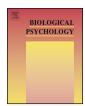
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## Oxytocin effects on neural correlates of self-referential processing



Yi Liu<sup>a,b</sup>, Feng Sheng<sup>a,b</sup>, Kate A. Woodcock<sup>a,c</sup>, Shihui Han<sup>a,b,\*</sup>

- <sup>a</sup> Department of Psychology, Peking University, Beijing, China
- <sup>b</sup> PKU-IDG/McGovern Institute for Brain Research, Peking University, Beijing, China
- <sup>c</sup> School of Psychology, University of Birmingham, Edgbaston, Birmingham, UK

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#### ABSTRACT

Oxytocin (OT) influences how humans process information about others. Whether OT affects the processing of information about oneself remains unknown. Using a double-blind, placebo-controlled within-subject design, we recorded event-related potentials (ERPs) from adults during trait judgments about oneself and a celebrity and during judgments on word valence, after intranasal OT or placebo administration. We found that OT vs. placebo treatment reduced the differential amplitudes of a fronto-central positivity at 220–280 ms (P2) during self- vs. valence-judgments. OT vs. placebo treatment tended to reduce the differential amplitude of a late positive potential at 520–1000 ms (LPP) during self-judgments but to increase the differential LPP amplitude during other-judgments. OT effects on the differential P2 and LPP amplitudes to self- vs. celebrity-judgments were positively correlated with a measure of interdependence of self-construals. Thus OT modulates the neural correlates of self-referential processing and this effect varies as a function of interdependence.

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#### 1. Introduction

Oxytocin (OT) is a peptide hormone produced in the hypothalamus and plays an important role in social cognition and social behavior. Animal studies have shown that OT contributes to the development of prosocial behavior such as mother-infant attachment, grooming, and approach behavior (see Lim & Young, 2006 for review). In humans, OT promotes social trust and cooperation such that individuals receiving intranasal sprays of OT compared to a placebo are more inclined to invest money in others even when there is no guarantee of reciprocation (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005). To account for the enhanced prosociality induced by OT, previous studies focused on how OT treatment affects the processing of information about conspecific others. It has been shown that, relative to placebo administration, intranasal OT results in increased sensitivity to others' facial expressions (Marsh, Yu, Pine, & Blair, 2010; Schulze et al., 2011), better understanding of others' thoughts and intentions (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007), and enhanced perception of trustworthy and attractiveness of others' faces (Theodoridou, Rowe, Penton-Voak, & Rogers, 2009, see Campbell, 2010 for review).

There is also increasing evidence that OT modulates neural activities involved in the processing of social cues (see Zink

E-mail address: shan@pku.edu.cn (S. Han).

& Meyer-Lindenberg, 2012 for review). Functional magnetic resonance imaging (fMRI) studies found that intranasal OT administration decreased neural responses in the amygdala during implicit (Domes, Heinrichs, Glascher, et al., 2007) and explicit (Gamer, Zurowski, & Buchel, 2010) processing of fearful facial expressions in males but increased amygdala activity during explicit processing of fearful faces in females (Domes et al., 2010). An electroencephalograph (EEG) study showed that, while perception of social stimuli (e.g., a point-light display of human biological motion) was associated with suppression of EEG activity in the mu/alpha and beta bands (Perry, Troje, & Bentin, 2010; Ulloa & Pineda, 2007), this suppression was significantly enhanced following intranasal OT versus placebo treatment (Perry, Bentin, et al., 2010). OT also modulated the amplitudes of event-related potentials (ERPs) elicited by facial stimuli such that OT, compared to a placebo, increased the amplitude of a frontal positivity at 140–180 ms and the amplitude of a late positive potential (LPP) at 400-800 ms over the parietal region in response to emotional faces (Huffmeijer et al., 2013). Moreover, OT interacts with social factors to modulate neural activities to emotional cues. Sheng, Liu, Zhou, Zhou, and Han (2013) recorded ERPs from Chinese adults while they perceived pain or neutral facial expressions of Asian and Caucasian models. They first showed that, in the placebo condition, pain compared to neutral expressions increased the amplitude of a fronto-central positive activity at 128-188 ms (P2) and this effect was evident for Asian but not for Caucasian models. This replicates the racial bias in empathic neural responses (Sheng & Han, 2012). Moreover, Sheng et al. (2013) found that OT compared to a placebo increased the P2 empathic neural responses to pain vs. neutral

<sup>\*</sup> Corresponding author at: Department of Psychology, Peking University, 5 Yiheyuan Road, Beijing 100871, China. Tel.: +86 10 6275 9138; fax: +86 10 6276 1081.

expressions of Asian but not Caucasian models, suggesting that OT may selectively enhanced the neural activity to facial expressions of racial in-group (but not out-group) members.

The reciprocally interconnected role of self related and other related processing in social cognition has been widely discussed. How one thinks of the self and the relationship between the self and others significantly influence social interaction. For example, a person may expend self-concept to include close others in order to acquire resources, perspectives, and identities from others and to enhance one's own ability to accomplish goals (Aron et al., 2004). Self-other merging facilitates cooperation in social dilemmas (Cremer & Stouten, 2003) and perceived "oneness" (i.e., one comes to incorporate the self within the boundaries of the other) or perceptions of self in relation to others links to emotional empathy (Burris & Rempel, 2012; Cialdini, Brown, Lewis, Luce, & Neuberg, 1997). Previous studies of OT effects on neural correlates of social cognition have focused exclusively on other-related processing. There has been no existing data so far on how OT affects neural correlates of self-related processing.

Consistent with the idea that the processes of the self and others are the two sides of social cognition (Iacoboni, 2006; Sedikides & Skowronski, 2009), it has been shown that priming independent vs. interdependent self-construals in Chinese participants speeded their responses to their own faces but slowed their responses to others' faces (Sui & Han, 2007). Moreover, while fMRI studies suggest that the medial prefrontal cortex and anterior cingulate cortex are engaged in self-referential processing of personality traits (Heatherton, 2011; Kelley et al., 2002; Ma & Han, 2011; Ma et al., 2013; Northoff et al., 2006; Wang et al., 2012; Zhu, Zhang, Fan, & Han, 2007), priming bicultural Chinese (i.e., students from Hong Kong) with Chinese vs. Western cultures enhanced the medial prefrontal activity related to self-referential processing but decreased the medial prefrontal activity involved in other-related processing (Ng, Han, Mao, & Lai, 2010). These findings suggest that the same psychological manipulation can modulate the neural processing of oneself and others in opposite directions. OT may produce similar effects, that is, if OT alters social cognition by increasing the salience of social cues related to others or enhancing attentional processing of others (Bartz, Zaki, Bolger, & Ochsner, 2011; Perry, Bentin, et al., 2010; Shamay-Tsoory et al., 2009), it may be proposed that OT would decrease the salience of self-related information or weaken self-related processing in tasks such as trait judgments.

A recent behavioral study found that intranasal OT versus placebo administration increased self-reported ratings of one's own extraversion and openness to experiences (Cardoso, Ellenbogen, & Linnen, 2012). This finding suggests that OT influences selfperceived personality traits that are important for social affiliation. However, measurements of subjective ratings do not reveal how the neurocognitive mechanisms involved in self-referential processing are affected by OT treatment. Thus the present study investigated how intranasal OT influences the neural activity involved in self-referential processing by recording ERPs during a self-referential task that requires judgments about the personality traits of oneself. A trait judgment task performed on a celebrity who was known to all participants was included to test whether OT also modulates the neural processing of others during trait judgments. A valence judgment task was included to serve as a baseline to control for semantic processing and motor responses.

Previous ERP research has linked self-referential processing to positive activities over broad regions (Fields & Kuperberg, 2012; Magno & Allan, 2007; Mu & Han, 2010). Particularly related to the current work, Mu and Han (2010) found that a fronto-central positive activity was associated with self-referential processing because trait judgments of oneself versus a celebrity elicited larger amplitudes of the fronto-central positivity as early as 200 ms after

sensory stimulation. Given that modulations of ERPs related to the processing of others (e.g., Sheng & Han, 2012; Sheng, Liu, Zhou, Zhou, & Han, 2013) and the self (e.g., Mu & Han, 2010) occurs in the same time course and over the same brain regions, it may be hypothesized that OT relative to a placebo may produce opposite effects on self- and other-referential processing during trait judgments. This hypothesis has a premise that the fronto-central activity in the P2 time window associated with self-referential processing and the processing of others arises from the same neural structure and OT effects occurs in the same time course during self-referential and other-referential processing. Specifically, we predicted that, relative to placebo treatment, OT treatment may decreases the fronto-central activity related to self-referential processing during the task of trait judgment. In contrast, OT vs. placebo may increase the frontal-central activity associated with the processing of others during the trait judgment task.

In addition, we examined whether OT effects on self-referential processing vary across individuals with different self-construals. It has been shown that the effects of OT in the social domain are constrained by features of situations and/or individuals (Bartz et al., 2011). OT (vs. placebo) effects on memories of childhood maternal care and closeness are moderated by the attachment representations people possess (Bartz, Zaki, Ochsner, et al., 2010). These findings suggest that OT effects on neural activities involved in social cognition may vary as a function of individuals' attributes. It is well known that individuals from Western cultures view the self as an autonomous entity that is independent of social contexts and others (i.e., having independent self-construals), whereas East Asians view the self as being strongly connected with others (i.e., having interdependent self-construals) (Han & Northoff, 2009; Markus & Kitayama, 1991, 2010; Zhu & Han, 2008). Moreover, the effect of social influences on self-related processing is stronger in individuals from sociocultural contexts that encourage interdependent than independent self-construals (Liew, Ma, Han, & Aziz-Zadeh, 2011; Ma & Han, 2009, 2010). Therefore, the current study tested whether differential self-versus other-referential processing is more sensitive to biological influences (i.e., intranasal OT treatment) in individuals with stronger interdependent selfconstruals.

#### 2. Methods

#### 2.1. Participants

Twenty male adults (mean age = 22.0, SD = 1.96 yrs) participated in this study as paid volunteers. Exclusion criteria included self-reported medical or psychiatric illness and use of medication. All were right-handed and had normal or corrected-to-normal vision. Informed consent was obtained prior to participation. This study was approved by a local ethics committee.

#### 2.2. Stimuli and procedure

288 Chinese trait adjectives, each consisting of two Chinese characters, were selected from an established personality trait adjective pool (Liu, 1990) for personality trait or valence judgments. For each participant these trait adjectives were randomly classified into 4 lists of 72 words with half positive and half negative words in each list.

In a double-blind, placebo-controlled within-subject design, participants participated in two EEG sessions with an interval of at least 6 days. Before each EEG session, 32 IU OT or placebo (containing all of the active ingredients except for the neuropeptide) was administered with a nasal spray. The spray was administered to participants four times to each nostril and each administration consisted of one inhalation of the spray with 4 IU. The procedure of OT and placebo administration was similar to the previous work that showed significant OT effects on either behavior (De Dreu et al., 2010; Mikolajczak, Pinon, Lane, de Timary, & Luminet, 2010) and brain activity (Petrovic, Kalisch, Singer, & Dolan, 2008; Sheng et al., 2013). Treatment (OT vs. placebo) orders were counterbalanced across participants. After OT or placebo administration, participants took a break of 45 min before EEG recording.

The experimental procedure is illustrated in Fig. 1. After OT or placebo administration, each participant performed 4 blocks of 72 trials for trait/valence judgments while EEG was recorded. Two lists of 72 words were used twice for each EEG session. Within each block participants had to make yes/no judgments on whether a trait

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