



THE EFFECT OF OXYTOCIN ON TRUST BETWEEN MOTHERS AND  
ADOLESCENTS AND THE MODERATING ROLE OF ATTACHMENT SECURITY

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A Dissertation

Presented to

The Faculty of the Department of Psychology

University of Houston

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In Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

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By

Amanda Venta

May, 2015

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Existing research with animals and human adults suggests that oxytocin is a promising therapeutic tool because it increases trust and attachment in social relationships—key factors in a range of psychiatric disorders. Oxytocin has been recommended as a treatment for adolescents, a population in which treatment providers are wary of other pharmacological options. However, this suggestion remains largely unstudied, with only one previous study administering oxytocin to adolescents with psychopathology. Against this background, the objectives of this study were to (a) examine the effect of intranasal oxytocin administration on trust behavior towards mothers in a game designed to assess in vivo, quantifiable social behavior, determining how this effect differs among inpatient and community control adolescents and (b) explore baseline attachment security as a moderator to determine whether the effect differs depending upon the existing social relationship. A secondary aim was to explore how internalizing and externalizing symptoms relate to the effect of oxytocin on trust. The central hypothesis was that oxytocin would increase trust behavior in the whole sample, and demonstrate clinical potential by raising the level of maternal trust in the inpatient sample nearer to the trust behavior of community adolescents. Within each group, oxytocin was expected to increase trust behavior to a greater degree among adolescents with a secure attachment style.  $N = 45$  inpatient adolescents and  $N = 35$  community controls participated in a randomized, double blind, placebo-controlled design in which they self-administered intranasal oxytocin or a placebo and played a trust game with their mother and a stranger over the internet. Findings suggested that oxytocin was associated with increased trust game investments for inpatient adolescents across both stranger and mother games, such

that their investments surpassed the investments of community controls. No evidence of a moderating role of attachment was noted. No associations between continuously rated internalizing symptoms, externalizing symptoms, and oxytocin effects were noted. This study takes a first step towards determining whether, and for whom, oxytocin may have clinical value, within the context of the critical variables of attachment and psychopathology in adolescents.

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## THE EFFECT OF OXYTOCIN ON TRUST BETWEEN MOTHERS AND ADOLESCENTS AND THE MODERATING ROLE OF ATTACHMENT SECURITY

Adolescence is a developmental stage that is often accompanied by psychopathology. The National Institute of Mental Health reports that 46.3% of adolescents have a psychiatric diagnosis (Merikangas et al., 2010) and the Center for Disease Control reports that adolescents are 90% more likely than children to use mental health services, stressing adolescent mental illness as a public health matter. Total mental health costs for American youth were estimated at 8.9 billion in 2006 (Agency for Healthcare Research and Quality, 2006), further illustrating the societal cost of adolescent mental illness. These statistics speak to the great need for improved interventions in this group, particularly because clinicians are wary of existing pharmacological options for adolescents (Netherton & Schatte, 2011). Oxytocin administration holds promise as a therapeutic technique because it increases trust and attachment in relationships—key factors in a range of psychiatric disorders.

### **Trust and attachment in psychopathology**

Trust is essential for adolescent well-being, particularly in the parent-child relationship (Smetana, 2010). Research suggests that youth who are more trusting engage in more socially responsible (Wentzel, 1991) and prosocial behavior (Rotenberg, McDougall, Boulton, Vaillancourt, Fox, & Hymel, 2004). Further, low trust has been associated with both depression and suicidal behavior in adolescents (Lester & Gatto, 1990) and with poorer psychosocial functioning (Rotenberg et al., 2010). While studies exploring parent-adolescent trust are limited, they suggest that trust is an important area for interventions research.

Attachment theory and research similarly provide rationale for the notion that parent-adolescent trust is an essential component of adolescent health. Trust has been called one of the primary ingredients contributing to attachment security (Levy, Ellison, Scott, & Bernecker, 2011) and is a fundamental component of attachment theory as conceived by its developers (Bowlby, 1969, 1982; Ainsworth, 1978). Attachment theory seeks to explain how the early stages of a parent-child relationship influence functioning across the lifespan. Childhood is viewed as a time during which a child vies for the attention of a caregiver whose responses contribute to the child's sense of being worthy of care and others as reliable caregivers (i.e., attachment security) to varying degrees (i.e., attachment insecurity). In this study, attachment security refers specifically to the adolescent's mental representation of their relationship with their mother, subdivided into secure and insecure groups (with the insecure group further subdivided into preoccupied, dismissing, and disorganized).

Existing research shows substantial links between adolescent attachment security (distinct from parenting and discipline practices; Scott, Briskman, Woolgar, Humayun, O'Connor, 2011) and psychological well-being. Similarly, research shows increased prevalence of attachment insecurity among adolescents in psychiatric hospitals (Allen, Hauser, Borman-Spurrell, 1996) and links it to depression, anxiety, suicidal behavior, delinquency, substance abuse, and conduct problems (Allen, 2008). Further, attachment insecurity appears to interfere with an adolescents' ability to receive help from others (Larose & Bernier, 2001) and use active coping strategies (Seiffge-Krenke & Beyers, 2005). This research highlights the importance of attachment security, and therefore

interpersonal trust, in adolescent mental health and shows that attachment insecurity presents a roadblock to the effective delivery of existing treatments.

### **Relations between oxytocin, trust, and attachment**

While clearly an important consideration in treatment and prevention, attachment style has historically been viewed as a relatively stable personal characteristic—one that persists throughout the lifespan, limiting the clinical and public health utility of attachment research. Recently, however, attachment security has been tied to the neuropeptide oxytocin, the chemical implicated in lactation, nurturance, and trust. In animals (Pedersen & Prange, 1979; Keverne & Kendrick, 1992), oxytocin increases nurturing behaviors and eliminates maternal rejection and aversive behaviors. Likewise, in humans, higher oxytocin levels are associated with maternal sensitivity to infants (Feldman, Weller, Zagoory-Sharon, & Levine, 2007) and quality of play and contact with infants (Feldman, Gordon, Schneiderman, Weisman, & Zagoory-Sharon, 2010). Not surprisingly, the repeated linking of parental nurturance to oxytocin has led to speculation that oxytocin is the attachment chemical of the brain, secreted during attachment experiences (e.g., childbirth, breastfeeding, and play) to create bonds between parents and children. Indeed, researchers exploring the neurobiology of attachment have now determined that securely attached mothers show greater activation in oxytocin-associated brain regions than insecurely attached mothers when viewing their infants smiling or crying (Strathearn et al., 2009).

While the idea that a mother's attachment circuitry would be implicated in response to seeing or touching her child is not new, the suggestion that this circuitry is associated with the oxytocin system of the brain, and that it is influenced by the mother's

own attachment experiences, is ground-breaking. These findings are most appreciated when considering that human fathers *given* oxytocin were more stimulating and less hostile towards toddlers (Naber, van IJzendoorn, Deschamps, van Engeland, & Bakermans-Kranenburg, 2010). Taken together, the implication of this research is that oxytocin is a neurobiological marker of attachment security that, when administered intranasally, will affect attachment and trust behavior in human adults.

Against this background, the first aim of this study was to examine the effect of intranasal oxytocin administration on trust behavior towards mothers in a neuroeconomic trust game designed to assess *in vivo*, quantifiable social behavior, determining how this effect differs among inpatient and community adolescents. In neuroeconomics, trust is defined as an exchange between two players in which trust is parameterized as the amount of money designated for the partner. The basic one-shot trust task was initially proposed by Camerer and Weigelt (1988) and further developed by Berg, Dickhaut and McCabe (1995). One player is given a certain amount of money and can keep all the money or decide to invest some amount with the partner. The amount invested is tripled as it is sent to the partner, who then decides what portion to return.

### **The trust game**

A meta-analysis conducted by Johnson and Mislin (2011) reveals that iterations of this basic game have been conducted more than 160 times, with more than 23,000 participants, and in 35 countries, providing substantial support for the use of this game as a measure of trust. Literature reviewed by Evans and Revelle (2008) shows that game investment is associated with positive affect (Dunn & Schweitzer, 2005) and closeness with the partner (Glaeser, Laibson, Scheinkman, & Soutter, 2000)—variables expected to

correlate with trust, contributing to the validity of this tool. Recently, there has been an explosion of research using trust games to study psychopathology in youth and adults (see Sharp, Monterosso & Montague, 2012 and Sharp, 2012 for reviews). No study to date, however, has explored the trust game as a proxy for parent-child trust behavior in either community or psychiatric adolescents. Additionally, no study has given oxytocin in order to determine the effect of oxytocin on adolescent trust game behavior. Adult research shows that intranasal administration of oxytocin significantly increases investments made in other people without increasing investments made in a lottery (Kosfeld et al., 2005), suggesting that this paradigm is an appropriate way to study the effect of oxytocin on trust.

The current study extended this paradigm by leading adolescents to believe that they were playing with their mother and a stranger and determining the effect of oxytocin on investments through comparison with a placebo control. Given evidence that lower trust is associated with psychopathology, we expected that community controls in both the placebo and oxytocin conditions would have higher investments than inpatient adolescents. However, oxytocin was expected to demonstrate clinical potential by raising the level of trust in the inpatient sample nearer to the trust behavior of community adolescents in the placebo group, thereby bringing inpatients to a “normal control” trust level.

### **Moderating effect of attachment security**

The second aim of this study was to explore baseline attachment security as a moderator within each group to determine whether the effect of oxytocin differed depending upon the existing social relationship. Importantly, research with adults playing

a trust game with and without oxytocin suggests that the effects of oxytocin on trust behavior are context specific—that is, the trust-inducing effect of oxytocin is overridden when the game partner is untrustworthy (Mikolajczak et al., 2010). Similarly, Strathearn and colleagues (2009) show that oxytocin circuitry is differentially activated in mothers with varying levels of attachment security. As previously noted, trust lies at the core of attachment security such that secure individuals “experience felt security by trusting that the attachment figure can be trusted in times of hardship” (Simmons, Gooty, Nolson, & Little, 2008, p. 234). Attachment insecurity, on the other hand, is associated with maternal unresponsiveness (Belsky, 1984), maltreatment (Cicchetti, Rogosch, & Toth, 2006), serious maternal psychopathology (Matrins & Gaffan, 2000), and maternal substance abuse (O’Connor, Sigman, & Brill, 1987), all of which interfere with a parent’s ability to be a trusted source of support. In other words, the trustworthiness of a caregiver is inextricably linked with the child’s attachment representation of them (Sharp & Fonagy, 2008).

Because the effects of oxytocin are context specific (Bartz, Zaki, Bolger, & Ochsner, 2011), it was expected that the effect of oxytocin on adolescent trust behavior towards their mother would depend upon their attachment representation of her. Indeed, adult research revealed that oxytocin administration increased positive attachment memories among securely attached individuals but increased negative attachment memories among anxiously attached (corresponding to preoccupied in the CAI) individuals (Bartz et al., 2011). Moreover, oxytocin has been shown to increase neuroeconomic cooperation game behavior of adults high in attachment avoidance (corresponding to dismissing in the CAI) in the presence of oxytocin, which was not the

case for those rated high in attachment anxiety (De Dreu, 2012). Therefore, we expected that within each sample (community v. inpatient), oxytocin would increase the trust game behavior of adolescents coded as secure and dismissing but not preoccupied. No study has explored the relation between oxytocin or trust behavior and disorganized attachment, so those analyses were solely exploratory.

### **Relation between oxytocin effect and psychopathology**

Given speculation about the clinical utility of oxytocin (e.g., Netherton & Schatte, 2011) for adolescents with psychopathology, the present study sought to examine the effect of oxytocin on trust in two subsamples—a group of healthy adolescents recruited from the community and a group of adolescents recruited from an inpatient psychiatric unit. Additionally, internalizing and externalizing symptoms were assessed continuously in both samples in order to adequately characterize both subgroups and explore how psychopathology relates to the effect of oxytocin.

Specific hypotheses about the relation between psychopathology and oxytocin effects in adolescents were precluded by the absence of prior research. Indeed, only one previous study has given oxytocin to adolescents with a psychiatric disorder (with autism) and, therefore, these analyses were exploratory.

### **The present study**

In sum, the present study had three aims. First, we sought to explore the effect of oxytocin on trust game behavior, exploring how this effect differs among inpatient and community control adolescents. We expected that community participants would demonstrate higher trust game investments than patients in the placebo conditions, and that oxytocin would demonstrate clinical potential by raising the level of trust in the

inpatient sample near to the trust behavior of community adolescents in the placebo group. Second, we aimed to test whether baseline attachment security would moderate the effect of oxytocin. Third, we aimed to explore how internalizing and externalizing symptoms related to the effect of oxytocin on trust.

## **Implications**

This study has significant implications for public health and the treatment of adolescent psychopathology because it contributes to knowledge regarding the clinical utility of oxytocin administration (suggested by Netherton & Schatte, 2011). As previously noted, attachment insecurity, and likely related perceptions of untrustworthiness in others, interfere with an adolescent's ability to seek help and make use of social support, and stand in the way of providing effective interventions to this group. In other words, even valuable interventions are rendered ineffective because adolescents will not ask for help from those capable of delivering it. The present study provides valuable information regarding the effect of oxytocin on adolescent trust behavior and speaks to individual differences in responsiveness by exploring both inpatient and community samples and assessing variables like attachment security and psychopathology.

## **Methods**

### **Participants**

Adolescents between the ages of 12<sup>1</sup> to 17 were recruited for this study. Inpatient adolescents were recruited from the Adolescent Treatment Program (ATP) of the Menninger Clinic, an inpatient unit which typically serves adolescents with severe

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<sup>1</sup> Age range was expanded from 15-17 to 12-17 in order to minimize exclusions, due to slow recruitment.



behavior and psychiatric disorders. Community adolescents were recruited from the Houston Independent School District and Craigslist advertising.

Inclusion criteria for participation were identical for both inpatient and community participants, except for the presence of psychiatric disorder in the inpatient sample. Inclusion criteria across both groups included parental consent, ages between 12 and 17, English fluency and literacy (based on the WRAT-IV in the community sample; English fluency was required at the inpatient facility), and a living mother. These inclusion criteria were selected in order to explore trust behavior towards mothers in the adolescent age group, a group largely affected by mental illness and therefore an important group in which to explore the role of oxytocin and attachment style on future interventions. English fluency was necessary because the trust game is programmed in English. Only mothers were used in this study for consistency and in light of preliminary work with the inpatient sample suggesting that over 85% of parent-report measures are completed by mothers.

Exclusion criteria for inpatients included a diagnosis of schizophrenia or any psychotic disorder and mental retardation (assessed at admission by clinical staff), as these disorders may affect an adolescent's investments in the trust game and obscure the effects of oxytocin and attachment style on trust behavior. Moreover, neurological disorders such as developmental or learning disabilities were excluded leaving only inpatients with emotional-behavior disorders in the psychiatric sample. We additionally excluded any adolescent who received a primary diagnosis of Attention Deficit Hyperactivity Disorder at admission, as this disorder is characterized by many as a neural dysfunction. A pregnancy test given before oxytocin administration was used to exclude

both community and inpatient adolescents who were pregnant, in light of previous clinical use of oxytocin to induce labor and the theoretical risks associated.

Exclusion criteria in the community sample included exclusion of any adolescent with significant symptoms of psychopathology. To that end, the Youth Self-Report (Achenbach & Rescorla, 2001) was used to exclude adolescents with symptoms of any psychiatric disorder that were two standard deviations above normative means. The Youth Self Report includes subscales related to all classifications of disorder (e.g., thought problems, attention problems, social problems, competence scales, etc.) and therefore served as the sole exclusion measure in the community sample. By excluding these adolescents, the community sample served as a community control group in order to understand the effect of oxytocin and moderating effect of attachment in the absence of clinically significant psychopathology. After consenting and assenting, community participants completed the Youth Self-Report and the measure was electronically scored. If the adolescent was excluded, he or she was thanked for participation and compensated with a \$30 gift card. If he or she was not excluded on the basis of the Youth Self-Report, study procedures including oxytocin administration continued. Youth identified through this screening procedure to be suffering from emotional-behavior problems were given a list of referral options, including the University of Houston Psychology Research and Services Center, where the proposed research was conducted.

In both the inpatient and community samples, participants were instructed that they would be excluded from the study for consumption or use of alcohol or tobacco during the 24 hours prior to oxytocin administration. Likewise, consumption of food or drink within 2 hours of oxytocin administration was prohibited.

A final sample of 50 inpatient adolescents was sought. To that end, 117 consecutive admissions to the adolescent unit of an inpatient psychiatric hospital (the Menninger Clinic's Adolescent Treatment Program; ATP) were approached for consent. Of those approached, 49 declined, one was discharged prior to completion of the assessments, one began assessments and then revoked consent, and 16 were excluded from the study based on the aforementioned criteria. Additionally, one adolescent was excluded due to a potential interfering medical treatment (i.e., chemotherapy). Four adolescents were statistical outliers with regard to a key outcome variable (Trust Game) and were therefore excluded from analyses, resulting in a final sample size of 45 in the inpatient sample. Regarding gender, 48.88% of the sample ( $n = 22$ ) identified as female and 51.11% of the sample ( $n = 23$ ) identified as male. The average age was 15.31 years ( $SD = 1.43$ ). Parent-reported ethnic background of the participants was as follows: 6.67% Hispanic, 80.00% Caucasian, 2.22% African-American, and 11.11% Multiracial, Other, or chose not to answer. Parental educational attainment was as follows: 6.67% some college, 44.44% Bachelor's or Associate's degree, 22.22% Master's degree, 17.78% professional degree (M.D, Ph.D, J.D.), and 8.89% chose not to answer. Adolescents with a history of treatment refractory emotional and behavioral symptoms typically populate the adolescent unit from which adolescents were recruited. Broadly, approximately 43.90% of the adolescents in this group had been admitted previously for acute psychiatric hospitalization (i.e., 1-5 days); 46.34% had been admitted previously for an extended psychiatry hospitalization (i.e., more than five days); and 80.00% were prescribed psychiatric medications at the time of admission. Overall, the rate of psychopathology in this sample was high (see Descriptive Analyses).

Additionally, a final sample of 50 adolescents was sought from the community. Between February of 2013 and December 2014, 41 community adolescents responded to an advertisement for this study and were approached for consent. Of those approached, one adolescent was excluded due to a previous diagnosis of an eating disorder. Additionally, three participants who participated were later excluded from analyses due to psychopathology that exceeded the clinical threshold ( $n = 1$ ) and for a WRAT grade reading level below fifth grade ( $n = 2$ ). Outlier analyses identified two community participants with problematic data who were subsequently excluded, resulting in a final sample size of 35 in the community sample. Regarding gender, 60.00% of the sample ( $n = 21$ ) identified as female and 40.00% of the sample ( $n = 14$ ) identified as male. The average age was 14.40 years ( $SD = 1.82$ ). Parent-reported ethnic background of the participants was as follows: 34.28% Hispanic, 17.14% Caucasian, 37.14% African-American, and 11.43% Multiracial or Other. Parental educational attainment was as follows: 2.86% completed some high school, 8.57% high school diploma or equivalent, 28.57% some college, 34.29% Bachelor's or Associate's degree, 20.00% Master's degree, and 5.71% other. Due to exclusionary criteria, the level of psychopathology in the community sample was low (see Descriptive Analyses).

## **Measures**

**Demographics.** To determine English fluency and literacy (an inclusion criterion), the reading test of the Wide Range Achievement Test (WRAT-IV; Wilkinson & Robertson, 2006) was used. This subtest consists of 15 letters and 42 individual words that the adolescent is asked to pronounce. Grade-equivalent scores are derived by using age-based normative values. Based upon the reading level required for other study

measures, adolescents below a 5<sup>th</sup> grade reading level were excluded. A questionnaire was used to assess demographics including age, birth date, birth sex, ethnic/racial background, and parental education. Likewise, use of oral contraception and menstrual cycle information was requested from female participants. These variables were assessed in order to identify possible confounds in trust behavior and in order to adequately describe the samples.

**Psychopathology.** Psychopathology was assessed using the Youth Self-Report (YSR; Achenbach & Rescorla, 2001) a widely used, gold-standard self-report questionnaire for use between the ages of 11 and 18. It includes 112 problem items, each scored on a 3-point scale and yields dimensional internalizing and externalizing scores used in this study to collect data on how the effect of oxytocin relates to symptomatology. A parent-report form, the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), was also used to assess parent perceptions of psychopathology.

**Attachment Organization.** Attachment organization was assessed using both interview and self-report based measures in order to have measures both with and without a social component and with varying levels of transparency. The interview-based Child Attachment Interview (CAI; Target, Fonagy, Shmueli-Goetz, Data, & Schneider, 2007) was used to assess attachment style by accessing adolescents' mental representations of their mother. Adequate validity for the CAI has been demonstrated both in the original measure's publication (Shmueli-Goetz, Target, Fonagy, & Datta, 2008) and in a sample of inpatient adolescents (Venta et al., 2014). The interview was conducted in private and videotaped in order to aid in coding the attachment style later on. Coding the CAI requires three days of training at University College London. These training sessions are

conducted by the measure's authors and focus upon the coding process, with secondary emphasis on the interview's administration. Specifically, attendees are trained to code interviews from videotapes and transcribed narratives on the basis of the following subscales: emotional openness, balance of positive and negative reference to attachment figures, use of examples, preoccupied anger, idealization, dismissal, resolution of conflicts, and overall coherence (a subscale of the CAI). These ratings are then used to assign an attachment classification (i.e., secure, dismissing, preoccupied, and disorganized) to each caregiver. Following the training, individuals interested in becoming certified interview coders must complete a lengthy reliability process and must achieve 85% agreement with the authors on a predetermined set of interviews.

In a previous sample recruited from ATP, 30.4% of adolescents were classified as secure, 38.1% as dismissing, 14.4% preoccupied, and 17.0% disorganized (Venta et al., 2014) and in a previous community sample the distribution was roughly 60% secure, 30% dismissing, 6% preoccupied, and 4% disorganized (Shmueli-Goetz et al., 2008), suggesting that all classifications would be represented in both samples. However, classifications on the CAI can be combined into secure and insecure (including dismissing, preoccupied, and disorganized) if needed.

The Kerns Security Scale (KSS; Kerns & Stevens, 1996) served as a self-report measure of attachment security to mothers. The measure contains 15 items rated on a 4-point scale and responses are selected based upon Harter's (1982) format (i.e., "some kids..." versus "other kids..."). An example is "Some kids find it easy to trust their mom but other kids are not sure if they can trust their mom" after deciding which statement applies most to them, they select "really true for me" or "sort of true for me." This

measure produces an index of total security. Adequate validity has been demonstrated in the original publication (Kerns, Schlegelmilch, Morgan, & Abraham, 2005). Cronbach's alpha for this measure in this sample was .90.

**Trust.** Trust was assessed using the trust game and a self-report measure to allow secondary analyses exploring the external validity of the trust game. Many variations of the trust game, created by Berg et al. (1995), currently exist. In this proposal, a slightly modified version of the tasks used by Unoka, Seres, Áspán, Bódi, and Kéri (2009) and Kosfeld et al. (2005) was used to probe the trust behavior of the adolescent without him or her needing to receive feedback from the partner. The researcher explained the directions as follows: "In this game, you will be the Investor. In each of 5 rounds, you will receive 12 dollars. You will then decide how many you want to send to your partner over the Internet. Whatever you decide to send will be tripled on the way to your partner. They then decide how many dollars they want to keep and how many they want to send back to you. The object of the game is to have as much money as possible. You will play two games that will come up in random order. You will play with your mother who is connecting over the Internet and with another woman, about her same age, who is a stranger to you. When you are playing with your mother, it is completely up to her how many dollars you get back in each round. When you are playing with the stranger, the amount you get back is completely up to her." The adolescent is told that their partner will receive the same instructions about game play. Despite not receiving feedback between trials (i.e., partner responses are not shown to the adolescent), this game has successfully discriminated between diagnostic groups expected to show differences in trust behavior (Unoka et al., 2009). The adolescent was provided a chance to ask

questions and was asked to repeat the instructions before progressing. Cronbach's alphas in this sample for investments across five trials were .80 for the stranger game and .80 for the mother game.

The Interpersonal Trust Belief Scale (ITBS; Rotenberg, Fox, Green, Ruderman, Slater, Stevents, & Carlo, 2005) was used to allow for analyses exploring the external validity of the trust game in these two samples. This is a 24-item self-report measure assessing 3 bases of trust (i.e. reliability, emotional, and honesty) towards mother, father, teacher, and peer and providing a total trust score. Each item is rated on a 5-point scale asking the adolescent to determine how likely each target is to display each of the bases. Reliability and validity of this measure have previously been established (Rotenberg et al., 2005). This measure was used to examine the external validity of the trust game. Cronbach's alpha for the ITBS in this sample was .89.

## **Procedures**

Data were collected at one time point, upon admission to the Adolescent Treatment Program of the Menninger Clinic (ATP) for the inpatient sample and in one assessment session at the University of Houston Psychology Research and Services Center (PRSC) for the community control sample. This study used a randomized, double-blind, placebo controlled design with type of game as a repeated measure. Adolescents from each sample were randomized to either a placebo or oxytocin condition. Both the researcher and the adolescent were blind to their assignment. The adolescent self-administered either oxytocin or placebo and played a trust game with two conditions. The order of these two conditions was randomized. In one, the adolescent believed that he or she was playing with his or her mother over the Internet. In the other, the adolescent



believed that he or she was playing with a stranger who was female and about the same age as the adolescent's mother. Adolescents also completed several other assessments, were debriefed about the deception involved (they were not really playing with partners over the Internet), and received compensation.

Initially, recruitment of an age and sex-matched community sample was sought. However, age and sex matching of inpatient and community adolescents reduced the total number of participants from 80 to 42 and, therefore, age and sex were explored as covariates rather than creating matched samples. Recruitment of community controls relied upon Craigslist advertisements and flyers at local youth organizations as well as recruitment from area public schools. All participants were compensated with \$30 gift cards to a nation-wide department store.

In both patient and community subgroups, informed consent from the parents was collected first and, if granted, assent from the adolescent was obtained. For the patient sample, this occurred on the first day of admission. For the community sample, this occurred during the sole assessment session, in person at the PRSC. Following consent, adolescents were separated from their parents and taken to a private room. Prior to oxytocin administration, adolescents were asked to complete self-report measures assessing demographics and psychopathology, and an interview-based measure of attachment security.

Once completed, oxytocin administration followed the procedures outlined by Kosfeld et al. (2005). Specifically, subjects self-administered 3 puffs of a nasal spray in each nostril for a total of one dose of 24 IU oxytocin (in the form of Syntocinon-Spray, Novartis) or one dose of a placebo spray containing all inactive ingredients, 50 minutes

before the start of the trust game. No dosage specifications currently exist for the use of oxytocin, however, this dosage and nasal spray supplier has been used in many studies (see MacDonald et al., 2011). A number was assigned to each bottle and was linked to either placebo or oxytocin in document prepared by the pharmacist bottling the nasal sprays and stored within a sealed envelope until study completion. Numbers were randomly assigned to placebo and oxytocin spray bottles in order to randomize assignment of each adolescent. No side-effects were expected, as a recent review of previous research with intranasal oxytocin determined that participants receiving oxytocin and a placebo could not be distinguished on the basis of reported side-effects and could not tell which substance they had received (MacDonald et al., 2011). Still, a symptom checklist was used to assess for any adverse side effects before administration, immediately after administration, and 45 minutes after administration. In this study, no adverse effects of oxytocin or the placebo were noted in either the community control or patient subgroups.

The effects of intranasal oxytocin are thought to peak at around 50 minutes post-administration, after which time testing began. Adolescents watched a predetermined movie (i.e., BBC's Planet Earth) without relevance to trust during the intervening time. Previous research suggests that a social environment is needed to trigger the effects of oxytocin (Insel & Shapiro, 1992; Kendrick, Da Costa, Broad, Kosfeld et al., 2005; Ohkura, Guevara, Lévy, & Keverne, 1997). In this study, the trust task served as the social trigger. Following the 50-minute wait, the researcher explained the trust game. Adolescents were told that they were going to play a game (see details above) with their mother who was connecting over the Internet and with a stranger about her same age.

These two conditions allowed data analyses comparing trust behavior towards a known, attachment-related target to trust behavior towards a human, non-attachment-related target. Only mothers were used in this study for consistency and in light of preliminary work with the inpatient sample suggesting that mothers complete over 85% of parent-report measures. Both game conditions were programmed electronically to randomize the order and simulate an Internet game. Adolescents then completed both games on the computer, received compensation, and were debriefed about the deception involved in the trust game. Specifically, it was explained that both games were identical, played solely with a computer. Because inpatient adolescents were assessed soon after admission to the hospital, they were unlikely to have been exposed to information about the study and were therefore likely naïve to the deception. Community controls were not expected to have any prior knowledge of the task. We asked each adolescent about their belief of the trust game after it as played in order to assess the external validity of this task (see Descriptive Analyses).

### **Data Analytic Strategy**

The first aim of this study was to determine the effect of oxytocin on trust game behavior. This aim was explored in two ways. First, the mean and median amounts invested were compared between groups and condition, as done by Kosfeld et al. (2005). Second, a four-way ANOVA with repeated measures explored subgroup (community v. patient) x condition (oxytocin v. placebo) x game (repeated: trust v. stranger) x trials (repeated: 1-5) effects and interaction effects.

The second aim was to determine whether attachment security moderated the relation between oxytocin and trust behavior. Moderation was explored in a subgroup

(community v. patient) x condition (oxytocin v. placebo) x attachment (secure, preoccupied, dismissing, disorganized) x trials (1-5) design. Moderation was explored separately for each game type.

Secondary analyses examined how the effect of oxytocin differed with regard to internalizing and externalizing symptoms by collecting dimensional symptom ratings that were correlated with mean and total trust behavior. Psychopathology was also explored as a moderator in the aforementioned models.

Finally, the external validity of the trust game and CAI was explored using self-report measures of trust and attachment and examining bivariate correlations among adolescents in the placebo condition.

## **Results**

### **Preliminary Analyses**

Normality was explored for all continuous measures: the YSR internalizing and externalizing subscales, the CBCL internalizing and externalizing subscales, the KSS total mother score, and the ITBS total score and are presented in Table 1. Evidence of non-normality was noted with regard to both the YSR externalizing and the CBCL internalizing scales.

Table 1

### **Randomization Preliminary Analyses**

Participants were randomly assigned to either receive a placebo nasal spray or an oxytocin nasal spray. In the community group, 15 adolescents received the oxytocin nasal spray and 20 received a placebo nasal spray. In the patient group, 25 adolescent received the oxytocin nasal spray and 20 received the placebo nasal spray. There were no

significant differences noted between the placebo and oxytocin groups (Table 2) with regard to age, gender, self-reported internalizing symptoms, self-reported externalizing symptoms, parent-reported internalizing, parent-reported externalizing, self-reported attachment security (KSS total), or self-reported trust (ITBS total).

Table 2

### **Descriptive Analyses**

Differences between the patient and community subgroups were assessed and descriptive data for age as well as the YSR, CBCL, KSS, and ITBS are presented in Table 3. The two groups differed only with regard to psychopathology. Specifically, the clinical subgroup had significantly higher parent-reported internalizing and externalizing symptoms and self-reported internalizing and externalizing symptoms. Pearson Chi-Square analyses provided no evidence of significant associations between gender and subgroup status (i.e., patient v. community; *Chi-Square* = .98,  $p = .323$ ) however, a significant relation between subgroup status and ethnicity was noted (*Chi-Square* = 18.44,  $p < .001$ ).

Table 3

CAI data on maternal attachment were available for 28 (out of  $n = 35$ ) community participants and 41 (out of  $n = 45$ ) patient participants. Missing data on the CAI was due to technical difficulties associated with video recording and/or saving the interview. In the two-way classification, 71.43% of community participants were coded as secure ( $n = 20$ ) and 28.57% ( $n = 8$ ) were coded as insecure (all were coded as dismissing). No community participants were coded as disorganized or preoccupied. In the patient sample, 19.51% ( $n = 8$ ) were coded as secure and 80.49% ( $n = 33$ ) were coded as

insecure (20 were coded as dismissing, 9 were coded as preoccupied, 4 were coded as disorganized). Due to a small number of insecurely attached participants, subtypes of attachment insecurity (i.e., preoccupied, dismissing, disorganized) were not explored and analyses relied, instead, on only the insecure versus secure classifications.

With regard to the trust game, responses that were out of range (0-12) were deleted, such that, in the community sample, one adolescent was missing data on two trials, and in the patient sample, one adolescent was missing data on one trial. All trust game data were missing for one adolescent in the patient sample. Repeated measures analyses (see below) require complete data across all trials of the trust game and therefore relied upon a sample of 33 community and 43 patient participants (with 38 in the oxytocin and 38 in the placebo conditions). Descriptive data for the trust game is presented in Table 4. No differences between subgroups or conditions were noted on any trial or in the mean scores for the stranger and mother conditions. Adolescents were asked to rate the degree to which they believed they were really playing with their mother on a scale from 1 to 7. Among community controls, scores ranged from 3 to 7, with an average score of 5.68 ( $SD = 1.25$ ) and a modal response of 7. Among patients, scores ranged from 1 to 7 with an average score of 4.80 ( $SD = 2.03$ ) and a modal response of 7.

Table 4

In the patient sample, seven adolescents stated that they were taking oral contraceptives and six stated that they were currently menstruating. Among community controls, no adolescents stated that they were taking oral contraceptives and two stated that they were currently menstruating. These variables were explored as moderators with regard to trust game behavior towards mothers and strangers. No evidence of a main

effect of current menstruation on trust game behavior [ $F(1, 38) = 0.713, p = .404$ ] or interaction of current menstruation with oxytocin condition [ $F(1, 38) = 0.640, p = .429$ ] was noted. Likewise, no evidence of a main effect of oral contraceptive use on trust game behavior [ $F(1, 37) = 0.228, p = .636$ ] or interaction of oral contraceptive use with oxytocin condition [ $F(1, 36) = 1.107, p = .300$ ] was noted. Given the absence of evidence suggesting significant relations between these variables and the effect of oxytocin, current menstruation and oral contraceptive use were not included in the final model (see “Effect of oxytocin on trust game behavior”). No participant was pregnant at the time of the study.

### **External validity of trust game and CAI**

Intercorrelations between trust game investments, dimensional CAI security rating (i.e., coherence subscale), the ITBS, and the KSS were computed and are presented in Table 5. These correlations were computed only in the placebo subgroups (i.e., patient placebo group and control placebo group) in order to examine the external validity of these measures under typical circumstances. Correlations suggested significant agreement between a dimensional subscale capturing attachment security globally (i.e., coherence) from the CAI and self-report measures of maternal attachment (KSS) and trust (ITBS). No significant correlations were noted between trust game behavior and other measures of trust or attachment.

Table 5

### **Effect of oxytocin on trust game behavior**

The first aim of this study was to determine the effect of oxytocin on trust game behavior. We expected that community controls in both placebo and oxytocin conditions

would have higher trust behavior than psychiatric adolescents and that oxytocin would demonstrate clinical potential by raising the level of trust in the inpatient sample nearer to the trust behavior of community adolescents in the placebo group.

A four-way repeated-measures ANOVA was used to explore subgroup (community v. patient) x condition (oxytocin v. placebo) x game (mother v. stranger) x trials (1-5) main and interaction effects. Results indicated a significant main effect of game (mother v. stranger) [ $F(1, 72) = 21.657, p < .001$ ] on investments overall and a significant main effect of trials (1-5) [ $F(4, 69) = 3.107, p = .021$ ]. These effects are presented visually in Figure 1, which shows that investments in the mother game were generally higher than investments in the stranger game and that investments (in both games) increased across trials.

Figure 1

A between-subjects interaction for subgroup (patient v. community) and condition (oxytocin v. placebo) was noted as approaching statistical significance [ $F(1, 72) = 3.875, p = .053$ ]. This interaction is presented visually in Figure 2, which indicates that oxytocin raised the level of trust in the patient group such that it surpassed the placebo level of trust displayed by the community group. This interaction corresponded to a moderate effect size ( $d = 0.458$ ).

Figure 2

Descriptive data for the trust game are presented in Table 4 and, visually, in Figure 3, and were used to further interpret these findings. This figure illustrates a significant between-subjects effect (i.e., community placebo, community oxytocin, inpatient placebo, vs. inpatient oxytocin) on investments [ $F(3, 75) = 2.96, p = .038$ ] with



regard to the stranger game. Specifically, the inpatient oxytocin group invested significantly more ( $M_{diff} = 1.32, p = .042$ ) than the inpatient placebo group and the community oxytocin group ( $M_{diff} = 1.86, p = .008$ ), with investments comparable to the community placebo group ( $M_{diff} = 0.55, p = .384$ ). A post-hoc equivalence test comparing the inpatient oxytocin and community placebo groups was not significant ( $t(43) = -0.81, \Delta = .30, p = .197$ ), indicating no statistically significant difference between the investments of these two groups in the stranger game (Weber & Popova, 2012). Equivalence tests were conducted using the custom dialog provided by Weber and Popova (2012).

Significant differences between groups were not evident when exploring investments in the mother game (see Table 4 and Figure 3), with no evidence of a significant between-subjects effect on investments [ $F(3, 72) = 0.60, p = .617$ ]. However, as in the stranger game, a post-hoc equivalence test comparing the inpatient oxytocin and community placebo groups was not significant ( $t(43) = -0.42, \Delta = .30, p = .108$ ), indicating no statistically significant difference between the investments of these two groups in the mother game (Weber & Popova, 2012).

Figure 3

### **Moderating role of attachment security**

The second aim of this study was to determine whether attachment security moderated the relation between oxytocin and trust behavior; moderation was explored separately for each game type. We expected that within each sample (community v. inpatient), oxytocin would increase the trust game behavior of adolescents coded as secure and dismissing but not preoccupied. No study has explored the relation between

oxytocin or trust behavior and dismissing attachment, so those analyses were solely exploratory. Due to small numbers of adolescents in the insecure subtypes (e.g., preoccupied, disorganized), these analyses relied on only the insecure versus secure classification.

Moderation was explored in a subgroup (community v. inpatient) x condition (oxytocin v. placebo) x attachment (secure v. insecure) x trials (1-5) design. With regard to the stranger game, no evidence of an interaction between attachment and condition [ $F(1, 60) = 1.32, p = .256$ ] or between subjects effect of attachment [ $F(1, 60) = 0.11, p = .742$ ] was noted. Likewise, with regard to the mother game, no evidence of an interaction between attachment and condition [ $F(1, 57) = 0.42, p = .516$ ] or between subjects effect of attachment [ $F(1, 57) = 0.18, p = .676$ ] was noted.

### **Relation to psychopathology**

Secondary analyses sought to examine how the effect of oxytocin related to psychopathology. No evidence of a significant relation between trust game investments (in either game) and internalizing symptoms was noted. At the bivariate level, self-reported internalizing symptoms did not significantly correlate with mean ( $r = .13, p = .272$ ) stranger investments or mean ( $r = .08, p = .514$ ) mother investments. Likewise, parent-reported internalizing symptoms did not significantly correlate with mean ( $r = .12, p = .309$ ) stranger investments or mean ( $r = .13, p = .275$ ) mother investments. At the multivariate level, internalizing symptoms were explored as moderators with regard to trust game behavior overall (across games). No evidence of a main effect of self-reported internalizing symptoms on trust game behavior [ $F(1, 70) = 0.869, p = .652$ ] or interaction of self-reported internalizing symptoms with condition [ $F(1, 70) = 0.668, p =$

.738] was noted. Likewise, no evidence of a main effect of parent-reported internalizing symptoms on trust game behavior [ $F(1, 69) = 0.982, p = .524$ ] or interaction of parent-reported internalizing symptoms with condition [ $F(1, 69) = 0.503, p = .902$ ] was noted.

No evidence of a significant relation between trust game investments (in either game) and externalizing symptoms was noted. At the bivariate level, self-reported externalizing symptoms did not significantly correlate with mean ( $r = -.09, p = .451$ ) stranger investments or mean ( $r = -.15, p = .202$ ) mother investments. Likewise, parent-reported externalizing symptoms did not significantly correlate with mean ( $r = -.01, p = .925$ ) stranger investments or mean ( $r = -.05, p = .673$ ) mother investments. At the multivariate level, externalizing symptoms were explored as moderators with regard to trust game behavior towards mothers and strangers. No evidence of a main effect of self-reported externalizing symptoms on trust game behavior [ $F(1, 70) = 1.514, p = .149$ ] or interaction of self-reported externalizing symptoms with condition [ $F(1, 70) = 0.567, p = .724$ ] was noted. Likewise, no evidence of a main effect of parent-reported externalizing symptoms on trust game behavior [ $F(1, 69) = 1.096, p = .405$ ] or interaction of parent-reported externalizing symptoms with condition [ $F(1, 69) = 0.704, p = .700$ ] was noted.

## **Discussion**

The present study had two primary aims, to (a) examine the effect of intranasal oxytocin administration on trust game behavior, determining how this effect differed among inpatient and community control adolescents and (b) explore baseline attachment security as a moderator within each group to determine whether the effect differed depending upon the existing social relationship. The central hypothesis was that oxytocin would increase trust behavior in the whole sample, and demonstrate clinical potential by

raising the level of maternal trust in the inpatient sample nearer to the trust behavior of community adolescents. Overall, findings supported this central hypothesis. A secondary aim was to explore how psychopathology related to the effect of oxytocin on trust.

Regarding the first aim, it was expected that (a) community controls would demonstrate higher trust than inpatient adolescents and that (b) oxytocin would demonstrate clinical potential by raising the level of trust in the inpatient sample nearer to the trust behavior of the community controls. With regard to hypothesis (a), Figure 3 illustrates increased investments among the community control groups, as expected. However, it should be noted that this difference was not statistically significant so the observed result cannot be inferred and generalized beyond this sample. Evidence for hypothesis (b) was found in a nearly significant interaction between subgroup and condition, which demonstrated that oxytocin raised the trust game investments of patients such that it surpassed the placebo-level of trust demonstrated by community controls. Likewise, equivalence testing indicated that the investments of adolescents in the inpatient oxytocin group were comparable to those in the community placebo group in both the mother and stranger games. Therefore, in this study, oxytocin demonstrated clinical potential by raising the level of trust demonstrated by patients to a “community control” trust level, as expected.

Although this interaction between subgroup and condition was true irrespective of game (i.e., stranger vs. mother), the effect of oxytocin is most clearly seen in the stranger game. In this game, post-hoc pairwise comparisons indicated that oxytocin significantly increased the level of investments among the inpatient group, making it significantly higher than their placebo counterparts, and indistinguishable from a “community control”

level. Notably, these pairwise comparisons provided no evidence of a significant effect of oxytocin on the community controls—that is, the community control oxytocin and placebo groups did not significantly differ with regard to trust game investments. Three possible explanations of this finding warrant further investigation.

Perhaps the most intuitive explanation for this finding is that oxytocin demonstrated clinical utility only in the inpatient subgroup because that was the group in which there was a clinical need (i.e., decreased trust). Psychopathology, generally, is associated with decreased trust among adolescents (e.g., Lester & Gatto, 1990; Rotenberg et al., 2010) and, in the present study, the trust game investments of patients in the placebo condition were lower (although not statistically significantly different) than those of the community participants in the placebo condition across both games (see Figures 2 and 3). Therefore, it may be that the effect of oxytocin was readily apparent only in the group that demonstrated decreased trust. Indeed, oxytocin effects are often conceptualized as mitigating an impairment— like decreasing anxiety following a stress induction (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003) or improving emotion recognition in patients with impaired social abilities (Averbeck et al., 2012). In this study, the community subgroup did not demonstrate impaired trust and therefore oxytocin could not demonstrate a mistrust-mitigating effect. In other words, a ceiling effect in the community subgroup may have suppressed the trust-enhancing effects of oxytocin noted in the patient subgroup.

However, the fact that oxytocin did not increase the investments of community controls in this study stands in contrast to prior research conducted with adults which indicated that oxytocin administration increased the investments that healthy young men

made in a trust game played with an anonymous partner (e.g., Kosfeld et al., 2005). The fact that oxytocin demonstrated a trust-enhancing effect in healthy adults but not healthy adolescents (in this study) suggests that alternate explanations—including possible moderators and mediators—warrant further investigation. Although speculative, we posit that developmental and genetic variables may be important to consider in future studies exploring the trust-enhancing effect of oxytocin.

In the present study, the patient group was, on average, about a year older than the community controls (although this difference lost statistical significance after applying a Bonferonni correction), suggesting that developmental differences may have contributed to differential oxytocin effects. Indeed, Hostinar, Cicchetti, and Rogosch (2014) highlight the importance of puberty for the maturation of the oxytocin system and highlight adolescence as an important developmental stage in which to explore oxytocin effects. Regarding trust specifically, prior studies of the trust game have shown that increased investments are associated with increased age, demonstrating decreased trust among younger adolescents (van den Bos, Westenberg, van Dijk, & Crone, 2009; Sutter & Kocher, 2007). Indeed, the trust game investments made by community controls in this study were lower than most of the trust game data reviewed by Johnson and Mislin (2011) and lower than the investments made by community control adults in Unoka et al.'s (2009) study, which used a similar game. Because no prior study has administered oxytocin to adolescents in the context of a trust game, the findings of the current study are somewhat hard to interpret. Therefore, future research should endeavor to replicate the findings of this study, exploring how age-related differences in trust may impact oxytocin responsiveness.

Additionally, the difference in oxytocin responsiveness between community controls and patients noted in this study could be indicative of underlying genetic differences that ought to be explored in future research. Although outside of the scope of this study, research is accumulating to suggest that variants of the oxytocin receptor gene are consistently linked to psychopathology. Indeed, oxytocin receptor gene variants have been associated with increased internalizing symptoms (Hostinar et al., 2014), aggression (Malik, Zai, Abu, Nowrouzi, & Beitchman, 2012), and psychopathic traits (Dadds et al., 2014) among youth. Studies conducted in adults echo the link between certain genotypes and varied forms of psychopathology (e.g., Costa et al., 2009; Montag et al., 2013; Saphire-Bernstein, Kim, Sherman, & Taylor, 2011;). Of particular relevance to this study is the fact that oxytocin gene polymorphism has also been linked to differential trust game behavior (Krueger et al., 2012). Given that individuals with psychopathology were excluded from the community control subgroup, and specifically recruited for the inpatient subgroup, it may be that the design of this study inadvertently selected groups that were different with regard to oxytocin receptor genotype. This is an essential area of future research in continuing to explore for whom oxytocin could hold clinical value.

Another finding of note in the present study is that the effect of oxytocin on trust behavior noted in this study was strongest (i.e., produced significant pairwise comparisons) for the stranger game. Although this was not anticipated, it echoes a larger body of research indicating that oxytocin-effects are context specific and depend upon characteristics of the game partner (Mikolajczak et al., 2010). Specifically, previous research indicates that oxytocin does not increase trust game investments overall, but rather that the trust-inducing effect of oxytocin can be overridden if a game partner has

proven untrustworthy (Mikolajczak et al., 2010). Curiously, the findings of the present study may provide a preliminary indication that the trust-inducing effect of oxytocin is also diminished when prior knowledge of the partner suggests trustworthiness. Indeed, adolescents in this study invested significantly more in their mothers than in the stranger, suggesting that perhaps oxytocin loses its trust-effect in the presence of existing levels of trust. To our knowledge, all oxytocin studies that have made use of a trust game have used anonymous game partners—that is, no previous study has explored the effect of oxytocin on trust game behavior towards a known target, an important area of research in unpacking the possible clinical applications of oxytocin for psychotherapy.

The second aim of this study was to explore baseline attachment security as a moderator within each group to determine whether the effect differed depending upon the existing social relationship. Based upon previous research with adults, it was expected that, within each sample (community v. inpatient), oxytocin would increase the trust game behavior of adolescents with secure and dismissing attachment styles but not a preoccupied attachment (see Bartz et al., 2011; De Dreu, 2012). Due to a small number of insecurely attached adolescents in the community control group, analyses relied on two-way (i.e., insecure v. secure) attachment classifications only—thereby collapsing preoccupied, disorganized, and dismissing adolescents in to one category. Contrary to the hypothesis, no evidence of a significant moderating role of attachment was noted in these analyses. However, this result was unsurprising, given that previous research has highlighted differences in oxytocin-effects *within* the insecure classification (De Dreu, 2012; Bartz et al., 2011) pointing to a suppressed oxytocin effect for anxious/preoccupied individuals. Notably, all insecurely attached community controls and the majority of



insecurely attached patients in this study were coded as dismissing (rather than preoccupied or disorganized) and, based on previous research, we expected that dismissing and secure adolescents would demonstrate similar trust-enhancing effects of oxytocin.. Therefore, the sample recruited in this study was not sufficiently diverse (with regard to attachment) to accurately evaluate the moderating role of attachment security—a limitation of this study and promising area for future research.

A final, exploratory aim of this study was to evaluate, for the first time, how psychopathology related to the effect of oxytocin on trust. In the present study, no evidence of significant relations among parent- or adolescent-rated internalizing or externalizing and trust game investments was found. Although the absence of significant findings could be interpreted as indicating that oxytocin response is unrelated to psychopathology, the broader interaction between subgroup and condition noted in this study speaks to the contrary. That is, overall, community and patient participants displayed different oxytocin effects. Notably, these two groups differed significantly with regard to psychopathology, implying a relation between psychopathology and oxytocin response. Why, then, was evidence of this relation not noted using self- and parent-reports of internalizing and externalizing symptoms? One explanation is that the dimensional symptom ratings used in these analyses did not adequately capture the differences in psychopathology between the two subgroups. That is, perhaps it is not psychopathology symptoms per se, but rather clinically significant or severe psychopathology that distinguishes these two groups and relates to oxytocin response. Although the sample size of the present study precluded comparison of adolescents with and without clinically significant psychopathology, this is an important direction for

future research evaluating the clinical utility of oxytocin. Likewise, the present study did not have a sufficiently large sample to thoroughly examine relations between oxytocin response and specific disorder pathology (i.e., depressive symptoms); this is an important area of future research bolstered by previous research (i.e., Unoka et al., 2009) pointing to diagnostic differences in trust game behavior.

A notable limitation of the present study is that it made use of two measures, the CAI and the trust game, that have not been extensively used among adolescents—producing uncertainty regarding the validity of these measures in the present study. With regard to the CAI, the rates of secure attachment on the CAI documented in this study (18.18% for patients and 75.86% for community controls) stand in contrast to previously published rates in a sample of inpatient adolescents (30.4% secure; Venta et al., 2014) and in a sample of community control children (60% secure). However, with no community comparison group of adolescents, and only one comparison group of inpatient adolescents, it cannot be determined whether the distribution of CAI classifications in this study is a marker of poor validity. Evidence in support of the CAI's external validity in this study is noted in a significant correlation with a widely used self-report measure of attachment (KSS).

In the same vein, the validity of the trust game in this study is uncertain and future research could benefit from a full validity study of the trust game in adolescents. In this study, no evidence of significant relations between trust game investments and the Interpersonal Trust Belief Scale (ITBS) was found. However, this should not necessarily be taken as an indicator of poor validity for the trust game. Indeed, it is well documented (see review Bernath & Feshbach, 1995) that the assessment of youth's trust varies widely

depending upon the mode of assessment and the theoretical rationale underlying the creation of the assessment tool. In this study, in vivo game behavior did not correlate with the ITBS, a self-report scale of trust beliefs. One possible explanation for the absence of a significant correlation is that the two measures access different levels of awareness. That is, the trust game measures in vivo behavior whereas the ITBS measures self-reported beliefs and the two tools use widely disparate assessment methods. Across psychological measurement, it is well known that self-report of beliefs does not necessarily correlate with behavior. Additionally, the ITBS and trust game conceptualize trust in different ways. The ITBS posits that trust is situationally determined by presenting respondents with varied interpersonal vignettes and assessing trust based on specific circumstances (Rotenberg et al., 2005). The ITBS is therefore based on a theoretical model of trust that views trust as dependent upon various situational factors, rather than as a stable personal trait. The trust game in this study, however, provided limited and tightly controlled information about the game and partners. Therefore, the information (e.g., situational description, names of characters, etc.) that adolescents in this study used to make trust determinations in the ITBS was not available for the trust game. In support of the trust game's external validity in this study, findings indicated strong relations between investments across trials (Cronbach's alphas), high self-reported belief in the trust game deception, significantly higher investments in the mother game than in the stranger game, and increasing trust across trials.

Several further limitations in the current study should be noted. First, as had been noted, recruitment (particularly of community controls) was difficult and, therefore, the final sample sizes were smaller than what a-priori power analyses had indicated.

Moreover, the small sample size meant that analyses relating to attachment and psychopathology could not attain large subsamples if adolescents were subdivided along clinically meaningful lines (e.g., clinically significant externalizing symptoms or preoccupied vs. dismissing attachment). Second, the inpatient and community control groups differed significantly with regard to ethnic make-up, a possible confounding factor in subsequent analyses. Again, a limited sample precluded dividing the inpatient and community groups into ethnic subgroups and analyses specifically controlling for ethnicity were not possible due to empty cells when considering ethnicity alongside subgroup and condition. Future research should seek to recruit samples with more closely aligned ethnic distributions or assess a sufficiently large group to specifically examine the role of ethnicity in oxytocin responsiveness. Johnson and Mislin (2011) provide robust evidence of geographic differences in trust game behavior that should be addressed in future research.

Still, the present study is strengthened in several ways. First, the study design cut across multiple levels of analyses, investigating aims across biology (oxytocin), behavior (trust game), interview, and self-report. Second, the present study made use of a randomized design in which adolescents assigned to the placebo and oxytocin conditions did not differ significantly from each other—limiting the effect of confounds on the findings of the current study. Third, data were analyzed using repeated-measures methodology, rather than collapsing across trials and focusing only on univariate analyses using mean or median investments as the sole outcome. Fourth, psychopathology was assessed and analyzed using parent- and self-report dimensional ratings. Fifth, biological confounds like the use of oral contraception and menstruation, for females, were assessed

and analyzed in relation to key study variables. Finally, the present study is the first to examine oxytocin response in adolescents with and without emotional-behavior disorders. To that end, this study provides first evidence for the potential clinical utility of oxytocin among adolescents—that it can increase the level of trust of inpatients to a “community control” level.

## Tables and Figures

*Table 1.*

Normality statistics for all continuous measures.

	<i>Skew</i>	<i>Kurtosis</i>	<i>Shapiro-Wilk</i>	<i>p</i>
YSR Internalizing	-.004	-.818	.972	.276
YSR Externalizing	.563	-.562	.946	.021*
CBCL Internalizing	-.328	-1.259	.920	.002*
CBCL Externalizing	.071	-1.037	.963	.113
SSM Total Score	-.221	-.975	.960	.085
ITBS Total Score	.080	.214	.986	.788

Table 2.

Randomization preliminary data for key study variables.

Measure	Oxytocin M (SD)	Placebo M (SD)	<i>t</i>	<i>p</i>
Age	14.63 (1.58)	15.20 (1.71)	-1.56	.123
CBCL Internalizing	62.79 (14.83)	58.58 (15.12)	1.24	.221
CBCL Externalizing	56.51 (10.93)	54.50 (11.62)	0.65	.436
YSR Internalizing	60.92 (15.05)	59.28 (13.14)	0.22	.608
YSR Externalizing	55.84 (10.03)	57.33 (10.85)	0.50	.533
KSS Total Security	2.71 (0.66)	2.92 (0.67)	0.80	.227
ITBS Total Trust	78.38 (10.72)	82.39 (14.09)	0.11	.222

*Notes.* CBCL = Child Behavior Checklist; YSR = Youth Self-Report; KSS = Kerns Security Scale; ITBS = Interpersonal Trust Belief Scale; M = Mean; SD = Standard Deviation.

Table 3.

Descriptive data for key study variables.

Measure	Community M (SD)	Patient M (SD)	<i>t</i>	<i>p</i>
Age	14.40 (1.82)	15.31 (1.43)	-2.44	.018
CBCL Internalizing	46.51 (9.04)	72.55 (5.92)	-14.62	>.001
CBCL Externalizing	48.09 (9.19)	61.71 (8.83)	-6.62	>.001
YSR Internalizing	49.49 (8.29)	68.70 (11.66)	-8.20	>.001
YSR Externalizing	52.46 (7.66)	59.98 (11.20)	-3.51	>.001
KSS Total Security	2.99 (0.65)	2.68 (0.66)	1.82	.074
ITBS Total Trust	81.67 (11.17)	79.45 (13.80)	0.67	.504

*Notes.* Bonferroni correction was applied such that a p-value of .007 (.05/7) was required for statistical significance. CBCL = Child Behavior Checklist; YSR = Youth Self-Report; KSS = Kerns Security Scale; ITBS = Interpersonal Trust Belief Scale; M = Mean; SD = Standard Deviation.



Table 4.

Descriptive data on trust game.

	Stranger						Mother					
	1	2	3	4	5	Average	1	2	3	4	5	Average
Community	4.40	4.77	5.37	5.29	5.37	5.04	5.41	5.88	6.00	6.34	7.03	6.14
Mean (SD)	(2.16)	(2.25)	(2.64)	(3.11)	(3.09)	(1.88)	(2.43)	(2.53)	(3.24)	(3.22)	(3.63)	(2.32)
Patient	4.84	5.55	5.95	5.52	6.05	5.58	6.07	6.49	6.57	6.84	5.77	6.35
Mean (SD)	(2.53)	(2.97)	(3.29)	(3.08)	(3.50)	(2.39)	(3.42)	(3.45)	(3.69)	(3.52)	(3.43)	(2.58)
<i>t</i> ( <i>p</i> )	-.82 (.415)	-1.28 (.205)	-.85 (.397)	-.34 (.736)	-.90 (.373)	-1.10 (.275)	-.99 (.325)	-.89 (.377)	-.72 (.476)	-.65 (.519)	1.58 (.12)	-.37 (.712)
Oxytocin	4.88	5.45	5.65	5.58	5.73	5.46	5.65	6.31	6.70	6.95	6.23	6.36
Mean (SD)	(2.58)	(2.75)	(3.13)	(3.19)	(3.27)	(2.28)	(2.77)	(3.12)	(3.51)	(3.44)	(3.21)	(2.28)
Placebo	4.41	4.95	5.74	5.26	5.77	5.23	5.92	6.13	5.92	6.28	6.44	6.15
Mean (SD)	(2.14)	(2.63)	(2.93)	(3.00)	(3.41)	(2.10)	(3.30)	(3.06)	(3.27)	(3.32)	(3.91)	(2.65)
<i>t</i> ( <i>p</i> )	.87 (.387)	.83 (.410)	-.137 (.891)	.46 (.649)	-.06 (.953)	.47 (.643)	-.41 (.683)	.25 (.803)	.99 (.325)	.88 (.383)	-.26 (.794)	.38 (.708)

Notes. SD = Standard Deviation

Table 5.

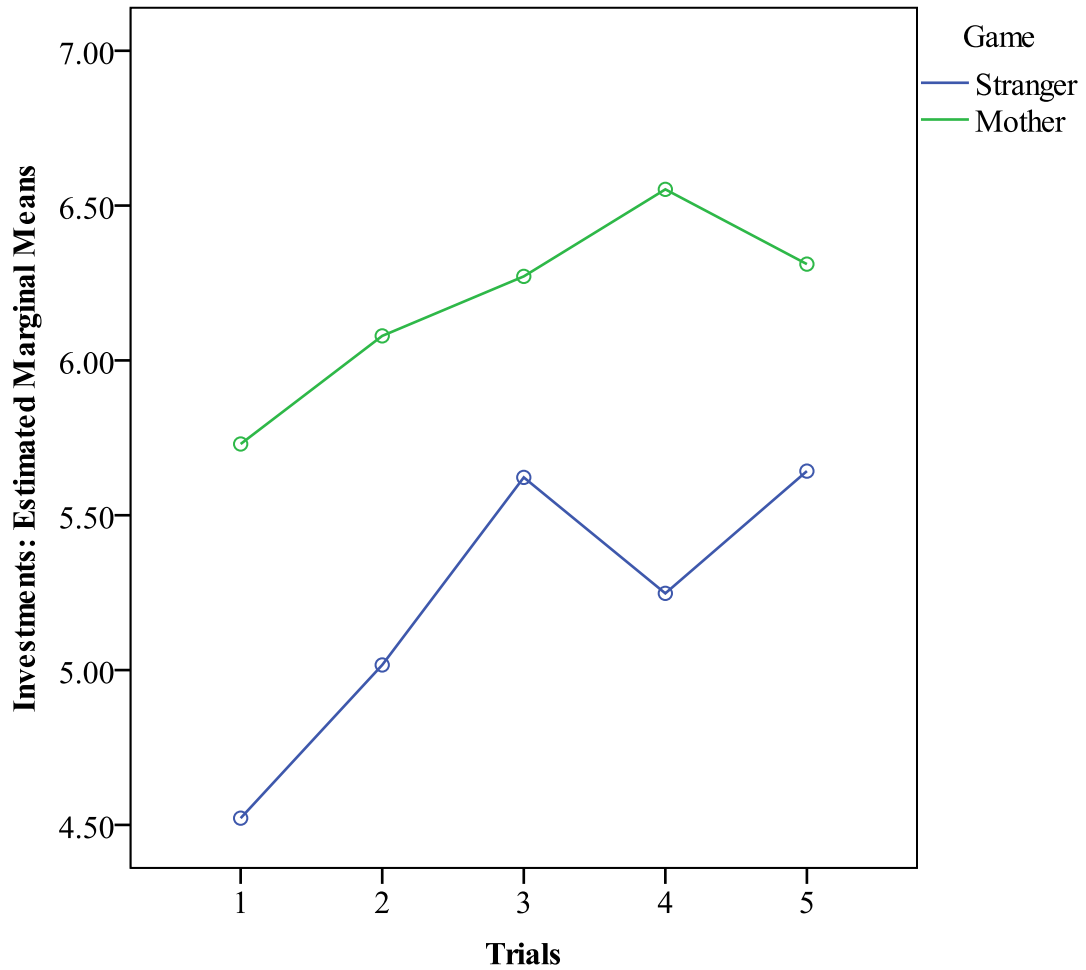
Correlations between attachment and trust measures in the placebo subgroups.

	Stranger	Mother		
	Mean	Mean	KSS Total	ITBS Total
Stranger Mean Trust	1.00			
Mother Mean Trust	0.72**	1.00		
KSS Total	-0.14	0.17	1.00	
ITBS Total	0.03	0.19	0.53**	1.00
CAI Coherence	0.30	0.29	0.56*	0.18

Notes. \*  $p < .05$ , \*\*  $p < .001$

Figure 1.

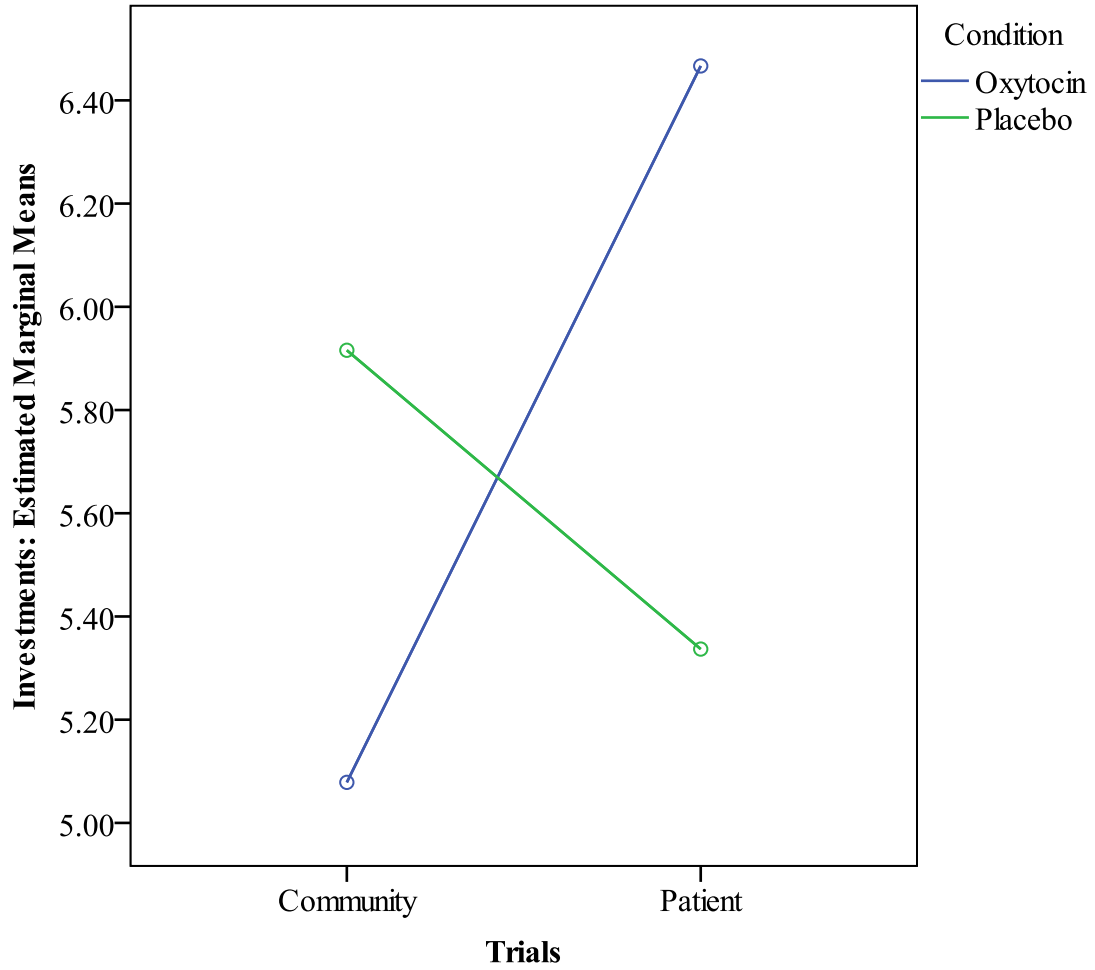
Investments in mother game were significantly higher than investments in stranger game overall and investments increased across trials in both games.



Notes. This figure illustrates a significant main effect of game (mother v. stranger) [ $F(1, 72) = 21.657, p < .001$ ] on investments overall and a significant main effect of trials (1-5) [ $F(4, 69) = 3.107, p = .021$ ].

Figure 2.

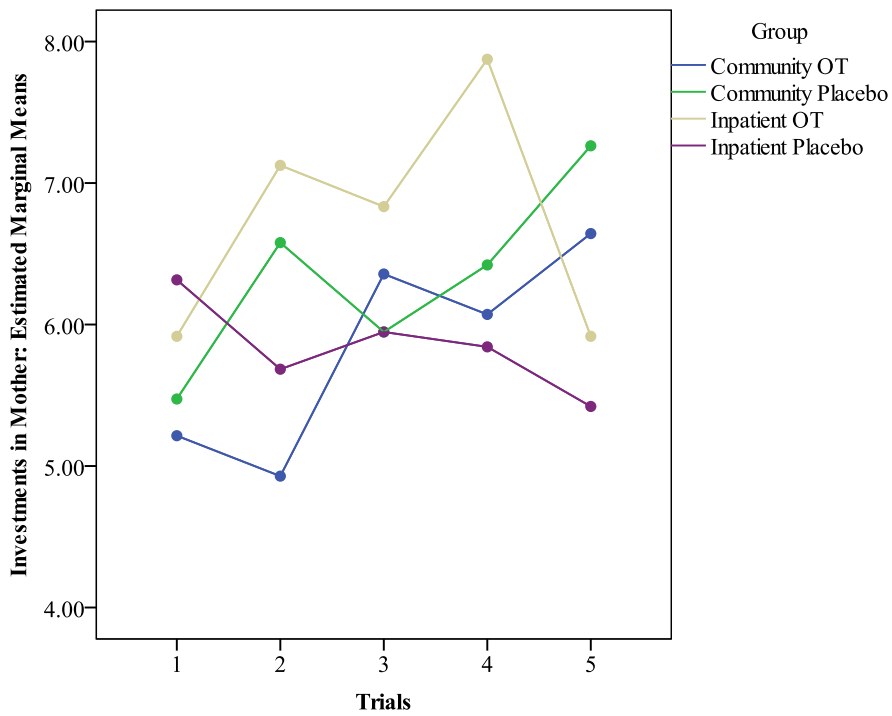
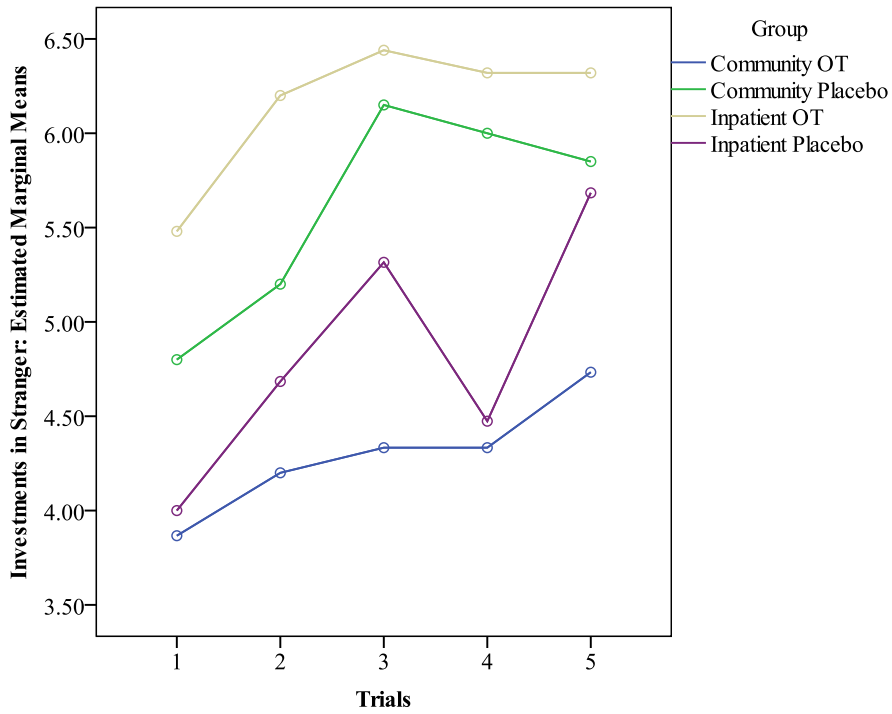
Patients in the oxytocin condition made higher investments in the stranger game than patients in the placebo group.



Notes. This figure illustrates a significant interaction between subgroup and condition [ $F(1, 72) = 3.875, p = .053$ ].

Figure 3.

Investments in stranger and mother games.



## Appendix

### Power Analyses

Power analyses were calculated based on the work of Unoka et al. (2009), who compared diagnostic groups on the trust game and reported moderate to large effects (Cohen, 1988), and Kosfeld et al. (2005), who compared oxytocin and placebo groups in trust behavior and reported moderate effect sizes (Cohen, 1988). Therefore, a moderate effect size (0.5) was entered into a sample size approximation method (WebPower) for the ANOVA design related to the first aim, using  $\alpha = 0.05$ . This method revealed estimated power equal to 0.94 if each level of the first factor (i.e., sample) has 25 adolescents. This procedure was replicated for the ANOVA design related to the second aim and revealed estimated power equal to 0.99 if each level of the first factor (i.e., sample) has 25 adolescents. Thus, the 50 inpatient and 50 community control adolescents expected, randomly assigned to oxytocin ( $n = 25, 25$ ) and placebo ( $n = 25, 25$ ) will be sufficient for all analyses proposed. To avoid missing data, all data is collected electronically and during one day. Preliminary analyses to explore group differences based upon demographic variables will be conducted in order to determine which variables should be controlled for in subsequent analyses.

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