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SHORT COMMUNICATION

Gender moderates the effect of oxytocin on social judgments

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Objective The neuropeptide oxytocin is implicated in social processing, and recent research has begun to explore how gender relates to the reported effects. This study examined the effects of oxytocin on social affective perception and learning.
Methods Forty-seven male and female participants made judgments of faces during two different tasks, after being randomized to either double-blinded intranasal oxytocin or placebo. In the first task, "unseen" affective stimuli were presented in a continuous flash suppression paradigm, and participants evaluated faces paired with these stimuli on dimensions of competence, trustworthiness, and warmth. In the second task, participants learned affective associations between neutral faces and affective acts through a gossip learning procedure and later made affective ratings of the faces.
Results In both tasks, we found that gender moderated the effect of oxytocin, such that male participants in the oxytocin condition rated faces more negatively, compared with placebo. The opposite pattern of findings emerged for female participants: they rated faces more positively in the oxytocin condition, compared with placebo.
Conclusions These findings contribute to a small but growing body of research demonstrating differential effects of oxytocin in men and women.

KEY WORDS—oxytocin; visual perception; affective learning; facial expression; social learning; neuropeptide

INTRODUCTION

Oxytocin is a hypothalamic neuropeptide that has been identified as an important neurochemical in mammalian social behavior. A growing body of work in humans has focused on the effect of oxytocin on social cognition and perception, such as higher ratings of trustworthiness and attractiveness of stranger's faces (Theodoridou *et al*., 2009).

Social perception and judgment tasks are influenced by the perceiver's affective state (Condon and DeSteno, 2011; Anderson *et al*., 2012). Affect can influence social perception through several mechanisms, but one of the most prominent theories is the "affect as information perspective" (Schwarz and Clore, 1983; Clore *et al*., 2001), which postulates that people use their feelings as a source of information about the world. From the affect as information perspective, oxytocin could increase prosocial behavior through different pathways. First, oxytocin could attenuate feelings of threat, fear, or anxiety induced by the approach of an unknown other (for review, see Bartz *et al*., 2011b). This is supported by research in animals, showing a general anxiolytic effect of oxytocin (Uvnäs-Moberg *et al*., 1994; Bale *et al*., 2001; Waldherr and Neumann, 2007). Second, oxytocin may facilitate social approach behavior in a broader way, independent of the valence (i.e., either aggressive or friendly) (Kemp and Guastella, 2011). This fits with the finding that oxytocin has not always been associated with positive prosocial effects (De Dreu *et al*., 2010; Bartz *et al*., 2011a, 2011b).

To explore the role oxytocin may play in social judgments, we conducted two different social affective experiments. First, to test whether oxytocin influences how people use affect as a source of information while

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making trait judgments, we employed an affective misattribution task that utilizes continuous flash suppression (CFS; Tsuchiya and Koch, 2005). In CFS, perceivers view a neutral face paired with a subliminal affective face. Previous work has demonstrated that the unseen face influences judgments of the seen faces (for details, see Anderson *et al*., 2012). Using this paradigm, we are therefore able to examine whether (and how) oxytocin might influence the use of affect in social judgments.

To explore whether oxytocin influences social affective learning, we used an affective "gossip" learning procedure as our second task. Gossip is a powerful way to learn whom to befriend and whom to avoid, and previous studies demonstrated that humans are remarkably good at learning about others in this way (Bliss-Moreau *et al*., 2008). In this study, we explored whether oxytocin would alter the effects of negative gossip (e.g., "threw a chair at a classmate"). We hypothesized that oxytocin would decrease the effects of negative gossip on later ratings, because attenuated negative learning has been demonstrated previously in negative associative learning studies. For example, Petrovic and colleagues paired an electric shock with faces in a fear conditioning procedure, and this aversive stimulus pairing produced a negative subjective rating to the faces; however, this negative rating was attenuated if oxytocin was administered (Petrovic *et al*., 2008).

Because the large majority of published work on intranasal oxytocin administration has been conducted in men, little is known about the differential effects by gender. Several recent studies found no gender differences (Savaskan *et al*. 2008; Ditzen *et al*., 2009; Guastella *et al*., 2009a; Shamay-Tsoory *et al*., 2009; Theodoridou *et al*., 2009), whereas others have reported gender differences (Gordon *et al*., 2010; Fischer-Shofty *et al*., 2012; Kubzansky *et al*., 2012). In our present studies, we therefore enrolled men and women and examined gender as a potential moderating factor.

MATERIALS AND METHODS

Participants

Adults with no current axis I DSM-IV psychiatric diagnosis were recruited to the Massachusetts General Hospital from March 2011 to September 2011. In total, 47 eligible participants completed the study, age 21 to 60 years old (mean = 43.3 years, *SD* = 10.7; 29 men; Table 1). All subjects gave informed consent in accordance with the policies of the Massachusetts General Hospital Institutional Review Board.

Table 1. Demographic information

		Complete sample		CFS task sample	
	Drug	*n*	Age, years (*SD*)	*n*	Age, years (*SD*)
Female	OT	10	42.2 (11.9)	7	42.1 (12.7)
	PL	8	46.0 (10.0)	7	49.0 (5.7)
Male	OT	15	42.3 (11.8)	14	42.2 (12.2)
	PL	14	43.6 (9.7)	8	45.8 (9.4)

CFS, continuous flash suppression; OT, oxytocin; PL, placebo.

Materials and procedure

Participants self-administered 30 IU of randomized, double-blinded intranasal oxytocin (Syntocinon, Novartis (Basel, Switzerland)) or placebo with a metered-dose spray vial and pump actuator (10 sprays, 3 IU per spray), in a similar dose and fashion to those of previous trials (Petrovic *et al*., 2008). To ensure a standardized experience while waiting for drug absorption, participants spent 25 min working on puzzles screened for neutral affective content before the 5-min set-up period, to allow the peptide to approach a peak in the central nervous system and remain at plateau during the tasks (Born *et al*., 2002).

Affective misattribution task (continuous flash suppression)

In the affective misattribution task, participants viewed stimuli through a mirror stereoscope with stimuli subtending approximately $3.5 \times 5.0°$ of visual angle. The affective misattribution task was identical to that previously reported by our laboratory (experiment 4 in Anderson *et al*., 2012; see Supporting information for task details).

During the misattribution task, the perceiver's dominant eye was presented with a "Mondrian" type image for 100 ms, followed by a structurally neutral face for 100 ms, and followed by another Mondrian image for 100 ms. Concurrent with the onset of the structurally neutral face, the perceiver's nondominant eye was presented with a low-contrast low-luminance smiling, scowling, or neutral face (of matching identity) for 200 ms that terminated with the offset of the final Mondrian image presented to the dominant eye. Following the stimuli presentation, perceivers were asked to make three trait judgments (trustworthiness, competence, and warmth) about the neutral target using four-point scales. Thirty unique identities were presented; 10 were paired with each type of suppressed face type (scowling, smiling, and neutral) for a total of 30 trials (shown twice to yield 60 trials). After the task, participants completed an awareness check that verified that they could not see the suppressed faces (for task details, see Anderson *et al*., 2012).

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Affective learning task (gossip)

The gossip task consisted of two phases: learning and test. During the learning phase, participants viewed 30 neutral faces, each paired with one sentence describing a negative positive, or neutral behavior, counterbalanced across participants (for details, see Supporting information and Anderson *et al.*, 2011). Each face–gossip pair was displayed for 5 s in random order, and four learning blocks were presented. During the test phase, participants rated the faces as negative, neutral, or positive. Participants saw all 30 neutral faces from the gossip manipulation plus an additional 10 novel neutral faces. Each face was presented only once. The faces in this task were not the same as the ones used in the affective misattribution task (CFS) task.

RESULTS

Affective misattribution (continuous flash suppression)

To explore how oxytocin influences affective misattribution when participants make trait judgments of faces, we conducted a series of 3 (suppressed face type) × 2 (gender) × 2 (drug) analyses of variance (ANOVAs) with valence of the suppressed face as the repeated measure (scowling, smiling, or neutral), gender and drug condition as the between-participant factors, and judgments of competence, trustworthiness, or warmth as the dependent variable (three separate ANOVAs). We replicated our previous studies (Anderson *et al.*, 2012), suppressed affective faces influenced trait udgments (Table 2). There was a main effect of suppressed face type for judgments of competence, $F(2, 64) = 10.07$, $p < 0.001$, partial $\eta^2 = 0.239$; trustworthiness, $F(2, 64) = 12.69$, $p < 0.001$, partial $\eta^2 = 0.284$; and warmth, $F(2, 64) = 24.49$, $p < 0.001$ partial $\eta^2 = 0.434$. Although there was no main effect for gender or drug condition, there was a significant gender × drug interaction, for judgments of competence, $F(1, 32) = 5.04$, $p < 0.033$, partial $\eta^2 = 0.136$; trustworthiness, $F(1, 32) = 4.27$, $p < 0.048$, partial $\eta^2 = 0.118$; and a trend level significant interaction for warmth, $F(1, 32) = 4.15$, $p < 0.051$, partial $\eta^2 = 0.115$. Male participants rated neutral faces more negatively in the oxytocin condition (vs. placebo condition), whereas female participants rated them more positively in the oxytocin condition (vs. placebo condition; Figure 1 and Table 3; see Supporting information for more details).

Table 2. Trait ratings by expression in affective misattribution task (continuous flash suppression)

	Expressions		
	Smiling	Neutral	Scowling
Trait judgments			
Competence (all)	2.91 (0.07)	2.72 (0.08)	2.65 (0.08)
Female	2.99 (0.11)	2.73 (0.12)	2.53 (0.13)
Male	2.82 (0.09)	2.72 (0.10)	2.77 (0.11)
Trustworthiness (all)	2.82 (0.07)	2.60 (0.06)	2.49 (0.07)
Female	2.89 (0.11)	2.59 (0.10)	2.38 (0.11)
Male	2.75 (0.09)	2.61 (0.08)	2.59 (0.09)
Warmth (all)	2.75 (0.09)	2.30 (0.07)	2.15 (0.08)
Female	2.89 (0.14)	2.32 (0.11)	2.08 (0.13)
Male	2.61 (0.11)	2.28 (0.09)	2.23 (0.11)

Note: Estimated marginal means. Standard errors in parentheses.

Affective learning (gossip)

To explore how oxytocin influences affective learning, we conducted a 4 (gossip type) × 2 (gender) × 2 (drug) ANOVA with the gossip type as the repeated measure (negative, positive, neutral, and novel), gender and drug condition as the between-participant factors, and the affective judgments as the dependent variable. Again, we replicated our previous studies (Anderson *et al.*, 2011), such that gossip influenced how neutral faces were evaluated, as shown by a main effect of gossip type, $F(3, 129) = 14.20$, $p < 0.001$, partial $\eta^2 = 0.248$ (Figure 2 and Table 4). Similar to the CFS task, although there were no significant main effects of gender or drug, the gender × drug interaction was significant, $F(1, 43) = 8.08$, $p < 0.008$, partial $\eta^2 = 0.158$. No other interaction effects were significant. As in the CFS task, male participants rated faces more negatively in the oxytocin condition (vs. placebo), whereas female participants rated faces more positively in the oxytocin condition (vs. placebo, Figure 2). Again, although there was no independent main effect of oxytocin on affective social learning, our findings suggest that gender moderates the influence of oxytocin on affective social learning oxytocin.

DISCUSSION

Our findings suggest that gender moderates the effect of oxytocin in social judgments. In both tasks, we found that intranasal oxytocin administration influenced male and female participants differently. Following oxytocin administration, male participants made more negative ratings, and female participants made more positive ones. In the affective misattribution task (e.g., CFS task), male participants judged physically neutral faces to be less competent, less trustworthy, and less warm after receiving oxytocin (compared with placebo). The opposite pattern was true for female participants. These findings held across all of the affective misattribution conditions: It did not matter whether the neutral faces being evaluated were paired with unseen scowling or smiling faces

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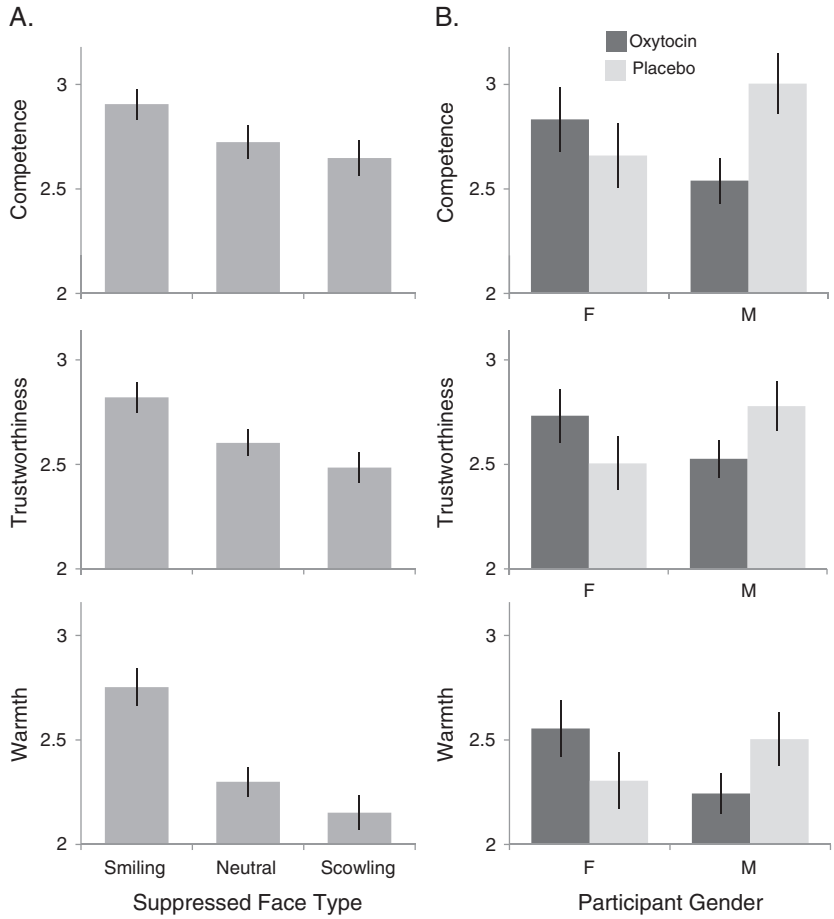

Figure 1. Trait ratings in affective misattribution task (continuous flash suppression)

Table 3. Trait ratings by gender and drug condition in affective misattribution task (continuous flash suppression)

		Participant gender	
	Drug	F	M
Trait judgment			
Competence	OT	2.83 (0.16)	2.54 (0.11)
	PL	2.66 (0.16)	3.00 (0.15)
Trustworthiness	OT	2.73 (0.13)	2.53 (0.09)
	PL	2.51 (0.13)	2.78 (0.12)
Warmth	OT	2.56 (0.14)	2.24 (0.10)
	PL	2.31 (0.14)	2.50 (0.13)

Note: Estimated marginal means. Standard errors in parentheses.

(although there was a main effect of suppressed face type that also independently influenced judgments). These findings suggest that gender moderates the influence of oxytocin on participants' social judgments but that there is no independent main effect of oxytocin on such judgments. Because of this differential effect of gender, our initial hypotheses were not supported. If oxytocin influences how affect is used as information, the effects depend on gender, which to our knowledge has never been demonstrated using the affect as information perspective.

A similar pattern emerged from the affective learning (gossip) data: Male participants rated faces more negatively after the gossip manipulation following oxytocin administration (compared with placebo). Female participants again showed the opposite pattern. Again, these findings held across stimulus conditions (suppressed face and gossip type)—there were no interactions between drug condition and stimulus conditions. It is important to note that both tasks replicated our previous findings, indicating that they were performed properly. Again, the findings did not support our initial hypothesis that oxytocin would attenuate negative learning.

These findings are consistent with a small literature, which suggests that gender may moderate the influence of oxytocin on social judgments and perception. For example, oxytocin administration led men to more accurately perceive competition interactions, whereas women

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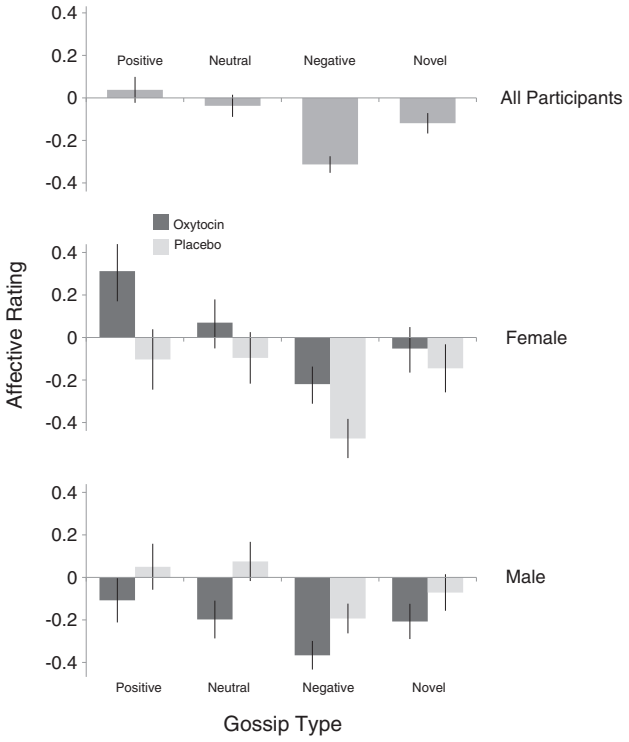

Figure 2. Affective ratings in affective learning task ("gossip" task)

more accurately perceived kinship interactions when watching realistic video interactions (compared with placebo; Fischer-Shofty *et al*., 2012). Our findings are also consistent with recent data suggesting that oxytocin might potentiate the protective and mnemonic effect of aversive social information (Striepens *et al*., 2012).

Interestingly, a study using a closely related neuropeptide found parallel effects to ours: Thompson and colleagues showed that intranasal administration of vasopressin (arginine vasopressin) decreased men's judgments of the friendliness of pictures of faces but *increased* women's judgments of friendliness (Thompson *et al*., 2006). Because oxytocin and arginine vasopressin are closely related and have an overlapping receptor activity (Chini and Manning, 2007), it is possible that these two findings are tapping a common pathway.

Currently, it is unclear why oxytocin influences men and women differently. One possibility is that there may be gender differences in the biochemical function of oxytocin, such as the number of receptors or binding action in particular brain networks (Uhl-Bronner *et al*., 2005). Second, the differential gender effects might happen downstream of oxytocin's biochemical functioning, perhaps due to differences in what is culturally accepted as appropriate behavior for men and women. Kemp and Guastella (2011) suggested that oxytocin increases approach motivation in both genders, which could involve either positive (enthusiasm and trust) or negative (aggression and anger) approach behaviors. Approach motivation behavior might look different for men and women, with male approach motivation being more aggressive and female being more prosocial. This way of conceptualizing the effect of oxytocin would be consistent with our findings.

There are several limitations of this study. First, our relatively small sample size may limit the generalizability of our findings. Second, we found an unexpected gender difference in misattribution effects. This finding is not relevant to our hypothesis as it does not involve oxytocin, and it could be the result of a relatively small sample size (previous studies with larger samples have consistently found no gender effects on this task, see Anderson *et al*., 2012). Third, menstrual status was not taken into account. Because gonadal steroids are involved in modulation of oxytocin signaling, there may have been baseline differences in oxytocinergic tone between women. It is possible that these differences could influence the response to oxytocin administration. However, other researchers have found no interactions with menstrual phase when measuring psychological behaviors (Cardoso *et al*., 2012; Fischer-Shofty *et al*., 2012).

If gender moderates the effects of oxytocin, there are important implications. Oxytocin has been considered as a treatment for a variety of mental health disorders. If the effects of oxytocin are different in men and

Table 4. Affective ratings in affective learning task (gossip task)

		Gossip type				
		Positive	Neutral	Negative	Novel	All stimuli
Female	OT	0.31 (0.13)	0.07 (0.11)	−0.22 (0.08)	−0.05 (0.10)	0.03 (0.08)
	PL	−0.10 (0.14)	−0.10 (0.12)	−0.48 (0.09)	−0.15 (0.11)	−0.21 (0.09)
Male	OT	−0.11 (0.10)	−0.20 (0.09)	−0.37 (0.07)	−0.21 (0.08)	−0.22 (0.06)
	PL	0.05 (0.11)	0.08 (0.09)	−0.19 (0.07)	−0.07 (0.09)	−0.04 (0.07)
All		0.04 (0.06)	−0.04 (0.05)	−0.31 (0.04)	−0.12 (0.05)	

Note: Estimated marginal means. Standard errors in parentheses.

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women, it is possible that its efficacy as a treatment might differ by gender. Clearly, more research is needed to further disentangle the mechanism by which oxytocin influences participants of different genders, but the gathering evidence suggests that it is untenable to ignore gender in oxytocin studies moving forward.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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REFERENCES

Anderson EC, Siegel EH, Bliss-Moreau E, Barrett LF. 2011. The visual impact of gossip. *Science* **332**: 1446–1448.

Anderson EC, Siegel EH, White D, Barrett LF. 2012. Out of sight but not out of mind: unseen affective faces influence evaluations and social impressions. *Emotion* **12**: 1210–1221.

Bale TL, Davis AM, Auger AP, Dorsa DM, McCarthy MM. 2001. CNS region-specific oxytocin receptor expression: importance in regulation of anxiety and sex behavior. *J Neurosci* **21**: 2546–2552.

Bartz J, Simeon D, Hamilton H, *et al*. 2011a. Oxytocin can hinder trust and cooperation in borderline personality disorder. *Soc Cogn Affect Neurosci* **6**: 556–563.

Bartz JA, Zaki J, Bolger N, Ochsner KN. 2011b. Social effects of oxytocin in humans: context and person matter. *Trends Cogn Sci* **15**: 301–309.

Bliss-Moreau E, Barrett LF, Wright CI. 2008. Individual differences in learning the affective value of others under minimal conditions. *Emotion* **8**: 479–493.

Born J, Lange T, Kern W, McGregor GP, Bickel U, Fehm HL. 2002. Sniffing neuropeptides: a transnasal approach to the human brain. *Nat Neurosci* **5**: 514–516.

Cardoso C, Ellenbogen MA, Linnen AM. 2012. Acute intranasal oxytocin improves positive self-perceptions of personality. *Psychopharmacology (Berl)* **220**: 741–749.

Chini B, Manning M. 2007. Agonist selectivity in the oxytocin/vasopressin receptor family: new insights and challenges. *Biochem Soc Trans* **35**: 737–741.

Clore GL, Wyer RS, Dienes B, Gasper K, Gohm C, Isbell L. 2001. Affective feelings as feedback: some cognitive consequences. In Theories of Mood and Cognition: A User's Guidebook, LL Marti (ed). Mahwah: Erlbaum; 63–84.

Condon P, DeSteno D, 2011. Compassion for one reduces punishment for another. *J Exp Soc Psychol* **47**: 698–701.

De Dreu CKW, Greer LL, Handgraaf MJJ, *et al*. 2010. The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans. *Science* **328**: 1408–1411.

Ditzen B, Schaer M, Gabriel B, Bodenmann G, Ehlert U, Heinrichs M. 2009. Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. *Biol Psychiatry* **65**: 728–731.

Fischer-Shofty M, Levkovitz Y, Shamay-Tsoory SG. 2012. Oxytocin facilitates accurate perception of competition in men and kinship in women. *Soc Cogn Affect Neurosci* **8**: 313–317.

Gordon I, Zagoory-Sharon O, Leckman JF, Feldman R. 2010. Oxytocin and the development of parenting in humans. *Biol Psychiatry* **68**: 377–382.

Guastella AJ, Carson DS, Dadds MR, Mitchell PB, Cox RE. 2009a. Does oxytocin influence the early detection of angry and happy faces? *Psychoneuroendocrinology* **34**: 220–225.

Guastella AJ, Howard AL, Dadds MR, Mitchell P, Carson DS. 2009b. A randomized controlled trial of intranasal oxytocin as an adjunct to exposure therapy for social anxiety disorder. *Psychoneuroendocrinology* **34**: 917–923.

Kemp AH, Guastella AJ. 2011. The role of oxytocin in human affect: a novel hypothesis. *Curr Dir Psychol Sci* **20**: 222–231.

Kubzansky LD, Mendes WB, Appleton AA, Block J, Adler GK. 2012. A heartfelt response: oxytocin effects on response to social stress in men and women. *Biol Psychol* **90**: 1–9.

Petrovic P, Kalisch R, Singe T, Dolan RJ. 2008. Oxytocin attenuates affective evaluations of conditioned faces and amygdala activity. *J Neurosci* **28**: 6607–6615.

Savaskan E, Ehrhardt R, Schulz A, Walter M, Schächinger H. 2008. Post-learning intranasal oxytocin modulates human memory for facial identity. *Psychoneuroendocrinology* **33**: 368–374.

Schwarz N, Clore GL. 1983. Mood, misattribution, and judgments of well-being: informative and directive functions of affective states. *J Pers Soc Psychol* **45**: 513–523.

Shamay-Tsoory SG, Fischer M, Dvash J, Harari H, Perach-Bloom N, Levkovitz Y. 2009. Intranasal administration of oxytocin increases envy and schadenfreude (gloating). *Biol Psychiatry* **66**: 864–870.

Striepens N, Scheele D, Kendrick KM, *et al*. 2012. Oxytocin facilitates protective responses to aversive social stimuli in males. *Proc Natl Acad Sci U S A* **109**: 18144–18149.

Theodoridou A, Rowe AC, Penton-Voak IS, Rogers PJ. 2009. Oxytocin and social perception: oxytocin increases perceived facial trustworthiness and attractiveness. *Horm Behav* **56**: 128–132.

Thompson RR, George K, Walton JC, Orr SP, Benson J. 2006. Sex-specific influences of vasopressin on human social communication. *Proc Natl Acad Sci U S A* **103**: 7889–7894.

Tsuchiya N, Koch C. 2005. Continuous flash suppression reduces negative afterimages. *Nat Neurosci* **8**: 1096–101.

Uhl-Bronner S, Waltisperger E, Martínez-Lorenzana G, Condes Lara M, Freund-Mercier MJ. 2005. Sexually dimorphic expression of oxytocin binding sites in forebrain and spinal cord of the rat. *Neuroscience* **135**: 147–154.

Uvnäs-Moberg K, Ahlenius S, Hillegaart V, Alster P. 1994. High doses of oxytocin cause sedation and low doses cause an anxiolytic-like effect in male rats. *Pharmacol Biochem Behav* **49**: 101–106.

Waldherr M, Neumann ID. 2007. Centrally released oxytocin mediates mating-induced anxiolysis in male rats. *Proc Natl Acad Sci U S A* **104**: 16681–16684.

SUPPORTING INFORMATION

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