Oxytocin Blurs the Self-Other Distinction During Trait Judgments and Reduces Medial Prefrontal Cortex Responses

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Abstract: The neuropeptide oxytocin (OXT) may act either to increase or blur the distinction between self and other and thereby promote either more selfish or altruistic behaviors. To attempt to distinguish between these two possibilities we performed a double-blind, between-subject, placebo-controlled design study to investigate the effect of intranasal OXT on self and other (mother, classmate, or stranger) trait judgments in conjunction with functional magnetic resonance imaging. Results showed that OXT reduced response times for making both self and other judgments, but also reduced the accuracy of their subsequent recall, thereby abolishing the normal self-bias observed in this task. OXT also abolished the positive correlation between response and self-esteem scale scores seen in the PLC group, suggesting that its effects were strongest in individuals with higher levels of self-esteem. A whole-brain functional magnetic resonance imaging analysis revealed that OXT also reduced responses during both self and other trait judgments in the dorsal (dmPFC) and ventral (vmPFC) medial prefrontal cortex. A subsequent region of interest analysis revealed that behavioral performance and self-esteem scale scores were associated with dmPFC activation and its functional connectivity with the anterior cingulate and between the vmPFC and posterior cingulate. Thus overall, while OXT may improve speed of decision making in self -vs. other trait judgments it also blunts the normal bias towards remembering self-attributes and reduces mPFC responses and connectivity with other cortical midline regions involved in self-processing. This is consistent with the view that OXT can reduce self-centered behavior. *Hum Brain Mapp* 37:2512–2527, 2016. © 2016 Wiley Periodicals, Inc.

Key words: self-referential effect; self- vs. other processing; oxytocin; cortical midline structures; self-esteem; medial prefrontal cortex

INTRODUCTION

A central feature of human experience is a sense of “self” that provides stability and continuity to the flow of subjective experience across space and time [Neisser, 1988]. Psychological aspects of the self tend to be operationalized with studies examining autobiographical memory and self-knowledge or self-referential processing of personality traits [Molnar-Szakacs and Uddin, 2013; Rogers et al., 1977; Symons and Johnson, 1997]. Self-referential processing is defined as the process by which a person becomes aware that specific contents are related to

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his or her own self [Symons and Johnson, 1997] and we tend to remember self-relevant more than irrelevant information [Rogers et al., 1977]. There are also cultural influences on our concept of self, with Asian collectivist cultures exhibiting an extended sense of self which can include close relatives, such as mother [Aron et al., 2004; Belk, 1988; Markus and Kitayama, 1991; Wang et al., 2012].

Neuroimaging studies have implicated parts of the default mode network (DMN) with self as opposed to other processing [Molnar-Szakacs and Uddin, 2013], with self-trait judgments being particularly associated with greater activity in the medial prefrontal cortex (mPFC) [Beer et al., 2010; Kelley et al., 2002; Kim and Johnson, 2014]. Thus the mPFC is engaged more when participants process information about themselves, as opposed to others, in terms of personality traits, mental states, or physical characteristics and when they access autobiographical knowledge [Amodio and Frith, 2006; Beer et al., 2010; Blair et al., 2008; Cikara et al., 2014]. The mPFC can be roughly divided into two overlapping subregions, relative to the genu of the corpus callosum—dorsal mPFC (dmPFC) and the ventral mPFC (vmPFC). Broadly defined, the dmPFC includes the supragenual anterior cingulate (ACC) and the medial frontal gyrus, whereas the vmPFC includes the supragenual anterior cingulate (ACC), ventromedial prefrontal and medial orbitofrontal cortex [Kim et al., 2011]. In addition to the mPFC and ACC, more posterior cortical midline structures are also implicated in self-processing including the posterior cingulate cortex (PCC) and precuneus [Meffert et al., 2013; Uddin et al., 2007; van der Meer et al., 2010].

The hypothalamic neuropeptide oxytocin (OXT) has been shown to influence many different aspects of social cognition and behavior in humans, particularly in relation to promoting social bonds, empathy and in-group preferences [Bartz et al., 2011; Bethlehem et al., 2013; Guastella and MacLeod, 2012; Striepens et al., 2011]. While there is an ongoing debate concerning the precise nature and mechanisms of OXT effects in humans, it is generally considered that it may act primarily to enhance the salience of social stimuli and affiliative behaviors [Bartz et al., 2011; Shamay-Tsoory and Abu-Akel, 2016], although there has also been increasing interest in its potential role in influencing aspects of self-processing and in particular distinctions between self and other. Thus intranasal OXT has been reported to increase memories for positive self-attributes [Colonnello and Heinrichs, 2014] and self-reported ratings of one's own extraversion and openness to experiences [Cardoso et al., 2012]. Another study has reported that OXT may sharpen self-other perceptual boundary by showing in a morphing paradigm that it increased the ability of subjects to discriminate between their own face (self) and that of an unfamiliar person (other) [Colonnello et al., 2013]. On the other hand, OXT has also been found to increase taking another—but not a self-perspective in a pain perception context [Abu-Akel

et al., 2015] and to increase other—but not self-orientation in terms of individuals perceiving themselves as being more communal [Bartz et al., 2015]. In this latter study OXT also reduced a sense of agency in anxiously attached individuals, indicative of a reduced self-orientation. Indeed, OXT's established role in promoting affiliative behavior and social bonds [Bartz et al., 2011; Bethlehem et al., 2013; Guastella and MacLeod, 2012; Striepens et al., 2011] would seem more consistent with it acting to decrease self-interest and to increase interest in others.

Several studies have reported OXT effects on DMN regions associated with self-processing, including increased activation in both the ACC and precuneus during self-processing of disgust and in the insula for both self and other processing [Scheele et al., 2014a,b]. Other studies have also reported OXT effects on functional connectivity involving the insula [Hu et al., 2015; Striepens et al., 2012] and mPFC [Sripada et al., 2013], although this has not been investigated in the context of self-processing. In another event related potential study, OXT was found to decrease the differential amplitudes of a frontocentral positivity at 220 to 280 ms (P200) in the area of the mPFC and ACC during self- vs. valence-judgments (self-referential processing) [Liu et al., 2013]. Thus OXT may play an important role in influencing some aspects self-processing, although whether it does act, as would be predicted from its role in affiliation, primarily to blur the distinction between self and other, and which specific neural mechanisms are involved remains unclear. It is also not known whether OXT effects on self-processing might be influenced by the extent to which others are included in the concept of self, which is a common feature of collectivist Asian cultures [Aron et al., 2004; Belk, 1988; Markus and Kitayama, 1991; Wang et al., 2012].

Self-perception can be modulated by self-esteem which can influence perception of social standing and evaluations individuals make about their personal worth [Somerville et al., 2010]. Whereas individuals with low self-esteem are more likely to experience negative affect and are more susceptible to interpersonal distress [Baumeister et al., 2003; Gyurak et al., 2012], those with high self-esteem can be aggressive and bullying [Baumeister et al., 2003] and tend to be liked less by their peers, especially following a threat to their self-esteem [Heatherton and Vohs, 2000; Somerville et al., 2010]. There are also some reported cultural differences in relation to self-esteem, although these mainly seem to occur in individuals with low self-esteem [Brown and Cai, 2010]. Individuals with high self-esteem tend to have a self-positivity bias [Tao et al., 2012] and increasingly research is showing overlap between neural substrates in the cortical midline system involved in self-referential processing and self-esteem [Frewen et al., 2013; Yang et al., 2012, 2014]. While there is no evidence to date that OXT effects may be modulated by levels of self-esteem there is growing evidence that they are influenced by a number of other different personality traits as well as

context [Bartz et al., 2011]. For example, OXT effects have been reported to be modified by trait forgiveness [Yao et al., 2014] and autism [Bartz et al., 2010; Scheele et al., 2014a; Xu et al., 2015] and depression [Ellenbogen et al., 2012] trait scores.

In the current study, we have carried out a task-dependent functional magnetic resonance imaging (fMRI) study to investigate the behavioral and neural effects of OXT on self- vs. other processing using the classic trait-judgment paradigm and subjects from a collectivist culture (Chinese). In this task, subjects reliably show an improved memory for both positive and negative valence trait judgments pertaining to self as opposed to others [Mu and Han, 2010; Symons and Johnson, 1997]. By using this behavioral paradigm together with an unbiased whole brain-based fMRI analysis we aimed to determine the specific neural substrates and their functional connections where OXT acts either to modulate self- vs. other distinctions. Furthermore, to identify potential moderating influences of an extended self, and/or levels of self-esteem, on OXT mediated effects, these traits were measured in all subjects through completion of inclusion of other self (IOS) [Aron et al., 1992], self-construal scale (SCS) [Singelis, 1994], and self-esteem scale (SES) [Rosenberg, 1989] questionnaires. We hypothesized that if OXT acts primarily to decrease the distinction between self and others by reducing self-interest then its effects might be more apparent in individuals with a more independent self-concept (i.e. those individuals with higher self-esteem and/or lower SCS/IOS scores).

MATERIALS AND METHODS

Participants and Treatment

In a double-blind, between-subject placebo (PLC)-controlled design with subjects randomly assigned to OXT and PLC treatment groups, a total of 41 male subjects (mean age $\pm$ SEM = 22.83 $\pm$ 0.34 years) participated in a task-dependent fMRI experiment [three subjects were excluded due to excessive head movement during scanning, OXT group: 18; PLC group: 20]. The subjects were all University students and were free of medical or psychiatric illness, drug or alcohol abuse. The study was approved by the ethical committee of the University of Electronic Science and Technology of China and all subjects gave informed consent to take part.

For the experiment, subjects were first administered a single intranasal dose of 40IU OXT (Oxytocin Spray—Sichuan Meike Pharmacy Co. Ltd, Sichuan, China; five puffs of 4 IU per nostril with 30 s between each puff) or PLC (also five puffs per nostril) using a standard protocol [Guastella et al., 2013]. The PLC treatment was provided in the same type of dispenser bottle by the pharmaceutical supply company providing the OXT nasal spray, and contained all of same ingredients other than the neuropeptide.

The experimental paradigm started 45 min after OXT or PLC treatment, which is estimated to allow increased concentrations of the peptide to occur within the cerebrospinal fluid [Born et al., 2002; Chang et al., 2012]. In postexperiment interviews, subjects were unable to identify better than chance whether they had received the OXT or PLC treatment.

Immediately before drug administration all subjects completed a range of questionnaires measuring personality and affective traits and levels of anxiety: Chinese versions of: NEO-Five Factor Inventory (NEO-FFI) [Costa and McCrae, 1989], Positive and Negative Affect Schedule (PANAS) [Watson et al., 1988], State-Trait Anxiety Inventory (STAI) [Spielberger et al., 1970], and SES [Rosenberg, 1989], Inclusion of Others in Self (IOS) [Aron et al., 1992], and Self-Construal Scale (SCS) [Singelis, 1994].

Experimental Design

After an 8.5 min resting state scan, subjects performed a self-referential task (trait judgment task), followed by a memory test for about 15 min after they came out of the scanner. The self-referential task used an identical overall design to that of a previously published study [Wang et al., 2012], other than that we only included a “mother” condition to test for an extended self (i.e. father was not included), a “class-mate” was used rather than “friend” for the familiar other condition and a “stranger” was used rather than a “famous person” to include an unfamiliar other category. The stimuli used in the task were 200 positive (clever, kind) and 200 negative (lazy, childish) trait adjectives which were all two Chinese character words selected from an established personality trait adjective pool [Wang and Cui, 2005], presented through an LCD projector onto a rear-projection screen and viewed with an angled mirror positioned on the head-coil. Trait adjectives were then divided into ten lists of forty words matched for valence and arousal (rated by a separate group of 20 subjects using a 7-point scale). Ratings by this separate group of subjects revealed no significant difference between positive (200) and negative (200) trait-adjectives for valence intensity ($t = 1.6$, $P = 0.1$) and arousal ($t = 0.86$, $P = 0.4$). There was also no significant difference between judgment (240) and memory (160) adjectives for valence intensity ($t = 0.56$, $P = 0.58$) and arousal ($t = 0.01$, $P = 0.99$), or between old (160) and new (160) adjectives used during the memory test for valence intensity ($t = 0.95$, $P = 0.34$) and arousal ($t = 0.01$, $P = 0.99$), or between self, mother, classmate, stranger and font (each with 48 words) conditions during judgments for valence intensity ($F = 1.4$, $P = 0.24$) and arousal ($F = 0.004$, $P = 1$).

From the 10 words lists, six were pseudorandomly selected for trait judgment tasks in the scanning session (48 words used in each of the five judgment conditions, 240 in total) while the other four were used as novel words in a “surprise” memory test after the scanning

Figure 1.

Self-referential trait-judgment task. Following a 4-s instruction period each block was presented for 28 s during which the subjects were asked to judge whether the adjective displayed was appropriate for describing a trait exhibited by themselves, their mother, a classmate or a stranger or to judge the font of the word. Eight adjectives were presented in each block and between each block

two rows of asterisks (*) were presented for 10 s. Each adjective was presented for 2 s during which subjects had to make a judgment by pressing a button (i.e. yes or no), with a “cue” word (either self, mother, classmate, stranger or font) shown above the centered trait adjective word on the screen.

session. Reaction time (RT) for making trait judgments was measured in each case. In the memory test afterwards, 32 trait adjectives used in each of the five judgment conditions (i.e. 160 in total) were randomly intermixed with 160 new trait adjectives, and subjects were required to identify old versus new items presented in a random order by pressing one of two buttons.

Functional scanning involved six sessions, with five blocks of trait judgments in each session. The order of the blocks was counterbalanced across scanning sessions. Following a 4-s instruction period each block was presented for 28 s during which the subjects were asked to judge whether the adjective displayed was suitable for describing a trait exhibited by themselves, their mother, a classmate, or a stranger. To control for nonspecific aspects of semantic processing and motor responses, a font judgment task (bold- vs. light-faced) was also included. For the trait adjective task, eight adjectives were presented in each block and between each block two rows of asterisks (*) were presented for 10 s. Each adjective was presented for 2 s during which subjects had to make a judgment by pressing a button (i.e. yes or no), with a “cue” word

(either self, mother, classmate, stranger, or font) shown above the centered trait adjective word on the screen [Wang et al., 2012; see Fig. 1].

fMRI Acquisition

We used a GE (General Electric Medical System, Milwaukee, WI) 750 3.0T MRI scanner to measure changes in blood oxygenation level-dependent (BOLD) activity. During each scan, a time series of volumes was acquired using a T2*-weighted echo planar imaging pulse sequence (repetition time, 2,000 ms; echo time, 30 ms; slices, 39; thickness, 4 mm; gap, 1 mm; field of view, 240 × 240 mm²; resolution, 64 × 64; flip angle, 90°). In addition, high-resolution whole-brain volume T1-weighted images were acquired obliquely with a three-dimensional spoiled gradient echo pulse sequence (repetition time, 6 ms; echo time, 2 ms; flip angle, 9°; field of view = 256 × 256 mm²; acquisition matrix, 256 × 256; thickness, 1 mm; number of slices, 156) to control for any anatomical abnormalities and increase normalization accuracy during preprocessing.

fMRI Data Processing

fMRI data were analyzed using SPM8 (Wellcome Department of Cognitive Neurology, London, UK, <http://www.fil.ion.ucl.ac.uk/spm/spm8>) [Friston et al., 1994]. Slice timing was used to correct slice order, images were realigned to correct for head movement based on a six-parameter rigid body algorithm and the first five were discarded to achieve magnet-steady images. These images were then normalized to MNI space in $3\text{ mm} \times 3\text{ mm} \times 3\text{ mm}$ voxel sizes. The normalized data were spatially smoothed with a Gaussian kernel; the full width at half maximum (FWHM) was specified as $8\text{ mm} \times 8\text{ mm} \times 8\text{ mm}$. After preprocessing, six regressors (self, mother, classmate, stranger, font, null) were modeled to create the design matrix. They were convolved with the canonical hemodynamic response function and the six realignment parameters for each subject were also included as confounding factors.

Whole-Brain Analysis

In order to investigate a possible role of other brain regions a whole brain analysis was performed to identify those whose activation was associated with OXT and the task. In the task, main effect of condition (self, mother, classmate, stranger) and interaction between condition and treatment were analyzed by ANOVA, and a main effect of treatment (OXT vs. PLC) was also analyzed by two-sample *t*-test. Differences between self and each of the other conditions (i.e. self- vs. mother, self- vs. classmate, and self- vs. stranger) were analyzed using two-sample *t*-tests. The significance threshold for fMRI data analysis was set to $P < 0.01$, FDR corrected, with a minimum cluster size of 10 contiguous voxels.

Regions of Interest (ROI) Analysis

Individual dmPFC ($-6, 46, 20$) activity was extracted from an 8 mm diameter sphere centered at coordinates previously identified in an independent sample [Wang et al., 2012]. Notably, the sphere also included the peak coordinates ($-3, 47, 19$) of self-processing related OXT effects in the dmPFC observed in the present study. In addition, vmPFC ($-6, 59, -2$) was chosen on the basis of our whole brain analysis in the self condition across the two groups. These ROIs were defined using MarsBar to extract the neural activation for further analysis [Brett et al., 2002]. Activation was extracted from 8 mm diameter spheres centered on these ROI coordinates and changes during performance of the trait-judgment task analyzed using a two-way ANOVA with treatment (OXT vs. PLC) as the between group factor and condition (self, mother, classmate, and stranger) as a within group factor. We next investigated whether activation in each ROI was significantly correlated with behavioral performance and questionnaire scores using a Pearson correlation analysis.

Psychophysiological Interaction (PPI) Analysis

Effects of OXT on functional connectivity during trait judgments were also investigated. We measured functional connectivity using a generalized form of context-dependent psychophysiological interactions (gPPI) analysis [Friston et al., 1994; McLaren et al., 2012; O'Reilly et al., 2012]. Based on ROI results, we chose the mPFC ROI (vmPFC and dmPFC) as seed regions separately to investigate functional connectivity. For the gPPI analysis, we extracted the de-convolved time-course of each seed region in each subject based on an 8 mm radius sphere centered on the peak-activation voxel from the mPFC ROIs [dmPFC ($-6, 46, 20$), vmPFC ($-6, 59, -2$)]. We calculated the product of this activation's time-course and the vector of the psychological variable of interest to create the psychophysiological interaction term. New SPMs were computed for each subject, including the interaction term, the physiological variable (i.e. the ROI activation time-course) and the psychological variable as regressors. We then identified areas where activation was predicted by the psychophysiological interaction term, with ROI activity and the psychological regressor treated as confound variables. These analyses were carried out separately for self, mother, classmate, or stranger conditions. Individual PPI SPMs were entered into a random-effects group analysis contrasting connectivity patterns in each condition using two-sample *t*-tests (OXT vs. PLC), with a threshold of $P < 0.001$, small volume corrected (SVC) and with a minimum cluster size of 10 voxels. Correlations in strengths of functional connections between the dmPFC seed region and different target regions and questionnaire scores were calculated using a Pearson correlation analysis.

RESULTS

Behavioral Results

Table I shows that there were no significant differences between the OXT and PLC treatment groups in terms of age or personality (NEO-Five Factor Inventory), emotion state (Positive and Negative Affective Schedule), anxiety (State-Trait Anxiety Inventory), self-esteem (SES), or self-construct (Self Construal Scale) scores. There were also no significant differences between scores on Inclusion of Others in Self (IOS) for mother and classmate in the two groups, with subjects showing the expected high score for inclusion of mother in self generally found in Asian collectivist culture.

Trait-judgment reaction time was subjected to a three-way ANOVA with treatment (OXT vs. PLC), condition (self, mother, classmate and stranger) and valence (positive vs. negative) of the adjectives as independent within-subjects variables. The results showed that there was a significant main effect of condition [$F_{(3,108)} = 5.88, P = 0.001, \eta^2 = 0.14$], due to faster responses to self ($P = 0.08$, Cohen's $d = 0.24$) and mother ($P = 0.012$, Cohen's $d = 0.39$)

TABLE I. Ages and questionnaire scores for study subjects (mean ± SEM)

Measurements	Placebo	Oxytocin	<i>t</i> -value	<i>P</i>
Age (yr)	23.10 ± 0.58	22.78 ± 0.43	0.438	0.664
NEO-Five Factor Inventory (NEO-FFI)				
Neuroticism	29.90 ± 1.42	31.50 ± 1.43	0.792	0.433
Extraversion	40.70 ± 1.22	43.28 ± 1.35	1.418	0.165
openness to experience	40.20 ± 1.01	40.22 ± 1.05	0.015	0.988
Agreeableness	42.50 ± 0.96	41.78 ± 0.88	0.550	0.586
conscientiousness	43.00 ± 0.71	43.33 ± 1.06	0.265	0.793
Positive and Negative Affective Scale (PANAS)—positive	30.70 ± 1.48	29.33 ± 1.43	0.660	0.513
Positive and Negative Affective Scale (PANAS)—negative	15.35 ± 1.16	16.00 ± 1.19	0.390	0.699
State-Trait Anxiety Inventory (STAI)—state	36.35 ± 1.83	37.22 ± 1.64	0.352	0.727
State-Trait Anxiety Inventory (STAI)—trait	43.05 ± 1.36	45.33 ± 1.41	1.159	0.254
Self-Esteem Scale (SES)	32.35 ± 0.87	32.72 ± 0.84	0.306	0.761
Self-Construal Scale (SCS)—independent	58.55 ± 1.32	57.5 ± 1.25	0.572	0.571
Self-Construal Scale (SCS)—interdependent	64.20 ± 1.40	62.33 ± 1.60	0.883	0.383
Inclusion of Others in Self (IOS)—mother	5.70 ± 0.27	5.83 ± 0.23	0.368	0.715
Inclusion of Others in Self (IOS)—classmate	2.85 ± 0.21	2.61 ± 0.23	0.770	0.446

judgments compared with stranger judgments across the two treatment groups. There was a significant main effect of treatment [$F_{(1,36)} = 4.63$, $P = 0.038$, $\eta^2 = 0.114$] and a marginal significant main effect of valence and medium effect size [$F_{(1,108)} = 2.87$, $P = 0.09$, $\eta^2 = 0.074$]. The interaction between condition and treatment was marginally significant, but with a medium effect size [$F_{(3,108)} = 2.56$, $P = 0.059$, $\eta^2 = 0.066$], and the interaction between condition and valence was significant [$F_{(3,108)} = 3.33$, $P = 0.022$, $\eta^2 = 0.085$]. Thus OXT tended to decrease RT compared with PLC across all conditions, although only with stranger traits did it achieve significance (self: $t = 3.35$, $P = 0.076$, Cohen's $d = 0.59$; mother: $t = 2.33$, $P = 0.13$; classmate: $t = 3.92$, $P = 0.055$, Cohen's $d = 0.64$; stranger: $t = 6.39$, $P = 0.016$, Cohen's $d = 0.82$). In the PLC, but not the OXT group, RTs to stranger trait judgments were also significantly longer than for self ($P = 0.022$, Cohen's $d = 0.66$), mother ($P = 0.002$, Cohen's $d = 0.66$), and classmate ($P = 0.022$, Cohen's $d = 0.44$, see Fig. 2a). Therefore, overall OXT reduced RT's across all conditions but particularly for stranger trait judgments which in the PLC group were longer than all the other conditions. In addition, RTs to negative but not positive valence stranger trait judgments were significantly longer than for self ($P = 0.013$, Cohen's $d = 0.38$) and mother ($P = 0.003$, Cohen's $d = 0.52$), but not for classmate ($P = 0.27$).

Independent sample *t*-tests were carried out on corrected recognition scores (the proportion of hits minus false alarms) for the memory test conducted after the scanning procedure and showed an overall significant difference between OXT and PLC groups [$t_{(36)} = 3.02$, $P = 0.005$, Cohen's $d = 0.95$], with OXT treatment decreasing recognition scores. A three-way ANOVA showed a significant main effect of condition [$F_{(3,108)} = 8.54$, $P < 0.001$, $\eta^2 = 0.192$], treatment [$F_{(1, 36)} = 4.77$, $P = 0.036$, $\eta^2 = 0.117$] and valence [$F_{(1,108)} = 21.02$, $P < 0.001$, $\eta^2 = 0.369$] and a treatment x valence x condition interaction [$F_{(3,108)} = 2.98$,

$P = 0.035$, $\eta^2 = 0.03$]. Post hoc analysis with Bonferroni correction showed that positive valence self-trait adjectives were remembered significantly better in the PLC group than any of the other conditions (mother: $P = 0.039$, Cohen's $d = 0.86$; classmate: $P = 0.003$, Cohen's $d = 0.94$; stranger: $P = 0.006$, Cohen's $d = 0.90$) whereas in the OXT group only for self- vs. mother ($P = 0.006$, Cohen's $d = 0.92$) and classmate ($P = 0.035$, Cohen's $d = 0.66$). Pairwise comparison analyses showed that positive trait adjectives used in the self ($t = 2.14$, $P = 0.039$, Cohen's $d = 0.72$) and mother ($t = 2.25$, $P = 0.031$, Cohen's $d = 0.75$) judgment conditions were remembered significantly better in PLC than OXT treatment groups (see Fig. 2b). For negative valence trait adjectives in the PLC group accuracy was significantly greater for self- vs. mother ($P = 0.038$, Cohen's $d = 0.59$) but not for classmate ($P = 0.453$) and stranger ($P = 0.573$), whereas in the OXT group there were no differences between self and other conditions ($P > 0.24$ in all cases). Negative valence trait words were also remembered more accurately in PLC than OXT treatment groups in self ($t = 2.74$, $P = 0.01$, Cohen's $d = 0.89$) and stranger ($t = 2.43$, $P = 0.02$, Cohen's $d = 0.80$) conditions (see Fig. 2c). Overall this confirmed the presence of the expected self-bias in remembering positive valence trait items [Mu and Han, 2010; Symons and Johnson, 1997] and that this self-bias was significantly weakened by OXT treatment. For negative valence items, there was only a self-bias in relation to close familiar others (mother) but not for less familiar others or strangers. However, again OXT also weakened this self-bias effect.

A correlation analysis revealed that there was no association between RT and subsequent accuracy in either the PLC (positive trait adjectives: $r = -0.012$, $P = 0.959$; negative trait adjectives: $r = -0.079$, $P = 0.74$ or OXT (positive trait adjectives: $r = -0.094$, $P = 0.709$; negative trait adjectives: $r = -0.038$, $P = 0.88$) groups. In PLC treated subjects there was a significant positive correlation between trait

Figure 2.

Trait-judgment reaction times and subsequent recall accuracy. **a–d**, Histograms show mean $\pm$ SEM reaction time (a) and accuracy for judging self-, mother-, classmate-, stranger-related positive (c), and negative (d) adjectives in OXT and PLC-treated groups. * $P < 0.05$ for differences within each group. # $P < 0.05$ for OXT vs. PLC.

judgment RTs and SES scores in both self ($r = 0.539$, $P = 0.014$) and mother ($r = 0.477$, $P = 0.034$) conditions, but not under OXT (self: $r = -0.196$, $P = 0.436$, mother: $r = -0.328$, $P = 0.183$). A Fisher's z -transformation revealed that these correlations were significantly different between PLC and OXT groups (self: $z = 2.26$, $P = 0.024$; mother: $z = 2.43$, $P = 0.015$). This suggested that effects of OXT treatment were strongest in individuals with higher SES scores, although there were no significant correlations between them and recognition accuracy. There were no significant behavioral correlations with IOS scores. However, there was a significant negative correlation between SES and the SCS interdependence score (subscale of SCS), $r = -0.413$, $P = 0.01$ suggesting that individuals with

higher self-esteem tend to have a more independent orientation.

For the font judgment (bold- vs. light-faced) condition there was no significant difference between the PLC and OXT group for either RT [$t_{(36)} = 0.165$, $P = 0.87$] or recognition accuracy [$t_{(36)} = 0.032$, $P = 0.97$]. This confirmed that OXT was not having any non-specific effects on making judgments per se.

Neuroimaging Results

Whole brain analysis revealed a main effect of condition with significant activation differences in superior frontal gyrus (SFG 24, 59, 4/21, 26, 49), medial frontal gyrus (MFG -27, 23, 49/42, 47, -11), mPFC (-6, 35, 40) and

TABLE II. Brain areas showing significant activation during trait judgments (MNI coordinates)

Brain region	BA	No. voxels	Peak <i>t</i> -value	<i>x</i>	<i>y</i>	<i>z</i>
Main effect of condition						
L. middle frontal gyrus		471	21.82	-27	23	49
Middle frontal gyrus			9.35	-45	23	34
Medial prefrontal cortex			8.92	-6	35	40
L. inferior parietal lobule	40	167	16.23	-45	-55	43
R. middle frontal gyrus	8	280	15.69	30	17	46
Superior frontal gyrus			12.69	21	26	49
Middle frontal gyrus			12.23	45	26	34
R. Inferior parietal lobule	40	149	14.15	42	-58	43
Inferior parietal lobule			12.71	48	-52	40
Supramarginal gyrus			9.48	45	-55	28
R. middle frontal gyrus	10	184	13.81	-39	44	-8
R. posterior cingulate gyrus	31	694	13.3	12	-58	25
Precuneus			11.46	-15	-61	25
L. middle frontal gyrus	11	76	12.67	42	47	-11
R. parahippocampal gyrus		12	8.94	-21	-10	-17
R. superior frontal gyrus	10	19	8.9	24	59	4
R. inferior temporal gyrus	21	18	8.77	-57	-7	-23
L. medial prefrontal cortex	10	28	8.33	-3	50	-5
Main effect of treatment (PLC > OXT)						
L. medial prefrontal cortex	10	25	2.45	-6	59	-2
L. medial prefrontal cortex	9	42	3.15	-15	35	34
L. medial prefrontal cortex	9	15	2.34	-3	47	19
Self condition (PLC > OXT)						
L. medial prefrontal cortex	10	21	2.40	-6	59	-2
L. medial prefrontal cortex	9	18	2.38	-3	47	19
L. medial prefrontal cortex	9	31	2.85	-18	38	34
Mother condition (PLC > OXT)						
L. medial prefrontal cortex	9	12	2.29	-3	47	19
L. medial prefrontal cortex	9	38	3.02	-15	35	34
Classmate condition (PLC > OXT)						
L. medial prefrontal cortex	10	41	2.36	-6	59	-2
L. medial prefrontal cortex	9	10	2.14	-3	47	19
L. medial prefrontal cortex	9	37	3.13	-15	35	34
Stranger condition (PLC > OXT)						
L. medial prefrontal cortex	10	10	2.43	-6	59	-2
L. medial prefrontal cortex	9	78	3.04	-18	38	34
L. medial prefrontal cortex	6	10	2.26	-15	2	55
Self vs. mother (PLC > OXT)						
R. medial prefrontal cortex	10	16	2.65	15	50	-2
R. medial prefrontal cortex	10	16	2.11	3	50	4
L. medial prefrontal cortex	10	31	2.21	-6	47	7
Self vs. stranger (PLC > OXT)						
R. medial prefrontal cortex		18	2.51	15	50	19

L, left; R, right; BA, Brodmann's areas.

posterior cingulate cortex (PCC 12, -58, 25) as well as a number of other regions ($P < 0.01$, FDR corrected, see Table II and Fig. 3a), but there was no interaction between treatment and condition. A main effect of treatment with small volume correction (SVC) ($P < 0.05$) was however found for a cluster of mPFC voxels (PLC > OXT, see Fig. 3b). Furthermore, two sample *t*-tests between OXT and PLC groups revealed that both dmPFC and vmPFC (SVC) exhibited greater activation for all conditions in the PLC group (see Fig. 3c). The contrast between self- vs. mother

yielded a significant difference in left vmPFC and self- vs. unfamiliar other (stranger) in the right dmPFC (SVC) (PLC > OXT; see Fig. 3d).

Two-way ANOVA for dmPFC ROI results showed main effects of condition [$F_{(3,108)} = 3.84$, $P = 0.012$, $\eta^2 = 0.096$] and treatment [$F_{(1,36)} = 4.65$, $P = 0.038$, $\eta^2 = 0.114$] due to OXT decreasing dmPFC activation, but there was no treatment $\times$ condition interaction [$F_{(3,108)} = 0.035$, $P = 0.853$]. Exploratory analysis showed that OXT decreased (or showed a trend towards decrease) dmPFC activation in all

Figure 3.

Whole-brain analysis of parametric responses to neural activation associated with self-referential processing and the effect of OXT. (a), Main effect of condition (self/mother/classmate/stranger). Activation was found in SFG (24, 59, 4/21, 26, 49), MFG (−27, 23, 49/42, 47, −11), mPFC (−6, 35, 40), PCC (12, −58, 25). Display threshold, $P < 0.01$, FDR corrected, voxels = 10. (b) Main effect of treatment (OXT vs. PLC). The contrast between OXT and PLC groups yielded significant activity differences in mPFC. Display threshold, $P < 0.05$, SVC corrected, voxels = 10. (c) The contrast between OXT and PLC

groups across the different trait-judgment conditions revealed reduced activation in both ventral and dorsal mPFC (i.e. PLC > OXT). Display threshold, $P < 0.05$, SVC corrected, voxels = 10. (d) The contrast between self- versus other in OXT and PLC groups. The contrast between self- versus mother yielded a significant greater activation difference in left ventral mPFC under PLC (i.e. PLC > OXT) and also for self- versus stranger in the right dorsal mPFC (i.e. PLC > OXT). Display threshold, $P < 0.05$, SVC corrected, voxels = 10.

conditions (self: $t = 3.60$, $P = 0.066$, Cohen's $d = 0.62$; mother: $t = 3.22$, $P = 0.081$, Cohen's $d = 0.57$; classmate: $t = 4.74$, $P = 0.036$, Cohen's $d = 0.071$; stranger: $t = 4.98$, $P = 0.032$, Cohen's $d = 0.72$). A two-way ANOVA for vmPFC ROI results showed a main effect of condition [$F_{(3,108)} = 8.35$, $P < 0.001$, $\eta^2 = 0.19$] and a marginal main effect of treatment [$F_{(1,36)} = 3.58$, $P = 0.067$, $\eta^2 = 0.09$] due to OXT decreasing activation compared with the PLC group. However, there was no interaction between treatment and condition [$F_{(3,108)} = 0.41$, $P = 0.75$]. Exploratory analysis showed that OXT decreased (or showed a trend towards decrease) vmPFC activation in self ($t = 3.27$, $P = 0.079$, Cohen's $d = 0.56$), classmate ($t = 4.22$, $P = 0.047$, Cohen's $d = 0.66$), stranger ($t = 3.56$, $P = 0.067$, Cohen's $d = 0.62$), but not mother ($t = 2.28$, $P = 0.14$, Cohen's $d = 0.5$) conditions. We next performed a Pearson correlation analysis between ROI activation [vmPFC (−6, 59, −2),

dmPFC (−6, 46, 20)], and subjects' RT in all conditions. Results showed that activation in the dmPFC was significantly positively correlated with RT in self, mother, and classmate conditions in the OXT but not PLC group (OXT: self: $r = 0.587$, $P = 0.01$; mother: $r = 0.632$, $P = 0.006$; classmate: $r = 0.547$, $P = 0.019$; stranger: $r = 0.478$, $P = 0.045$; PLC: self: $r = -0.079$, $P = 0.739$; mother: $r = -0.198$, $P = 0.402$; classmate: $r = 0.045$, $P = 0.850$; stranger: $r = 0.016$, $P = 0.946$, see Fig. 4b–e). Fisher z-transformation results showed the correlation coefficient in the OXT group was significant higher than that in the PLC group for dmPFC in both self ($z = 2.12$, $P = 0.03$) and mother ($z = 2.39$, $P = 0.02$) conditions. However, activation in the vmPFC and RT was not significantly correlated with any conditions across the two groups (OXT: self: $r = 0.293$, $P = 0.239$; mother: $r = 0.424$, $P = 0.08$; classmate: $r = 0.288$, $P = 0.246$; stranger: $r = 0.286$, $P = 0.251$; PLC: self: $r = -0.114$, $P =$

Figure 4.

Region of interest analysis for dmPFC. (a) Brain activation was extracted from an 8 mm diameter spherical dmPFC (−6, 46, 20) ROI. (b–e) Scatterplot of a regression analysis between neural parameter estimates of dmPFC and behavioral reaction time for self (b)/mother (c)/classmate (d)/stranger (e). (f–i) Scatterplot of a regression analysis between neural parameter estimates

of dmPFC for self (f)/mother (g)/classmate (h)/stranger (i) and self-esteem scale score. The averaged β -weights for each subject were extracted from the voxels in the same ROI where the correlation was significant in the random effects group analysis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

0.633; mother: $r = -0.061$, $P = 0.798$; classmate: $r = 0.019$, $P = 0.937$; stranger: $r = -0.118$, $P = 0.622$).

A correlation analysis was also carried out between ROI activations in all subjects in the OXT or PLC groups and SES score. This showed that in the OXT group, but not the PLC one, dmPFC activation was positively correlated with SES score in all conditions (OXT: self: $r = 0.580$, $P = 0.015$; mother: $r = 0.395$, $P = 0.058$; classmate: $r = 0.621$, $P = 0.008$; stranger: $r = 0.478$, $P = 0.052$; PLC: self: $r = -0.109$, $P = 0.647$; mother: $r = -0.102$, $P = 0.669$; classmate: $r = -0.097$, $P = 0.685$; stranger: $r = -0.144$, $P = 0.544$, see Fig. 3f–i). Fisher z -transformation results showed that the correlation coefficient in the OXT group was significant greater than in the PLC group in self ($z = 2.14$, $P = 0.03$) and classmate ($z = 2.28$, $P = 0.02$) conditions and marginally in the stranger one ($z = 1.84$, $P = 0.06$). However, there was no significant correlation between vmPFC and SES scores in all conditions across two groups (OXT: self: $r = -0.033$, $P = 0.895$; mother: $r = -0.294$, $P = 0.237$; classmate: $r = -0.359$, $P = 0.143$; stranger: $r = -0.221$, $P = 0.378$; PLC: self: $r = 0.115$, $P = 0.628$; mother: $r = 0.077$,

$P = 0.748$; classmate: $r = 0.057$, $P = 0.810$; stranger: $r = 0.126$, $P = 0.597$).

The PPI analysis revealed that in the OXT group the dmPFC (−6, 46, 20) showed decreased functional connectivity with the ACC (15, 29, 25) during the self condition and with the hippocampus (−33, −22, −17) in the mother condition compared with PLC (see Fig. 5a–c). Additionally, the strength of dmPFC–ACC functional connectivity in the self and mother conditions was negatively correlated with SES score in the OXT but not the PLC group (OXT: self: $r = -0.455$, $P = 0.067$; mother: $r = -0.484$, $P = 0.049$; PLC: self: $r = 0.211$, $P = 0.372$; mother: $r = -0.189$, $P = 0.425$). Fisher z -transformation results revealed that the correlation coefficient for the OXT group was significantly different from the PLC group in the self ($z = 1.96$, $P = 0.05$) condition. The connectivity strength between dmPFC and ACC was not significantly correlated with RT in either OXT or PLC group (OXT: $r < 0.458$, $P > 0.065$; PLC: $r < 0.373$, $P > 0.105$ in all cases). On the other hand, the vmPFC (−6, 59, −2) showed decreased functional connectivity with bilateral PCC (−3, −52, 10/2, −46, 28), and precuneus (−18, −61, 31) during the

Figure 5.

Functional connectivity changes following PPI analysis. (a) dmPFC (−6, 46, 20) and vmPFC (−6, 59, −2) seed regions. (b, c) dmPFC seed was accompanied by decreased functional interaction with ACC (15, 29, 25) during the self condition (b) and with hippocampus (−33, −22, −17) during the mother condi-

tion (c) compared with PLC group. d, vmPFC seed was accompanied by decreased functional interaction with left PCC (−3, −52, 10), right PCC (2, −46, 28), and precuneus (−18, −61, 31) during the self condition compared with PLC group. $P < 0.001$, SVC corrected, voxels = 10.

self condition compared with PLC (see Fig. 5d). The functional connectivity between vmPFC and right PCC in the self and mother conditions was positively correlated with SES score in the PLC but not the OXT group (OXT: self: $r = -0.336$, $P = 0.173$; mother: $r = -0.232$, $P = 0.354$; PLC: self: $r = 0.506$, $P = 0.023$; mother: $r = 0.646$, $P = 0.002$). Fisher z -transformation results revealed that the correlation coefficient for the PLC group was significantly greater than for the OXT group in the self ($z = 2.56$, $P = 0.01$) and mother ($z = 2.83$, $P = 0.004$) conditions. The functional connectivity between vmPFC and right PCC in the self and mother conditions was also positively correlated with RT in the OXT but not the PLC group (OXT: self: $r = 0.649$, $P = 0.004$; mother: $r = 0.484$, $P = 0.042$; PLC: self: $r = -0.222$, $P = 0.346$; mother: $r = -0.344$, $P = 0.138$). Fisher z -transformation results revealed that the correlation coefficient for the OXT group was significant greater than for the PLC group in the self ($z = 2.82$, $P = 0.005$) and mother ($z = 2.50$, $P = 0.01$) conditions. However, the strength of vmPFC-precuneus (OXT: $r < 0.194$, $P > 0.413$; PLC: $r > -0.184$, $P > 0.465$, all cases) and vmPFC-left PCC (OXT: $r > -0.321$, $P > 0.194$; PLC: $r < 0.356$, $P > 0.123$, all cases) functional connectivity showed no significant correlation with either the SES score or RT in either the OXT or PLC groups.

DISCUSSION

The present study aimed to determine whether OXT acts primarily to increase or decrease self- vs. other discrimina-

tion using a classical self-referential task (self and other trait-judgments) in conjunction with fMRI. Overall our findings showed that while OXT reduces RTs for making both self and other trait judgments, suggestive of improved decision making, it also reduced their subsequent recall, thereby preventing the normal advantage for remembering self-attributed traits. These behavioral effects of OXT were associated with reduced dmPFC and vmPFC responses and functional connectivity between them and other cortical midline regions (vmPFC—precuneus/PCC, dmPFC—ACC/hippocampus) important for self- vs. other processing [Berkovich-Ohana, 2012; Qin and Northoff, 2011; Sheline et al., 2009; Uddin et al., 2009]. The effects of OXT on dmPFC, but not vmPFC, activation were positively associated with task RTs and self-esteem scores whereas the functional connectivity between dmPFC and ACC was negatively associated with self-esteem. The vmPFC connectivity with PCC on the other hand was positively correlated with RT under OXT, and OXT treatment abolished the positive correlation between the strength of this connection and self-esteem score in the PLC group. Thus both behavioral and neural findings support an action of OXT in decreasing the distinction between self and other at both behavioral and neural levels. Furthermore, behavioral and neural OXT effects were modulated by trait self-esteem although not by that of inclusion of other in self.

Our behavioral findings confirmed the presence of a self-bias for remembering positive valence trait adjectives

compared to both familiar and unfamiliar others in the PLC group [Mu and Han, 2010; Symons and Johnson, 1997]. On the other hand, for negative valence trait adjectives differences in recognition accuracy were only found between self and close familiar others (mother). This so-called “self-reference” effect is a unique encoding phenomenon whereby memory for previously presented trait adjectives is better if they have been processed with reference to the self. In other words, as traits are incorporated into the self-schema subsequent memory for them is increased [Molnar-Szakacs and Uddin, 2013]. As with other studies, there was less evidence for a self-reference effect with RTs, although overall across the OXT and PLC groups these were significantly shorter for both self and mother compared to stranger, providing further support for the presence of an extended self in Chinese subjects [Markus and Kitayama, 1991; Zhu et al., 2007]. However, contrary to findings in some previous studies [Cardoso et al., 2012; Colonnello et al., 2013; Liu et al., 2013], OXT treatment neither enhanced this self-bias per se nor sharpened the distinction between self and other. Instead, it both reduced RTs across self and other conditions and subsequent memory for trait judgments. Indeed, OXT treatment clearly weakened the self- vs. other bias in recall accuracy suggesting that it was blurring the self-other distinction rather than sharpening it. The contrast between these findings with previous ones is most notable with the Colonnello et al. [2013] study which reported that OXT sharpened the perceptual boundary between self and other using face stimuli. However, Colonnello et al.’s [2013] paradigm measured only perceptual differences between self and other using a face morphing approach, and it is possible that OXT can improve perceptual discrimination between self and other using visual cues from the face but also at the same time weaken a more cognitive bias for remembering self- as opposed to other-attributed personal traits. A greater ability to discriminate self from other perceptually clearly does not necessarily imply improved memory for self- vs. other trait characteristics. It should also be noted that the Colonnello et al. [2013] study did not include a control condition and therefore results could have been influenced by a nonspecific reduction of RT’s by OXT. This possibility receives some support from our current findings where OXT reduced RT’s in both self and other conditions. While we also used a higher dose of OXT than that in the latter study (40 vs. 24IU), no dose-dependent effects have so far been reported in humans. Finally, our findings of a reduced self-bias effect are consistent with those reported by Abu-Akel et al. (2015) where OXT increased perception of other- but not of self-experienced pain and by Bartz et al. (2015) of an increased sense of communion with others. Both these latter studies used a lower 24IU dose of OXT.

The reduction in RTs by OXT in both self- and other-trait judgment conditions might indicate that it facilitated decision making in this trait-judgment task. Since RTs

were not correlated with recognition accuracy in either PLC or OXT groups, this suggests that they represent two relatively independent constructs in this task and that OXT may have had separate actions on them. Self-descriptiveness judgment RTs are shortened by reduced task difficulty [Meffert et al., 2013] and by the degree of certainty in the decision made [D’Argembeau et al., 2012]. Given previous evidence for OXT sharpening self- vs. other perceptual recognition [Colonnello et al., 2013], the reduced RTs we observed might therefore represent a more automatic and efficient categorization of the different self and other trait attribution conditions, leading to greater certainty and faster decision making. On the other hand OXT may have also reduced the motivation to remember trait judgments which distinguish self from other and this could explain the reduced accuracy in their subsequent recall.

Importantly, our behavioral results suggesting that OXT may blur the distinction between self and others are consistent with the finding that it also significantly decreased dmPFC and vmPFC responses and their functional connectivity with other cortical midline structures (vmPFC—PCC/precuneus and dmPFC—ACC) associated with self- vs. other processing [Berkovich-Ohana, 2012; Sheline et al., 2009; Uddin et al., 2009]. This finding contrasts to some extent with a previous study reporting that OXT increased self- vs. other activation in both ACC and precuneus (parts of the CMS) when subjects were presented with faces expressing disgust and required to consider their own as opposed to the other person’s feelings of disgust [Scheele et al., 2014b]. However, this neural effect did not occur when happy faces were used as stimuli and there were no associated behavioral effects of OXT. The same study also reported greater endorsement of self-benefit moral dilemmas by male subjects after OXT and interpreted their findings in terms of promoting more selfish behaviors in men. It is possible that increased activation in ACC and precuneus reported by Scheele et al. [2014b] during self- vs. other-perspective taking may be specific to the domain of disgust and in our current study none of the trait adjectives used is likely to have evoked this emotion. Also, the close association between our behavioral and fMRI findings supports the conclusion that in the context of self- vs. other perspective taking in trait judgment tasks, OXT does appear to blur rather than enhance distinctions between self and others by reducing activation in the mPFC and weakening its functional connections with other cortical midline regions.

The frontal cortex has long been established as playing an important role in self-evaluation and self-reflection [Beer et al., 2010; Feng et al., 2013; Kelley et al., 2002; Moran et al., 2006] and we also found differences across self- and other-trait judgment conditions in MFG, SFG and mPFC. Our results showed that OXT decreased activation in both dmPFC and vmPFC regions in self and other conditions and also reduced the difference between self and

other for both mother and stranger. Several recent meta-analyses of mPFC activations have reported involvement of both dmPFC and vmPFC in self-referential processing [Amodio and Frith, 2006; Martinelli et al., 2013; Murray et al., 2012; van der Meer et al., 2010] and our findings are consistent with this, as well as demonstrating that OXT influences responses in both mPFC regions. Self-esteem scores have also been found to be positively correlated with mPFC activation [Yang et al., 2014].

Interestingly, our findings showed that despite OXT reducing mPFC activation in self and other trait judgments, it also resulted in a significantly greater association between dmPFC activity and both reaction times for trait-judgments and SES scores. The mPFC has been shown to be engaged during tasks which require making specific judgments about both one's own traits and those of others' [Cikara et al., 2014; Kim and Johnson, 2012, 2014; Yang et al., 2012]. Thus, despite mainly reducing activation changes OXT might at the same time be reducing noise in this neural system, thereby revealing a closer association with both RTs and behavioral traits. While there was no overall significant association between the OXT reduction in mPFC activation and subsequent recall accuracy of both self and other trait adjectives, this may nevertheless reflect its effect in reducing the perceived value of such judgments. The vmPFC in particular has been implicated with the subjective value of rewards [Levy and Glimcher, 2012; Sescousse et al., 2013] and has been hypothesized to play a role in assigning personal value or significance to self-related contents [see D'Argembeau, 2013]. Thus the magnitude of mPFC activation reflects both the personal importance attributed to self-representations and the degree of interest in self-reflection [D'Argembeau et al., 2012; D'Argembeau and Salmon, 2012]. Reduced mPFC activity following OXT treatment may therefore reflect individuals valuing representations of both self and other traits less with a resultant reduction in accuracy of their recall.

The PPI analysis showed that OXT decreased functional connectivity between the dmPFC and ACC in the self condition and between dmPFC and hippocampus in the mother condition. The strength of dmPFC-ACC functional connectivity was also negatively correlated with SES score in both self and mother conditions in the OXT group. On the other hand, OXT decreased functional connectivity between vmPFC and PCC/precuneus only in the self condition. Activity in the dmPFC has been consistently associated with tasks related to social cognition, theory of mind (i.e., perspective-taking), episodic memory retrieval, as well as face emotion processing [Bzdok et al., 2013]. Macrae et al. [2004] found remembered items induced activation in dmPFC, lateral prefrontal cortex, and bilateral hippocampus/parahippocampal gyrus when compared to forgotten items, while the self-descriptive versus nonself-descriptive contrast revealed activation in the dmPFC during the retrieval of visually presented self- and nonself-related adjectives describing personality traits [Macrae

et al., 2004]. Regions associated with self-relatedness were located in the anterior CMS including vmPFC, ACC, and dmPFC, the latter two appearing only with increasing degrees of self-relatedness during emotional processing. In other words, the more self-related the picture content was appraised, the more activation was observed in these regions [Phan et al., 2002, 2004]. These findings support our results that dmPFC activity was positively correlated with SES scores. It has been proposed by Northoff et al. [2006] that the dmPFC and ACC form a continuum in coding information for self-relevance in both cognitive and emotional domains [Northoff et al., 2006; Wagner et al., 2013]. Since there is an inherent emotional component to self-relevant processing, stronger connectivity between ACC and mPFC may contribute to the memory bias for self-trait judgments. Thus, OXT effects in weakening functional connectivity between these two regions might particularly contribute to reduced recognition memory accuracy for self-trait judgments, thereby blurring the distinction between self and other. The negative association between the self-esteem score and the strength of the dmPFC-ACC connection in both self and mother conditions is also consistent with this interpretation with low-esteem individuals reported to have stronger functional connectivity between mPFC and ACC than high-esteem ones in the context of a social exclusion task [Onoda et al., 2010]. Although the functional connection between the dmPFC and hippocampus was only significantly weakened in the mother condition under OXT, this may similarly have contributed to reduced accuracy in recall of trait judgments. Moreover, activity in the vmPFC was consistently associated with tasks related to general cognition, social cognition, as well as emotion and reward processing [Bzdok et al., 2013]. One study reported that the emotional pictures' degree of self-relatedness parametrically modulated subsequent resting state signal changes in various CMS regions, including vmPFC, dmPFC, and PCC/precuneus [Schneider et al., 2008]. In addition, the vmPFC (versus dmPFC) was more consistently associated with reward processing and general cognition, while the dmPFC (versus vmPFC) was more consistently associated with (episodic) memory retrieval and theory-of-mind processing. Thus overall the vmPFC appears to be more associated with processing approach- and avoidance-relevant stimuli whereas the dmPFC is more connected with higher associative cortical areas involved in processing mental states and episodic memory [Bzdok et al., 2013].

It is possible that our current findings supporting a role for OXT in blurring rather than enhancing the distinction between self and others may have been contributed to by cultural differences. Compared with Western cultures where individuals have a more independent sense of self, and therefore more marked self-other distinctions, Asian collectivist cultures typically exhibit a much more interdependent and extended sense of self, and therefore a weaker self-other distinction [Aron et al., 2004; Belk, 1988;

Markus and Kitayama, 1991; Wang et al., 2012]. A recent genetic study has also reported that while the OXT receptor (rs53576) polymorphism is associated with emotional social support seeking in Americans, it is not in Koreans [Kim et al., 2010]. However, to date no studies have found cultural differences in responses to intranasal OXT and we have recently shown very similar effects on facilitation of learning with social feedback in Caucasian and Chinese subjects [Hu et al., 2015; Hurlemann et al., 2010]. A limitation of the current study is that it only included male subjects and several recent studies have reported gender differences in OXT effects [Scheele et al., 2014b; Yao et al., 2014]. While, to the best of our knowledge, gender differences have not been reported in the trait-judgment task used in the current study it is possible that OXT might have different effects in females than in males.

In summary, the current study has provided evidence that OXT appears to blur the distinction between self and other in the context of weakening the bias for remembering self-assigned traits in the widely used trait-judgment self-referential task. However, there was also evidence that OXT shortened RTs for both self- and other-trait judgments. This suggests a possible improvement in decision making when making trait attributions. These behavioral effects were associated with reduced mPFC activation associated with self- vs. other referential processing and with a reduction in functional connectivity between dmPFC and ACC when making self-trait judgments. We hypothesize from these findings that OXT may act both to reduce noise in the mPFC to improve speed of decision making on self and other trait judgments but at the same time weaken the influence of the emotional significance of self-assigned traits resulting in reduced subsequent memory for them. In short, while OXT may make individuals better at judging both self and other-trait attributes it may at the same time make them less self-centered by reducing their interest in assessing the differences between themselves and others.

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