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Biological Psychology 92 (2013) 380–386

Contents lists available at SciVerse ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Oxytocin modulates the racial bias in neural responses to others' suffering

Feng Sheng[a,b], Yi Liu[a], Bin Zhou[c], Wen Zhou[c], Shihui Han[a,*]

[a] Department of Psychology, Peking University, Beijing, PR China
[b] Guanghua School of Management, Peking University, Beijing, PR China
[c] Institute of Psychology, Chinese Academy of Sciences, Beijing, PR China

ARTICLE INFO

Article history:
Received 2 July 2012
Accepted 29 November 2012
Available online xxx

Keywords:
Empathy
Oxytocin
ERP
Racial bias

ABSTRACT

The intergroup relationship between a perceiver and a target person influences empathic neural responses to others' suffering, which are increased for racial in-group members compared to out-group members. The current study investigated whether oxytocin (OT), a neuropeptide that has been linked to empathic concern and in-group favoritism, contributes to the racial bias in empathic neural responses. Event-related brain potentials were recorded in Chinese male adults during race judgments on Asian and Caucasian faces expressing pain or showing a neutral expression after intranasal self-administration of OT or placebo. A fronto-central positive activity at 128–188 ms (P2) was of larger amplitude in response to the pain expressions compared with the neutral expressions of racial in-group members but not of racial out-group members. OT treatment increased this racial in-group bias in neural responses and resulted in its correlation with a positive implicit attitude toward racial in-group members. Our findings suggest that OT interacts with the intergroup relationship to modulate empathic neural responses to others' suffering.

1. Introduction

Empathy is the ability to understand and share the emotional states of others, and it plays a key role in prosocial behavior (Batson, 1998; de Waal, 2008). Recent neuroimaging research has resulted in increased interest in the neural mechanisms underlying empathy. One line of research has shown that viewing others in pain activates the midcingulate cortex, the anterior insula, and the sensorimotor cortex (Singe et al., 2004; Avenanti et al., 2005; Gu and Han, 2007; Saarela et al., 2007; Han et al., 2009; Ma et al., 2011). Because these brain regions are engaged in the first-hand experience of pain (Rainville et al., 1997; Wager et al., 2004), it has been proposed that empathy for pain shares the neural mechanisms with the first-hand experience of pain.

Recent studies have shown that empathic neural responses to perceived pain in others are strongly shaped by the social relationship between an observer and a target person. Using functional magnetic resonance imaging (fMRI), Xu et al. (2009) scanned Chinese and Caucasian participants while they watched video segments showing a Chinese or a Caucasian model receiving painful (needle penetration) versus non-painful (Q-tip touch) stimulation. In both Chinese and Caucasian participants, the empathic neural activity in the midcingulate region was much stronger when viewing painful stimulation applied to same-race models compared to other-race models. A subsequent event-related brain potential (ERP) study found that a positive activity at 128–188 ms over the frontal/central brain regions (P2) increased in response to pain expressions versus neutral expressions and that the P2 empathic responses were significantly reduced toward racial out-group faces compared to racial in-group faces (Sheng and Han, 2012). Source estimation suggested that the P2 component may arise from the midcingulate region, which is consistent with the previous fMRI findings (Xu et al., 2009). Avenanti et al. (2010) found that observing the pain of racial in-group but not racial out-group models inhibited the onlookers' sensorimotor activity, as if they were receiving painful stimulation. These results indicate that empathic neural responses to others' suffering are modulated by the intergroup relationships between a perceiver and a target person and that neural responses to others' pain are stronger for racial in-group members compared with racial out-group members.

While the prior studies have demonstrated a racial bias in empathic neural responses, it remains unclear how neurobiological factors may contribute to this effect. Oxytocin (OT) is a neuropeptide that is important for the maintenance of social groups and the development of trust among in-group members (see De Dreu, 2012 for a review). It has been demonstrated that intranasally administered OT, versus placebo, can enhance the behavioral index of emotional empathy in response to positive and negative stimuli (Hurlemann et al., 2010). OT can improve performance during inference of others' emotion (Domes et al., 2007), suggesting that OT

* Corresponding author at: Department of Psychology, Peking University, 5 Yiheyuan Road, Beijing 100871, PR China. Tel.: +86 10 6275 9138; fax: +86 10 6276 1081.
E-mail address: shan@pku.edu.cn (S. Han).

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http://dx.doi.org/10.1016/j.biopsycho.2012.11.018

may up-regulate empathic concern for others. However, the effects of OT on social cognition and prosocial behavior are influenced by the social context (Bartz et al., 2011). OT promoted trust or cooperation with in-group members but not with out-group members (De Dreu et al., 2010, 2011). Thus it is likely that OT may improve empathic neural responses specifically to racial in-group members rather than function as a general facilitator of empathy.

The current study tested this

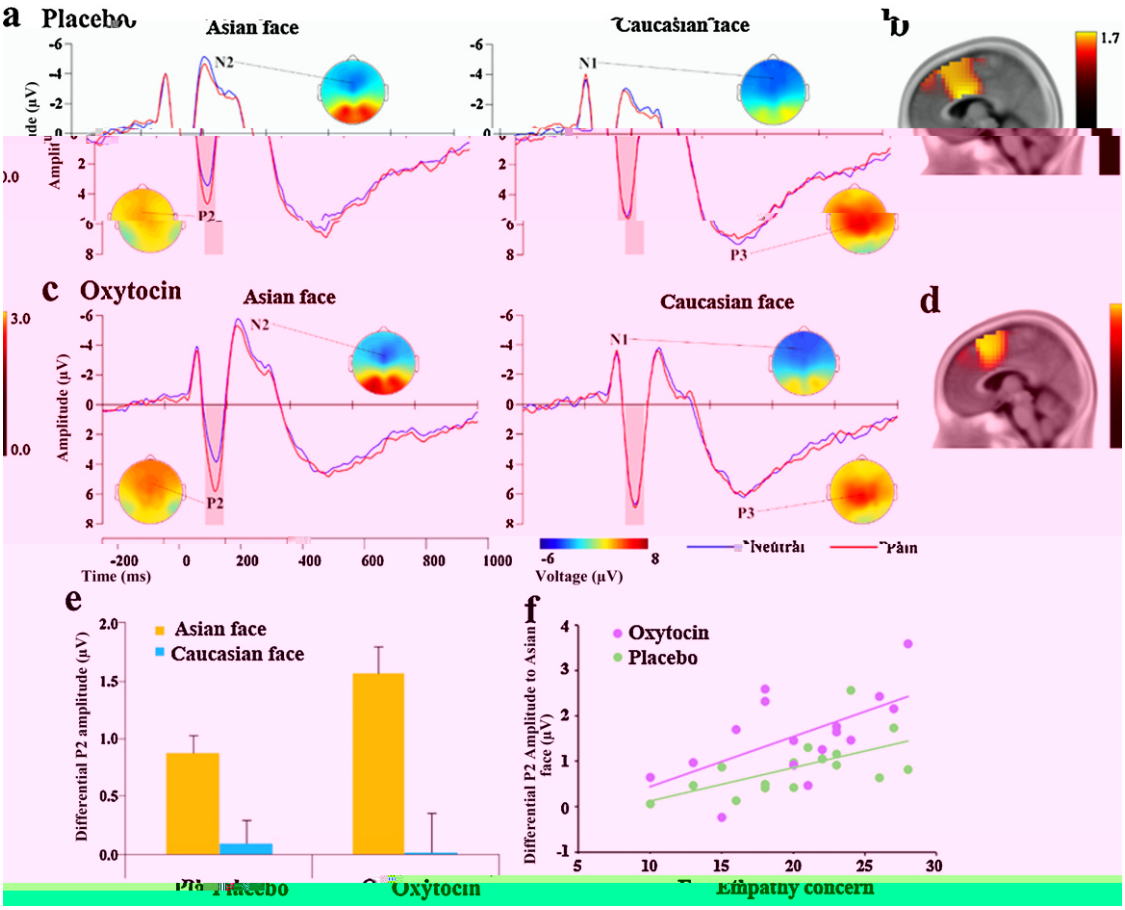

Fig. 2. Illustration of the OT effects on empathic neural responses. (a) ERPs recorded at FCz to pain and neutral expressions after placebo treatment. (b) Source estimation of the neural activity in the P2 time window that differentiated between pain and neutral expressions of Asian faces in the placebo condition. The scale bar represents the log of *F*-ratio for comparisons between ERPs to pain and neutral expressions in the P2 time window. (c) ERPs recorded at FCz to pain and neutral expressions after OT treatment. (d) Source estimation of the neural activity in the P2 time window that differentiated between pain and neutral expressions of Asian faces in the OT condition. (e) The amplitude of the difference wave at 128–188 ms obtained by subtracting ERPs to neutral expression from those to pain expression in the OT and placebo conditions. (f) The correlation between the differential P2 amplitude to pain versus neutral expressions and rating scores of empathy concern in the OT and placebo conditions.

Brain Electromagnetic Tomography (sLORETA, Pascual-Marqui, 2002) were used to estimate potential sources of empathic neural responses.

3. Results

3.1. Behavioral results

The ANOVAs of RTs and accuracy showed significant interactions of race × expression ($F(1,15) = 38.00$ and 14.66, both $p < 0.005$). Participants responded slower ($F(1,15) = 15.27$, $p < 0.001$) and less accurately ($F(1,15) = 5.45$, $p < 0.05$) to pain versus neutral expressions of Asian faces, whereas a reverse pattern was observed for Caucasian faces (RTs, ($F(1,15) = 20.02$, $p < 0.001$; accuracy, $F(1,15) = 10.91$, $p < 0.01$, Table 1). Pain intensity and self-unpleasantness were rated higher on pain expressions than on neutral expressions ($F(1,15) = 168.16$ and 56.11, both $p < 0.001$), but these effects were not modulated by race or treatment (both $p > 0.1$). The explicit likability rating showed a preference for neutral over pain expressions ($F(1,16) = 48.47$, $p < 0.001$). The *D* score in the Implicit Association Test did not differ significantly from zero in the placebo condition ($M = 0.16$, SD = 0.49, $t(1,15) = 1.43$, $p = 0.173$), but was significantly larger than zero in the OT condition ($M = 0.33$, SD = 0.58, $t(15) = 2.36$, $p < 0.05$). These results suggest that, relative to Caucasian faces, Asian faces were significantly associated with a positive rather than negative attitude after OT treatment.

3.2. Electrophysiological results

Fig. 2 illustrates the ERPs at a fronto-central electrode to pain and neutral expressions in the OT and placebo conditions. The ERPs were characterized by a negative wave at 84–116 ms (N1) and a positive deflection at 128–188 ms (P2) over the frontal–central area, which were followed by a negative wave at 200–300 ms (N2) over the frontal region and a long-latency positivity at 400–700 ms (P3) over the parietal area. The face stimuli also elicited a posterior P1 at 88–148 ms and a N170 at 140–180 ms over the occipito-temporal electrodes.

The ANOVAs of the P2 amplitudes at 128–188 ms showed significant main effects of race (Fz: $F(1,15) = 24.81$, $p < 0.001$; FCz: $F(1,15) = 27.14$, $p < 0.001$; Cz: $F(1,15) = 28.44$, $p < 0.001$; F3–F4: $F(1,15) = 20.47$, $p < 0.001$; FC3–FC4: $F(1,15) = 25.89$, $p < 0.001$; C3–C4: $F(1,15) = 33.31$, $p < 0.001$) and expression (Fz: $F(1,15) = 10.94$, $p = 0.005$; FCz: $F(1,15) = 28.07$, $p < 0.001$; Cz: $F(1,15) = 35.19$, $p < 0.001$; F3–F4: $F(1,15) = 8.88$, $p = 0.009$; FC3–FC4: $F(1,15) = 22.23$, $p < 0.001$; C3–C4: $F(1,15) = 24.39$, $p < 0.001$). The P2 amplitudes were increased in response to Caucasian versus Asian faces and in response to expressions of pain versus neutral expressions. These main effects are consistent with previous findings (Ito and Bartholow, 2009; Sheng and Han, 2012) and suggest that the P2 is engaged in coding both race and pain expression. There was a significant main effect of treatment on the P2 amplitude (Fz: $F(1,15) = 7.71$, $p = 0.014$; FCz: $F(1,15) = 5.30$, $p = 0.036$;

Table 1
Behavioral performances and subjective rating scores (mean ± SD).

	Expression	Placebo		Oxytocin	
		Asian	Caucasian	Asian	Caucasian
Reaction time (ms)	Neutral	535 ± 71	533 ± 72	535 ± 57	523 ± 57
	Pain	546 ± 76	522 ± 73	544 ± 70	516 ± 49
Accuracy (%)	Neutral	91 ± 5	90 ± 5	93 ± 5	92 ± 5
	Pain	89 ± 7	92 ± 5	91 ± 7	94 ± 4
Pain intensity	Neutral	2.03 ± 1.22	1.92 ± 1.11	1.82 ± 0.96	1.91 ± 1.04
	Pain	6.80 ± 1.16	6.55 ± 1.40	6.75 ± 1.10	6.65 ± 1.25
Self-unpleasantness	Neutral	2.88 ± 1.65	2.80 ± 1.84	3.01 ± 1.69	2.50 ± 1.34
	Pain	5.48 ± 1.69	5.33 ± 1.35	5.41 ± 1.44	5.66 ± 1.80
Likability	Neutral	4.98 ± 1.02	5.20 ± 1.11	5.02 ± 1.25	5.38 ± 0.96
	Pain	4.10 ± 0.84	4.08 ± 0.91	4.31 ± 1.22	4.37 ± 1.04

F3–F4: $F(1,15) = 6.62$, $p = 0.021$; FC3–FC4: $F(1,15) = 4.95$, $p = 0.042$), as the OT treatment significantly increased the P2 amplitude, compared to the placebo treatment. There was also a significant interaction of expression × race (Fz: $F(1,15) = 19.34$, p

Fig. 3. Illustration of the correlation between the racial bias in empathic neural responses and the *D* score in the placebo and OT conditions, respectively. Each individual participant was indicated with a number.

in-group members and the racial bias in empathic neural responses in the P2 time window, after the OT treatment.

The ANOVAs of the N2 amplitudes showed significant main effects of race (Fz: $F(1,15) = 49.35$, $p < 0.001$; FCz: $F(1,15) = 47.61$, $p < 0.001$; Cz: $F(1,15) = 49.65$, $p < 0.001$; F3–F4: $F(1,15) = 36.28$, $p < 0.001$; FC3–FC4: $F(1,15) = 46.24$, $p < 0.001$; C3–C4: $F(1,15) = 53.36$, $p < 0.001$) and expression (Fz: $F(1,15) = 3.49$, $p = 0.081$; FCz: $F(1,15) = 7.87$, $p = 0.013$; Cz: $F(1,15) = 6.74$, $p = 0.020$; FC3–FC4: $F(1,15) = 5.56$, $p = 0.032$; C3–C4: $F(1,15) = 3.91$, $p = 0.067$), due to that the N2 was of larger amplitude to Asian than Caucasian faces and to neutral than pain expressions (Fig. 2a and c). There were also significant main effects of race on P3 amplitude (Pz: $F(1,15) = 8.38$, $p = 0.011$; P3–P4: $F(1,15) = 6.29$, $p = 0.023$) and N170 amplitudes (P7–P8: $F(1,15) = 38.13$, $p < 0.001$; PO7–PO8: $F(1,15) = 26.01$, $p < 0.001$), suggesting larger P3 for Caucasian faces than for Asian faces and larger N170 amplitudes for Asian faces than for Caucasian faces. The ANOVAs of the N2, P3, P1, and N170 amplitudes showed that neither the main effect of treatment nor its interaction with race and expression was significant (all $p > 0.1$). Correlation analyses failed to find a significant correlation between the *D* score in the Implicit Association Test and the race effect on the P2, N170, N2, and P3 components (all $p > 0.1$).

4. Discussion

The modulation of the P2 amplitude by facial expression of pain is consistent with the previous findings that perception of human body parts (e.g., hand or foot) receiving painful versus neutral stimulation elicits increased positivity over the fronto-central region (Fan and Han, 2008; Han et al., 2008; Li and Han, 2010; Decety et al., 2010). The source estimation suggests that the P2 empathic neural responses might arise from the midcingulate and the supplementary motor area. Moreover, the P2 empathic response was greater to racial in-group faces than to out-group faces. The P2 effect is consistent with the previous findings of a racial in-group bias in empathic neural responses within the same time window (Sheng and Han, 2012) and in a similar brain region (Xu et al., 2009). Moreover, we found that, relative to the placebo treatment, the OT treatment selectively increased neural responses to pain expression of racial in-group faces in the context of racial categorization and thus increased the racial bias in empathic neural responses in the P2 time window.

Although behavioral research suggests that OT facilitates understanding or sharing of others' emotions (Domes et al., 2007; Hurlemann et al., 2010; Bartz et al., 2010), there has been no evidence for the modulation of empathic neural responses by OT treatment. Singer et al. (2008) found that, relative to treatment with a placebo, OT treatment reduced amygdala activation when participants received painful stimulation themselves but did not modulate empathy-relevant brain activation in the anterior insula. This study did not investigate the OT effects on empathic neural responses in a specific social context. Our ERP findings suggest an effect of OT that was specific to an in-group versus out-group context and support the existence of an interaction between social (e.g., intergroup relationship) and biological (e.g., OT) factors in the modulation of empathic neural responses to perceived pain in others.

The effect of OT on empathic neural responses took place between 100 and 200 ms after sensory stimulation. Sheng and Han (2012) showed that empathic neural responses in this time window were modulated by manipulation of cognitive strategies and intergroup relationships. Enhanced attention to an individual's feelings and inclusion of other-race individuals on one's own team for competitions reduced the racial bias in empathic neural responses, by increasing empathic neural activity to other-race individuals rather than by decreasing empathic neural activity to same-race individuals. Unlike the manipulation of cognitive strategies and intergroup relationships, intranasally administered OT increased the empathic neural responses in the P2 time window to same-race individuals but produced little effect on the P2 empathic neural responses to other-race individuals. Thus P2 empathic neural responses to same-race and other-race individuals seem to be sensitive to psychological manipulations and neuropeptide, respectively.

Interestingly, neither intranasally administered OT (the current work) nor manipulation of cognitive strategies and intergroup relationships (Sheng and Han, 2012) affected the rating scores of self-reported unpleasantness induced by viewing pain expressions. Rating scores are explicit measurements of subjective feelings and are sensitive to social contexts and social desire. It is likely that our participants were concerned about overtly expressing greater empathy for racial in-group members than for out-group members because racial in-group bias is apparently not encouraged by current societies. OT treatment appeared to modulate participants' implicit attitudes toward racial in-group members because the *D* score of the Implicit Associate Test was larger than zero after the OT treatment. The OT treatment resulted in a significant association between racial bias in empathic neural responses and participants' implicit attitudes toward racial in-group faces. The previous studies have shown that OT treatment significantly affects attitudes, such as social trust, toward others (Kosfeld et al., 2005; Baumgartner et al., 2008; De Dreu, 2012). One possibility is that, in our study, the OT treatment might have changed participants' implicit attitudes toward racial in-group and out-group members. The resulting

sustained variation of implicit attitudes might have modified the neural activity to perceived pain in racial in-group members in a top-down manner. This possibility should be investigated in future research.

Empathic neural responses are associated with altruistic behavior. Neural activity to perceived pain predicts how much money participants donate (Ma et al., 2011) and how often participants sacrifice themselves to help in-group members (Hein et al., 2010). The racial bias in empathy-related neural activity may lead to racial in-group preference during altruistic behavior. Indeed, individuals with racial bias in empathy tend to assign more lenient punishments (Johnson et al., 2002) and show pain treatment biases (Drwecki et al., 2011) toward racial in-group compared to out-group members. The racial bias in empathy may reflect an evolutionary strategy to prevent an inappropriate extension of in-group generosity to out-group members in order to benefit the survival of in-group individuals. Recent research suggests that OT motivates in-group favoritism and parochial cooperation instead of creating more benevolent views of others generally (De Dreu et al., 2010, 2011). The effect of OT on empathic neural responses to in-group members may play a role in the modulation of social behavior toward in-group members. OT is a highly reserved neuropeptide and has been a hormone throughout evolution (Meyer-Lindenberg et al., 2011). It may signal its adaptive value in protecting in-group benefit by facilitating in-group favoritism in empathy.

There has been evidence for OT engagement in first-hand pain experience. Animal studies have shown that OT administration reduces pain sensitivity to thermal heat (Agren et al., 1997) and mechanical pain (Petersson et al., 2001). In contrast, an OT antagonist increases pain sensitivity (Uvnas-Moberg et al., 1992). Intrathecal OT administration in humans reduces pain in individuals with acute or chronic low back pain (Yang et al., 2002). The effect of OT on pain experience may arise from an enhancement of endogenous opioid activity (Miranda-Cardenas et al., 2006) and a reduction of sympathetic nervous system activity (Sofroniew, 1980). These studies did not consider whether the effect of OT on pain experience is influenced by the social relationship between a giver and a receiver of pain stimulation. Our findings indicate that the effect of OT on empathic neural responses to others' suffering is sensitive to the social relationship between an observer and a target person. Future research should clarify whether the effect of OT characterizes the key difference between first-hand pain experience and empathy for others' pain.

A recent behavioral study showed that, relative to placebo treatment, OT treatment increased the feeling of envy when an individual gained less money than another player and increased the feeling of gloating when one player gained more money than the other (Shamay-Tsoory et al., 2009). Thus, OT may enhance the social comparison that produce a negative effect on prosocial behaviors. Hein et al. (2010) found that, when seeing out-group members in pain, participants with more negative impressions of out-group members showed stronger activity in the right nucleus accumbens, a brain region that has been associated with schadenfreude (Takahashi et al., 2009). These findings leave an open question of whether OT influences the neural activity in the reward-related system while perceiving out-group members' pain.

Previous studies have shown that other facial expressions also modulate the P2 amplitude. Kubota and Ito, 2007 recorded ERP to black and white faces from Caucasians. They found enlarged P2 amplitudes to angry and happy faces compared to neutral faces. The P2 modulation by angry/happy expressions did not differ between racial in-group and out-group faces. The P2 modulation by pain expression seemed to be different from that observed by Kubota and Ito, 2007, in terms of the effect of the racial relationship between an observer and a target person. Previous research has shown that the P2 is sensitive to novel or negative stimuli because the P2 is enlarged by negative-arousing pictures (Bar-Haim et al., 2005) and threat-related pictures or words (Taake et al., 2009; Thomas et al., 2007; Weymar et al., in press). These findings suggest that the P2 amplitude may reflect enhanced attention to novel stimuli that are relevant to one's own safety. From an evolutionary perspective, intergroup competition for resources results in antagonism between in-group and out-group members and leads to the stereotype that out-group members are dangerous. Faces of out-group members may be perceived with higher novelty compared to faces of in-group members regardless of facial expression (e.g., painful versus neutral faces). This hypothesis may explain the race effect on the P2 amplitude observed in our study and others. In-group members are usually not dangerous. Pain expression of an in-group member may signal a need for help and have higher novelty compared to neutral faces. This impression may result in higher sensitivity to pain expression of in-group versus out-group members, as indicated by the greater P2 amplitude and delayed responses to pain versus neutral expressions of racial in-group members in a race judgment task. The P2 modulation by in-group members' pain expressions in particular is associated with empathy because we showed that the P2 amplitude to pain versus neutral expressions was correlated with an individual's empathy concern capacity.

In conclusion, our ERP results showed that, relative to the placebo treatment, the OT treatment increased the empathic neural responses to racial in-group faces at 128–188 ms after stimulus onset but failed to modulate the empathic neural responses to racial out-group faces. Our findings suggest that OT may interact with the social relationship between an observer and a target person to modulate human empathy for the suffering of others. Future research should address how the interaction between the social relationship and biological factors, such as OT, influences human social behaviors.

Acknowledgements

This work was supported by Beijing Municipal Natural Science Foundation (No. Z111107067311058), the National Natural Science Foundation of China (Project 30910103901, 91024032, 81161120539), and the National Basic Research Program of China (973 Program 2010CB833903). We thank Kate Woodcock for proofreading the manuscript.

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