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Intranasal administration of oxytocin increases compassion toward women

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It has been suggested that the degree of compassion—the feeling of warmth, understanding and kindness that motivates the desire to help others, is modulated by observers' views regarding the target's vulnerability and suffering. This study tested the hypothesis that as compassion developed to protect vulnerable kinships, hormones such as oxytocin, which have been suggested as playing a key role in 'tend-and-befriend' behaviors among women, will enhance compassion toward women but not toward men. Thirty subjects participated in a double-blind, placebo-controlled, within-subject study. Following administration of oxytocin/placebo, participants listened to recordings of different female/male protagonists describing distressful emotional conflicts and were then asked to provide compassionate advice to the protagonist. The participants' responses were coded according to various components of compassion by two clinical psychologists who were blind to the treatment. The results showed that in women and men participants oxytocin enhanced compassion toward women, but did not affect compassion toward men. These findings indicate that the oxytocinergic system differentially mediates compassion toward women and toward men, emphasizing an evolutionary perspective that views compassion as a caregiving behavior designed to help vulnerable individuals.

Keywords: oxytocin; compassion; empathy; sex differences

INTRODUCTION

Human pro-social behaviors are characterized by acts undertaken to protect or promote the welfare and safety of other persons or groups (Schwartz and Bilsky, 1990). These behaviors, which integrate individuals into a cohesive and united society, have social evolutionary value as through such behaviors humans provide physical and mental levels of security to each other, well beyond what individuals could possibly achieve alone (Darwin, 1871/2004; De Dreu, 2012). One of the salient pro-social feelings that drive us to help others is compassion. Compassion may be defined as the feeling of warmth, understanding, sadness and kindness that arises in witnessing the distress and suffering of others. This feeling motivates the desire to help and care for others (Lazarus, 1991; Goetz *et al.*, 2010). Compassion is a complex and multidimensional feeling that integrates not only the sense of empathy—the ability to recognize, understand and metalize the thoughts, desires and feelings of others (Davis, 1996; Batson, 2009)—but also the ability to recognize that someone else suffers and to separate the distress of the other from self-distress (Lazarus, 1991; Nussbaum, 1996). Furthermore, compassion motivates caring behaviors aimed at relieving the suffering and distress of others (Batson, 1998; Goetz *et al.*, 2010). Thus, compassion is a complex emotional state that motivates pro-social behavior. Zaki and Ochsner (2012) recently proposed, a model of empathy, which includes three components: (i) affective empathy and experience sharing, (ii) cognitive empathy and mentalization ability, (iii) empathic motivation and empathic concern, the third component includes the pro-social motivation to help others as a result of using one or both components of empathy (affective and cognitive).

As such, compassion appears to be based on both components of empathy and therefore, empathy seems to be the initial trigger of compassion and may motivate the compassionate reaction.

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Evolutionary accounts view compassion as a survival affective state that is oriented toward enhancing the welfare of those who suffer, and especially intended to protect vulnerable offspring (Darwin, 1871/2004; Frank, 1988; Sober and Wilson, 1998). A central characteristic of compassion is the adjustment of the appropriate response to the target distress. Goetz *et al.* (2010) propose that degree of compassion is shaped by the assumptions of the observer about the other's suffering. For example, individuals and groups who are stereotypically perceived as affectionate and warm may trigger more compassion in an observer than those who are perceived as cold and aloof. Thus, because women are perceived as more warm and compassionate than men (e.g. Rudman *et al.*, 2001; Fiske *et al.*, 2002), their distress may provoke more compassion in an observer than will the distress of men. This assumption receives support from a meta-analysis review on helping behavior, showing that women in trouble received more help than men (Eagly and Crowley, 1986), perhaps since they evoked a higher sense of compassion.

Although compassion is central to human behavior, its biological underpinnings are largely unknown. Neuroscience studies suggest that several regions of the brain are involved in compassion, among them the interior frontal cortex, the insula and the temporal pole, which may mediate mirroring the emotions of the other; the middle and ventral prefrontal cortex involved in cognitive assessment and understanding of the other's suffering; the periaqueductal gray (PAG), substantia nigra and ventral tegmental area involved in feeling warmth or tenderness toward others; the midbrain PAG involved the perception of other's pain; and networks within the left hemisphere involved in overarching motivation to approach (for review, Goetz *et al.*, 2010; Simon-Thomas *et al.*, 2012). Nonetheless, studies on the neurobiological mechanisms that mediate compassion are scarce.

Because compassion is a social emotion, it is reasonable to assume that neuropeptides such as oxytocin (OT), which has been found to mediate complex pro-social, affective and tending behaviors, should play a key role in mediating compassion. OT is a nine amino-acid cyclic neuropeptide produced in the brain, which is synthesized in the hypothalamic paraventricular (PVN) and supraoptic nuclei (SON), and store and released into the brain and bloodstream from

the posterior lobe of the pituitary gland. It functions as both a neurotransmitter and a hormone. OT targets are widespread across several brain regions, including the amygdala, the hippocampus, the paraventricular nucleus of the hypothalamus and the brainstem, and peripheral sites including the heart, the uterus and regions of the spinal cord that regulate the autonomic nervous system (Huber *et al.*, 2005; Langford *et al.*, 2006; Neumann, 2008). Moreover, OT functions as one of the hormones in the hypothalamic–pituitary–adrenal axis that mediates, among others, the stress response (Heinrichs *et al.*, 2009; Dabrowska *et al.*, 2011). During the past decade, ample evidence has shown that the OT mediates complex pro-social, affective and tending behaviors (for review, Heinrichs *et al.*, 2009; Bethlehem *et al.*, 2012; Graustella and MacLeod, 2012).

OT has been shown to play a critical role in the expression of maternal behavior across a variety of species (Uvnas-Moberg, 1998; Szyf *et al.*, 2008; Zhang and Meaney, 2010), including human mothers (Feldman *et al.*, 2004; Levine *et al.*, 2007; Feldman, 2011), and in parental attachment and bonding between infants and mothers (Lee *et al.*, 2000).

Interestingly, Taylor *et al.* (2000) suggest that OT is involved in sexually differentiated reactions to stress. According to this view, the familiar 'fight-and-flight' human response to stress may particularly characterize male behavior, whereas women are more likely to react to stress through social communication or 'tend-and-befriend' behaviors—the response of bonding, nurturing others and creating social networks. These behaviors, which have been suggested to be mediated by OT (Taylor, 2006; Olff *et al.*, 2007), rely on the ability to feel compassion and have selectively evolved to maximize the survival of weaker individuals within groups. Therefore, Taylor *et al.* (2000) suggest those behaviors are mainly directed toward females and offspring with the intention of increasing their ability to survive and maximizing their welfare.

Throughout evolution, men were often fighters and attackers, whereas women were the caregivers and caretakers of the offspring. Nevertheless, in a safety context, as with in-group members, both men and women can show tend and befriend behavior. Recent findings suggest that OT may particularly enhance pro-social behaviors toward those with whom we feel safe and close to, and have less of an impact upon such behaviors toward people who may endanger us, i.e. in-group members *vs* to out-group members (Declerck *et al.*, 2010; De Dreu *et al.*, 2011; De Dreu, 2012).

Furthermore, current studies show that OT moderates paternal behavior and attachment bonding between infants and fathers (Feldman *et al.*, 2010; Gordon *et al.*, 2010a,b), and romantic attachments between men and women (Schneiderman *et al.*, 2011). Likewise, OT enhances emotional empathy (Hurlemann *et al.*, 2010), trust (Kosfeld *et al.*, 2005) and recognition facial expressions (Domes *et al.*, 2007; Fischer-Shofty *et al.*, 2010).

As tend-and-befriend behaviors occur mostly toward women, and as it has been found that OT mediates tending and caring behaviors in both men and women, OT may enhance increased compassion in both men and women toward women targets as opposed to men targets.

Nevertheless, recent studies report inconsistent findings about the differential effect of OT and AVP on men and women. Although some of the studies found that OT affects similarly women and men both genders (e.g. Ditzen *et al.*, 2009; Theodoridou *et al.*, 2009; Feldman *et al.*, 2010), other find some gender-differential effects (e.g. Domes *et al.*, 2010; Fischer-Shofty *et al.*, 2013; Prehn *et al.*, 2013). As such, this study sought to examine whether OT moderates pro-social and tending behaviors in either sex, or whether OT will differentially affect women and men.

It was hypothesized that subjects' compassion toward women may be overall higher from their compassion toward men, and that OT may differentially affect compassion toward the distress of women and of men. In addition we examined whether OT enhances compassion toward women, both in men and women participants. We measured compassion using a situation that resembles real inter-personal everyday interactions: the participants were requested to listen to four recorded stories of protagonists describing distressful emotional conflicts, and then asked to briefly provide compassionate advice regarding the distressful event described in the tapes. Each story was rated on four sub-scales, taking in account four different aspects of compassion.

METHODS

Participants

Thirty healthy subjects participated in the study (19 men, 11 women, mean age = 39.2, s.d. = 10.72; male and female groups did not differ in age, $t = 0.677$, $P = 0.494$, or with respect to education, $t = 0.944$, $P = 0.353$). All participants reported normal or corrected-to-normal visual acuity, and had no history of neurological or psychiatric disorders, as confirmed by the Hebrew version of the Mini International Neuropsychiatric Interview as a screening interview (Sheehan *et al.*, 1998). Exclusion criteria were (i) an acute, unstable, significant, or untreated medical illness (including arrhythmia, psychiatric conditions and head injury); (ii) a history of alcohol or drug abuse; (iii) mental retardation; (iv) disturbances in vasomotor coordination; and (v) pregnant, lactating or menopausal females. Baseline questionnaires, which assessed information regarding menstrual cycle phase, indicated that seven women were in there follicular phase, two were in there luteal phase, and two were menopause; only one woman used contraceptive pills. Previous studies have shown that the phases in the cycle period (Theodoridou *et al.*, 2009; Domes *et al.*, 2010) and use of contraceptive pills (Arueti *et al.*, 2013) do not modulate the effects of OT administration. All participants were instructed to avoid using psychotropic substances (such as caffeine and nicotine) at least 12 h prior to the experiment. All participants gave written consent before participation. The study protocol was approved by the Helsinki committee of Rambam Health Care Campus, as well as by the Israel Ministry of Health.

Treatment administration

A double-blind placebo-controlled within-subject design was used. Participants were randomly assigned into groups for the first administration of either OT or placebo (18 participants received OT in the first session of the experiment and a placebo in the second session, whereas 12 participants received a placebo in the first session and OT in the second session). One week later, each participant underwent a second administration, switching to the other treatment arm.

The current design was based on previous studies which report that intranasal administration of OT affects plasma levels of OT (Domes *et al.*, 2010) and salivary cortisol levels (Heinrichs *et al.*, 2003), and that various neuropeptides achieves directed access to the CNS within 30 min of intranasal administration (Born *et al.*, 2002). Based on these findings, 45 min prior to task performance, a single dose of 24 IU, given as three puffs per nostril, with each puff containing 4 IU OT (syntocinon spray, Defiante) or placebo (consisting of the same salt solution in which the hormone was dissolved but without the hormone itself) was administered intranasally. This dosage and waiting time correspond to those previously used in experiments designed to investigate the human behavioral effects of intranasally administered OT (Kirsch *et al.*, 2005; Kosfeld *et al.*, 2005; Domes *et al.*, 2007). None of the participants reported side effects following the use of the OT or the placebo.

The compassion task

Participants were requested to listen to four recorded stories of protagonists describing distressful emotional conflicts. The stories are based on Truax's (1961) tasks of empathy and compassion in clinical setting of real psychotherapies. For example, in one story a young woman describes feelings of rejection she felt from her peer group. Participants were then asked to briefly provide compassionate advice regarding the distressful event described in the tapes. The participants' verbal responses (between 7 and 130 words) to the stories were recorded, and further analyzed by two clinical psychologists who were blind to the OT or placebo condition. The two psychologists separately rated each participant's responses for level of compassion. To reflect the complexity of the compassion ability, each story was rated on four sub-scales, adapted from Truax (1967). The compassion total score was the average of these four sub-scales. The four sub-scales were developed according to a new model that views compassion as a complex multidimensional emotion (Goetz *et al.*, 2010) involving the following components:

(i) *Ability to listen*: Participants' ability to be attentive to the story, ranging from complete lack of attention (1 point) to full reference to the story (7 points).
(ii) *Separation ability*: Participants' ability to see the protagonist of the story as separate from themselves, ranging from complete identification and fusion with the protagonist (1 point) to perceiving the protagonist as a separate object (7 points).
(iii) *Identifying distress*: The ability to recognize the distress of the protagonist and his or her mental state that led to the distressful conflict, ranging from inability to recognize the distress (1 point) to ability to identify and refer to a variety of emotions, including conscious and unconscious feelings (7 points).
(iv) *Adjusted solution*: The ability to offer a solution adjusted to the distressful conflict, ranging from absence of a solution or a solution that is totally inappropriate (1 point) to a solution that conformed to the protagonist's needs, distress and feelings (7 points).
(v) Correlation between the ratings of the two judges was extremely high (ability to listen, $r = 0.996$; separation ability, $r = 0.998$; identifying distress, $r = 0.993$; adjusted solution, $r = 0.997$; total compassion score, $r = 0.998$), confirming high inter-judge reliability. Therefore, the average scores of both judges were computed to create the compassion scores (sub-scores and total score). For an example of a story, and its possible answers and scoring (see Appendix S1, Supplementary Material).

RESULTS

To confirm that the four stories provoked a similar degree of compassion, the compassions sub-scores were analyzed by a two-way repeated measures analysis, with the four stories and four sub-scales as the within-participants factors. No main effect of stories was found [$F(1,29) = 1.434$, $P = 0.241$, $\eta^2 = 0.047$] and no significant interaction was found between stories and the sub-scales [$F(1,29) = 0.258$, $P = 0.615$, $\eta^2 = 0.009$], indicating that the stories did not differ from each other in the degree of compassion they provoked. There was significant sub-scale effect [$F(1,29) = 66.099$, $P < 0.0001$, $\eta^2 = 0.695$], with significantly higher score in the separation ability sub-scale ($M = 5.704$, s.d. $= 1.00$), following the ability to listen sub-scale ($M = 5.313$, s.d. $= 0.915$), the adjusted solution sub-scale ($M = 4.483$, s.d. $= 0.120$) and then identifying distress sub-scale ($M = 4.521$, s.d. $= 1.203$). Finally, a one-way repeated measures analysis of the total compassion score was carried out with the four stories as the within-participants factor. No main effect of stories was found [$F(1,29) = 1.434$, $P = 0.241$, $\eta^2 = 0.047$], confirming that the stories did not differ from each other in the degree of total compassion they provoked.

OT enhances compassion toward women

The compassion sub-scores were analyzed by a four-way repeated measures analysis, with treatment (OT, placebo), protagonist-gender (male, female) and the type of compassion sub-scale (ability to listen, separation ability, identifying distress and adjusted solution) as the within-participants factors, and participant-gender (male, female) as the between-participants factor.

The main effect of protagonist-gender was not significant [$F(1,28) = 0.462$, $P = 0.502$, $\eta^2 = 0.016$], indicating that overall and beyond the treatment effect, subjects' compassion toward women did not differ from the compassion toward men. Yet, the interaction between treatment and protagonist-gender was significant [$F(1,28) = 5.686$, $P = 0.024$, $\eta^2 = 0.169$, observed power $= 0.78$], suggesting that drug administration had a differential effect on the degree of compassion toward women and toward men.

In addition, no main effect of treatment [$F(1,28) = 0.869$, $P = 0.359$, $\eta^2 = 0.30$] or of protagonist-gender [$F(1,28) = 0.462$, $P = 0.502$, $\eta^2 = 0.16$] was found. There was no significant interaction effect between the participant-gender and treatment [$F(1,28) = 0.950$, $P = 0.338$, $\eta^2 = 0.033$], between the participant-gender and protagonist-gender [$F(1,28) = 0.107$, $P = 0.747$, $\eta^2 = 0.004$], or three-way interaction effect between treatment, protagonist-gender and participant-gender [$F(1,28) = 0.390$, $P = 0.537$, $\eta^2 = 0.014$], indicating that there were no differential effects of drug administration on degree of compassion beyond participant-gender.

There was significant main effect for type of sub-scale [$F(3,28) = 20.276$, $P < 0.0001$, $\eta^2 = 0.701$], indicating that the scores of sub-scales compassion are different, regardless of treatment, the protagonist-gender, or the participant-gender, with 'separation ability' sub-scale had the highest score [5.704 (1.004)], followed by the 'ability to listen' sub-scale [5.313 (0.915)], and then the 'identifying distress' sub-scale [4.521 (1.023)], and 'adjusted solution' [4.483 (1.203)]. There were no differential effects of the OT on the type of sub-scale [$F(3,28) = 1.61$, $P = 0.211$, $\eta^2 = 0.157$], between protagonist-gender and type of sub-scale [$F(3,28) = 1.006$, $P = 0.408$, $\eta^2 = 0.104$], between participant-gender and type of sub-scale [$F(3,28) = 0.292$, $P = 0.831$, $\eta^2 = 0.033$], nor any significant three-way or four-way interaction [i.e. between treatment, protagonist-gender and participant-gender, $F(1,28) = 0.390$, $P = 0.537$, $\eta^2 = 0.014$; between treatment, type of sub-scale and participant-gender, $F(3,28) = 2.152$, $P = 0.118$, $\eta^2 = 0.199$; between protagonist-gender, type of sub-scale and participant-gender, $F(3,28) = 1.271$, $P = 0.305$, $\eta^2 = 0.128$; between treatment, protagonist-gender and type of sub-scale, $F(3,28) = 2.041$, $P = 0.133$, $\eta^2 = 0.191$; and between treatment, protagonist-gender, type of sub-scale and participant-gender, $F(3,28) = 1.122$, $P = 0.358$, $\eta^2 = 0.155$], indicating that the effects of OT and the protagonist-gender do not interact with the subscales of the task. Table 1 summarized the compassion sub-scales scores, for male and female protagonist, in the OT and placebo conditions.

Follow-up paired-samples *t*-test comparisons were carried out to detect the source of the treatment and protagonist-gender interaction. As the interaction effect of OT and the protagonist-gender was beyond the subscales, these comparisons were carried out with the total compassion score.

These analyses revealed that although in the placebo condition, there was no difference between the compassion toward women ($M = 4.792$, s.d. $= 1.321$) and the compassion toward men ($M = 5.063$, s.d. $= 1.289$), [$t(29) = 1.1017$, $P = 0.317$], in the OT condition the

Table 1 Compassion sub-scales scores, for male and female protagonist, fallowing OT and placebo administration

	Male protagonist		Female protagonist	
Sub-scale	OT	Placebo	OT	Placebo
Compassion total score	4.8 (1.439)	5.063 (1.289)	5.367 (1.209)	4.792 (1.21)
Ability to listen	5.00 (1.503)	5.400 (1.435)	5.583 (1.352)	5.267 (1.337)
Separation	5.433 (1.874)	5.933 (1.513)	6.167 (1.392)	5.283 (1.715)
Identifying distress	4.467 (1.874)	4.517 (1.432)	4.750 (1.305)	4.350 (1.475)
Adjusted solution	4.300 (1.687)	4.300 (1.719)	4.967 (1.456)	4.267 (1.552)

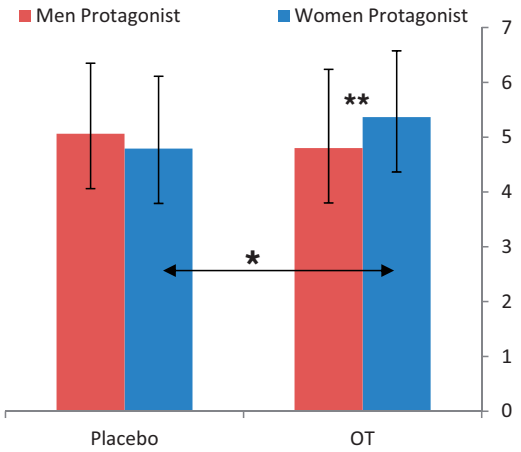

Fig. 1 Repeated measures ANOVA revealed a significant interaction between treatment and protagonist-gender [$F(1,28) = 4.526$, $P = 0.042$]. Follow-up t-tests revealed that in the placebo condition there was no difference in compassion toward a women ($M = 4.7917$, s.d. $= 1.3209$) compared with compassion toward a men [($M = 5.0625$, s.d. $= 1.2881$), $t(29) = 1.1017$, $P = 0.317$]. In the OT condition, however, compassion toward women ($M = 5.3667$, s.d. $= 1.2092$) was significantly higher than compassion toward men [($M = 4.800$, s.d. $= 1.4389$), $t(29) = 2.296$, $P = 0.029$]. When a woman was the protagonist, OT tended to improve the total compassion score in the task [OT ($M = 5.3667$, s.d. $= 1.209$), placebo ($M = 4.7917$, s.d. $= 1.3209$), $t(29) = 1.955$, $P = 0.060$, Cohen's $d = 0.454$]. $^{**}P < 0.5$, $^{*}P = 0.060$.

compassion toward women ($M = 5.367$, s.d. $= 1.209$) was significantly higher than the compassion toward men ($M = 4.80$, s.d. $= 1.439$), [$t(29) = 2.296$, $P = 0.029$, Cohen's $d = 0.426$], indicating that OT enhanced compassion toward women, whereas it did not affect compassion toward men (Figure 1).

Moreover, when a woman was the protagonist, OT tended to improve the total compassion score in the task [OT ($M = 5.3667$, s.d. $= 1.209$), placebo ($M = 4.7917$, s.d. $= 1.3209$), $t(29) = 1.955$, $P = 0.060$, Cohen's $d = 0.454$]. While it did not affect the total compassion score when a man was the protagonist [OT ($M = 4.8$, s.d. $= 1.439$), placebo ($M = 5.0625$, s.d. $= 1.2881$), $t(29) = -0.937$, $P = 0.357$].

To confirm that the order of the drug administration did not interact with the treatment effect, the compassion total scores were analyzed by a three-way repeated measures analysis, with treatment (OT, placebo) and protagonist-gender (male, female) as the within-participants factors, and treatment order (OT first, placebo first) as the between-participants factor. This analysis indicated that there was no order effect [$F(1,28) = 0.614$, $P = 0.440$, $\eta^2 = 0.021$], no significant interaction effect between the order and treatment [$F(1,28) = 1.764$, $P = 0.195$, $\eta^2 = 0.059$], nor three-way interaction effect between treatment, protagonist-gender and order [$F(1,28) = 0.410$, $P = 0.527$, $\eta^2 = 0.014$], indicating that there were no differences in compassion scores between those participants who received OT treatment first and those who received the placebo first.

DISCUSSION

In this study, we examined whether OT differentially affects compassion toward women compared with compassion toward men. In contrast to our original hypothesis, we did not find that the compassion toward the distress of women is higher from the compassion toward the distress of men. Nevertheless, the results did support the hypothesis that OT enhances compassion toward women, whereas it does not affect compassion toward men, and that this differential effect occurs both in men and in women.

Compassion is a complex pro-social response that involves several neural networks and neurochemicals (for review, Goetz *et al.*, 2010; Simon-Thomas *et al.*, 2012). Our findings indicate that OT is one of the neurochemicals that modulates compassion. Although compassion toward women is not overall higher from compassion toward men, OT enhances compassion toward women. These findings provide evidence for the notion that biochemical mechanisms, and specially the oxytocinergic system, differentially mediate affective behaviors, in particular compassion toward male and female targets. This theoretical framework extends Taylor's idea that OT mediates tend-and-befriend behaviors—the response of bonding, caring about and tending to others due to stress (Taylor *et al.*, 2000; Taylor, 2006; Olff *et al.*, 2007). Although Taylor suggests that these behaviors are mainly feminine behaviors, we suggest that OT enhances compassion and tending behaviors primarily toward women who feel distress, and this is the case both in men and in women.

The current findings are in line with De Dreu (2012) who argue that OT may particularly increase pro-social behaviors toward in-group members (Chen *et al.*, 2011; De Dreu *et al.*, 2011; De Dreu, 2012). Our findings that OT enhances compassion toward women whereas it does not affect compassion toward men may indicate that OT increases particularly pro-social behaviors toward those with whom we feel safe and close to, and do not affect behaviors toward people who may endanger us, that is, in-group members *vs* to out-group members. Future studies may compare the effect of OT on compassion toward women, men and children, in-group/out-group protagonists.

Moreover, the increased compassion toward women following the administration of OT was found both for men and for women participants. To date, most of the studies investigating the effects of OT in humans have restricted their samples to male participants (Heinrichs *et al.*, 2009; Theodoridou *et al.*, 2009). Recent studies that include both genders participants found contradictory evidence. Although several studies report that OT affects similarly women and men (e.g. Ditzen *et al.*, 2009; Theodoridou *et al.*, 2009; Feldman *et al.*, 2010), other find some gender-differential effects (e.g. Domes *et al.*, 2010; Fischer-Shofty *et al.*, 2013; Prehn *et al.*, 2013). One of the recent leading hypotheses about the mechanism underlying the social effects of OT, that may explain these conflicting reports, is the 'social salience hypothesis'. This salience hypothesis suggests that OT alters the perceptual salience and/or processing of social cues, thus having a differential effect on individuals depending on dispositional traits and on the interpersonal situation (Shamay-Tsoory *et al.*, 2009; Bartz *et al.*, 2011). OT may increase the individual's attention to social agents, which may result in more trustworthiness and generosity in positive contexts (e.g. Kosfeld *et al.*, 2005; Guastella *et al.*, 2008), while leading to more envy and schadenfruede (Shamay-Tsoory *et al.*, 2009) or out-group derogation (De Dreu *et al.*, 2011; De Dreu, 2012) in competitive contexts. Building on this hypothesis, it is possible that when certain context/behavior equally characterizes both genders (e.g.

trustworthiness), OT may alter similarly the behavior of women and men; however when the behavior is more characteristic of a particular gender (e.g. competition in men), OT may alter the behavior differently for each gender. Thus, although Fischer-Shofty *et al.* (2010) found that OT had a general effect on improving accurate perception of social interactions, they found that it involves gender-specific characteristics; OT had a selective effect on improving kinship recognition in women, but not in men, whereas men's performance was improved following OT administration only for competition recognition. This gender-specific effect may be related to the relevance of kinship recognition in female and competition recognition in males. Similarly, Gordon *et al.* (2010a) have reported that the level of OT plasma in parents was associated with differential parental affectionate touch during parent–infant interactions. Although OT in mothers correlated with the social affective repertoire, including maternal gaze, affect, vocalizations and affectionate touch, the levels of OT in fathers was associated with the object-oriented stimulatory play, consisting of positive arousal, object exploration and stimulatory touch. In this vein, our findings may indicate that compassion toward women is a behavior which is characteristic of both men and women.

In contrast to the present findings, Prehn *et al.* (2013) recently reported that OT diminished gender-specific stimulus in a task that involved looking at men and women faces. The authors suggested that this effect may be due to an intensified processing of stimuli that usually do not recruit much attention. In contrast to Prehn *et al.* (2013), this study did not find gender differences in the degree of compassion toward men *vs* women, indicating that although men participants have lower interest looking at male faces compared with women faces (Prehn *et al.*, 2013), men and women participants show similar levels of compassion to the distress of males and females. These differences may strengthen the 'social salience hypothesis', indicating that OT alters the perceptual salience of social cues, thus having a differential effect on individuals depending on dispositional traits and on the interpersonal situation (Shamay-Tsoory *et al.*, 2009; Bartz *et al.*, 2011). It is possible that the current task design, which was highly emotional and provoked compassion in the participants, increased compassion toward women in the OT condition, whereas the dynamic facial emotion recognition task reported by Prehn *et al.* (2013) was less emotionally arousing and therefore OT did not have a differential effect on women *vs* men protagonists.

Our findings can be integrated with current reports (e.g. Shamay-Tsoory *et al.*, 2009; Bartz *et al.*, 2010, 2011; Arueti *et al.*, 2013; MacDonald *et al.*, 2013) showing that the effect of OT depends on its contexts. It seems that OT has differential effects depending on different variables such as the social context [e.g. provoke cooperation (Arueti *et al.*, 2013), *vs* envy (Shamay-Tsoory *et al.*, 2009)], the attachment style of the participant (Bartz *et al.*, 2010), or psychiatric diagnosis the patients suffering from (e.g. Bartz *et al.*, 2011; MacDonald *et al.*, 2013). Future research may benefit from examining the mutual influence of such individual differences on the effect of OT on compassion.

In line with this, it can be assumed that other neurochemical mechanisms mediate affective responses toward men. Arginine-vasopressin (AVP) may be an appropriate candidate for mediating bonding behaviors toward men. AVP is a neuropeptide that differs from OT by only two amino acids, and is known to play an important role in modulating social behaviors, especially aggressive responses to others (Zink *et al.*, 2010). Interestingly, it has been recently reported that AVP leads to a significant decrease in men's ability to recognize negative emotions of other men, whereas it does not affect their ability to recognize emotions of women (Uzefovsky *et al.*, 2012). Further studies can benefit from studying both these hormones among both genders, and the ways in which they influence differential affective responses toward men and women.

The literature dealing with differences in affective behaviors toward signals of distress from women and from men is limited, and inconsistent. In a recent study, Chun *et al.* (2012) examined the neural responses to crying vocalization produced by the same and the opposite sex. They found that the posterior cingulate was more activate in both men and women, while hearing someone of the opposite sex crying. In line with this, it has been shown that a stimulus causing self-pain in both male and female participants increased perception of men's expressions of pain, but decreased perception of women's expressions of pain (Coll *et al.*, 2012). Yet, other studies found no differences between men and women in facial electromyography (EMG) activity toward male and female facial expressions (Dimberg and Lundquist, 1990). Examining differential hormonal responses toward women and toward men could clarify these inconsistent findings. Although our study examines compassion as a complex and multidimensional behavior defined by four separate scales of compassion, those aforementioned studies examined basic and immediate emotional responses, such as neural responses (Chun *et al.*, 2012), EMG activity (Dimberg and Lundquist, 1990) or degree of pain perception (Coll *et al.*, 2012).

It should be noted that in contrast to the current results, Theodoridou *et al.* (2013) did not find that OT had an effect on self-reported empathy scales, after reading vignettes in which a woman described an unfortunate plight. Similarly, Singer *et al.* (2008) report that OT did not increase men self-reported unpleasantness ratings, of their female partner's experience of painful hand stimulation. It may be assumed that these differences may reflect the different tasks used and different types of assessments. In this study, we measured compassion using an open-ended interview taking in account four different aspects of compassion. Contrary to these previous studies, our findings relay on analysis of the interviews rather than on self-report scales. It is possible that self-report measures are less sensitive to the effects of OT, as opposed to open-ended interviews which allow the participants to provide elaborated meaningful information using their own knowledge and feelings.

This study has some limitations that need to be acknowledged. First, our sample included an unequal number of men and women participants (19 men and 11 women). Likewise, the study includes four stories, two for each participant-gender, and the protagonists of all four stories were adolescents or young adults. Future studies should include more stories, including protagonists from a wider range of ages. Moreover, considering that tending behaviors commonly occur toward offspring, it is possible that OT enhances compassion toward babies and children more than toward adult targets. Finally, basal levels of peripheral OT were not tested in our study. The current design was based on previous studies which report that intranasal administration of OT affects plasma levels of OT (Domes *et al.*, 2010) and salivary cortisol levels (Heinrichs *et al.*, 2003), and that various neuropeptides achieves directed access to the CNS within 30 min of intranasal administration (Born *et al.*, 2002). Yet, future research may examine whether prolonged used of OT can improve compassion toward women over time, and whether people with a higher OT plasma level demonstrate more compassion toward women.

In summary, our findings suggest that both in men and in women OT enhances compassion toward women, whereas it does not affect compassion toward men. This differential effect may have evolved during the course of human development to provide more affective and pro-social behaviors toward vulnerable individuals. These findings may expand the existing knowledge about the role played by the oxytocinergic system in social behaviors, and may indicate that not only

the gender of the participant should be examined but also the gender of the target of the pro-social behavior.

These results may have important clinical implications for treatment of psychopathology, that involve aberrant social behavior including autism spectrum disorders (Hollander *et al.*, 2007), Post traumatic stress disorder - PTSD (Pitman *et al.*, 1993; Olff, 2012), Obsessive-Compulsive disorder OCD (Swedo *et al.*, 1992; Meinlschmidt and Heim, 2007), schizophrenia (Pedersen *et al.*, 2011) or social anxiety disorder (Guastella *et al.*, 2009), and suggest that OT may improve some symptoms, and in particular the social impairments symptoms of these patients (for review, Heinrichs *et al.*, 2009; Matsuzaki *et al.*, 2012). This study suggests that the effect of OT may be not generalized positive effects, but the OT effect depends on the context in which the patient is in. More particularly, OT may affect the social behavior toward women. Future studies on the effect of OT on psychiatric disorders should take in a count these findings.

SUPPLEMENTARY DATA

Supplementary data are available at *SCAN* online.

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