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Effects of Oxytocin on Cortisol Reactivity and Conflict Resolution Behaviors among Couples with Substance Misuse

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Keywords

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1. Introduction

Social stress is a well-established correlate of substance use disorders (SUD). Clinical studies indicate that social stress exacerbates craving, substance use, and relapse among individuals with SUD (Back et al., 2010; Higley et al., 2011). One particular type of social stress which is especially salient in the development, maintenance, and treatment of SUD is dyadic conflict among couples. Existing research indicates that SUD has detrimental effects on dyadic functioning acutely and over time (Boden et al., 2013). Maladaptive dyadic functioning can precipitate excessive substance use and impede effective treatment outcomes (Cranford et al., 2011; Keyes et al., 2011; Quigley et al., 2013; Rodriguez et al., 2013; Testa et al., 2014). For example, research has established a strong temporal association between dyadic conflict (e.g., verbal and physical intimate partner violence) and excessive substance use (Elkins et al., 2012; Mattson et al., 2010; Parks et al., 2008; Testa et al., 2012; Testa et al., 2003). A related body of research indicates that adaptive dyadic functioning facilitates effective SUD treatment and maintenance of abstinence (Grosso et al., 2013). For example, one recent study demonstrated that higher relationship satisfaction among women in SUD treatment was associated with experiencing fewer cravings (Owens et al., 2013). Findings from clinical trials also consistently demonstrate that dyadic interventions for SUD result in significantly higher rates of abstinence compared to individual treatments for SUD (Powers et al., 2008; Stanton and Shadish, 1997). While the efficacy of addressing dyadic functioning within behavioral SUD interventions is well-established, much remains unknown about the efficacy of medications to address dyadic functioning as well as concurrent substance use problems.

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The neuropeptide oxytocin (OT) is associated most saliently with parturition and lactation (Ludwig and Leng, 2006). OT is commonly administered as an intranasal spray and may enhance dyadic functioning and mitigate addictive behaviors simultaneously. Research examining the effects of OT on addictive behaviors is an area of intense scientific inquiry (McGregor and Bowen, 2012; Olff et al., 2010). Recent findings demonstrate that OT has the ability to reduce stress-induced craving, drug-seeking behaviors, and relapse among individuals with alcohol, marijuana, cocaine, or stimulant use disorders (Carson et al., 2010; McGregor and Bowen, 2012; McRae-Clark et al., 2013b; Pedersen et al., 2013; Peters et al., 2013).

OT has also demonstrated anxiolytic and prosocial effects in both animal and human studies (Campbell and Hausmann, 2013; De Dreu et al., 2010; Heinrichs and Domes, 2008; Kirsch et al., 2005; MacDonald and MacDonald, 2010). While some research asserts that OT's prosocial effects are due to its influence on humans' capacity to read and respond to social cues and to better retain positive social memories (Groppe et al., 2013; Guzmán et al., 2014; Olff et al., 2013), other findings caution that amplifying one's capacity to interpret social cues may not always be adaptive (Shamay-Tsoory and Abu-Akel, 2016). A variety of individual and contextual factors such as sex, social context, and psychiatric history may influence response to OT (Bartels, 2012; Bartz et al., 2011b; Flanagan et al., 2015; Hoge et al., 2014). For example, some studies have found that women and men respond differently to OT, both neurobiologically and behaviorally (Hoge et al., 2014; Lynn et al., 2014; Yao et al., 2014), and others suggest that women have higher endogenous OT levels than men (Weisman et al., 2013). Research also demonstrates that individuals with psychiatric diagnoses or trait characteristics such as depression, borderline personality disorder, or high trait aggression may incur negative social or affective effects following OT administration (Bartz et al., 2011a; DeWall et al., 2014; Mah et al., 2013). However, other studies indicate that individuals with more severe trauma history or mental health symptom severity yield more positive OT response compared to healthy controls (Flanagan et al., 2015; Macdonald and Feifel, 2013). Social context also appears to inform OT response in some samples (Bartz et al., 2010; Bartz et al., 2011b; De Dreu et al., 2010). For example, Mah and colleagues found that oxytocin increased protective aggression among mothers with postpartum depression in an intrusive stranger laboratory paradigm (Mah et al., 2015).

The nuances and mechanisms of action underlying the neurobiological effects of OT in humans are complex and many questions remain. However, there is consensus in the existing literature that OT modulates hypothalamic-pituitary-adrenal axis (HPA) reactivity to stressful social stimuli (Neumann et al., 2000; Quirin et al., 2011; Simeon et al., 2011). Salivary cortisol is among the most accessible and commonly studied measure of HPA axis functioning among humans. Several studies have found that intranasally-administered OT reduces cortisol reactivity to stressful stimuli (Cardoso et al., 2013; Ditzen et al., 2009; Heinrichs et al., 2003; Linnen et al., 2012).

Only one previous study has examined the effects of OT on neurobiological reactivity and dyadic conflict behaviors. In a sample of normative heterosexual couples ($N=94$ total participants), Ditzen and colleagues (2009) found that participants who received OT, as compared to placebo, demonstrated more positive conflict resolution behaviors and lower

cortisol levels in a single conflict resolution task. In the same sample, women who received OT, as compared to men who received OT, demonstrated lower salivary alpha amylase levels during the conflict task. However, the higher salivary alpha amylase levels among men were also associated with greater emotional arousal and more positive conflict resolution behaviors (Ditzen et al., 2012).

The current study utilized a randomized, double-blind, placebo controlled and repeated-measures design to extend this line of inquiry to couples with substance misuse. Specifically, we examined the effects of OT on couples' cortisol reactivity and conflict resolution behaviors. We hypothesized that participants who received OT would demonstrate more positive and less negative conflict behaviors and decreased cortisol reactivity compared to participants who received placebo. Additionally, because some animal and human studies have demonstrated sexual dimorphisms in the endogenous OT system as well as HPA functioning in the context of social stress tasks (Ditzen et al., 2012; MacDonald, 2015; Rilling et al., 2014), we expected that the response among men and women might differ.

2. Methods

2.1 Participants

A total of 33 couples (66 individuals) were enrolled in the study during 2014–2015. Participants of any sex and sexual orientation were eligible for the study. However, only two female same-sex couples enrolled. They were excluded from the present analyses given that the small number of same-sex couples and overall sample size was not sufficient to estimate effects for men and women simultaneously while also accounting for sex constellations within couples in the multilevel growth-curve models. In addition, one couple was excluded from the analyses due to unreliable data. The study team discovered that this couple had presented false identities during the self-report portion of the study and did not complete remaining study procedures. Thus, the final analysis sample consisted of 30 heterosexual couples.

Potential participants responded to advertisements placed in the community, local treatment clinics, and on the internet. Inclusion criteria were 1) 18–65 years of age, and 2) one or both partners within each dyad must have engaged in hazardous drinking (i.e., 4 or more standard drinks for women, 6 or more for men on one occasion) or illicit drug use during the past 60 days. Exclusion criteria were 1) pregnancy or breastfeeding for women, 2) history of or current significant hematological, endocrine, cardiovascular, pulmonary, renal, gastrointestinal, or neurological diseases, 3) BMI ≥ 39 , 4) history of or current psychotic, panic, eating, major depressive, or bipolar affective disorders as these may affect HPA and cortisol levels, 5) use of prescribed medications that might interfere with HPA axis activity, 6) active suicidal or homicidal ideation and intent, or 7) severe, unilateral intimate partner violence in the past year as determined by the Revised Conflict Resolution Tactics Scale (CTS-2; Straus et al., 1996)).

2.2 Measures

2.2.1 Diagnostic evaluation—The Mini-International Neuropsychiatric Interview (MINI; 1998) was used to assess current and history of DSM-IV psychiatric diagnoses, including substance abuse and dependence.

2.2.2 Clinical characteristics—The Time Line Followback (TLFB; Sobell and Sobell, 1992) is a calendar-assisted, semi-structured interview which was used to assess quantity and frequency of alcohol, illicit drugs, and prescription drugs (e.g., prescription opioids, benzodiazepines, and psychostimulants). Participants reported the total number of days each substance use and the amount of substance used (e.g., standard drink units for alcohol, number of joints for marijuana) during the 90 days prior to participating in the study.

Alcohol use problem severity was assessed using the 10-item, self-report Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 2001). Items are rated on a scale from 0 (*never*) to 4 (*more than 4 times per week*) and summed to obtain a total score (Cronbach's $\alpha = 0.83$). Drug use problems were assessed with the 10-item version of the Drug Abuse Screening Test (DAST; Skinner, 1982). Each affirmatively endorsed item 0 (*no*)/1 (*yes*) was summed to produce a total drug problems score (Cronbach's $\alpha = 0.59$).

The Dyadic Adjustment Scale (DAS; Spanier, 1976) is a self-report questionnaire used to assess couple functioning. Higher scores reflect higher levels of relationship adjustment, and scores below 97 reflect relationship distress (Cronbach's $\alpha = 0.94$).

2.2.3 Neuroendocrine assay—Unstimulated salivary samples were collected by passive drool in polypropylene vials and immediately iced. Samples were aliquoted into 1.8 mL tubes and saliva was then frozen at -70°C until assayed. Samples were assayed in duplicate using a high sensitivity salivary cortisol enzyme immunoassay system that has an intra-assay precision (coefficient of variation, CV) of 3.35%–3.65% with a lower sensitivity limit of $<0.003\text{ }\mu\text{g/dL}$ (Salimetrics, LLC). Samples were analyzed using a PowerWave HT Microplate Spectrophotometer in conjunction with a Precision Series Automated Liquid Handling System (BioTek Instruments, Inc.).

2.3 Procedures

All procedures were approved by the Institutional Review Board of the Medical University of South Carolina. Participants were scheduled at the same time of day (i.e., 8 a.m.) and during the luteal phase of women's menstrual cycles to control for diurnal and menstrual cycle variations in HPA function. Participants completed informed consent and baseline assessment procedures in a private room separate from their partner. Women completed a urine pregnancy test. If negative, both partners completed breathalyzer tests and urine drug screens. OT and matching placebo were compounded by Investigational Drug Services at MUSC, which also implemented the block-design randomization scheme and kept a record of the blind. The dose and timing of drug administration was selected based on previous OT studies (Ditzen et al., 2009; McRae-Clark et al., 2013a).

2.3.1 Laboratory procedures—At approximately 9:00 am (Time 1), a baseline saliva sample was collected. Participants then completed a 10-minute acclimation period, followed by the first 10-minute conflict resolution task at approximately 9:30 am. Participants then provided a saliva sample immediately afterwards (Time 2). Participants were randomly assigned in a double-blind manner (1:1) to receive intranasal oxytocin (40 IU) or placebo. Both partners within a dyad were randomized to the same drug condition. Participants self-administered 40 IUs of OT nasal spray or matching placebo (i.e., saline) at approximately 9:35 am. Following a 45-minute rest period during which time participants read a book or magazine, watched movies, or read content of their choice on their mobile phones. Participants provided another saliva sample at approximately 10:20 am (Time 3) and began the second conflict resolution task. Data including saliva samples were collected from participants immediately upon completion of the second conflict resolution task at 10:35am (Time 4), and at 15- (Time 5), 30- (Time 6), and 60- minutes (Time 7) post-task. Participants were then debriefed and compensated.

2.3.2 Conflict resolution task—Couples completed two 10-minute, video recorded problem-solving tasks using the Rapid Marital Interaction Coding Scheme (RMICS; Heyman, 2004; Heyman et al., 1995b). Each partner identified a topic of relationship difficulty and a coin flip determined the topic of the discussion. The couple was asked to work towards a resolution or agreement on that topic. Each partners' conflict resolution behaviors were estimated by coding the frequency of the following domains: *psychological abuse* (e.g., verbal statements or nonverbal behaviors indicating disgust, contempt, mocking, domineering, or devaluation), *distress-maintaining attributions* (e.g., statements of blame or negative attributions, denying responsibility), *hostility* (e.g., angry or irritable negative affect, statements of negative content that do not constitute psychological abuse), *dysphoric affect* (e.g., sad or depressed emotional state, whiny tone, self-derogatory statements), *withdrawal* (e.g., behaviors intended to pull back from interaction), *acceptance* (e.g., active listening to help validate or understand partner), *relationship-enhancing attributions* (e.g., statements exempting partner from blame for a negative event, positive attributions), *self-disclosure* (e.g., statements about one's emotions, wishes or beliefs), *humor* (e.g., genuine demonstrations of good humor not including hostile sarcasm), *constructive problem discussion* (e.g., all constructive efforts to problem-solve), and other (e.g., other than a personal or relationship topic). The RMICS is widely used and has demonstrated excellent psychometric properties (Gottman and Notarius, 2000; Heyman et al., 1995a). Coding was completed by the developers of the RMICS. Coders were blind to treatment condition. Inter-rater reliability in the present study was good (Cohen's $\kappa=.56$), with average agreement exceeding 70% across behavioral subscales.

2.4 Data Analytic Plan

Cortisol reactivity was examined using two-intercept, multi-level growth curve models (Kenny et al., 2006), a type of general linear mixed model (GLMM) which allows for the analysis of the effects for both members of the couple simultaneously, while accounting for dependence in the data (i.e., repeated measures nested within individuals, individuals nested within couples). To model the typical inverted U-shape of cortisol reactivity, linear and quadratic effects for time were included starting with Time 3 (i.e., the beginning of the

second conflict resolution task after drug administration), along with interaction effects for experimental condition (dummy coded with placebo as the reference group). Mean-centered, pre-medication baseline cortisol (average of Time 1 and Time 2) and a binary indicator representing whether the participant had a positive urine drug screen for at least one substance were included as covariates. The model also included random intercepts, and allowed for correlation within-couple and within individual over repeated measures. A reduced model was analyzed removing any non-significant interactions with drug condition, resulting in a more parsimonious model with the best fit to the data. GLMMs were also used to model changes in the frequency counts of the various behaviors observed between the first and second conflict resolution tasks. Separate GLMMs were constructed for each behavioral subscale, and each model included fixed main effects for sex and treatment and a sex by treatment interaction term. They also include random couple effects to account for within-couple correlation. Sensitivity analyses were also performed, in which the previously described GLMMs also included a binary indicator representing whether the subject screened positive for at least one substance during the study. All analyses were conducted in SAS 9.4 (SAS Institute Inc, 2013). P-values < 0.05 were considered statistically significant.

3. Results

3.1 Demographics and Baseline Characteristics

Demographic and clinical characteristics are presented in Table 1. The mean age of study participants was 32.18 years (SD=9.9 years). Approximately half of participants were Black (53.3%), and the majority of couples were cohabitating but not married (80%). Participants reported mean DAS scores of 94.08 (SD=11.33). Scores below 97 on the DAS typically indicate relationship distress (Jacobson et al., 1984). Among the 37 participants who tested positive for use of at least one substance on a 6-panel UDS, six tested positive for more than one substance. The most common drug used was marijuana ($n=33$), followed by cocaine ($n=8$), amphetamines ($n=3$), benzodiazepines ($n=2$), methamphetamine ($n=2$), opiates ($n=1$). Fourteen couples in this sample presented with both partners having a positive urine drug screen. There were no between-group differences in any baseline demographic or clinical characteristics.

3.2 Cortisol Reactivity

There were no significant between-group differences in cortisol levels at the beginning of the first conflict resolution task (Time 3). Among women, significant between-group differences emerged (see Table 2), with women in the OT group, as compared to the placebo group, evidencing significantly less stress-induced cortisol reactivity. As shown in Figure 1, among women who received placebo, cortisol levels increased immediately following the task and then decreased. In contrast, among women who received OT, cortisol levels stayed relatively low following the task and did not significantly increase at any post-task assessment period. As a result, cortisol levels among women who received placebo, as compared to OT, were significantly higher at each of the three time points (T3-T6) following the second conflict resolution task. At the final post-task assessment period of the second conflict resolution task (T7), cortisol levels had decreased among women who received placebo, and cortisol was no longer significantly higher than women who received OT (see Figure 1).

In contrast, men's cortisol levels did not significantly change over time (no linear or quadratic effects, see Table 2), and there were no significant differences between the OT and placebo groups for men in either the linear or quadratic effects. Thus, no interactions with drug condition were retained for men in the reduced model (see Table 2).

3.3 Conflict Resolution Behaviors

Table 3 summarizes the estimated mean changes in the counts of each of the 11 behavioral domains observed during conflict resolution tasks. Positive change values reflect increases in counts from the first task (before drug administration) to the second (after drug administration), while negative values indicate declines from the first to the second task. Significant ($p < 0.05$) sex by drug interactions were noted for two of the 11 behavior domains (i.e., Distress Maintaining Attributions and Relationship Enhancing Attributions), indicating that acute administration of OT affected men and women's conflict resolution behaviors differently (see Figure 2). Statistically significant sex by drug interactions on conflict resolution behaviors are depicted in Figure 2. Among women, OT was associated with increased Distress Maintaining Attributions and decreased Relationship Enhancing Attributions. Placebo among women was associated with decreased Distress Maintaining Attributions and increased Relationship Enhancing Attributions. Among men, however, OT was associated with decreased Distress Maintaining Attributions, while placebo yielded no significant change in Distress Maintaining Attributions. Also among men, both placebo and OT yielded declines in Relationship Enhancing Attributions. In the sensitivity analyses, the inclusion of a positive drug screen as an additional covariate in the models summarized in Table 3 did not impact on our conclusions. All statistically significant findings remained significant, and all non-significant findings remained non-significant.

4. Discussion

This study examined the effects of a 40 IU dose of intranasal oxytocin (OT) on cortisol reactivity and conflict resolution behaviors among couples with substance misuse, extending previous work by Ditzen and colleagues (Ditzen et al., 2012; Ditzen et al., 2009). The study employed a behavioral coding system with various positive, negative, and neutral subscales to account for pre-medication behaviors and more clearly ascertain the types of behaviors that may be influenced by OT. Results indicate that among women, but not men, OT significantly attenuated cortisol responses to the laboratory conflict resolution task. These findings are consistent with the hypotheses and encouraging given that the literature on the effects of OT on cortisol and other HPA axis function measurements are ambiguous. Some recent studies have found positive cortisol outcomes among humans while others have found that OT may increase or have no effect on cortisol reactivity (Cardoso et al., 2014). Sex differences in the neurobiological effects of OT are also emerging in the clinical literature. Notably, Ditzen and colleagues' couples study found prominent sex differences in the effects of OT on salivary alpha amylase reactivity (Ditzen et al., 2012).

The findings regarding the behavioral outcomes were also different among men and women; however, these results were inconsistent with hypotheses. Among women, OT increased Distress Maintaining Attributions and decreased Relationship Enhancing Attributions.

Among men, OT decreased Distress Maintaining Attributions and men in both the OT and placebo conditions decreased Relationship Enhancing Attributions over time. These results are surprising in light of existing literature documenting OT's anxiolytic and prosocial effects (MacDonald and MacDonald, 2010), and the positive effects of OT on women's cortisol reactivity in this sample. Previous research asserts that the positive effects of OT on social behaviors may be, in part, a result of attenuated HPA axis reactivity. However, emerging literature suggests that the association between neurobiological stress reactivity and social behavior may not be as closely, or directly, related as previously hypothesized. Indeed, Ditzen and colleagues (Ditzen et al., 2012) found that men demonstrated increased salivary alpha amylase in response to dyadic conflict in the laboratory, but that increase was associated with more positive conflict resolution behavior. The differential findings between men and women in this sample may also be explained by sex differences in the physiology of the endogenous OT system (MacDonald, 2015; Weisman et al., 2013). Considering some previous findings that women and men with SUDs respond differently to laboratory stress paradigms (Back et al., 2005), an additional hypothesis is that men in this sample may not have responded to the dyadic conflict task with as much intensity as women. Future studies should examine subjective responses in order to determine how patients experience the dyadic conflict task before and after drug administration. While the present study was not designed or sufficiently powered to directly test causal association between cortisol reactivity and behavioral responses, future research is necessary to clarify the associations between HPA axis function and social behavior, as well as the impact that sex has on this association.

In conjunction with previous research examining the effects of OT on couple functioning, the current study suggests that adaptive and maladaptive effects of OT may be dependent on both individual and interpersonal contexts. For example, OT's ability to influence HPA axis reactivity and social behavior may differ according to sex, psychiatric diagnostic history, and preexisting relationship patterns. Thus, an additional consideration is that as OT research is rapidly expanding in the field of psychiatry and addiction, new evidence is emerging that highlights the complexity and inconsistency of human OT treatment outcome (Bartels, 2012; Bartz et al., 2011b). Perhaps, in addition to the previously noted nuances associated with OT response, the dyadic context moderates OT response. The vast majority of OT studies to date have been conducted among individuals, and the present study is the first to control for baseline conflict resolution behaviors. We found that the strongest predictor of behaviors in the second conflict resolution task was the behavior used in the first conflict resolution task. Indeed, compared to Ditzen and colleagues study, which did not report on overall couple functioning, the participants in this study consistently reported distressed relationship functioning, which is a common correlate of substance misuse. Although some recent studies suggest that OT may be more effective for individuals who have more prominent psychiatric or social vulnerabilities compared to healthy controls (Bartz et al., 2011b; Flanagan et al., 2015), it is also possible that the pre-existing, maladaptive behavioral patterns common within distressed couples are more persistent and less disposed to OT's influence compared to individual behaviors in laboratory stress paradigms. Like most other human laboratory studies on OT to date, this study used a single drug administration. Differences may emerge over time in studies utilizing multiple repeated drug

administrations. Thus, OT should also be examined as an adjunct to behavioral treatments that facilitate change in deeply ingrained behavioral interaction patterns.

4.1 Limitations

Several limitations should be considered. The small sample size limited statistical power to make inferences about the complex findings. The small sample size also limited our ability to examine moderators of OT response which have been emerging in recent OT studies (Bartz et al., 2011b). Future studies should examine the moderating role of sex, substance use problem severity, and baseline dyadic functioning. This exploratory study also did not examine endogenous OT levels or mental health symptoms such as PTSD or childhood trauma exposure which may influence individual OT responses (Flanagan et al., 2015). The generalizability of these findings is also limited in that while participants in this sample reported high levels of substance-related problems, participants were primarily recruited from the community and were not seeking treatment for SUD. Findings from a similarly designed study may have differed among treatment-engaged couples, who may find greater utility in pharmacological intervention compared to community samples.

While this study employed a multimethod approach, we did not examine more in-depth neurobiological or genetic factors such as functioning of the dopaminergic system, oxytocin receptor genes, or brain-derived neurotrophic factor, which are hypothesized to play an important role in individual differences observed in HPA axis function and the effects of oxytocin administration (MacDonald, 2015; Ortiz et al., 2014; Shamay-Tsoory and Abu-Akel, 2016). An important step forward for future studies examining the relational effects of oxytocin are to employ methods such as neuroimaging to more aptly explain possible drug effects of oxytocin.

Despite these limitations, this is the first to examine the effects of OT on conflict behaviors among couples with substance misuse. Additionally, this study utilized a rigorous and well-controlled laboratory procedure and an evidence-based behavioral coding system, and these findings add to the literature on the effects of OT among men and women.

4.2 Conclusions

Complex neurobiological and behavioral findings were observed in response to a conflict resolution task among couples who received OT or placebo. Future studies examining the use of OT among couples are needed to replicate and expand the current findings. In this sample, a single dose of OT treatment alone was insufficient to mitigate negative dyadic conflict behaviors, and in fact, among some participants, resulted in increased maladaptive conflict behaviors. Future research should examine the utility of pairing OT with behavioral interventions to maximize the opportunity for couples to improve their conflict resolution behaviors and mitigate the common negative outcomes associated with dyadic conflict.

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Figure 1.

Cortisol reactivity in women in response to second conflict resolution task, controlling for baseline cortisol levels and UDS drug screen status. Curves are model-implied based on the reduced quadratic growth curve model, and represent expected cortisol reactivity for women with average baseline (T1 and T2) cortisol. Differences between point estimates for the oxytocin and placebo groups significant at 20, 35, and 50 minutes ($p < 0.01$). Error bars represent standard errors.

Figure 2.
Statistically significant changes in frequency of conflict resolution behaviors among men and women, controlling for baseline frequency of behaviors.

Table 1

Demographic and Clinical Characteristics (N=60)

Characteristics	Overall N=60	Group	
		Placebo n=30	Oxytocin n=30
Demographics			
Age (years)	32.08 ± 9.88	32.21 ± 9.73	31.97 ± 10.17
Employment, n (%)			
Unemployed	26 (86.7%)	14 (46.7%)	12 (40.0%)
Part-time	17 (28.3%)	5 (16.7%)	12 (40.0%)
Full-time	15 (25.0%)	9 (30.0%)	6 (20.0%)
Student	2 (3.3%)	2 (6.7%)	0 (0.0%)
Household Income	30,022±\$20,389	\$28,186±\$17,832	\$31,947±\$23,054
Race, n (%)			
Black/African American	31 (51.7%)	14 (46.7%)	17 (56.7%)
White/Caucasian	24 (40%)	11 (36.7%)	13 (43.3%)
Other	4 (6.7%)	2 (6.7%)	2 (6.7%)
Bi-racial	1 (1.7%)	1 (3.3%)	0
Relationship Status, n (%)			
Married	3 (5.0%)	1 (3.3%)	2 (6.7%)
Cohabitating	50 (83.3%)	25 (83.3%)	25 (83.3%)
Dating	7 (11.7%)	2 (6.7%)	5 (16.7%)
Relationship Length (months)	51.43±60.03	40.95±32.43	60.61±75.87
Clinical Characteristics			
^Substance use disorder, n (%)			
Alcohol Abuse	6 (10.0%)	1 (3.3%)	5 (16.7%)
Alcohol Dependence	3 (5.0%)	1 (3.3%)	2 (6.7%)
Drug Abuse	6 (10.0%)	3 (10.0%)	3 (10.0%)
Drug Dependence	7 (11.7%)	5 (16.7%)	2 (6.7%)
Alcohol Problems (AUDIT)	5.96±5.62	5.86±5.25	6.06±6.03
Drug Problems (DAST)	1.85±1.62	1.86±1.64	1.84±1.63
Dyadic Adjustment	94.11±11.24	93.59±1.85	94.58±12.43

Note.

^ Denotes current (past 6 months) substance use disorders. No statistically significant differences emerged between groups.

Table 2

Salivary Cortisol Reactivity to 2nd Conflict Resolution Task: Results from Reduced¹ Two-Intercept, Multilevel Growth Curve Model Predicting Cortisol Levels Over Time

		Estimate	SE
Women	Intercept	0.19***	0.02
	Effect of baseline cortisol ²	0.38***	0.09
	Linear effect of time ³ in placebo group	0.02*	0.01
	Difference in linear effect for oxytocin group compared to placebo	-0.03**	0.01
	Quadratic effect of time in placebo group	-0.002**	0.001
	Difference in quadratic effect for oxytocin group compared to placebo	0.004**	0.001
Men	Intercept	0.19***	0.02
	Linear effect of time	0.003	0.01
	Quadratic effect of time	-0.0003	0.001

Note. Average baseline cortisol level (T1-T2) was controlled for in the analyses.

¹Retaining intercepts, effects of time, and all significant effects for drug condition from full model. There were no significant differences based on drug condition for intercepts for both men and women, as well as for linear and quadratic effects for men.

²Mean-centered around gender-specific means, i.e., all other effects can be interpreted as effects for women/men with average baseline cortisol.

³Time elapsed since T3, coded in 10-minute increments to avoid computational problems with small estimates for 1-minute increments

Table 3

Estimated ^f Mean Changes in Counts of Problem Solving Behaviors

Behavior	Women (n=16)			Men (n=16)			Sex × OT Interaction	
	PL (n=14)	OT (n=16)	P-Value	PL (n=14)	OT (n=16)	P-Value	P-Value ^f	
Psychological Abuse	0.14	0.47	0.27	0.22	0.15	0.83	0.25	
Distress Maintaining Attribution	-0.51	0.79	0.07	-0.04	-0.44	0.58	0.04 [*]	
Hostility	-7.14	-1.03	0.12	-7.25	-2.25	0.22	0.70	
Dysphoric Affect	0.38	-0.05	0.05 [*]	-0.05	-0.05	0.99	0.14	
Withdrawal	-0.17	2.10	0.15	-0.73	2.06	0.10	0.78	
Acceptance	0.11	0.07	0.86	-0.05	0.07	0.56	0.55	
Relationship Enhancing Attribution	0.97	-0.99	0.02 [*]	-0.91	-0.93	0.98	0.05 [*]	
Self-Disclosure	-0.42	-0.62	0.75	-0.19	0.03	0.72	0.60	
Humor	-0.31	-0.20	0.96	-1.04	-1.24	0.92	0.84	
Constructive Problem Solving Discussion	-2.02	-4.24	0.57	0.68	-1.72	0.55	0.96	
Other	-0.34	1.88	0.29	-0.82	1.82	0.21	0.58	

Note. Changes reflect counts of behaviors during the second conflict resolution task minus counts during the first conflict resolution task.

^fLeast square mean estimates were obtained from general linear mixed models that adjusted for within-couple correlation and baseline behavior counts.

PL = placebo, OT = oxytocin.

^{*}
p .05.