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

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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

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 hypothesis using a randomized double-blind within-subjects placebo-controlled design. From male adult subjects, we recorded ERPs to racial in-group and out-group faces expressing pain or showing a neutral expression. The facial stimuli were adopted from our previous research (Sheng and Han, 2012). Intranasally administered OT or a placebo was administered to participants on two separate days before the ERPs were recorded. Our previous work showed that the racial bias in fronto-central P2 empathic neural responses was modulated by manipulation of cognitive strategies and intergroup relationships. Specifically, the racial bias was reduced by enhanced attention to individuals' emotions and by including other-race individuals in one's own team for competitions (Sheng and Han, 2012). The current study investigated whether and how P2 empathic neural responses are modulated by OT treatment. If OT plays a role in racial bias in empathy, the in-group bias in the P2 effect observed in Sheng and Han (2012) should be increased by OT, as compared to the placebo treatment. Because Avenanti et al. (2010) found that a deficit in empathic reactivity to racial out-group members was greater in the onlookers who exhibited stronger implicit racial bias in their attitudes, we measured participants' implicit attitudes toward racial in-group and out-group faces. We used

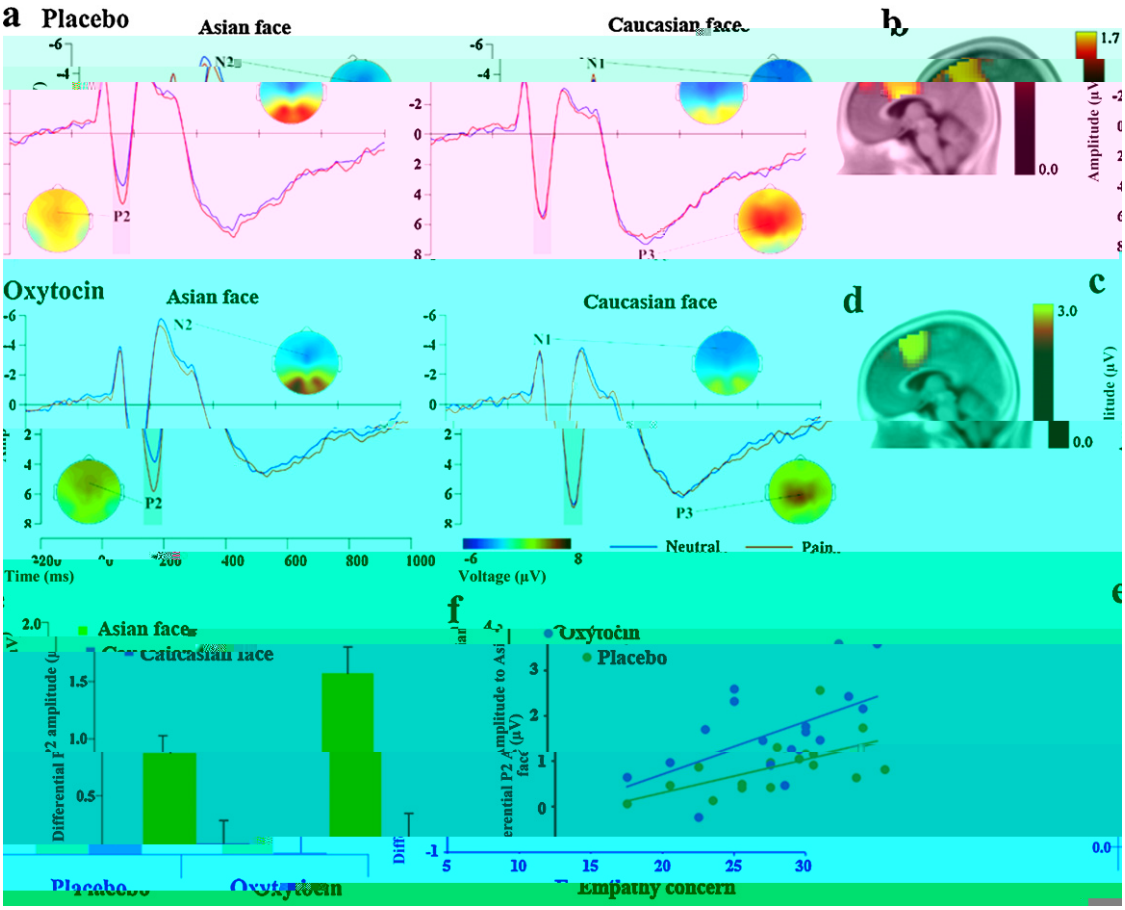

Fig. 2. Illustration of the OT effects on empathic neural responses. (a) ERPs recorded at FCz to pain and neutral expressions after placebo treatment. (b) Source estimation of the neural activity in the P2 time window that differentiated between pain and neutral expressions of Asian faces in the placebo condition. The scale bar represents the log of -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. t

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

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: (1,15) = 24.81, < 0.001; FCz: (1,15) = 27.14, < 0.001; Cz: (1,15) = 28.44, < 0.001; F3–F4: (1,15) = 20.47, < 0.001; FC3–FC4: (1,15) = 25.89, < 0.001; C3–C4: (1,15) = 33.31, < 0.001) and expression (Fz: (1,15) = 10.94, = 0.005; FCz: (1,15) = 28.07, < 0.001; Cz: (1,15) = 35.19, < 0.001; F3–F4: (1,15) = 8.88, = 0.009; FC3–FC4: (1,15) = 22.23, < 0.001; C3–C4: (1,15) = 24.39, < 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: (1,15) = 7.71, = 0.014; FCz: (1,15) = 5.30, = 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: (1,15) = 6.62, = 0.021; FC3–FC4: (1,15) = 4.95, = 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: (1,15) = 19.34, = 0.001; FCz: (1,15) = 22.75, < 0.001; Cz: (1,15) = 29.86, < 0.001; F3–F4: (1,15) = 11.90, = 0.004; FC3–FC4: (1,15) = 17.97, = 0.001; C3–C4: (1,15) = 18.56, = 0.001), indicating that the effect of pain expression on the P2 amplitude was stronger for Asian than Caucasian faces. Simple effect analysis revealed that the P2 amplitude was enlarged to pain expression, compared to neutral expression of Asian faces (Fz: (1,15) = 43.91, < 0.001; FCz: (1,15) = 76.57, < 0.001; Cz: (1,15) = 84.95, < 0.001; F3–F4: (1,15) = 27.59, < 0.001; FC3–FC4: (1,15) = 61.82, < 0.001; C3–C4: (1,15) = 60.68, < 0.001), but not of Caucasian faces (all < 1). This result replicates our previous findings (Sheng and Han, 2012) and suggests an in-group bias in neural responses to others' suffering. Source estimation suggested that the neural activity in the P2 time window that differentiated between pain and neutral expressions of Asian faces had potential sources in the dorsal ACC and supplementary motor cortex (peak MNI coordinates: 5, 10, 25 and 5, 25, 55 in placebo and OT conditions, respectively; Fig. 2b and d). This result is similar to our previous finding (Sheng and Han, 2012).

Most importantly, the ANOVAs of the P2 amplitudes showed a significant three-way interaction of treatment × race × expression (Fz: (1,15) = 5.21, = 0.037; FCz: (1,15) = 4.87, = 0.043; FC3–FC4: (1,15) = 3.19, = 0.094). Separate analysis revealed that treatment × expression interaction was significant for Asian faces (Fz: (1,15) = 3.77, = 0.071; FCz: (1,15) = 6.11, = 0.026; Cz: (1,15) = 5.78, = 0.03; F3–F4: (1,15) = 10.36, = 0.006; FC3–FC4: (1,15) = 4.84, = 0.044; C3–C4: (1,15) = 6.22, = 0.025), as OT compared to placebo significantly increased the P2 amplitude to pain expressions (Fz: (1,15) = 7.63, = 0.015; FCz: (1,15) = 5.87, = 0.028; F3–F4: (1,15) = 6.56, = 0.022; FC3–FC4: (1,15) = 3.89, = 0.069), but did not affect the P2 amplitude to neutral expressions (all > 0.1). However, the interaction of treatment × expression was not significant for Caucasian faces (all > 0.1), suggesting that OT treatment failed to modulate the P2 amplitude to pain versus neutral expressions of racial out-group members. Separate analysis revealed significant interactions of race × expression in both the placebo (Fz: (1,15) = 4.46, = 0.052; FCz: (1,15) = 12.20, = 0.003; Cz: (1,15) = 15.02, = 0.001; F3–F4: (1,15) = 7.204, = 0.017; FC3–FC4: (1,15) = 11.22, = 0.004; C3–C4: (1,15) = 10.35, = 0.006) and OT conditions (Fz: (1,15) = 15.57, = 0.001; FCz: (1,15) = 18.42, = 0.001; Cz: (1,15) = 17.21, = 0.001; F3–F4: (1,15) = 8.21, = 0.012; FC3–FC4: (1,15) = 12.74, = 0.003; C3–C4:

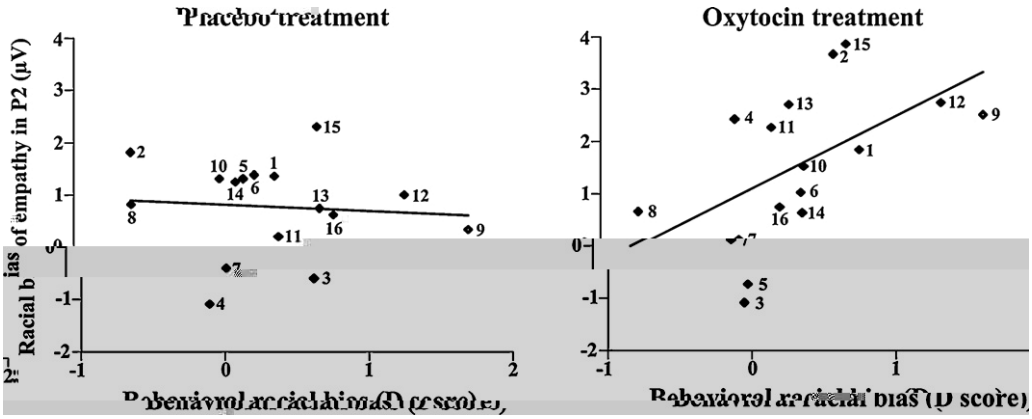

Fig. 3. Illustration of the correlation between the racial bias in empathic neural responses and the score in the placebo and OT conditions, respectively. Each individual participant was indicated with a number.

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: (1,15) = 49.35, < 0.001; FCz: (1,15) = 47.61, < 0.001; Cz: (1,15) = 49.65, < 0.001; F3–F4: (1,15) = 36.28, < 0.001; FC3–FC4: (1,15) = 46.24, < 0.001; C3–C4: (1,15) = 53.36, < 0.001) and expression (Fz: (1,15) = 3.49, = 0.081; FCz: (1,15) = 7.87, = 0.013; Cz: (1,15) = 6.74, = 0.020; FC3–FC4: (1,15) = 5.56, = 0.032; C3–C4: (1,15) = 3.91, = 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: (1,15) = 8.38, = 0.011; P3–P4: (1,15) = 6.29, = 0.023) and N170 amplitudes (P7–P8: (1,15) = 38.13, < 0.001; PO7–PO8: (1,15) = 26.01, < 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 > 0.1). Correlation analyses failed to find a significant correlation between the score in the Implicit Association Test and the race effect on the P2, N170, N2, and P3 components (all > 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 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

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