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Does oxytocin affect mind-reading? A replication study

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Summary One of the most well-known findings in human oxytocin research is its beneficial effect on ''mind-reading'', i.e., inferring others' mental states just from the eye region in the Reading the Mind in the Eyes Test (RMET). Previous studies have partially confirmed these improvements and have further shown that they depend both on baseline social-emotional abilities and on specific item characteristics such as difficulty. Following the original design of Domes et al. (2007), the aim of the current study was to replicate and extend previous findings by thoroughly investigating the impact of oxytocin administration on RMET performance. We tested for potential moderation effects involving item difficulty, valence, intensity, sex of poser as well as individual differences in trait empathy measured with the Empathy Quotient (EQ) for a general score and the Interpersonal Reactivity Index (IRI) for a multidimensional assessment of cognitive and emotional empathy. Oxytocin did not affect mind-reading, neither in general nor when considering specific item characteristics. An association between oxytocin-induced changes in RMET performance and emotional empathy (the empathic concern scale of the IRI) was evident, with individuals low in emotional empathy showing greater improvement after oxytocin administration compared to placebo. The reproducibility and variability of these and prior findings needs to be addressed in future experiments. As true effects may not replicate across different studies for various reasons, this should not discourage, but encourage further research.

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1. Introduction

In oxytocin research, one of the most referenced and well-known finding constitutes its benefits on mind-reading (Domes et al., 2007). Mind-reading, i.e., the ability to infer others' mental states, also referred to as mentalizing or cognitive empathy, is integral for social interactions (Amodio and Frith, 2006). It is regarded as being distinct from emotional empathy, i.e., the ability to emotionally share another's affective state as both enable the understanding of others' states via different neural networks (Dziobek et al., 2008; Shamay-Tsoory et al., 2009). In general, empathy is a broad construct, consisting of both cognitive and emotional reactions to others' experiences (see e.g., Shamay-Tsoory, 2011).

The observation from Domes et al. (2007) that oxytocin enhances interpretation of subtle social-affective cues from the eye region, measured by the Reading the Mind in the Eyes Test (RMET), has only recently been fully replicated (Feeser et al., 2015) including both general effects and item difficulty as an additional modulator. Other oxytocin administration studies did not elicit these broad improvements on the RMET in healthy individuals (Kuypers et al., 2014; Luminet et al., 2011; Pincus et al., 2010; Riem et al., 2014; Woolley et al., 2014) and could only partially confirm increased accuracy on difficult items after oxytocin (Woolley et al., 2014). A more pronounced impact of oxytocin on difficult mental inferences might be due to the greater challenge they present to healthy participants (Feeser et al., 2015; Kuypers et al., 2014), which fits with oxytocin-induced benefits in RMET performance specifically in less socially proficient individuals (Feeser et al., 2015; Luminet et al., 2011; Riem et al., 2014) as well as clinical populations such as autism spectrum disorder (e.g., Guastella et al., 2010). Interestingly, facilitated mental state attribution after oxytocin administration for individuals scoring high on alexithymia was further moderated by the type of material, i.e., increased accuracy was driven by negative and highly intense expressions (Luminet et al., 2011). These emotion-specific effects might indicate that oxytocin influences emotional rather than cognitive processing. Likewise, in the Multifaceted Empathy Test (Dziobek et al., 2008) where stimuli include additional facial and contextual features, oxytocin enhanced the intensity of emotional reactions (emotional empathy), but not the identification of others' mental states (cognitive empathy) (Hurlemann et al., 2010).

Taken together, these findings suggest that oxytocin effects on mind-reading depend on both baseline social-emotional abilities and properties of the environment that contribute to the interaction. As the influence of personal variability and contextual factors has been demonstrated in the domain of social cognition and other areas of oxytocin research (for a review see Bartz et al., 2011), investigating the stability and replicability of (interaction) effects remains important to evaluate its therapeutic potential.

The current study follows the randomized, double-blind, placebo-controlled, cross-over design from Domes et al. (2007) to test the impact of oxytocin on RMET performance, measured by accuracy, and potential moderation by item characteristics (difficulty, valence, intensity, sex of poser). Because previous studies vary in their choice of item categories, we aimed to thoroughly investigate in how far these different classifications yield the same result within one oxytocin administration study.

Our second aim was to determine the role of individual differences in trait empathy, assessed with two commonly used self-report inventories, the Empathy Quotient (EQ; Baron-Cohen and Wheelwright, 2004) and the Interpersonal Reactivity Index (IRI; Davis, 1983). Whereas the EQ yields an aggregated empathy score, the IRI is a multidimensional empathy questionnaire that differentiates between two subcomponents of cognitive and emotional empathy. Of these, cognitive empathy is best operationalized by the perspective-taking scale, and emotional empathy is best operationalized by the empathic concern scale. If cognitive empathy underlies mind-reading as in the RMET, improved accuracy after oxytocin administration specifically for individuals low in cognitive empathy might be expected. Alternatively, however, if oxytocin affects rather emotional than cognitive empathy (Hurlemann et al., 2010; Shamay-Tsoory, 2011), oxytocin administration should lead to facilitated performance for those low in emotional empathy.

2. Methods

2.1. Subjects

Twenty-four healthy males (M_{age} = 21.46 years, SD = 1.93) participated for financial compensation. All of them were students and recruited through advertisements placed across campus and in an online recruitment system (Sona System: http://radboud.sona-systems.com). The data were collected at the Donders Institute of Brain Cognition and Behavior (Nijmegen, The Netherlands) in spring 2011. Subjects were screened according to in- and exclusion criteria and received information about the study several days before their first visit. Exclusion criteria included age of <18 or >30, current/past neurological or endocrine disease, medication use, drug or alcohol abuse, smoking >5 cigarettes a day, participating in another pharmacological study within 2 months prior to inclusion, and having fever, common cold, or allergic rhinitis (''hay fever'') on test days. Participants abstained from caffeine, alcohol, and nicotine for 24 h, and from eating and drinking (except water) for 2 h before substance administration. Sample characteristics are reported in Table 1.

All participants gave their written informed consent. Procedures were in accordance with the Declaration of Helsinki and had been approved by the Medical Ethics Committee of the Radboud University Nijmegen Medical Centre.

2.2. Procedure

A randomized, placebo-controlled, double-blind, within-subjects design was applied. During two sessions separated by 14 days, participants self-administered oxytocin (Syntocinon; Novartis) or a saline solution via a nasal spray with three puffs per nostril over a time of about 3 min (total dose of 24 IU). To avoid any bias due to potential differences in scent between the two sprays, not the experimenter, but an independent assistant blind to the experimental hypotheses