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ORIGINAL ARTICLE

The role of oxytocin in empathy to the pain of conflictual out-group members among patients with schizophrenia

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Background. Oxytocin (OT) is associated with our ability to empathize and has been shown to play a major role in mediating social behaviors within the context of intergroup dynamics. Schizophrenia is associated with impaired empathy, and with a dysfunctional oxytocinergic system. The effect of OT on the empathic responses of patients with schizophrenia within the context of intergroup relationships has not been studied. The present study examined the effect of OT on the patients' empathic responses to pain experienced by in-group, conflictual out-group and neutral out-group members.

Method. In a double-blind, placebo-controlled, within-subject cross-over design, the responses on the Pain Evaluation Task of 28 male patients with schizophrenia were compared to 27 healthy male controls. All participants received a single intranasal dose of 24 IU OT or placebo, 1 week apart.

Results. OT induced an empathy bias in the healthy controls towards the conflictual out-group members. Although this effect was absent in the patient group, OT seems to heighten an empathic bias in the patient group towards the in-group members when rating non-painful stimuli.

Conclusions. The study demonstrates that the administration of OT can result in empathic bias towards adversary out-group members in healthy controls but not in patients with schizophrenia. However, the OT-induced bias in both the patients (in the no-pain condition towards the in-group members) and the healthy controls (in the no-pain and pain conditions towards the adversary out-group) suggests that OT enhances the distinction between conflictual in-group and out-group members.

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Introduction

Empathy can generally be defined as an affective response to another's individual distress, which requires an accurate understanding of another's mental state or frame of reference (Batson *et al.* 1987). In addition to its association with a myriad of sociocognitive dysfunctions, schizophrenia is associated with impaired empathy (Abu-Akel & Abushua'leh, 2004; Bora *et al.* 2008; Derntl *et al.* 2009; Smith *et al.* 2013). For example, Bora *et al.* (2008) reported that, compared to healthy controls, patients with schizophrenia exhibited severe empathy dysfunctions as measured by the Empathy Quotient questionnaire (Baron-Cohen & Wheelwright, 2004). They also found impairments in the ability of the patients with schizophrenia to recognize and reason about emotions, which are considered core components of empathy (Blair, 2005; Shamay-Tsoory, 2011). Similarly, Derntl *et al.* (2009) found that patients with schizophrenia exhibited a generalized deficit in all core components of empathy, including emotion recognition, perspective taking and affective responsiveness. More recently, Lee *et al.* (2011) investigated empathic accuracy (defined as the ability to accurately infer the affective state of another person) and reported that patients with schizophrenia not only have lower empathic accuracy compared to controls but also are less sensitive to the social cues of others when making those judgments.

Several studies have suggested that the neuropeptide oxytocin (OT) mediates empathy (Rosenfeld *et al.* 2011; Striepens *et al.* 2011). This has been demonstrated in both healthy (Hurlemann *et al.* 2010) and pathological populations such as those with autism (Guastella *et al.* 2010). Studies have also shown

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abnormal levels of OT in the plasma (Goldman *et al.* 2008) and cerebrospinal fluid (Linkowski *et al.* 1984; Beckmann *et al.* 1985; Legros *et al.* 1992) of patients with schizophrenia and, more recently, variations in the OT receptor gene have been linked to schizophrenia (Souza *et al.* 2010; Montag *et al.* 2012*a*, *b*). Because of these associations, research concerned with the therapeutic potential of OT in schizophrenia has intensified over the past few years (Davis *et al.* 2013). Findings suggest that endogenous OT levels are significantly associated with social functioning (Keri *et al.* 2009; Rubin *et al.* 2010; Sasayama *et al.* 2012) and that the administration of OT improves symptomatology (Bujanow, 1974; Caldwell *et al.* 2009; Feifel *et al.* 2010; Pedersen *et al.* 2011), social perception (Fischer-Shofty *et al.* 2013) and verbal memory (Feifel *et al.* 2012). In addition, OT has been shown to improve emotion recognition (Averbeck *et al.* 2012) and theory of mind abilities (Pedersen *et al.* 2011). These associations suggest that OT might have a bearing on both the psychopathology and sociocognitive functioning of individuals with schizophrenia. Thus, in considering the general role of OT in social interaction and empathy, the established abnormalities of individuals with schizophrenia in sociocognitive and empathic abilities and the positive normalizing effect of OT on various aspects of social dysfunction seen in schizophrenia, it can be hypothesized that the normalizing effect of OT in schizophrenia can also be extended to empathy.

One of the most rudimentary empathy mechanisms is that of empathy to pain, a concept that describes our tendency to automatically experience distress when facing someone else's pain. Previous human imaging studies focusing on empathy for others' pain have consistently shown activations in regions also involved in direct pain experience (Jackson & Decety, 2004; Singer *et al.* 2004; Decety & Lamm, 2006). Specifically, a neural network including the anterior cingulate cortex and the anterior insula was reported to respond to both felt and observed pain (Decety *et al.* 2010). The same sets of regions have been reliably observed across a wide range of individuals and circumstances, suggesting that empathy to pain is, at least in part, an automatic, bottom-up process and perhaps an evolved adaptation (Decety & Svetlova, 2012). However, research strongly suggests that empathy is also mediated by top-down processing. Indeed, neuroimaging studies have demonstrated that the empathic response to pain is either strengthened or weakened when contextual and interpersonal variables are manipulated, including the intent of the inflictor of pain to harm the target (Akitsuki & Decety, 2009), and whether the person in pain belongs to a stigmatized group (Tarrant *et al.* 2009; Decety *et al.* 2010). This suggests that empathy to pain is also modulated by top-down processes such as group membership. Although this 'in-group empathy bias' has been repeatedly reported in healthy participants (Trawalter *et al.* 2012), it is not known whether patients with schizophrenia also exhibit this bias.

The role of OT and empathy has been extensively researched in the context of intergroup relationships in healthy controls, showing that the administration of OT favorably promotes empathy towards in-group members (De Dreu *et al.* 2011). The work of De Dreu *et al.* (2010, 2011) has also shown that raising OT levels can lead to negative reactions towards out-group members such as out-group derogations and defensive aggression. To our knowledge, the effect of the administration of OT on such bias among patients with schizophrenia has not been investigated. In addition, we are not aware of any studies that have examined whether patients with schizophrenia have inherent social biases towards in-group *versus* out-group members. With respect to studying the effect of OT on empathy in schizophrenia, we are aware of only one study (Davis *et al.* 2013). In this double-blind, placebo-controlled study, the administration of a single dose of 40 IU intranasal OT did not improve the patients' empathic responses as measured by the Emotional Perspective Taking Task (EPTT; Derntl *et al.* 2009), in which participants were required to infer the emotional expression of a masked-face individual taking part in a two-person social interaction. Of note, however, the authors reported a positive effect on the composite score of several higher-level processes, including the detection of sarcasm and deception in addition to empathy.

Accordingly, using a double-blind cross-over design, we sought to examine in a group of individuals with schizophrenia the effect of intranasal administration of OT on their empathic responses to the pain of others. A unique aspect of our study is that we tested the influence of OT on the empathic responses of patients within the context of the Israeli–Palestinian conflict in Israel. This allowed us to examine, in an ecologically valid environment, the role of this neuropeptide in modulating the patients' empathic responses to members of a group who are part of a protracted intergroup violent conflict. Accordingly, this study evaluated whether patients with schizophrenia have a group bias, often exhibited by healthy participants, towards in-group *versus* out-group members, and the extent to which this bias, or lack thereof, is moderated by the administration of intranasal OT.

Method

Participants

Twenty-eight healthy men, ranging in age from 20 to 37 years (mean age=27.43 years, S.D.=3.44), and

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28 male patients with schizophrenia, ranging in age from 22 to 45 years (mean age=32.21 years, S.D.=6.05) were included in the study. Because of known significant hormonal interactions between OT and estrogen in women (McCarthy, 1995), an all-male sample eliminates this possible confound. During the course of the experiment, one participant from the control group dropped out, bringing the final sample to a total of 55 participants. The data reported here are thus for 27 healthy participants and 28 patients with schizophrenia. All participants were Israeli Jews and living in Israel at the time of assessment. Healthy participants were recruited through advertisement posted across campus at the University of Haifa, and the patients were recruited from out-patient and day clinics. Diagnosis of schizophrenia was based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) and confirmed by two psychiatrists. The individuals with schizophrenia were stabilized on fixed doses of an equivalent antipsychotic medication with or without trihexyphenidyl (Artane, 5–0 mg/day) or biperiden (Dekinet, 2–4 mg/day). Exclusion criteria were acute, unstable, significant or untreated medical illnesses (including arrhythmia, psychiatric conditions and head injury), mental retardation (IQ<75), and disturbances in visuomotor coordination. The study was approved by the National Institutional Review Board of Israel and all participants gave their signed informed consent.

Clinical assessment

The patients with schizophrenia were assessed by a clinical psychologist with validated clinical tests suitable for evaluating their condition and the severity of specific symptoms. The Positive and Negative Syndrome Scale (PANSS; Kay *et al.* 1987) was used to evaluate the presence/absence and severity of positive, negative and general psychopathology. This was assessed during the screening session. The Clinical Global Impression (CGI) scale was used to estimate the severity of each patient's illness. This was administered during the first and second sessions of the treatment protocol. Finally, the Shipley Institute of Living Scale (SILS; Shipley, 1940) was used to assess the intellectual abilities of the participants.

After giving their oral and written informed consent, the participants were instructed to avoid using psychotropic substances (e.g. caffeine and nicotine) for at least 12 h prior to the experiment.

Treatment administration

A double-blind, within-subject, cross-over design was used, with participants randomly assigned to groups for the first administration of either OT or placebo 45 min prior to performing the behavioral task. Those initially receiving OT were administered a single intranasal dose of 24 IU (Syntocinon-Spray, Novartis, Switzerland) by three puffs in each nostril (each puff contains 4 IU). The placebo contained all inactive ingredients without the neuropeptide. Seven days later, at the second session of the experiment, participants underwent the same procedure with the other substance (i.e. placebo or OT). Previous studies show that the elevation of OT following intranasal administration (24 IU) usually lasts for only 1–2 h (Born *et al.* 2002; Gossen *et al.* 2012). Hence, it was safe to assume that there was no carry-over effect between the two sessions.

Assessment of empathy to pain: the Pain Evaluation Task

In this study, we used the Pain Evaluation Task designed by Jackson *et al.* (2005). We chose this task because previous research using this task and similar empathy-for-pain paradigms has shown that it reliably induces an empathy bias towards in-group compared to out-group members (Hein *et al.* 2010; Shamay-Tsoory *et al.* 2013). The task consists of showing a series of digital color photographs depicting right hands and right feet in painful and non-painful situations as follows: (1) right hands in painful situations, (2) right hands in neutral situations, (3) right feet in painful situations, and (4) right feet in neutral situations. All situations depict familiar events that can occur in everyday life. Various types of pain (mechanical, thermal and pressure) are represented. For each painful situation there is a corresponding neutral picture that involved the same setting without any painful component. Stimuli were presented randomly, following a 750-ms presentation of different common names of Jews (representing the in-group members), Palestinian Arabs (representing the adversary out-group members) or Europeans (representing the neutral out-group members). Following each name, a picture showing either a painful or a non-painful situation was presented (see Fig. 1). Participants were then asked to rate, as quickly as possible, the intensity of the pain experienced by the target using a visual analog scale (VAS) using the computer mouse (from 0=no pain to 10=most painful). The experiment consisted of 30 trials in total (15 painful and 15 non-painful stimuli). The same name was always tagged with the same picture in all sessions, but the order of presentation of the pain and no-pain stimuli were randomized separately for each participant. The task began with three practice trials, followed by the test blocks. The task was administered using E-prime 2.1 (Psychology Software Tools Inc., USA).

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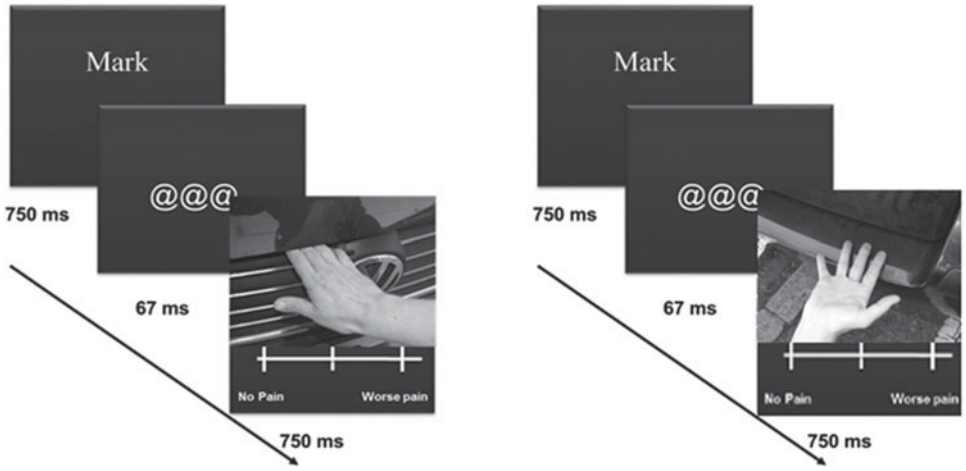

Fig. 1. Sample presentation of a right hand in a pain and no-pain situation.

Selection of the protagonist names

The selection of the targets' names was based on a preliminary study in which 120 students from the University of Haifa (60 Palestinian Arabs and 60 Jews), all Israeli citizens, were asked to report what they believe are the five most common names of Palestinian Arabs, Jews and Europeans. From a total list of 96 names, five names with the highest frequency were selected for each group. Because, in the current study, all the participants were Israeli Jews, we only used the prototypical names reported by the Jewish students. Accordingly, the stereotypical Jewish names were Moshe, Avi, Yits'hak, Yesrael and Shimon. The Arab names were Ahmad, Mohammed, Abed, Saleem and Ali. The European (neutral out-group) names were Chris, John, Mark, Martin and Paul. The use of names to prime group membership is motivated by studies showing that the presentation of prototypical names is sufficient to prime affiliative biases of in-group and out-group membership (De Dreu *et al.* 2011; Bruneau *et al.* 2012; Shamay-Tsoory *et al.* 2013).

Statistical approach and analysis

The double-blind, placebo-controlled design adopted in the current study enabled us to assess within and across groups the effect of OT *versus* placebo on the empathy rating of perceived pain when viewing in-group, adversary or neutral out-group members (primed by their respective prototypical names) in painful and non-painful familiar situations. The current study thus used a 2×3×2×2 design, where treatment (placebo *versus* OT), target (Jew *versus* Palestinian Arab *versus* European) and stimuli (painful *versus* non-painful) were entered as within-subject factors and patients *versus* healthy controls as between-subjects factors. In addition, independent-sample *t* tests and correlation analyses were carried out. All analyses were performed using IBM SPSS version 21 (SPSS Inc., USA).

Results

Independent-sample *t* tests indicated that the control and patient groups differed in age ($t_{53}=-3.54$, $p=0.001$) but not intelligence ($t_{53}=1.74$, $p=0.09$). None of the empathy responses of both groups correlated with either the intelligence score or age. In addition, none of the empathy responses within the schizophrenia group correlated with age of disease onset, duration of illness, positive or negative symptoms, or general psychopathology. There were also no associations between the patients' responses and severity of illness as measured by the CGI scale during the first or the second session. Moreover, there was no difference in the patients' severity of illness during the first *versus* the second session. The clinical and demographic data for the patient and healthy control groups are presented in Table 1.

Effect of OT on empathy to pain

The full model of the study design included three within-subject variables (target, pain condition and treatment) and one between-subjects variable (group). To examine the interaction between treatment (placebo/OT), target (Arab/European/Jew), pain condition (pain/no-pain) and group (control/schizophrenia), a four-way (2×3×2×2) repeated-measures ANOVA was performed. The results show a non-significant treatment effect ($F_{1,53}=1.02$, $p=0.32$), a non-significant target effect ($F_{2,106}=0.75$, $p=0.47$) and a non-significant group effect ($F_{1,53}=0.45$, $p=0.51$). The pain condition effect was highly significant ($F_{1,53}=48.50$, $p<0.001$, $\eta^2_P=0.90$), indicating that overall the ratings for the

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Table 1. *Clinical and demographic data of the patient and healthy control groups*

	Schizophrenia sample (n=28 males)	Healthy controls (n=27 males)
Age (years)	32.21±6.05	27.48±3.49
Intelligence (SILS)	25.21±8.39	29.64±6.20
Age of onset (years)	20.21±4.20	–
Duration of illness (years)	11.93±6.54	–
PANSS Negative	18.68±4.70	–
PANSS Positive	15.14±3.73	–
PANSS General	33.79±6.03	–
CGI Session 1	4.71±0.66	–
CGI Session 2	4.61±0.83	–

SILS, Shipley Institute of Living Scale; PANSS, Positive and Negative Syndrome Scale; CGI, Clinical Global Impression.

Values given as mean±standard deviation.

painful stimuli were higher than the non-painful stimuli. Furthermore, the two-way interactions of group × treatment ($F_{1,53}$=2.52, p=0.12) and target × group ($F_{2,106}$=2.75, p=0.07) were also not significant. Importantly, the three-way interaction of treatment × target × group ($F_{2,106}$=4.05, p=0.020, η^2_p=0.07) was significant, indicating that the treatment affected the groups differently when judging the stimuli associated with the different targets. The within-subjects contrast for this interaction is linearly significant ($F_{1,53}$=8.17, p=0.006, η^2_p=0.13), suggesting that the participants' ratings across the three targets followed a linear trend. The four-way interaction of treatment × target × condition × group was not significant ($F_{2,106}$=0.260, p=0.772).

To further explore the source of the three-way interaction, we carried out separate repeated-measures ANOVAs for each group. Using a three-way repeated-measures ANOVA, we examined the interaction between treatment (placebo/OT), target (Arab/European/Jew) and pain condition (pain/no-pain) within the healthy controls. As shown in Fig. 2, a significant treatment by target effect ($F_{2,53}$=6.74, p=0.002, η^2_p=0.21) indicated that, in the healthy controls, the treatment differentially affected the pain ratings of the different target groups. Although the pain condition was highly significant ($F_{1,26}$=183.95, p<0.001, η^2_p=0.88), indicating higher pain ratings in the pain *versus* no-pain condition, the three-way interaction of treatment × target × pain condition was not significant ($F_{2,52}$=0.66, p=0.52). The target ($F_{2,52}$=0.434, p=0.65) and treatment ($F_{2,52}$=2.62, p=0.12) effects were also not significant. To further explore the source of the two-way treatment by target interaction, follow-up t tests were carried out. This analysis indicated that OT had a significant effect on increasing the pain rating for the Arab protagonists (t_{26}=2.06, p=0.049) but it did not affect the pain rating for the European (t_{26}=−0.59, p=0.56) or Jewish targets (t_{26}=−0.56, p=0.58). Of note, similarly to the pain ratings, in the no-pain condition, OT had a significant effect on increasing the empathy to pain ratings for the Arab targets (t_{26}=3.27, p=0.003) and for the European targets (t_{26}=2.31, p=0.029) but non-significantly for the Jewish targets (t_{26}=1.37, p=0.18).

Within the patient group, we similarly examined the interaction between treatment (placebo/OT), target (Arab/European/Jew) and pain condition (pain/no-pain) using a three-way repeated-measures ANOVA. As shown in Fig. 3, a non-significant treatment by target effect ($F_{2,54}$=0.82, p=0.45) indicated that, in the patient group, the treatment did not differentially affect their empathy to the pain of the different targets. Although the pain condition was highly significant ($F_{1,27}$=318.07, p<0.001, η^2_p=0.92), indicating higher pain ratings in the pain *versus* no-pain condition, the three-way interaction of treatment × target × pain condition was not significant ($F_{2,54}$=0.12, p=0.89). The target ($F_{2,54}$=2.70, p=0.11) and treatment ($F_{2,54}$=0.23, p=0.64) effects were also not significant.

When examining the within-subject contrasts reported above, no significant differences were discerned across the targets in the placebo condition for both the painful and non-painful stimuli. However, under the OT condition, the patients, but not the controls, rated the non-painful stimuli differently across the targets. Paired t tests reveal that the Jewish targets received significantly higher ratings than both the Arab targets (t_{27}=3.17, p=0.004) and the European targets (t_{27}=2.38, p=0.024). The European targets also received higher rating than the Arab targets, but the difference did not reach significance (t_{27}=1.34, p=0.19).

Discussion

The current study sought to investigate the effect of OT on the empathic responses of male patients with schizophrenia and male healthy controls within the context of intergroup relationships. The healthy and the patient groups behaved differently in their empathic responses towards the conflictual group members as a function of OT administration. Within the controls, OT induced a significant empathy bias towards the Arab targets in the painful condition. A similar but a more robust bias towards the Arab targets was also observed under the OT condition when rating non-painful stimuli. Within the schizophrenia group,

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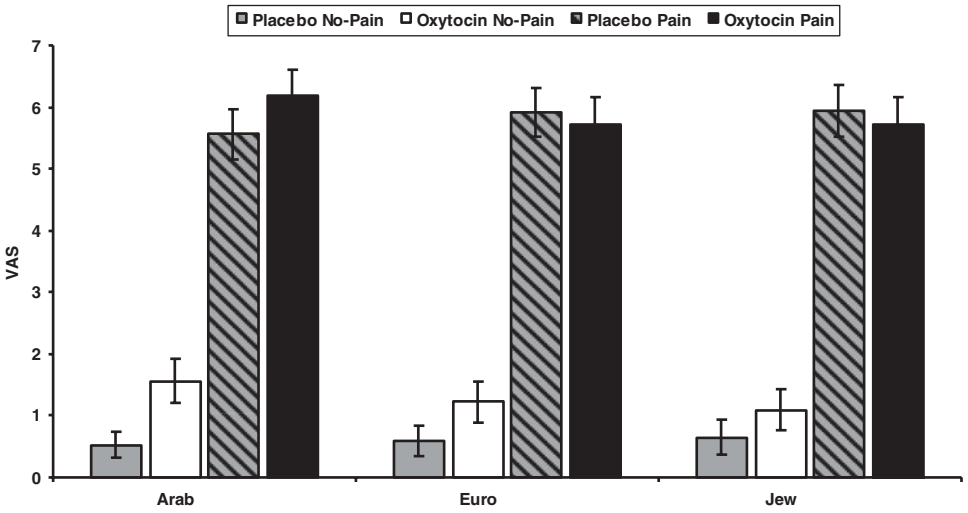

Fig. 2. Mean empathic ratings (± standard error) of the healthy controls as a function of treatment condition (placebo *versus* oxytocin), pain condition (pain *versus* no-pain) and target (Arabs *versus* Europeans *versus* Jews). VAS, Visual analog scale.

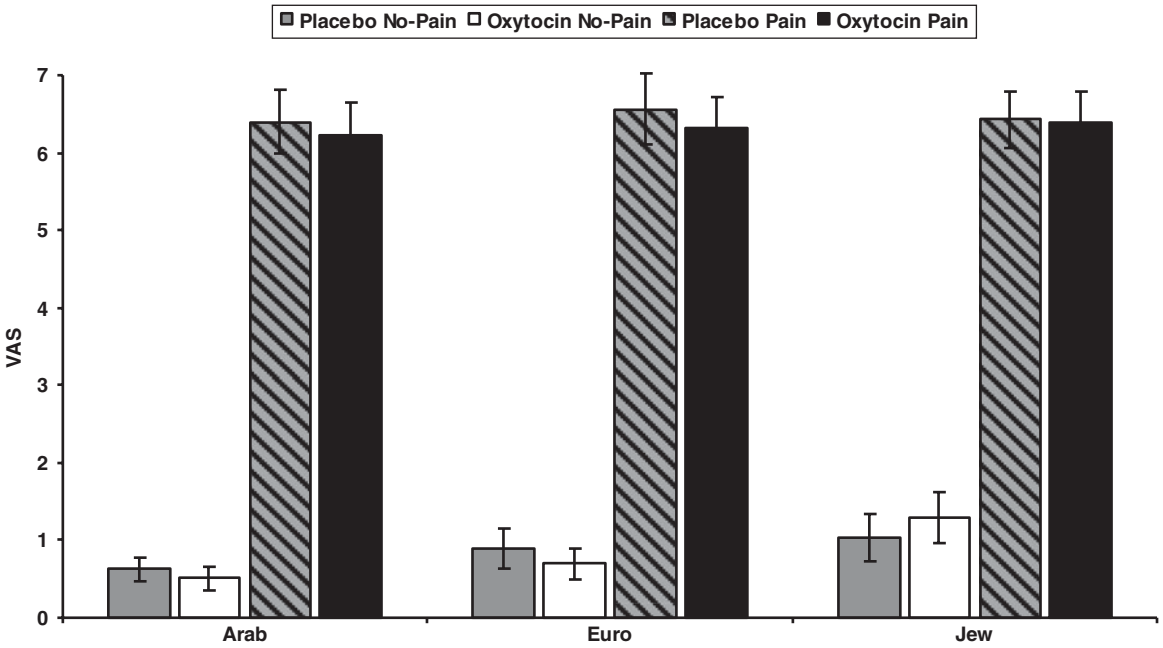

Fig. 3. Mean empathic ratings (± standard error) of the patients with schizophrenia as a function of treatment condition (placebo *versus* oxytocin), pain condition (pain *versus* no-pain) and target (Arabs *versus* Europeans *versus* Jews). VAS, Visual analog scale.

the empathy ratings of the targets did not differ as a function of treatment condition when evaluating others in pain. However, OT seems to heighten the bias within the patients when rating non-painful stimuli. Under this condition, the patients significantly conferred higher empathy ratings to the Jewish targets (i.e. the in-group members), followed by the European targets and then the Arab targets. Thus it seems that OT exerts opposing effects on the rating of non-painful stimuli within the healthy and patient groups; although OT increased the level of empathy in the healthy participants towards out-group members, it increased the bias among the patients towards the in-group members.

From a clinical perspective, OT did not increase the patients' empathic responses in the painful condition. This finding partially overlaps with the study by Davis *et al.* (2013), who reported that OT did not improve the empathic responses of their patients as measured by the EPTT. However, as noted earlier,

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that study found a positive effect on a composite score of several higher-level cognitive processes, including empathy. The absence of the effect of OT among the patients can be attributed to variations within the patients' neurochemical profile with which OT interacts, including variation in endogenous OT and the possible modulatory effect it may have on exogenous OT (Bartz *et al.* 2011). As such, the lack of a baseline measure of endogenous OT levels is a limitation in our study that should be addressed in future studies. Another possibility is that the administration of one dose of OT may not be sufficient to induce an effect on complex sociocognitive abilities, such as empathy, in the patient group. It is conceivable that a higher dosage and/or a protracted regimen of daily intranasal OT administration may be necessary for such an effect to transpire (Feifel *et al.* 2010; Pedersen *et al.* 2011).

A surpising finding is that OT increased empathic responses towards the non-painful stimuli, albeit in opposite trends, in both the patient and healthy participants. Although the opposing effect in terms of the in-group bias (in the patient group) *versus* the out-group bias (in the heathy controls) is open to speculation, our findings suggest that increasing OT levels facilitate social categorization of others as in-group *versus* out-group (Kavaliers & Choleris, 2011; De Dreu, 2012). Moreover, the enhanced empathic response towards non-painful stimuli after the administration of OT might be a consequence of an overdrive of endogenous OT leading to hyper-vigilance/sensitivity. This may in turn have led participants to attribute social meaning to visual information with when none is required. This is akin to inducing some form of hyper-mentalism, which is a common feature in schizophrenia present with positive symptoms (Abu-Akel & Bailey, 2000; Frith, 2004; Abu-Akel, 2008; Montag *et al.* 2011; Walss-Bass *et al.* 2013). Another explanation is that both pain and non-pain stimuli rely on similar neural substrates including the thalamus, insula and anterior cingulate cortex (Mouraux *et al.* 2011; Hayes & Northoff, 2012), whose activity correlates significantly with the perceived saliency of the stimulus (Mouraux *et al.* 2011). Speculatively, the modulation of the oxytocinergic system of the regional, along with the connectivity between these different regions (Bethlehem *et al.* 2013), may explain the increased ratings we observe for both the painful and non-painful stimuli.

Within the healthy controls, there was an increase in the pain ratings to both painful and non-painful stimuli in the OT condition, which suggests that OT may have a general effect on pain perception. This finding is commensurate with evidence suggesting that OT potently affects the nociceptive system when administered directly (Juif & Poisbeau, 2013). Moreover, our study can inform research using intergroup conflict paradigms, particularly in light of the finding that OT did not lead the healthy participants to change their overall ratings towards their in-group members. Indeed, our finding suggests that OT can induce an empathic response towards out-group members even if the out-group members are part of a social group with which the participants are engaged in a protracted political and violent conflict. As such, our finding does not support claims suggesting that OT promotes, in healthy controls, out-group derogation or enhances in-group bias (De Dreu *et al.* 2010, 2011), and replicates our earlier results in this regard (Shamay-Tsoory *et al.* 2013). This finding might be explained within the framework of prosocial theories positing that trust and concern for others tend to increase towards others in anticipation of future interaction (Komorita & Parks, 1995). It is conceivable that the administration of OT increases the salience of this likely interaction, which could explain why the effect was only observed when rating the Palestinian Arabs (with whom there is a greater likelihood of interaction) and not the Europeans. Other possible interpretations pertain to the role of OT in increasing approach-related behaviors (Kemp & Guastella, 2011), abolishing negative affect (Petrovic *et al.* 2008) and increasing attention to socially relevant information (Leknes *et al.* 2013), which together constitute mechanisms that could facilitate increased empathic responses towards others. The selectivity of OT to increasing the empathic response towards the out-group rather than the in-group suggests that, in certain contexts, exogenous OT may not necessarily have an additive value to what is already salient to the individual (i.e. the in-group member). In this regard there is evidence showing that the administration of OT to individuals with high emotional sensitivity afforded little or no improvement in detecting subtle social cues (Leknes *et al.* 2013). Thus, our finding provides further support for the view suggesting that the effect of OT on sociocognitive abilities is not uniform and is susceptible to changes in context, whether it is the environment or the persons with whom we interact (Bartz *et al.* 2011).

To conclude, this study demonstrates that the administration of OT induces an empathic bias towards the adversary out-group members in healthy male controls but not in male individuals with schizophrenia. This suggests that OT, within the context of intergroup conflict, does not affect the patients' empathic judgments of either neutral or adversary out-group members. In this context we should note that the reliance on an all-male sample may limit the generalizability of our findings, particularly in light of evidence suggesting that male and female individuals with schizophrenia differ in baseline OT levels and OT response

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(Rubin *et al.* 2010), and also in their affective mentalizing abilities (Abu-Akel & Bo, 2013). However, OT does seem to enhance the distinction between the conflictual in-group and out-group in both the healthy and patient groups. This is evidenced by the OT-induced bias in both the patient (in the no-pain condition towards the in-group members) and the healthy control groups (in both the pain and no-pain conditions towards the adversary out-group members), and the absence of such an effect towards the neutral European group. This finding thus underscores the importance of using both neutral and conflict groups in future studies concerned with intergroup dynamics (see also Bruneau *et al.* 2012). The effect of OT on enhancing the salience and/or social relevance of non-painful stimuli is intriguing and warrants further investigation, particularly within the framework of the 'aberrant salience' hypothesis of schizophrenia (Kapur, 2003).

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Declaration of Interest

None.

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