International Journal of Psychophysiology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Psychophysiology

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

The Other and Me: Effects of oxytocin on self-other distinction

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ARTICLE INFO

Keywords:
Oxytocin
Self-other distinction
Perspective-taking
Imitation
Social approach

ABSTRACT

Distinguishing self- from other-related representations plays an important role in social interactions. The neuropeptide oxytocin has been shown to modulate social behavior as well as underlying social cognitions and emotions. However, how exactly oxytocin modulates representations of self and other is still unclear. The present study therefore aimed to assess effects of oxytocin on self-other distinction on two different processing levels (i.e., lower-level imitation-inhibition and higher-level perspective taking) in a male sample (n = 56) by performing a double-blind, placebo-controlled oxytocin administration study. Oxytocin improved visual perspective-taking and thus affected self-other distinction on the cognitive level, but had no effects on self-other distinction on the perceptual-motor level nor on a control task measuring attention reorientation. Thus, our findings suggest that oxytocin reduces ambiguity during perspective-taking in social interactions, which in turn may encourage social approach motivation and affiliative behavior.

1. Introduction

It has been shown that the neuropeptide oxytocin can improve social interactions in healthy as well as psychiatric populations (Domes et al., 2007; Meyer-Lindenberg et al., 2011). The exact mechanisms by which oxytocin is able to facilitate social interactions have not been identified so far. As oxytocin has been shown to improve a variety of distinct social processes – e.g., mind-reading (Domes et al., 2007), trust (Baumgartner et al., 2008; Kosfeld et al., 2005) and emotional empathy (Hurlemann et al., 2010) - it has been proposed that oxytocin might exert its effects by a more general mechanism, which might be to increase the salience of social signals (Bartz et al., 2011) and (Olff et al., 2013; Shamay-Tsoory and Abu-Akel, 2016). However, this notion has limited empirical evidence so far. As many social cognitive processes require a successful interplay of sharing and differentiating between self- and other related cognitions and emotions (Epley et al., 2004; Lamm et al., 2016; Singer and Klimecki, 2014), a possible mechanism (potentially occurring in interaction with increased social salience) might be that oxytocin improves social cognition via improvements of self-other distinction. Self-other distinction describes the ability to distinguish between the representations of our own actions, perceptions, sensations and emotions, and those of others. In the perception-action domain, self-other distinction is required to enable flexibly regulated mimicry (Rauchbauer et al., 2015; Rauchbauer et al., 2016; Wang and Hamilton, 2012) which is known to have widespread effects on social interactions (Chartrand and Lakin, 2013). Self-other distinction is also fundamental in high-level cognitive processes such as perspective taking, as perceiving the world in another's stead requires disentangling one's own views and intentions from those of the other (Epley et al., 2004). Specifically, it has been proposed that people adopt a perspective of someone else, by starting at their own perspective and then serially accounting for the perspective of the other person (Epley et al., 2004). Furthermore, experimental evidence indicates that self-other distinction on the perceptual-motor level and the cognitive level might rely on similar processes and functions, as it was found that training the inhibition to imitate the actions of others enhances performance in the ability to adopt a (differing) perspective of others (Santiesteban et al., 2012b). Moreover, it has been shown that self-other distinction during imitation-inhibition as well as perspective-taking relies on neural processes conjointly localized to the right temporo-parietal junction (see e.g., Lamm et al., 2016 for recent review), indicating that both may rely on similar underlying mechanisms.

These findings directly motivated the second research goal of the present study, which was to test whether oxytocin affects self-other distinction on a perceptual-motor level (e.g., during imitation-inhibition) and a cognitive level (e.g., during perspective taking) in similar

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https://doi.org/10.1016/j.ijpsycho.2018.03.008
Received 22 April 2017; Received in revised form 19 January 2018; Accepted 12 March 2018

ways. Prior research has shown that oxytocin can sharpen visual self-other distinction (Colonnello et al., 2013) and increase empathy for pain when adopting an other-oriented perspective (Abu-Akel et al., 2015). In addition, in a previous study we found that under stress, women showed improved self-other distinction while men showed impaired self-other distinction. A putative candidate to explain such the gender differences on a physiological level is the oxytocin system (Heinrichs et al., 2009; Meyer-Lindenberg et al., 2011), because there is some evidence that women might show higher oxytocin release under stress than men (Carter, 2007; Jezova et al., 1996; Sanders et al., 1990). Thus, if oxytocin indeed improves self-other distinction and women and men differ in their availability of oxytocin under stress, the oxytocin system might be a putative candidate to explain such gender differences in stress research on a physiological level (see also Tomova et al., 2014 for a similar reasoning). However, recent research has also found opposite effects of oxytocin by showing increased self-other merging (i.e., increased sharing of self- and other related representations) in an automatic imitation-inhibition task (De Coster et al., 2014), and increases in self-other integration during joint task performance (i.e., Social Simon task, (Ruissen and de Bruijn, 2015)). Thus, it is still unclear whether oxytocin affects representations of self and other by increasing self-other merging or rather by improving self-other distinction. Furthermore, it is also unclear via which route oxytocin might affect self-other distinction/merging – i.e. by acting on lower-level perceptual processes or on more deliberate higher-level cognitive processes, or both. In addition, because self-other distinction has been shown to represent an effortful cognitive process, there might be the third possibility that oxytocin improves self-other distinction via enhancement of general cognitive processes. Therefore, using double-blind, placebo-controlled oxytocin administration, the present study specifically assessed the effects of oxytocin on self-other distinction during lower-level imitation-inhibition and during higher-level perspective-taking. In addition, we tested the effects of oxytocin on a non-social selective attention task which requires participants to inhibit an automatic first response in favor of the correct response to assess unspecific effects of oxytocin on non-social cognitive processing. Due to previous findings that self-other distinction on the perceptual-motor level and the cognitive level might rely on similar processes, we hypothesized that oxytocin would improve self-other distinction on both lower-level perceptual as well as higher-level cognitive processes.

2. Methods

2.1. Participants

Fifty-six healthy male participants between 18 and 40 years were included in the study. All participants, except for two (one in oxytocin group and one in placebo group) were currently enrolled as students at the University of Freiburg. Socio-cognitive abilities were determined using an online questionnaire using the Reading the eyes in the mind test (RMET; Baron-Cohen et al., 2001) and the perspective taking scale of the Interpersonal Reactivity Index (IRI; Davis, 1983, see Appendix 6.2.2 for descriptive statistics on each scale of the online questionnaire). The study was approved by the institutional review board of the University of Freiburg, and performed in agreement with the latest revision of the Declaration of Helsinki (2013) regarding the treatment of human research participants. Written informed consent was obtained, and all participants received 50 € for participation. We excluded four participants due to incorrect task understanding in either the perspective-taking or imitation-inhibition task, resulting in very high error rates (> 70% of trials wrong). Additionally, we excluded four participants who were strong outliers in the data (> 3 SDs from the mean in either of the tasks). The final sample consisted of 48 participants (24 oxytocin and 24 placebo).

2.2. Self-other distinction paradigms

2.2.1. Imitation-inhibition task

This paradigm requires participants to lift their index or middle finger in response to a visual cue, while they are simultaneously viewing congruent or incongruent finger movements of a hand of another person shown on the screen (Brass et al., 2009). Importantly, this paradigm does not measure imitation in a classical sense, but instead it represents a measure of the ability to inhibit automatic imitation tendencies and therefore self-other distinction on an automatic-perceptual level. Perceiving these movements activates automatic imitation tendencies, and in the case of incongruent movements, these imitation tendencies interfere with the instructed movement execution and therefore need to be inhibited. As established by previous investigations (Brass et al., 2009), self-other distinction was assessed by means of the interference effect, which was computed by subtraction of response times and error rates, respectively, of congruent from incongruent trials. Higher interference indicated reduced self-other distinction.

2.2.2. Perspective-taking task

Self-other distinction in the cognitive domain was investigated using a perspective-taking paradigm (Keysar et al., 2000; Santiesteban et al., 2012a). Participants were asked to move objects on a shelf according to the instructions of a “director”. On congruent trials, participants and the “director” saw the same objects on the shelf. On incongruent trials, the view of the participant and the director differed. Thus the task required participants to disentangle their own visual perspective from the one of the director. We computed differences in response times and error rates between congruent and incongruent trials. Higher differences indicated reduced self-other distinction. Importantly, this measure does not represent a perspective-taking, or theory of mind task in a classical sense, but rather investigates the ability to overcome egocentric biases during perspective taking and therefore self-other distinction on a cognitive level.

2.2.3. Attention-reorientation task

Participants completed an attention-reorientation task (Posner et al., 1984) during which they had to indicate the location of a visual target stimulus that appeared in either a cued or miscued location. The task was chosen as it requires participants to inhibit an automatic first response in favor of the correct response. This cognitive process as well as the neural bases involved in this task are closely related to mechanisms involved in self-other distinction (Decety and Lamm, 2007; Mitchell, 2008). However, it is a purely non-social task and therefore a well-suited control condition to specify whether effects might be explained by other, non-social processes.

More detailed information on the paradigms (i.e., number of conditions and trials, durations of stimuli presentation and examples of stimuli) is reported in the Appendix (6.1 Detailed description of paradigms).

2.3. Procedure

All experimental sessions took place between 1 and 5 pm in order to keep timing constant across participants and groups. To control for possible non-specific mood differences in baseline and following substance administration, the participants completed the Multidimensional Mood Questionnaire (MDBF; Steyer et al., 1994) before substance administration (T1), 45 min after administration (T2) and after the experimental tasks (T3). Forty-five minutes before the experiment, each participant received a single dose of either oxytocin (24 I.U. in 6 puffs of Syntocinon-Spray, Novartis, Basel, Switzerland) or placebo (containing all ingredients except for the neuropeptide; (see Heinrichs et al., 2003) intranasally. Participants were randomly assigned to the oxytocin or placebo group. The order of the experimental paradigms was fixed across participants as we expected carry-over effects from the

individual tasks. Task order was as follows: (1) imitation-inhibition task, (2) perspective-taking task, (3) attention-reorientation task. We chose this order based on the rationale that the two experimental paradigms (i.e., imitation-inhibition task and perspective-taking task) should precede the control tasks (i.e., attention-reorientation task). We chose to implement the imitation-inhibition task before the perspective-taking task based on the rationale that a lower level task (i.e., imitation-inhibition task) might interfere less with a higher level task (i.e., perspective-taking task) than vice versa, due to the stronger engagement of meta-cognitive processes in the latter. After the experiment, participants were debriefed and received their payment of 50 €.

2.4. Measures

In order to assure that the oxytocin and placebo groups did not differ in variables such as age and socio-cognitive abilities, we calculated two-sample *t*-tests for IRI perspective taking scale and RMET. Changes in mood were assessed for each subscale of the MBDF (i.e., subscale *GS* indicating valence of mood, *WM* indicating alterness and *RU* indicating calmness; (Steyer et al., 1994)) using a mixed model ANOVA with the within subject factors *time* (T1, T2 and T3) and *scale* (GS, WM and RU) and the between subject factor *substance* (oxytocin, placebo). Behavioral data of the self-other distinction paradigms were preprocessed by calculating the bias between congruent and incongruent trials (i.e., difference scores of incongruent minus congruent trials) for response times (RT) and error rates separately. This enabled us to compare values across tasks in one statistical model. The effect of oxytocin on self-other distinction was then assessed by calculating a repeated measures ANOVA with the within subject factor *task* (imitation-inhibition, perspective taking, attentional reorientation) and the between subject factor *substance* (oxytocin, placebo). We calculated two separate ANOVAs, one using the biases in response times as the dependent variables and one using the biases in error rates. Greenhouse-Geisser corrections were used when the homogeneity of covariances assumption was violated (as determined by Mauchly tests of sphericity). Correlations between tasks were calculated using Pearson correlations. All data were analyzed using SPSS v. 20 and the significance threshold was set to $p < 0.05$. Effect sizes are reported as η_p^2.

3. Results

Oxytocin and placebo group did not differ in self-reported socio-cognitive abilities, nor in their scores in the mood questionnaire during the experimental session (all p-values ≥0.072). The repeated measures ANOVA for bias in *response times* showed a main effect of task ($F(1.01,46.36) = 24.133$, $p < 0.001$, $\eta_p^2 = 0.34$), but no significant effect of substance nor any interaction between task and substance (p-values ≥0.204). The repeated measures ANOVA for *error rates* showed a main effect of task ($F(2,92) = 12.670$, $p < 0.001$, $\eta_p^2 = 0.22$) and a significant substance x task interaction ($F(2,92) = 3.287$, $p = 0.042$, $\eta_p^2 = 0.07$). The main effect of substance was not significant ($F(1,46) = 1.522$, $p = 0.224$, $\eta_p^2 = 0.03$). Fig. 1 shows the mean bias in error rates for each paradigm. Bonferroni corrected post-hoc tests revealed that in the perspective taking task, the oxytocin group showed lower error rates than the placebo group ($p = 0.017$; mean difference ± standard deviation: 0.055 ± 0.017, $\eta_p^2 = 0.12$) indicating better self-other distinction performance in the perspective-taking task in the oxytocin group. There was no significant group difference for the other two paradigms (i.e., imitation-inhibition and attentional reorientation; p-values ≥0.727). In order to verify that the measures showed main effects of congruency and to more specifically determine the effects of substance, we additionally ran another repeated measures ANOVA for *error rates* including the factors task, congruency and substance. Here, we found a main effect of task ($F(1.56,71.94) = 4.318$, $p = 0.025$, $\eta_p^2 = 0.09$) and a main effect of congruency ($F(1,46) = 40.855$, $p < 0.001$, $\eta_p^2 = 0.47$). In addition, we found a three-way interaction of task x congruency x substance ($F(2,92) = 3.287$, $p = 0.042$, $\eta_p^2 = 0.07$). We did not find any significant correlations between measures of the imitation-inhibition and the perspective-taking task (all p-values ≥0.137). Both tasks also did not correlate with the attention-reorientation task (all p-values ≥0.568). The descriptive statistics for each measure are provided in the Appendix (Descriptive statistics 6.2).

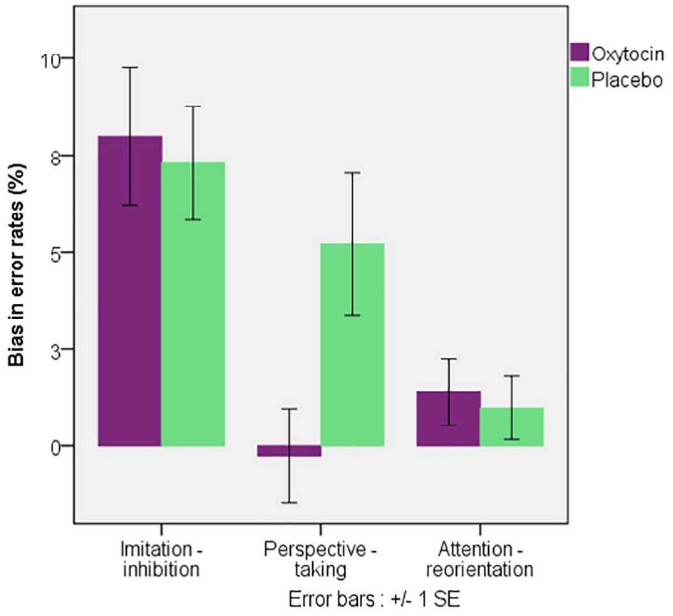

Fig. 1. Mean bias for error rates (i.e., differences between congruent and incongruent trials) for the three paradigms: imitation-inhibition task, perspective-taking task and attention-reorientation task. Error bars indicate standard error of the mean.

4. Discussion

The present study assessed the effects of oxytocin on the ability to distinguish self- from other-related representations, across two different processing levels. Furthermore, we included a non-social attention-reorientation task in order to test for potentially unspecific effects of oxytocin on non-social cognitive processing. We found that oxytocin improved self-other distinction on the cognitive level but did not affect self-other distinction on the perceptual-motor level. The effects on the perspective taking task could not be explained by differences in attention-reorientation, as this was not affected by oxytocin.

More specifically, participants in the oxytocin group showed a lower bias in error rates (i.e., difference in error rates between a condition in which they had to adjust for a mismatch between their own and the "director's" perspective versus a condition where no adjustment was necessary) compared to the placebo group. Our findings of improved self-other distinction during visual perspective-taking are in line with prior research showing oxytocin induced improvements in mind-reading (Domes et al., 2007; although see also Radke and de Bruijn, 2015), improvements in visual self-other differentiation (Colonnello et al., 2013) and decreased self-centeredness in trait judgments (Zhao et al., 2016). The present study merges this line of research by showing that a single dose of intranasally administered oxytocin causes an increase in the ability to differentiate the visual perspective of oneself from that of another person. Prior studies on oxytocin effects in humans and animals suggest that oxytocin increases approach behavior, improves trust and has stress-protective effects (e.g., Heinrichs et al., 2009). Our findings suggest that by reducing the interference of the self when taking the perspective of others, oxytocin might reduce ambiguity or miscommunication in social interactions, which in turn may encourage social approach, affiliation, and trusting behavior.

Notably, we did not find any effects of oxytocin on self-other distinction on the perceptual-motor level. Although prior research has shown oxytocin induced increases in self-other integration during a joint task performance (Ruissen and de Bruijn, 2015) and self-other merging in the imitation-inhibition task (De Coster et al., 2014), the present experiment could not replicate these findings. Thus, more research is needed to further specify the effects of oxytocin on lower level automatic social processes. In addition, our research only partially supports the hypothesis that gender differences in self-other distinction under stress (Tomova et al., 2014) might be routed in different availability of oxytocin under stress (Carter, 2007; Jezova et al., 1996; Sanders et al., 1990), because oxytocin was only found to improve self-other distinction during perspective taking.

Crucially, we can rule out oxytocin-induced improvements in attention-reorientation as a mechanism driving our results, as we did not find any effects of oxytocin on measures of attention-reorientation capacity. In addition, as oxytocin and placebo groups did not differ in trait perspective-taking abilities and we did not find any association between trait perspective-taking abilities and performance in paradigms, we can rule out that oxytocin induced modulations in self-other distinction are related to a priori perspective taking-abilities. In addition, self-report measures of mood did not differ between placebo and oxytocin group. We, however, did find that overall participants reported a decrease in alertness over the time course of the experiment.

Importantly, when interpreting our results, it should be kept in mind that we did not measure perspective taking in a more classical sense (i.e., adopting the perspective of another person on a topic or opinion) or theory of mind (i.e. understanding the beliefs of others). Instead, our task represents a very targeted paradigm to measure the ability to overcome egocentric biases during visual perspective taking and represents a measure of self-other distinction in the cognitive domain (Santiesteban et al., 2012a; Santiesteban et al., 2012b). Furthermore, it should be noted that improvements in self-other distinction during perspective taking might either come from enhancements of the representation of the other, or from increased suppression of the egocentric representation (Bartz, 2016; Bartz et al., 2015; Epley et al., 2004; Lamm et al., 2016, for review). However, the present study was not designed to disambiguate which of the two processes was affected by oxytocin when increasing self-other distinction during perspective taking. Future studies should test in more detail whether oxytocin facilitates the suppression of an egocentric view, or rather enhances the representation of another person's view.

Some possible limitations should be kept in mind when interpreting the results. First, as oxytocin has been shown to affect particularly challenging items (Domes et al., 2007), we cannot rule out a possible interaction between the difficulty of tasks and oxytocin effects. Indeed, Fig. A5 in the Supplemental material shows that while error rates on incongruent trials for imitation-inhibition and perspective-taking tasks are similar, error rates for attention-reorientation are much lower, hence indicating that this task might have been easier than the other two. However, the fact that we do see a differentiation in oxytocin effects between imitation-inhibition and perspective-taking, although they appear to have similar difficulty, speaks for the fact that our effects are not driven by difficulty alone. Additionally, the present study only included young (i.e., 18–40 years) male participants and therefore we cannot draw conclusions on effects of oxytocin on self-other distinction in women and individuals outside of this age range. Future studies should therefore assess whether oxytocin affects self-other distinction in women and participants of different age groups in distinct ways. Additionally, we were not able to replicate prior findings of increased self-other merging in the automatic-motor domain (De Coster et al., 2014) using the same paradigm as we did. However, the differences in results might be attributed to several methodological differences between the two studies. Most importantly, in our study the duration of each paradigm (including the imitation-inhibition task) was kept to approximately 5 min, while De Coster et al.'s task duration was 30 min. We did this in order to ensure that assessments of self-other distinction were conducted during a time window in which oxytocin effects were still peaking and not already declining (Born et al., 2002). Although prior research from our group has shown that the interference effect in the imitation-inhibition task is not attenuated when using a shortened version (e.g., Tomova et al., 2014), it might be that performing the task for different durations affects oxytocin effects on performance. Several other differences in methodological procedures may have contributed to a failure to replicate De Coster et al.'s finding: 1) After administration of oxytocin, De Coster et al. gave participants questionnaires on affect and empathy in addition to the instructions for the subsequent paradigms. We, on the other hand, gave the instructions to participants before administration and our questionnaire data was collected via an online questionnaire prior to the experiment. Thus, our participants did not encounter any stimuli related to social cognition/affect after oxytocin administration while the participants in De Coster's study were given such stimuli. Oxytocin effects might be sensitive to contextual effects of a social situation and therefore it could be that presenting participants with social stimuli after oxytocin administration somehow affected effects of oxytocin in De Coster's study. 2) De Coster et al. counterbalanced the order of their tasks, while in our experiment participants always started with the imitation-inhibition task after a ramping period of 45 min after oxytocin administration (which was the same in both studies). 3) It should be also noted that De Coster et al. found oxytocin effects on response time measures while we only found oxytocin effects on error rates. It might very well be that subtle differences in experimental procedures affect results in oxytocin studies, which, in addition to the differences in task duration, might have contributed to the different results between De Coster et al. and our study. Ultimately, we think a replication study which very carefully takes such differences in experimental design into account, is necessary in order to gain further understanding of the effects of oxytocin on self-other distinction in the perceptual-motor domain.

One additional limitation of this study is the fixed order of the self-other distinction paradigms, which was chosen based on the rationale that lower-level tasks should interfere less with higher-level tasks. This approach, however, precluded to control for carry-over or order effects. Future replication studies should therefore consider randomized task ordering. In addition, while our sample size is comparable to those of other oxytocin administration studies addressing similar research questions (e.g., Colonnello et al., 2013; De Coster et al., 2014; Abu-Akel et al., 2015; Ruissen and de Bruijn, 2015), replication studies should employ larger sample sizes in order to verify the reliability of our results. Furthermore, the visual complexity between the three tasks was different and might have contributed to the reported effects. Thus, future studies should try to modify the different paradigms in order to be more comparable with each other. This might rule out possible interactions between oxytocin and such low-level features of the tasks.

In sum, our study provides a further step in the specification of oxytocin effects on social cognition by showing that self-other distinction during visual perspective-taking is improved by a single dose of oxytocin compared to placebo. This extends and merges prior research on the effects of oxytocin on self-other distinction and mind reading (Colonnello et al., 2013; Domes et al., 2007) and proposes a possible underlying mechanism by which oxytocin might increase social approach motivation - i.e., reduced ambiguity and miscommunications with others might increase motivation to engage in social interactions. We, however, did not find oxytocin effects on self-other distinction during lower level automatic motor-mimicry. Thus, our results suggest that oxytocin specifically affects self-other distinction processes during non-automatic, deliberate social processing. Future research is needed to understand oxytocin's role in more basic, lower-level social processing.

Acknowledgements

This research was supported by a research grant from the Federal Ministry of Science, Research and Economics Austria (BMWFW, Marietta-Blau grant) to Livia Tomova. We thank Mareike Makosch and Anna Gronewold for their support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2018.03.008.

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