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Oxytocin improves compassion toward women among patients with PTSD

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ABSTRACT

Although impairments in social skills, including empathic abilities, are common in post-traumatic stress disorder (PTSD), the ability to feel compassion—a pro-social behavior that is based on empathy and drives us to help others—has never been assessed among these patients. The first aim of this study was to examine whether patients with PTSD suffer from deficits in compassion and to examine the association between the clusters of PTSD symptoms and these deficits. Furthermore, given that intranasal oxytocin (OT) has been suggested to possibly modulate social behaviors, the second aim of this study was to investigate whether intranasal OT may enhance compassion in these patients. Using a randomized, double-blind, placebo-controlled crossover design, we administered 24 IU of OT and placebo at a one-week interval to 32 patients with PTSD and to 30 matched healthy control participants. The results indicate that patients with PTSD exhibit deficits in compassion and that the numbing cluster emerged as the key predictor of those deficits. Moreover, the results indicate that a single intranasal dose of OT enhances compassion toward women (but not towards men), both in patients with PTSD and in controls. These results offer support for recent suggestions that intranasal OT may potentially be an effective pharmacological intervention for patients with PTSD.

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1. Introduction

Post-Traumatic Stress Disorder (PTSD) is a disorder that develops following one or more traumatic events and is characterized by intrusion memories, avoidance of trauma-related stimuli, negative alteration in cognition and mood and hyper-arousal (American Psychiatric Association, [APA] 2013). This disorder causes significant distress and impairs broad areas of functioning, including social and interpersonal skills (Charuvastra and Cloitre, 2008; Maercker and Horn, 2013). Studies among patients with PTSD have shown that this disorder is related to difficulties across several domains involving social relationships difficulties, including problems with partners, children and friends (see Maercker and Horn, 2013; Monson et al., 2009 for review). In particular, *emotional numbing* symptoms – a cluster of symptoms characterized by a restricted range of affect, anhedonia and detachment (e.g., Kashdan et al., 2006; Orsillo et al., 2007) – were significantly associated with these relationship difficulties (e.g., Cook et al., 2004; Kuhn et al., 2003; Samper et al., 2004).

Recent studies have suggested that the social difficulties characterizing patients with PTSD are caused, at least in part, by impairment in *empathy*—the ability to understand the other's thoughts, desires and feelings (Nietlisbach and Maercker, 2009; Nietlisbach et al., 2010; Plana et al., 2013). In this study we take a further step in attempting to understand empathy deficits in PTSD and examine levels of compassion among these patients.

Recently it has been suggested that the ability to respond in a compassionate way is a key factor of the empathic response (Goetz et al., 2010). *Compassion* is a combination of salient pro-social feelings that drive us to help others. Compassion may be defined as the multi-dimensional feeling of warmth, understanding, sadness and kindness that arises in witnessing the distress and suffering of others and that motivates the desire to help and care for others (Goetz et al., 2010; Singer and Klimecki, 2014). It has been suggested that compassion is based on empathy, and that the compassionate response rely on two different components of empathy: *emotional empathy* – the ability to automatically experience affective reactions of others and to recognize their feelings, and *cognitive empathy* – the ability to cognitively understand and represent the thoughts, desires and feelings of others.

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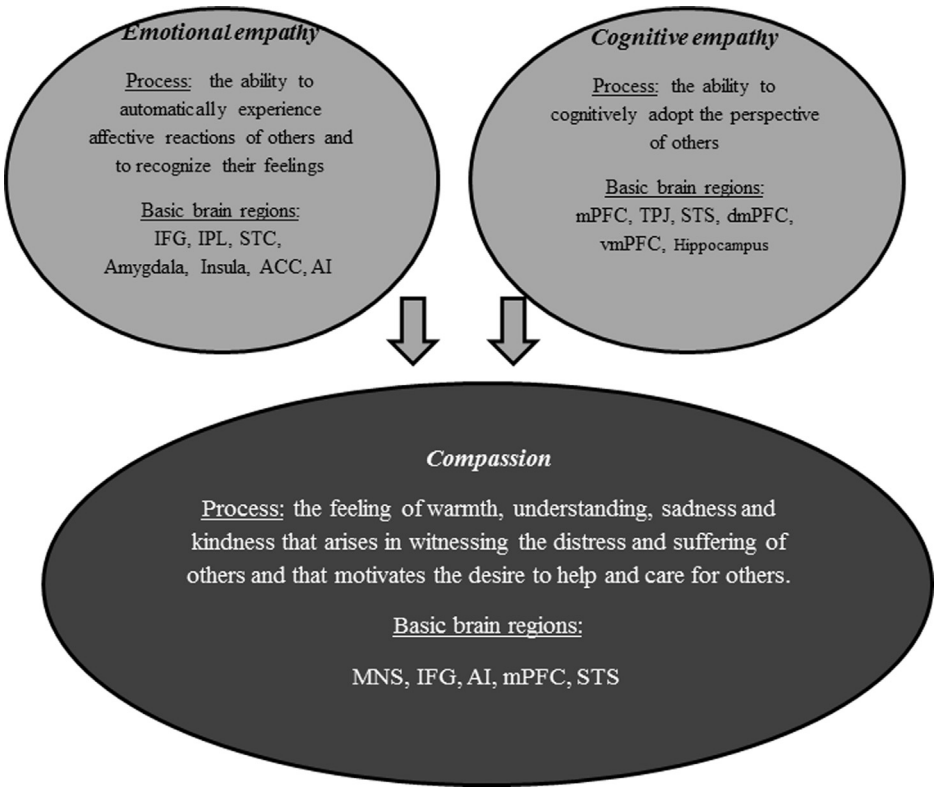

Fig. 1. Compassion integrates *emotional empathy* and *cognitive empathy* with pro-social motivation to help others.
ACC—anterior cingulate, AI—anterior insula, dmPFC—dorsa-medial prefrontal cortex, IFG—inferior frontal gyrus, IPL—inferior parietal lobulem, PFC—medial prefrontal cortex, STC—superior temporal cortex, STS—superior temporal sulcus, TPJ—temporal parietal junction, vmPFC—ventromedial prefrontal cortex.

Thus, compassion—the pro-social motivation to help others who are in distress, is an outcome of cognitive and emotional of empathy (Palgi et al., 2015) (see Fig. 1). In line with this theoretical framework, Zaki and Ochsner (2012) recently proposed, a model of empathy, which includes three components: (a) affective empathy and experience sharing, (b) cognitive empathy and mentalization ability, (c) empathic motivation and empathic concern. The third component includes the pro-social motivation to help others, e.g., compassion response, as a result of using one or both components of empathy (affective and cognitive). Thus, compassion appears to be based on both components of empathy: based on empathy that helps one to identify and understand the distress of other compassion encourages improving the other's wellbeing and motivates pro-social behavior (Singer and Klimecki, 2014). Accordingly, recent studies have found that compassion is mediated by brain areas associated both with emotional empathy [i.e., inferior frontal gyrus (IFG), anterior insula (AI) and dorsal anterior cingulate (ACC)] and with cognitive empathy [i.e., superior temporal sulcus (STS), medial prefrontal cortex (mPFC)] (Goetz et al., 2010).

A growing number of studies have recently shown that patients with PTSD exhibit impairments in pro-social behaviors (Charuvastra and Cloitre, 2008), including emotional empathy and cognitive empathy (also known as *Theory of Mind—ToM*) (see Plana et al., 2013; for review)—abilities that underlie the ability to respond compassionately. Moreover, accumulating neuroimaging studies have shown altered activity in the amygdala, mPFC and ACC, as well as in the hippocampus and insular cortex in patients with PTSD (Pitman et al., 2012; Zoladz and Diamond, 2013), all areas that moderate empathy (Shamay-Tsoory, 2011) and compassion (Goetz et al., 2010). For example, neuroimaging studies found that patients with PTSD have hyper-activation in the amygdala during the presentation of fearful stimuli (e.g., Rauch et al., 1996; Shin et al., 2005), a core region in the emotional empathy. Moreover, other studies found that patients with PTSD have small volume (e.g., Rauch et al., 2003) and hypo-activation (e.g., Shin et al., 2004) of the mPFC, as well as small volume (e.g., Rauch et al., 2003; Schuff et al., 2008) and hypo-activation (e.g., Semple et al., 2000; Milad and Quirk, 2012) of the ACC, both core regions in the empathy network (for review see: Pitman et al., 2012; Zoladz and Diamond, 2013). Yet to the best of our knowledge, the impairments in compassion among these patients have never been assessed. Therefore, the rationale behind this study was to take a further step in understanding empathy deficits in PTSD by examining levels of compassion in these patients. Furthermore, since symptoms of emotional numbing are significantly associated with relationship difficulties among patients with PTSD (e.g., Cook et al., 2004; Kuhn et al., 2003; Samper et al., 2004), we hypothesized that the intensity of the symptoms would predict the intensity of the compassion deficit.

The neurochemical underpinnings of compassion are still largely unknown. Since 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 caring behaviors, should play a key role in mediating compassion. OT is a nine amino-acid cyclic neuropeptide produced in the brain that functions both as a neurotransmitter and as a hormone. During the past decade, ample evidence has shown that the OT system serves as a key mediator of complex social behaviors, including empathy (Kanat et al., 2013). The original speculation was that intranasal administration of OT would have general positive effects on social behaviors (Heinrichs et al., 2009). Nevertheless, recently it has been suggested that the effects of OT are more contextual and are affected by inter-individual factors, including gender and personal traits. Moreover, recent studies have shown gender differences in behavioral and neural responses to intranasal OT (Domes et al., 2010; Rilling et al., 2014). One leading hypothesis regarding these diverse effects of OT is the *social salience hypothesis* (Bartz

et al., 2011; Olff et al., 2013; Shamay-Tsoory et al., 2009), according to which OT alters the perceptual salience of social cues. In the context of compassion, OT has recently been found to enhance compassion toward women in both male and female participants, while it does not affect compassion toward men either in male or in female participants. It was suggested that this differential effect may have evolved during the course of human development to provide more effective and pro-social behaviors toward vulnerable individuals, including women (Palgi et al., 2015).

Several recent theoretical frameworks suggest that the oxytocinergic system functions abnormally among patients with PTSD and that intranasal OT may potentially serve as an effective pharmacological intervention for ameliorating symptoms of PTSD (Charuvastra and Cloitre, 2008; Koch et al., 2014; Olff et al., 2007, 2010). Yet very few studies have examined the effects of OT administration among patients with PTSD. Pitman et al. (1993) found that OT decreases physiological responses when individuals are confronted with combat imagery, and Yatzkar and Klein (2010) showed that OT may decrease anxiety and irritability among these patients. Nevertheless, to the best of our knowledge the effects of OT on compassion among patients with PTSD have never been assessed.

Therefore, the second aim of this study was to examine the effects of OT administration on the capacity for compassion among patients with PTSD and among healthy control (HC) participants. We measured compassion using a situation that resembles a real interpersonal everyday interaction. Given that OT was found to enhance compassion only toward women but not toward men, we hypothesized that this effect would be found both in the PTSD and in the control groups. Given the proposed gender differences in the effects of OT (Domes et al., 2010; Rilling et al., 2014), we carried out a secondary analysis to examine a possible interaction between participant gender and the effects of OT on compassion.

2. Material and methods

2.1. Participants

Study participants included 32 patients with PTSD [male = 23, age 22–60 years, $M = 43.44$ (11.14)] and 30HC participants matched for age and sex [male = 19, age 21–59 years, $M = 39.2$ (10.72)]. The data for the HC group were the same as reported in Palgi et al. (2015), and participants in the PTSD group were recruited for the current study. Participants in the HC group had no history of psychiatric disorders, as confirmed by the Hebrew version of the Mini International Neuropsychiatric Interview (MINI) used as a screening interview (Sheehan et al., 2001).

Participants with PTSD were outpatients with a certified DSM-IV diagnosis of PTSD who were receiving treatment at the Rambam Health Care Campus. The PTSD diagnosis was made by two senior psychiatrists and was confirmed by the Clinician-Administered PTSD Scale (CAPS, Blake et al., 2000). All patients had chronic PTSD ($M = 9.78$ years, SD = 10.1); 50% of them suffered from PTSD symptoms immediate after the trauma event, and 50% suffered from delayed onset of PTSD. The unequal number of male and female participants in this study derives from the fact that the study included only participants whose PTSD was the result of combat and terror attacks (40.6%), traffic accidents (28.1%) and work accidents (15.6 %). We did not include patients that suffer from PTSD due to sexual or relational trauma, since accumulating evidence indicates that such patients exhibit different symptoms of PTSD that tend to be more dissociative (Cloitre et al., 2009; D'Andrea et al., 2012). Furthermore, it has recently been suggested that the OT system works differently in these patients (Olff et al., 2013). Since combat and terror attacks, traffic accidents and work accidents are more common traumatic events among men (Kessler et al., 2005), the gender distribution in this study represents the gender distribution of PTSD in the general population. Chi-square testing confirmed that the type of trauma did not differ between men and women [$\chi 2(2) = 4.682$, $p = 0.611$].

Participants with a history of neurological disorder, head injury, disturbances in vasomotor coordination, significant medical illness or substance abuse were excluded from both groups, as were pregnant or lactating women. Chi-square testing confirmed that the women in both groups did not differ in menstrual cycle phase [$\chi 2(3) = 1.818$, $p = 0.611$], only one woman in the study, from the HC group, was taking contraceptive pills.

All participants were instructed to avoid using caffeine and nicotine at least 12 h prior to the experiment. All gave their written consent before participation and were compensated for their time and expenses. The study protocol was approved by the Helsinki committee of the Rambam Health Care Campus and by the Israel Ministry of Health.

2.2. Treatment administration

A single intranasal dose of 24 IU was administered 45 min prior to task performance in the form of three puffs per nostril, with each puff containing 4 IU OT (syntocinon spray, Defiante) or placebo (consisting of the same saline solution in which the hormone was dissolved but without the hormone itself). This dosage and the waiting time were based on assumptions derived from the study by Born et al. (2002). The procedure was in line with previous studies (e.g., Domes et al., 2010; Guastella et al., 2010; Kirsch et al., 2005; Kosfeld et al., 2005) which used similar dosages and waiting times. Moreover, it has recently been shown that intranasal OT indeed changes OT plasma levels in rodents and influences brain areas relevant to social behavior (Neumann et al., 2013).

2.3. Measures

2.3.1. The clinician-administered PTSD scale (CAPS)

Symptoms of PTSD were evaluated by the Hebrew translation of the CAPS for PTSD, according to the DSM-IV-TR (Blake et al., 2000). The scale comprised a 17-item structured interview that assesses symptom frequency and intensity on a 5-point Likert scale, yielding a total PTSD combined summary score, with total scores ranging from 0 to 136. Additionally, separate scores were calculated for every cluster of PTSD symptoms, and cluster C symptoms were separated into effortful avoidance and emotional numbing symptom clusters. Thus, severity was calculated for four symptom clusters: experience-again, active-avoidance, hyper-arousal and emotional numbing. The CAPS has good internal consistency, with alpha coefficients of 0.89 for the total score and of 0.63, 0.78, 0.78 and 0.79 (respectively) for each cluster separately.

2.3.2. The compassion task

Participants were requested to listen to four recorded stories (based on Truax, 1961) of protagonists describing distressful emotional conflicts. For example, in one story a young woman describes feelings of rejection she felt from her peer group. In each session, the participants were presented with two different stories (one with male protagonists and one with female protagonists). Thus, each participant was interviewed about four different stories, two with male protagonists and two with female protagonists. Participants were then asked to briefly provide compassionate advice regarding the distressful event described in the recorded story (see detailed description of the task in Palgi et al., 2015).

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. To reflect the complexity of the capacity for compassion, each story

was rated on four sub-scales based on the notion that compassion is a complex multidimensional emotion (Goetz et al., 2010). The total compassion score was the average of these four sub-scales (ranging from 1 to 7 points):

a.) *Ability to listen*: the ability to be attentive to the story.
b.) *Separation ability*: the ability to see the protagonist of the story as separate from themselves.
c.) *Identifying distress*: the ability to recognize the distress of the protagonist and his or her mental state that led to the distressful conflict.
d.) *Adjusted solution*: the ability to offer a solution adjusted to the distressful conflict.

2.4. Procedure

A double-blind placebo-controlled within-subject design was used. All participants were randomly assigned to groups for the first administration of either OT or placebo. One week later, each participant underwent a second administration, switching to the other treatment administration. In the first meeting before OT administration, patients with PTSD were assessed by a clinical psychologist by means of a comprehensive structured interview of PTSD symptoms (CAPS, Blake et al., 2000). Forty-five minutes after the administration, all participants were requested to listen to two randomly chosen different stories from the compassion task (one with a male protagonist and one with a female protagonist) and to provide compassionate advice regarding the distressful event described.

3. Results

Independent sample *t*-tests confirmed that the groups did not differ in age [$t(60) = 1.525$, $p = 0.133$], years of education [$t(60) = -0.196$, $p = 0.845$] or estimated verbal IQ as measured by the "similarity" sub-test from WAIS-III (Wechsler, 1999) [$t(57) = -1.95$, $p = 0.056$]. Chi-square testing indicated that the groups did not differ in participant gender [$\chi 2(1) = 0.517$, $p = .472$]. The PTSD group demonstrated high scores on PTSD symptoms, as measured by the CAPS [CAPS total score, $M = 87.88(17.08)$: re-experiencing, $M = 26.41(6.89)$; numbing, $M = 25.03(6.58)$; effortful avoidance, $M = 10.22$ (3.75); hyperarousal, $M = 26.22(5.60)$].

To determine that the stories did not differ in the total compassion score they arise, beyond participant group (PTSD, HC) and treatment conditions (OT, placebo), we conducted a one-way repeated measures ANOVA with type of story as a within-participants factor. This analysis revealed no significant differences between the stories [$F(3183) = 0.448$, $p = 0.713$, $\eta^2 = .007$]. Moreover, paired-samples T-test comparisons indicate no significant differences between the stories with female protagonists and those with male protagonists [$t\,(62) = .859$, $p = 0.394$]. These results confirmed that neither the four stories nor the protagonist gender differed from one another in the degree of compassion they provoked.

An additional analysis using the additional factor of sub-scale scores (Ability to listen, Separation ability, Identifying distress, Adjusted solution) revealed no significant differences between the stories [$F(3183) = 0.444$, $p = 0.713$, $\eta^2 = 0.007$] or in the interaction between type of story and type of sub-scale [$F(9540) = 0.884$, $p = 0.476$, $\eta^2 = 0.014$]. A significant sub-scale effect [$F(3183) = 39.665$, $p < 0.001$, $\eta^2 = 0.394$] was found. Post hoc analysis (Bonferroni) indicated that the scores on the separation ability sub-scale [$M = 4.638$ (0.206)] were higher than those on the identifying distress sub-scale [$M = 3.883(0.146)$, $p < 0.0001$]. There were no other significant differences between the other sub-scale scores.

Each of the four stories demonstrated high internal consistency between the four sub-scales in the present sample (Cronbach's alpha ranging from 0.91 to 0.933), indicating that total compassion score can be used as a single consistent measure of compassion.

3.1. The effects of intranasal administration of OT on compassion

To examine the effects of oxytocin on the total compassion score, we conducted a three-way repeated measure ANOVA, with treatment (OT, placebo) and protagonist-gender (male, female) as the within-participants factors and group (PTSD, HC) as the between-participants factor. This analysis revealed a significant group effect [$F(1,58) = 5.952$, $p = 0.018$, $\eta^2 = 0.093$], indicating that overall the PTSD patients scored lower on the compassion task compared to the HC group (Fig. 2).

Moreover, a significant treatment × protagonist-gender interaction was found [$F(1,60) = 7.204$, $p = 0.009$, $\eta^2 = 0.107$], indicating that drug administration had a differential effect on the degree of compassion toward women and toward men. No main effects of treatment [$F(1,60) = 0.671$, $p = 0.461$, $\eta^2 = 0.011$] or of protagonist-gender [$F(1,60) = 0.142$, $p = 0.708$, $\eta^2 = 0.002$] were found, nor were there any other significant interactions.

Follow-up paired-samples *T*-test comparisons were carried out to detect the source of the interaction between treatment and protagonist-gender. These analyses revealed that when a woman was the protagonist, OT significantly improved the total compassion score [$t(61) = 2.234$, $p = 0.029$, *Cohen's d* = 0.288; OT condition, $M = 4.433(1.595)$; placebo condition, $M = 3.964(1.663)$], while OT did not affect the total compassion score when a man was the protagonist [$t(61) = -0.902$, $p = 0.370$, *Cohen's d* = −0.117; OT condition, $M = 4.054(1.615)$; placebo condition, $M = 4.244(1.618)$]. This result indicates that in general OT enhanced compassion toward women, while it did not affect compassion toward men (Fig 2). Paired *t*-tests carried out separately for each group did not reveal any significant effects for any of the comparisons, indicating that the effect of OT is similar for both groups. [for the PTSD group: in the male-protagonist condition; $t(31) = -.385$, $p = 0.703$, *Cohen's d* = 0.081, OT condition, $M = 3.356(1.467)$; placebo condition, $M = 3.476(1.503)$; in the female-protagonist condition; $t(31) = 1.223$, $p = 0.231$, *Cohen's d* = 0.246, OT condition, $M = 3.558(1.415)$; placebo condition, M = 3.187(1.589); for the HC group: in the male-protagonist condition; $t(29) = -0.937$, $p = 0.357$, *Cohen's d* = 0.191, OT condition, $M = 4.80(1.439)$; placebo condition, $M = 5.062(1.288)$, in the female-protagonist condition; $t(31) = 1.955$, $p = 0.060$, *Cohen's d* = 0.454, OT condition, $M = 5.367(1.209)$; placebo condition, $M = 4.791(1.321)$].

To examine the possibility that the effects of OT are gender dependent, we conducted an analysis with participant-gender (male, female) as an additional factor. This analysis did not reveal any main effects for participant-gender [$F(1,58) = 0.411$, $p = 0.524$, $\eta^2 = 0.007$] or any other significant interaction effect with the participant-gender factor, indicating that our finding that OT enhances compassion toward women while it does not affect compassion toward men occurs both in men and in women participants. Moreover, an analysis with the additional factor sub-scale (Ability to listen, Separation ability, Identifying distress, Adjusted solution) did not reveal any significant interaction between effect of OT and sub-scale [$F(3183) = 1.723$, $p = 0.164$, $\eta^2 = 0.027$] or any other significant interaction.

To examine possible effects of oxytocin on number of words used in the compassion task, we conducted a three-way repeated measure ANOVA, with treatment (OT, placebo) and protagonist-gender (male, female) as within-participants factors and group (PTSD, HC) as the between-participants factor. This analysis revealed a significant group effect [$F(1,60) = 15.310$, $p < 0.008$, $\eta^2 = 0.203$], indicating that the PTSD patients were generally less talkative on the compassion task compared to the HC group. No

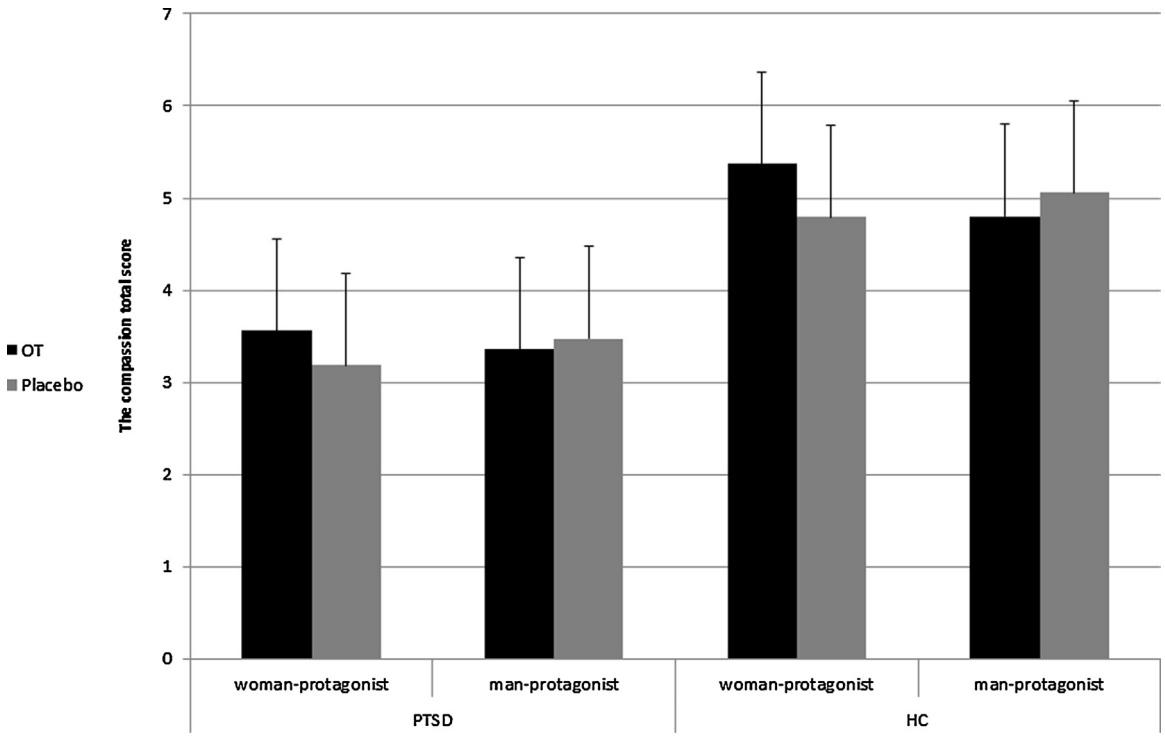

Fig. 2. The effect of OT and placebo on the total score of compassion for the PTSD and the HC groups. Showing: (a) Differences between groups in the total compassion score [$F(1,58) = 5.952, p = 0.018, \eta^2 = 0.093$]. (b) Significant interaction treatment X protagonist-gender [$F(1,60) = 7.204, p = 0.009, \eta^2 = 0.107$]. The error bars represent standard deviations.

main effects of treatment [$F(1,60) = 0.109$, $p = 0.742$, $\eta^2 = 0.002$] were found, nor were there any other significant interactions with treatment, indicating that OT did not affect levels of talkativeness.

3.2. The relationship between compassion and PTSD symptomatology

Stepwise analyses of multiple regressions were conducted to examine the relationship between PTSD symptomatology and compassion as measured by the compassion task. The independent variables were the four PTSD symptom clusters (re-experiencing, numbing, effortful avoidance and hyperarousal), and the dependent variable was the average total compassion score, beyond protagonist-gender (male, female) and treatment condition (OT, placebo).

The stepwise multiple regression analysis revealed that 34% of the variance in the average total compassion score [$R^2 = 0.34$] could be accounted for by symptomatology [$F(1,30) = 15.44$, $p < 0.001$]. The numbing cluster emerged as the only significant predictor of the total compassion score ($R^2 = 0.34$, $\beta = -0.583$, $t = -3.90$, $p < 0.0001$), which was found to be significant. These results indicate that the numbing cluster was the only cluster that could explain some of the variance in the capacity for compassion. Thus, the more patients suffer from emotional numbness, the more difficult it is for them to show compassion toward others. These results were replicated even when the multiple regressions were conducted separately for each treatment condition (Table 1).

Table 1
Multiple regressions with stepwise method: associations between PTSD symptom clusters and compassion abilities on the compassion task.

Predicted variable	Predictor cluster	β	t	p
All stories (OT & placebo condition)	Numbing	−0.583	−3.930	>0.001s***
	Re-experiencing	−0.024	−0.147	0.884
	Effortful avoidance	−0.154	−1.039	0.308
	Hyperarousal	0.052	0.344	0.733
OT condition	Numbing	−0.393	−2.342	0.026*
	Re-experiencing	−0.217	−1.202	0.239
	Effortful avoidance	−0.178	−1.060	0.298
	Hyperarousal	−0.042	−0.241	0.881
Placebo condition	Numbing	−0.560	−3.702	0.001**
	Re-experiencing	0.149	0.904	0.374
	Effortful avoidance	−0.085	−0.553	0.584
	Hyperarousal	0.116	0.754	0.457

* <0.05.
** <0.01.
*** <0.001.

4. Discussion

In the present study we sought to explore compassion deficits among patients with PTSD and to examine the effect of intranasal administered OT on the capacity for compassion.

In line with our predictions, the current study found that compared to HC, patients with PTSD suffered from significant deficits in compassion and were less talkative, as measured by a task that resembles real interpersonal everyday interactions. These current findings are in accordance with recent findings showing deficits in emotional and cognitive empathy among patients with PTSD (for review see: Plana et al., 2013). Additionally, these deficits are in accordance with neuroanatomical evidence pointing to abnormalities in the volume and function of brain regions associated with empathy and compassion among patients with PTSD (i.e., the amygdala, mPFC, IFG, ACC) (for review see: Pitman et al., 2012; Zoladz, and Diamond, 2013). The deficits in compassion observed here may lead to, or alternatively may arise from, the deficits in emotional and cognitive empathy, and from the impairment of social and interpersonal skills characterizing these patients (Charuvastra and Cloitre, 2008; Maercker and Horn, 2013). Future research may benefit from examining the association between deficits in empa-

thy and compassion, among patients with PTSD as well as in the general population.

Furthermore, the current study shows that among the four PTSD symptom clusters (re-experiencing, numbing, effortful avoidance and hyperarousal), the numbing cluster emerges as the only consistent predictor of deficits in compassion. This finding is consistent with our predictions, as well as with studies demonstrating that the severity of numbing symptoms is significantly associated with relationship difficulties among patients with PTSD (e.g., Cook et al., 2004; Kuhn et al., 2003; Samper et al., 2004). Until recently, according to the DSM-IV-TR (American Psychiatric Association, [APA] 2000) this cluster of symptoms was included in the avoidance symptoms cluster, along with active avoidance symptoms. Yet, numerous studies found that these symptoms differ from each other and suggested that PTSD symptoms are associated with four main factors: experience-again, active-avoidance, hyper-arousal and emotional numbing (e.g., King et al., 1998; Naifeh et al., 2008). Consequently, the DSM-5 (2013) divided PTSD symptoms into four clusters, with emotional numbness symptoms included in a new cluster [Cluster D: negative alteration in cognition and mood associated with traumatic event(s)]. Since the current study was conducted before the DSM-5 was published, we did not examine all the symptoms included in cluster D (e.g., persistent and exaggerated negative beliefs or distorted cognitions about the cause of the traumatic event). Future research may benefit from examining the association between these symptoms and deficits in empathy and compassion.

The findings about deficits in compassion among patients with PTSD have therapeutic clinical implications. First, the results about compassion deficits indicate that patients with PTSD may benefit from psychotherapeutic interventions aimed at improving their compassion abilities, e.g., mindfulness-based compassion meditation (Hofmann et al., 2011). Moreover, the association between numbing symptoms and deficiencies in empathy and compassion may emphasize the importance of focusing on these symptoms in treating patients with PTSD.

Furthermore, the results of this study suggest that among patients with PTSD as well as among HC participants, a single dose of intranasal OT enhanced compassion toward women, while it did not affect compassion toward men. This differential effect occurs both in male and in female participants. This finding is in line with our predictions and our findings about the effect of OT on compassion among HC subjects (Palgi et al., 2015). However, although previous studies (Bartz et al., 2010) have suggested that OT may have stronger effects among individuals with impaired social behavior, the current study found that OT had the same effect on patients with PTSD and on HC patients. Moreover, we found that OT did not affect the level of talkativeness toward women or men, as reported in recent studies (Lane et al., 2013; Scheele et al., 2015).

The current findings support several recent theoretical frameworks which suggest that intranasal OT may potentially be an effective pharmacological intervention for ameliorating PTSD symptoms (Charuvastra and Cloitre, 2008; Olff et al., 2010; Koch et al., 2014). Therefore, our results have pharmacologic clinical implications supporting recent suggestions that intranasal OT may potentially be an effective pharmacological intervention for patients with PTSD (Olff et al., 2010; Koch et al., 2014). In particular, the current findings that OT increases compassion toward women may indicate that OT may enhance the tolerance and caring behaviors of men with PTSD toward their wives. This indication is in line with recent suggestions that OT may be used as a psychobiological treatment option in couple therapy as it may increase positive communication behavior among partners (Ditzen et al., 2009; Wudarczyk et al., 2013) and in particular may increase these behaviors among men toward their wives (Ditzen et al., 2013). This potential treatment use of OT may be particularly important for men with PTSD, and especially for war veterans who tend to have difficulties in their family and intimate relationships (Monson et al., 2009). These relationships frequently manifest aggressive behaviors, especially toward their partners (Beckham et al., 2000).

The current study has some limitations that need to be acknowledged. First, since this is a retrospective study, it cannot conclude whether the compassion deficits stem from the PTSD or whether they preceded it. A future prospective research study should examine this issue. Second, the compassion task included only 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. In addition, this study examined a single administration of intranasal OT and therefore it is impossible to generalize the current findings to chronic OT treatment of PTSD. It is important to further investigate the sustained effects of intranasal OT among such patients in the future. Finally, basal levels of peripheral OT or cortisol were not tested in our study. Future research should examine whether individuals with lower levels of OT plasma exhibit more compassion impairment.

5. Conclusions

Our findings suggest that patients with PTSD suffer from significant and comprehensive deficits in compassion. These deficits may indicate that in response to the distress of the other, patients with PTSD may have difficulty in inferring and understanding the circumstances leading to this distress and in being motivated to help and care for others. In addition, our findings suggest that among the four PTSD symptom clusters, the numbing cluster emerges as the only consistent predictor of such deficits. Furthermore, our findings suggest that a single intranasal dose of OT enhances compassion toward women, while it does not affect compassion toward men, both in patients with PTSD and in HC participants. These results are novel and fill a gap in the study of the oxytocinergic system among patients with PTSD. The results offer initial support for recent suggestions that intranasal OT may potentially be an effective pharmacological intervention for patients with PTSD, and in particular may be used as a psychobiological treatment option in couple therapy for patients with PTSD.

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Conflict of interest

The authors declare no conflict of interest.

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