all of the instructions. Following completion of the PDG, participants underwent blood draws or saliva collection and completed a series of self-report questionnaires (described below). They were debriefed about the study and paid for their participation.

Procedural Differences Between Phase I and Phase II. In phase I, participants completed the PDG in a large computer lab in groups of 8-20. In phase II, participants completed the PDG in a small computer lab in groups of 1-4. Because of the small and/or odd number of participants who participated in the smaller room in phase II, one aspect of the procedure was changed: participants were deceived into thinking that they could be paired against other participants in the room that they were in, as well as another room that was "networked" with their room when playing the PDG. [2] There were no significant differences in any of the outcome or control variables based on phase membership. Therefore, participant data from both phases were combined.

[2] In the phase II initial instructions, participants were told the following: "You are about to play two games with another person who is either in this room or the room next door that has been networked with these computers." Within the E-prime paradigm, a recording was used in which a female voice (acting as the controller of both testing rooms) first asked, "is room 1 ready?" A response was then provided by a male voice (acting as a research assistant facilitating the session in another testing room) by replying, "all set." The female voice then asked, "is room 2 ready?" Research assistants in the present study were instructed to say "almost ready, just reviewing the last slide." The female voice then said "room 1 is all set to go so you can begin as soon as you're ready." At this point, research assistants would complete the tutorial and proceed.

Iterated Prisoner's Dilemma Game. The iterated prisoner's dilemma is a paradigm that is commonly used to study cooperation in interpersonal interactions (Axelrod & Hamilton, 1981) and reciprocal altruism (Trivers, 1971). In the present study, a modified version of the iterated PDG used by Rilling and colleagues (2007; 2002) was used through E-prime software (Psychology Software Tools, Pittsburgh, Pennsylvania). Participants' behavior, emotions, and ratings of their perceptions of their partners' level of agreeableness during the iterated prisoner's dilemma were recorded to examine individual differences in cooperation, reactions to betrayal, and perceptions of their "betrayers." Participants believed that they were playing the PDG in dyads and each round they selected to either cooperate or defect both independently and anonymously of their "partner." Participants earned a certain amount of points per round depending on the integrated outcome of both their selection and their partner's. Following completion of the PDG, total points were converted to real money. During each round there were four possible outcomes: Mutual cooperation (CC), one player cooperates and the other player defects (CD or DC), or mutual defection (DD). Each outcome corresponds to a different amount of points: CC represents the highest collective payoff (2,2), DD represents the lowest collective payoff (1,1), and DC or CD represent the maximum payoff for the defector and zero payoff for the cooperator (3,0 or 0,3).

Pre-programmed Computer Strategy for the PDG. The computer cooperated 100% of the time in the first round. During rounds 2-12 the computer played a generous-tit-for-tat strategy in which a cooperative choice by the participant was responded to with 100% cooperation in the following round, and a defection by the participant was responded to with defection in the next round 50% of the time. Importantly, the generous-

tit-for-tat strategy was modified from the original strategy used by Rilling et al. (2007), which included a computer defection 67% of the time following defection by the participant. To further elicit high levels of cooperation, participants received a message, "lets keep cooperating" (intentionally misspelled), from their anonymous partner after the initial 8 rounds of the generous-tit-for-tat strategy. Based on studies indicating that breaches in trust that occur during later rounds are more likely to increase negative emotional reactions and decrease cooperation (Bottom, et al., 2008; Lount, et al., 2008), the computer strategy defected 100% of the time during rounds 13-18.

Biological Assessment. Following completion of the PDG participants provided three 6ml vacutainer tubes of blood or 2mls of saliva via Oragene DNA saliva kit (DNAGenotek, Ottawa, Ontario, Canada). After blood samples were collected, tubes were placed in a standard refrigerator for approximately two days until they were transported to the John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine for DNA extraction. The Oragene samples were kept at room temperature and transported.

Genotyping. SNP genotyping was conducted at the John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine using Taqman allelic discrimination assays from Applied Biosystems (ABI). Three ng of genomic DNA, extracted from whole blood or saliva according to established protocols, was used in the amplification reaction. Cycling was performed on GeneAmp PCR Systems 9700 thermocyclers, with conditions recommended by ABI. End-point fluorescence was measured on the ABI 7900 HT system. Genotype discrimination of experimental results was then conducted using ABI's 7900 HT Sequence detection Systems version 2.3

analysis software. In order to ensure genotyping accuracy, 32 quality control samples per 384 well plate that match within and across plates, were included.

Measures

Behavioral Measures During the PDG

Initial Rates of Cooperation. The computer program (i.e., participants' anonymous partners during the PDG) played a cooperative and forgiving "generous tit-for-tat" strategy (Nowak & Sigmund, 1992) during the first 12 rounds of the iterated PDG (this strategy was previously described in the Procedure section). Participants' rates of cooperation during the first 12 rounds were used to represent initial rates of cooperation.

Rates of Cooperation Post-betrayal. Following 12 rounds of cooperative play (i.e., the generous tit-for-tat strategy), the computer-simulated "partner" proceeded to defect on five consecutive rounds (details regarding this strategy were previously described in the Procedure section). Participants' rates of cooperation during the five rounds of consecutive defections were used to represent behavioral reactions to betrayals.

Self-report Measures During the PDG

Emotional Reactions. Participants rated their emotional experiences on three positive emotions (happy, content, relaxed) and five negative emotions (insulted, disrespected, bitter, resentful, angry) on two occasions (following round 7 and round 18) during the PDG in response to the instructions, "Next, we would like you to please rate how YOU are feeling about your partner's behavior at this time. How are you currently feeling about your partner's behavior so far in the game?" Responses were made on a 7-point Likert-type scale (*1 = not at all, 7 = extremely*). Both scales demonstrated adequate

to high internal consistency for both the first (positive emotions, α = .81; negative emotions, α = .91) and second set of ratings (positive emotions, α = .77; negative emotions, α = .87).

Perceived Agreeableness. Following round 7 and round 18, participants were prompted to rate their perceptions of their "partners" agreeableness on four randomly ordered descriptors (sympathetic, considerate, cooperative, and fair and just) drawn from the NEO-FFI (P. T. Costa & McCrae, 1992), the Big Five Inventory (BFI; John, Donahue, & Kentle, 1991), and research investigating ideal personality traits among potential relationship partners (Cottrell, Neuberg, & Li, 2007). As described in Tabak, McCullough, Luna, Bono, and Berry (in press), adjectives and phrases were rated on a 7-point Likert-type scale (*1 = not at all, 7 = extremely).* Randomly ordered distracter adjectives that were not examined in the present study were also included. The mean of the four target descriptors demonstrated high internal consistency for the both sets of ratings (α = .87, .91).

Self-report Measures

Depression Symptoms. Following completion of the PDG, participants completed the Beck Depression Inventory (BDI; Beck, et al., 1961). The BDI is a self-report measuring the degree of current depressive symptomology. Participants rated the extent to which they had experienced 21 depression symptoms over the past 2 weeks on a 4-point Likert-type scale *(e.g., loss of interest: 1 = "I have not lost interest in other people or activities," 4 = "It's hard to get interested in anything")*. Items were summed and demonstrated high internal consistency (α = .92).

CHAPTER THREE: RESULTS

Statistical Analysis

All genotype distributions were tested for adherence to Hardy-Weinberg Equilibrium using PLINK version 1.07 (Purcell, et al., 2007; http://pngu.mgh.harvard.edu/purcell/plink). Adherence to Hardy-Weinberg Equilibrium assumes that genetic data have come from a population in which variations in allele and genotype frequencies have remained relatively consistent for generations. This assumption suggests the data are of high quality and have not come from a population that has been subject to inbreeding, population stratification, or selection (Balding, 2006). In the present study, nine SNPs on OXTR were chosen based on previous research that identified these markers as htSNPs and found associations among these nine htSNPs on OXTR and various aspects of social behavior (for review see, Ebstein, et al., 2009). According to the International HapMap Consortium (2005), the use of htSNPs, or tag SNPs, improves the ability to identify relevant markers in association studies by taking advantage of the redundancy associated with SNPs that are highly correlated and tend to be in close proximity to one another. The use of these nine htSNPs can be thought of as "maximally informative" exemplars of genetic variation on a particular region of the gene of interest (Carlson, et al., 2004), which therefore prevents the need to genotype the thirty or more polymorphisms that have already been identified on OXTR (Insel, 2010). In addition, an additional SNP was examined (rs53576) due to recent research that has found that variation on rs53576 contributes to individual differences in social-cognitive and behavioral functioning (e.g., Rodrigues, et al., 2009; Tost, et al., 2010).

Crawford and Nickerson (2005) note that since many SNPs are intercorrelated, there is potential utility involved in conducting haplotype analyses. Haplotypes are inferred and inherited "combinations of alleles at different loci on the same chromosome" that can be used to "capture the correlation structure of SNPs in regions of little recombination" (Balding, 2006, p. 781). Examining haplotypes, which are based on patterns of Linkage Disequilibrium (LD), or non-random statistical association of alleles at two or more loci (Balding, 2006), may increase power in tests of genetic association (de Bakker, Yelensky, Pe'er, Gabriel, Daly, & Altshuler, 2005). Determination of LD between SNPs was analyzed using Haploview version 4.2 (Barrett, et al., 2005; http://www.broadinstitute.org/mpg/haploview) and haplotype block identification was conducted using the Gabriel method (Gabriel, et al., 2002). The same software was used to estimate haplotype distributions for each participant via the Expectation-Maximization (EM) algorithm (Dempster, Laird, & Rubin, 1977). PLINK version 1.07 (Purcell, et al., 2007; http://pngu.mgh.harvard.edu/purcell/plink) was then used to estimate haplotype frequencies. As in previous research (Kawamura, et al., 2010), based on the present study's relatively small sample size, only haplotypes with frequencies greater than 0.15 were analyzed. PLINK was used for permutation-based multiple test correction (1000 iterations). This method is less conservative than the Bonferroni method because it accounts for correlations between the genetic markers (Gao, Starmer, & Martin, 2008), thus making it more appropriate for the present investigation.

Linear regression analyses were performed with PLINK version 1.07 (Purcell, et al., 2007; http://pngu.mgh.harvard.edu/purcell/plink) to evaluate single-marker and haplotype associations among the following dependant variables: (a) initial levels of

cooperation (i.e., rates of cooperation during the first twelve rounds), (b) reactions to betrayal (i.e., rates of cooperation during the five rounds post-betrayal), (c) positive and negative emotional reactions to betrayal, and (d) participants' perceptions of their betrayers' personalities. To control for baseline differences in cooperation, positive and negative emotional reactions, as well as perceptions of participants' partners, initial rates of cooperation, initial positive and negative emotional reactions, and initial perceptions of partners' personalities were included as control variables in multiple regression analyses. In the event that any of the variables were not normally distributed, the data were transformed to better approximate a normal distribution.

Descriptive Statistics

Table 1 displays means and standard deviations for major study variables. Initial rates of cooperation in the first twelve rounds of the PDG were high (M = 0.85, SD = .26), initial ratings of positive emotions were high (M =5.51, SD = 1.24), initial ratings of negative emotions were low (M = 1.72, SD = 1.12), and initial ratings of perceived agreeableness were high (M = 5.69, SD = 1.19). Thus, both initial ratings of positive and negative emotions, as well as initial levels of cooperation and initial levels of perceived agreeableness suggest that the computer strategy successfully elicited participants' trust.

Single-marker Analyses

As shown in Table 2, all genotype distributions were in Hardy-Weinberg equilibrium (p > .05). Single-marker association tests were conducted with the 10 SNPs on OXTR using the additive model (see Table 3). As detailed on p. 116 in the PLINK version 1.07 documentation (Purcell, et al., 2007; http://pngu.mgh.harvard.edu/purcell/plink), "For the additive effects of SNPs, the

direction of the regression coefficient represents the effect of each extra minor allele (i.e. a positive regression coefficient means that the minor allele increases risk/phenotype mean).” Thus, in the additive model, the combined effect of the genotype that is homozygous for the minor allele is equivalent to the sum of the individual effect of genotypes with one minor allele (i.e., the heterozygous genotypes). Nominal associations (uncorrected for multiple testing) were found in the following: initial rates of cooperation and rs237887 (b = .05, p = .042); positive emotional reactions post-betrayal (controlling for initial ratings of positive emotions) and rs53576 (b = -.36, p = .01), rs237887 (b = -.38, p = .006), rs237897 (b = -.37, p = .006), and rs1042778 (b = .36, p = .007); and negative emotional reactions post-betrayal (controlling for initial ratings of negative emotions) and rs53576 (b = .41, p =.017), rs237897 (b = .35, p = .036), rs9840864 (b = .39, p = .036), and rs1042778 (b = -.38, p = .021). No significant single-marker associations were found with rates of cooperation post-betrayal (controlling for initial rates of cooperation) or post-betrayal perceived agreeableness (controlling for initial rates of perceived agreeableness). Following correction for multiple testing, the association of rs237887 and positive emotional reactions post-betrayal (controlling for initial ratings of positive emotions) remained significant (p = .047). Specifically, with the addition of the G allele on rs237887, self-reported positive emotional reactions significantly decreased (see Figure 1). Based on recent findings identifying an association between OXTR and risk for depression (B. Costa, et al., 2009; Kawamura, et al., 2010; Thompson, et al., 2010), as well as the relationship between depression, emotion dysregulation, and social-cognitive dysfunction (Harlé, Allen, & Sanfey, 2010; Joormann & Gotlib, 2010;

Wolkenstein, et al., in press), the analyses between rs237887 and positive emotional reactions post-betrayal were re-run controlling for current depression symptoms. The results remained unchanged.

In addition, following multiple test correction, the association of positive emotional reactions post-betrayal and three other SNPs approached statistical significance, rs1042778, $p = .058$; rs237897, $p = .055$; rs53576, $p = .081$). Due to previous research demonstrating sex-specific effects of OXTR on aspects of social cognition and behavior (e.g., Tost, et al., 2010), single-marker by sex interactions were conducted using IBM SPSS version 19. A sex by rs1042778 interaction significantly predicted post-betrayal perceived agreeableness (controlling for initial rates of perceived agreeableness), F (3, 156) = 5.25, $p < .01$. Follow-up analyses revealed that this appeared to be driven by females; however, the result would not maintain significance following permutation test correction and therefore, no additional follow up analyses were conducted. No other sex by OXTR interaction effects were significant.

Multi-marker Analyses

Figure 2 shows the r^2 measure of LD between SNPs as well as the two haplotype blocks that were identified. Block 1 contained rs237887 and rs2268490, and Block 2 contained rs9840864 and rs2268490. Haplotype-based association tests were performed via linear regression analyses using allelic combinations of each haplotype block with frequencies greater than 0.15. This resulted in four haplotype association tests that were performed on each of the dependent variables. As shown in Table 4, nominal associations were found in the following: initial rates of cooperation and the Block 1 AC haplotype ($b = .05$, $p = .042$); positive emotional reactions post-betrayal (controlling for initial ratings

of positive emotions) and the Block 1 AC haplotype (b = -.38, p = .006), the Block 1 GC haplotype (b = -.42, p = .009), and the Block 2 CT haplotype (b = -.39, p = .041); and negative emotional reactions post-betrayal (controlling for initial ratings of negative emotions) and the Block 2 CT haplotype (b = .69, p = .003) as well as the Block 2 GT haplotype (b = .39, p = .036). Haplotypes were not associated with rates of cooperation post-betrayal (controlling for initial rates of cooperation) or post-betrayal rates of perceived agreeableness in either haplotype block. Three associations remained significant following permutation-based correction for multiple testing: the Block 1 AC haplotype and positive emotional reactions post-betrayal (p = .019), the Block 1 GC haplotype and positive emotional reactions post-betrayal (p = .032), and the Block 2 CT haplotype and negative emotional reactions post-betrayal (p = .014). All significant analyses were re-run controlling for current depression symptoms and results remained unchanged. Due to the potential for variation in participants' computer strategies on occasions in which participants defected during the first 12 rounds (i.e., the computer responded with defection 50% of the time), all analyses were re-run controlling for the computers' initial rates of cooperation. Results of single and multi-marker analyses remained unchanged.

CHAPTER FOUR: DISCUSSION

Following the establishment of trust and high rates of cooperation through the use of the iterated prisoner's dilemma, the present study revealed that variation in one SNP (rs237887) and three haplotypes (A-rs237887, C-rs2268490; G-rs237887, C-rs2268490; and C-rs9840864, T-rs2268494) on OXTR contributed to individual differences in both positive and negative emotional reactions to betrayals in trust. The present study is the first to examine OXTR and emotional reactions to interpersonal betrayal, and the first to investigate OXTR in the context of an iterated prisoner's dilemma.

These findings are in agreement with previous research that has revealed associations between markers on OXTR and aspects of social cognition and behavior in both clinical (B. Costa, et al., 2009; Gregory, et al., 2009; Jacob, et al., 2007; Lerer, et al., 2008; Liu, et al., 2010; Riem, et al., in press; Thompson, et al., 2011; Wu, et al., 2005; Yrigollen, et al., 2008) and non-clinical populations (Bakermans-Kranenburg & van IJzendoorn, 2008; Israel, et al., 2009; Kim, et al., 2010; Montag, et al., 2010; Rodrigues, et al., 2009; Tost, et al., 2010). The present results are also in agreement with recent research associating variation on OXTR with individual differences in affectivity or emotionality (Kawamura, et al., 2010; Lucht, et al., 2009; Montag, et al., 2010; Tost, et al., 2010). Following multiple test correction, no significant associations were found among markers on OXTR and initial levels of cooperation, post-betrayal levels of cooperation, or post-betrayal levels of perceived transgressor agreeableness.

The most robust findings in the present study involve SNP rs237887. In single-marker analyses, the presence of the G allele in rs237887 was significantly associated with lower levels of positive emotions following betrayal. This association maintained

significance when controlling for current depression symptoms and following multiple test correction. In multi-marker analyses, SNP rs237887 was also part of the Block 1 haplotype comprising rs237887 and rs2268490. Following multiple test correction, the haplotypes within this block were significantly associated with positive emotional reactions post-betrayal. Whereas single-marker analyses determined that the G allele in rs237887 was associated with lower levels of positive emotions post-betrayal, in haplotype analyses the presence of either the A or the G allele in rs237887 (in addition to the C allele in rs2268490) was significantly associated with lower positive emotional reactions following betrayal. In addition, a significant association was also found in the Block 2 haplotype (comprising rs9840864 and rs2268494) in which the C allele in rs9840864 and the T allele in rs2268494 predicted higher levels of negative emotional reactions post-betrayal.

One explanation for the present findings is that variation in the associated markers are associated with prosociality—an interpretation corroborated by the nominal association between the rs237887 G allele, as well as the Block 1 AC haplotype and the Block 1 GC haplotype (which was trending in the same direction, $p = .07$), and higher initial rates of cooperation, which can be viewed as a behavioral measurement of prosocial disposition. If this is the case, then individuals with the Block 1 AC or GC haplotype and/or individuals with the Block 2 CT haplotype may have more intense emotional reactions because they have made stronger investments in establishing a cooperative relationship with their partners than did individuals who do not carry these haplotypes. Fabes and Eisenberg (1992) have suggested that increased emotionality in general is not indicative of a lack of prosocial functioning, but rather, learning to

adaptively self-regulate emotions may be the most optimal strategy for positive social functioning. In this way, people with the associated haplotypes may be demonstrating increased prosociality by regulating their emotions so as to prevent themselves from responding more negatively (i.e., with more defections in the PDG post-betrayal). This is demonstrated by the significant differences in positive and negative emotional reactions to betrayal, but the lack of significant differences in post-betrayal rates of cooperation among single and multi-marker tests of association. This interpretation is militated by the fact that these haplotypes were not significantly associated with higher rates of cooperation either during the generous tit-for-tat regime or the betrayal regime following multiple test correction. Such a lack of behavioral differences could have been due, however, to low statistical power.

A second possible explanation for these results is that the associated genetic markers in the present study are in LD with other markers that have true functional relevance (Lin, Vance, Pericak-Vance, & Martin, 2007), and therefore, the markers themselves may not have casual relationships to emotional reactions to betrayal. As discussed in Lucht et al. (2009), it is important to note that in the present study some results might represent "flip-flop associations," or associations of opposite alleles at the same genetic marker with a similar phenotype (Lin, et al., 2007). Previous research investigating the SNPs examined in the present study with other aspects of social-cognitive and behavioral functioning have found variable patterns of allelic association. Israel and colleagues (2009) found associations with generosity and Social Value Orientation and several 3-8 locus haplotypes that included either the A or G alleles in rs237887, the C or T alleles in rs2268490, and/or the C or G alleles in rs9840864 (Israel,

personal correspondence). Similarly, Liu at al. (2010) found nominal associations between prevalence of Autism Spectrum Disorders and rs237887 as well as haplotypes containing both the A and G alleles in rs237887 respectively. In addition, Lerer et al. (2008) found that haplotypes that included either the A or T alleles on rs2268494 and/or the C and G alleles on rs9840864 significantly predicted risk for ASDs. In addition, several studies investigating how variation in rs237887, rs2268490, rs2268494 and rs9840864 may contribute to individual differences in social-cognitive and behavioral functioning have found non-significant nominal associations (Apicella, et al., 2010; Campbell, et al., in press; Kawamura, et al., 2010; Tansey, et al., 2010) or associations that become non-significant following multiple test correction (Liu, et al., 2010; Tansey, et al., 2010).

Across these studies, there are many potential explanations for the inconsistencies in findings, including type I error, which is characteristic of candidate gene studies (Ioannidis, Tarone, & McLaughlin, in press), and publication and reporting bias (Lin, et al., 2007). There are also biologically substantive explanations for "flip-flop associations" including: sampling variation among homogenous racial groups in combination with low LD between loci in the same genetic marker (Lin, et al., 2007); variation in LD or haplotype variance associated with different racial groups (Lin, et al., 2007; Zaykin & Shibata, 2008), and unexamined associations among multi-loci genetic and environmental factors that are correlated with the markers examined (Lin, et al., 2007). To date, the presence of potentially genuine allelic heterogeneity (i.e., "flip-flop")

in genetic association studies has been largely overlooked (Clarke & Cardon, 2010; Maher, Reimers, Riley, & Kendler, 2010). Additional research is needed to disentangle these inconsistencies.

Limitations and Future Directions

There are several limitations in the present study. First, the present study's sample size was relatively small for a population-based association study of unrelated individuals. Due to this constraint, only haplotypes with frequencies greater than 0.15 were examined (as in Kawamura, et al., 2010), which limits the ability to discuss how other haplotypes may be related to the major variables of interest. As noted by Apicella et al. (2010), a greater sample size may be necessary to further clarify the association between genetic markers and the complex phenotypes examined in the present study. However, the study sample size is similar to other recent genetic association studies examining aspects of social-cognitive functioning (e.g., Reuter, Frenzel, Walter, Markett, & Montag, in press), and given the number of SNPs analyzed and the potential difficulty in finding significant associations following multiple test correction when examining complex phenotypes (Cardon & Bell, 2001), the present results appear somewhat robust given the size of the sample.

Second, although research on OXTR is rapidly progressing, and several studies have found associations between variation on OXTR and brain structure and function (e.g., Furman, et al., 2011; Inoue, et al., 2010; Tost, et al., 2010), the functionality of the polymorphisms examined in the present study are not yet known. As discussed previously, given the complexity of social-cognitive and emotional processes, the associations observed in the present study may result from LD associations with other

functional markers on OXTR (Lin, et al., 2007), or in other genes (e.g., Montag, et al., 2010). As a result, the present results should be viewed as preliminary.

A third limitation is that the use of self-reported non-Hispanic White undergraduates limits the generalizability of the present findings to people from other racial and cultural groups, as well as those in other phases of the life course. Although results from the present study may not be generalizable to other racial and cultural groups, the inclusion of participants from a homogenous racial group increases the likelihood that the present findings are not the result of type I error associated with population stratification (Cardon & Palmer, 2003; Risch, Burchard, Ziv, & Tang, 2007). In addition, examining individuals from a similar age group prevented the potentially confounding influence of age-related differences in social decision-making (Nielsen & Mather, 2011).

In the present study, participants interacted with anonymous partners with whom they had not interacted and may not have seen before or during the PDG. Previous research examining the effects of oxytocin administration on peoples' willingness to cooperate with others found that oxytocin increased cooperation among participants who had met their partner before beginning the game; however, for those who played against anonymous partners, oxytocin actually decreased peoples' willingness to cooperate (Declerck, Boone, & Kiyonari, 2010). Thus, future research would benefit from examining how variation on OXTR may contribute to individual differences in emotional reactions to betrayals in trust in a non-anonymous context. In addition, research combining behavioral economic paradigms and neuroimaging (see Baumgartner, et al., 2008) with genetic analysis may further elucidate the neural mechanisms that correlate

with the present findings. Finally, investigating the influence of OXTR on interpersonal emotional reactions through gene by gene interactions (e.g., Montag, et al., 2010) and gene by environment interactions (e.g., Kim, et al., 2010) would increase our overall understanding of OXTR's influence on social-cognitive and emotional functioning.

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Table 1

Means and Standard Deviations for Major Study Variables

Measure	All Participants Mean (SD) $N = 165$	Male Mean (SD) $n = 83$	Female Mean (SD) $n = 82$
Initial Cooperation	0.85 (.26)	0.85 (.2)	0.85 (.2)
Pb Cooperation	0.34 (.26)	0.39 (.29)	0.3 (.23)
Initial Pos Emotions	5.51(1.24)	5.47 (1.39)	5.6 (1.09)
Pb Pos Emotions	3.2 (1.2)	3.25 (1.27)	3.15 (1.14)
Initial Neg Emotions	1.72 (1.12)	1.93 (1.25)	1.51 (.94)
Pb Neg Emotions	3.97 (1.5)	3.97 (1.43)	3.98 (1.55)
Initial Perceived Ag	5.69 (1.19)	5.47 (1.34)	5.91 (.97)
Pb Perceived Ag	2.42 (1.18)	2.32 (1.25)	2.52 (1.11)

Note. Pb = Post-betrayal; Pos = Positive; Neg = Negative; Ag = Agreeableness.

Table 2

OXTR Descriptive Statistics

Measure	Position	Genotype	Genotype Frequency	Minor Allele	mAF	HapMap CEU mAF	HWE
rs53576	8779371	AA/AG/GG	17/61/84 *n* = 162	A	0.29	0.29*	0.26
rs237887	8772042	GG/AG/AA	23/80/62 *n* = 165	G	0.38	0.41	0.87
rs237888	8772095	CC/CT/TT	2/17/146 *n* = 165	C	0.09	0.08	0.13
rs237889	8777483	TT/CT/CC	22/74/59 *n* = 155	T	0.38	0.37	1
rs237897	8783285	AA/AG/GG	25/72/66 *n* = 163	A	0.37	0.39	0.5
rs2254298	8777228	AA/AG/GG	1/35/127 *n* = 163	A	0.11	0.07	0.7
rs2268494	8777046	AA/AT/TT	4/26/135 *n* = 165	A	0.10	0.05	0.07
rs2268490	8772085	TT/CT/CC	2/40/123 *n* = 165	T	0.13	0.12	0.74
rs9840864	8773477	GG/GC/CC	11/68/85 *n* = 164	C	0.27	0.23	0.7
rs1042778	8769545	TT/GT/GG	28/78/57 *n* = 163	T	0.41	0.37	0.87

Note. mAF = Minor allele frequency. HapMap CEU = Utah residents with Northern and Western European ancestry. NA = Not available. HWE = Hardy Weinberg Equilibrium. *Value obtained from HapMap pilot 1 CEU.

Table 3

Regression Analyses with SNPs for the Additive Model

SNP	Allele	Initial Cooperation	Pb Cooperation	Pb Pos emotions	Pb Neg emotions	Pb Perceived Agreeableness
rs53576	A	.011	-.039	-.359**	.415*	-.051
rs237887	G	.046*	.008	**-.381****	.326	-.231
rs237888	C	.043	-.087	.051	.156	-.367
rs237889	T	-.008	-.006	-.133	.232	-.222
rs237897	A	-.014	-.051	-.365**	.346*	-.148
rs2254298	A	.014	-.013	-.36	.271	-.073
rs2268494	A	-.054	.039	.386	-.099	-.039
rs2268490	T	.022	.012	-.159	.312	-.271
rs9840864	C	-.008	.001	-.033	.393*	-.24
rs1042778	T	-.01	.036	.362**	-.382*	.135

Note. Pb = post-betrayal; Pos = positive; Neg = negative. n = 155-165. **Bold** represents $p < .05$ following permutation test correction. *$p < .05$; **$p < .01$

Table 4

Regression Analyses with Haplotype Blocks

SNP	Alleles	Initial Cooperation	Pb Cooperation	Pb Pos emotions	Pb Neg emotions	Pb Perceived Agreeableness
Block 1						
rs237887	AC	.046*	.008	**-.381****	.326	-.231
rs2268490	F = .62					
rs237887	GC	.048	.003	**-.42****	.243	-.14
rs2268490	F = .25					
Block 2						
rs9840864	CT	.035	-.031	-.385*	**.69****	-.34
rs2268494	F = .17					
rs9840864	GT	-.008	.001	-.033	.393*	-.24
rs2268494	F = .73					

Note. F = frequency; Pb = post-betrayal; Pos = positive; Neg = negative. n = 155-165.
Bold represents $p < .05$ following permutation test correction.*$p < .05$; **$p < .01$

Figure 1

The Addition of the G allele in rs237887 Significantly Decreases Positive Emotional Reactions Post-betrayal (Controlling for Initial Ratings of Positive Emotions)

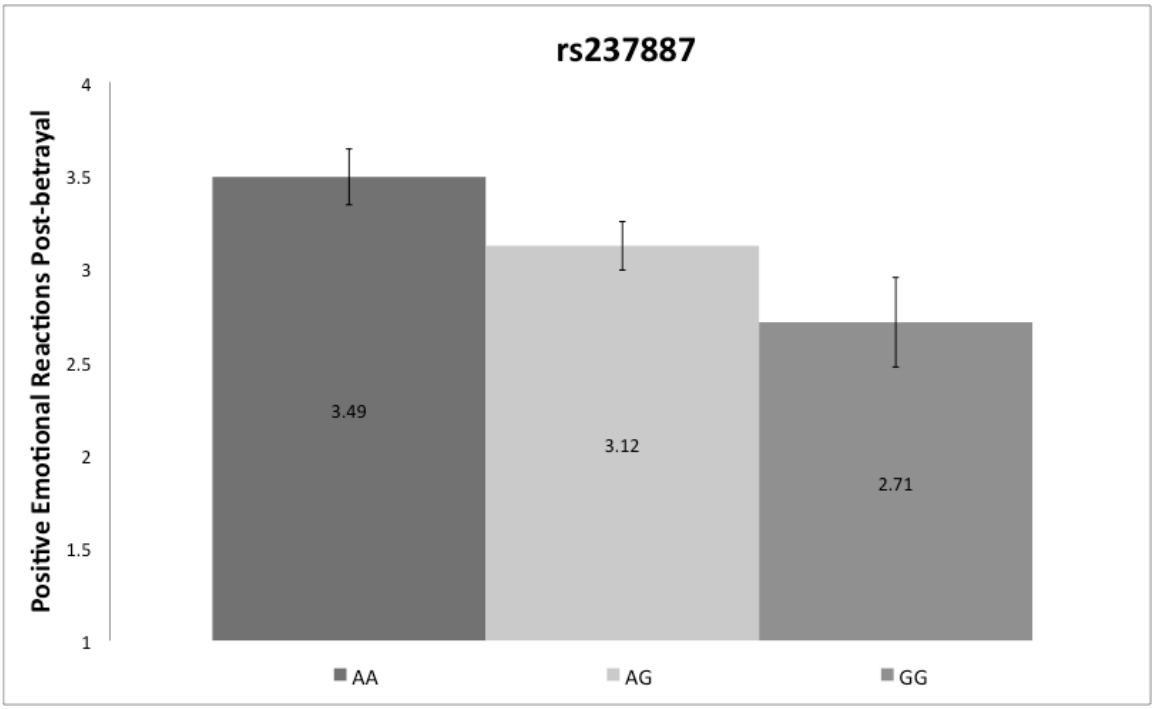
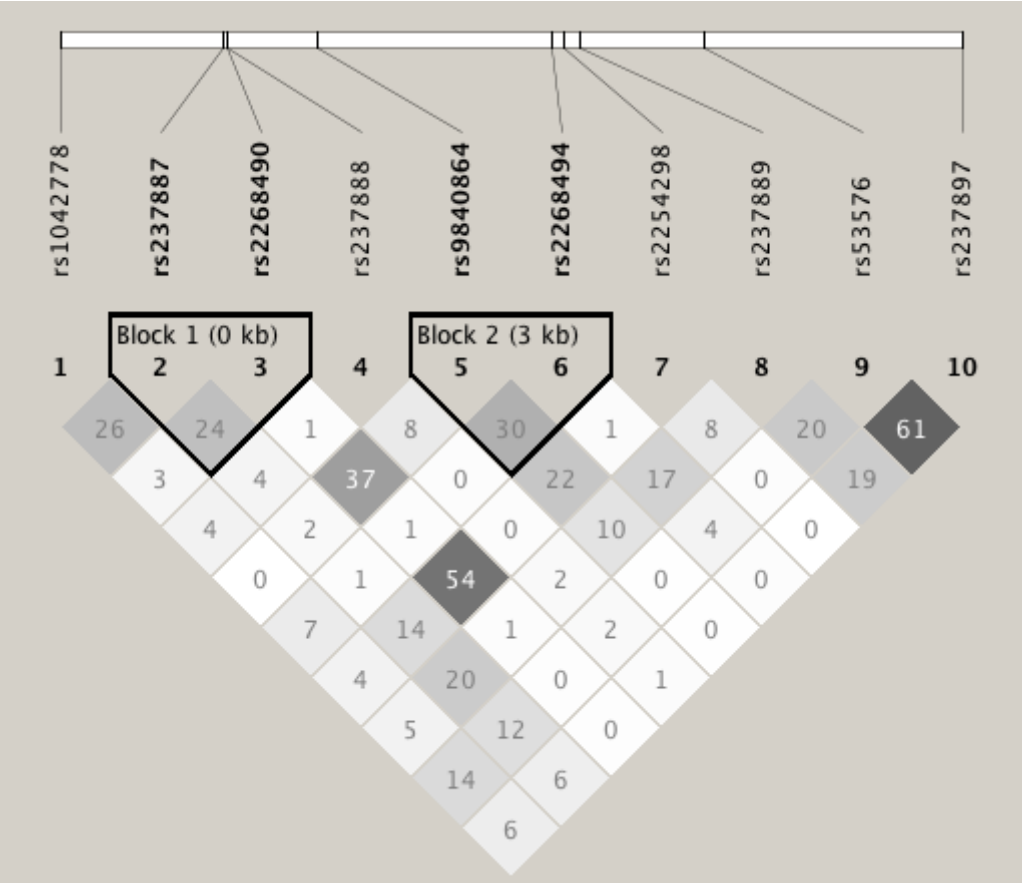


Figure 2

R^2 Values and Haplotype Block Structure



Note. R^2 values displayed are equivalent to 100X their value (i.e, 1 = .01).