



Oxytocin improves mentalizing – Pronounced effects for individuals with attenuated ability to empathize



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Received 7 July 2014; received in revised form 19 December 2014; accepted 23 December 2014

KEYWORDS

Oxytocin;
Neuropeptide;
Mentalizing;
Empathy

Summary The ability to predict the behavior of others based on their mental states is crucial for social functioning. Previous studies have provided evidence for the role of Oxytocin (OXT) in enhancing the ability to mentalize. It has also been demonstrated that the effect of OXT seems to strongly depend on socio-cognitive skills with more pronounced effects in individuals with lower socio-cognitive skills. Although recent studies indicate that mentalizing is related to empathy, no study has yet examined whether the effects of OXT on mentalizing depend on the ability to empathize.

71 male participants participated in a double-blind, between-subjects, placebo-controlled experiment. The Reading the Mind in the Eye Test (RMET) was used to investigate mentalizing abilities. We analyzed the effect of OXT on easy and difficult items of the RMET depending on differential empathy scores of the participants as assessed with the Empathy Quotient (EQ).

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Our results showed that OXT improves mentalizing for difficult but not for easy items. We generally observed increased mentalizing accuracy in participants with higher empathy scores. Importantly, however, whereas the performance in participants with higher empathy scores was comparable in both OXT and placebo condition, OXT specifically enhanced mentalizing accuracy in participants with lower empathy scores.

Our findings suggest that OXT enhances mentalizing abilities. However, we also demonstrate that not all participants benefited from OXT application. It seems that the effects of OXT strongly depend on baseline social-cognitive skills such as empathy.

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1. Introduction

The ability to identify internal states of another person plays an important role in human social cognition (Humphrey, 1976). During social interactions, humans need to perceive, represent and reason about their own and others' intentions. This ability is called 'mentalizing' (Frith and Frith, 2006a). Mentalizing implies the ability to infer mental and emotional states from multiple sources, e.g. understanding the other person's perspectives and beliefs, as well as interpreting non-verbal cues such as facial expressions and gaze direction (Baron-Cohen, 1995). The foundation for mentalizing is partly rooted in infant-caregiving attachment relationships and matures over the lifespan with increased interpersonal interactions (Fonagy et al., 2007).

Several studies have shown the strong relationship between mentalizing and empathy (Martin et al., 1996; Besel and Yuille, 2010). Findings from neuroimaging studies suggest that greater neural activity in brain circuits underlying mentalizing is related to more self-reported empathy (Hooker et al., 2008, 2013).

Even though mentalizing and empathy are often used as synonyms, they represent different skills that rely on distinct neuronal circuitries (Singer, 2006). Empathy is a multidimensional construct combining cognitive and affective components. For example, previous studies have shown that empathic responses can be evoked automatically in participants through observation, without specific evaluation of the feelings of others (Singer et al., 2004; Blakemore et al., 2005). This can be referred to as the 'affective–perceptual' form of empathy and defines empathy as the emotional reaction to the observed experience of others. Other studies have reported that empathic responses depend on whether or not one attends to the others' feelings by imagining and evaluating them (Preston et al., 2007; Fan and Han, 2008). This can be termed as the 'cognitive–evaluative' form of empathy. The concept of mentalizing overlaps with the latter described cognitive–evaluative' form of empathy as it also includes the immediate recognition and cognitive inference about other persons' emotional states (Frith and Frith, 2006b).

However, previous imaging studies have shown that empathy and mentalizing are distinct and rely on different neural circuits (Singer, 2006). Specifically, empathy relies on somatosensory and insular cortices as well as limbic areas and anterior cingulate cortex (Singer, 2006; Hein and Singer, 2008). In contrast, mentalizing relies on structures of the prefrontal cortex, superior temporal sulcus (STS), the temporo-parietal junction (TPJ) and the

anterior temporal poles (TP) (Saxe et al., 2004; Frith and Frith, 2006b). Additionally, studies have indicated that empathy and mentalizing display distinct ontogenetic trajectories (Baron-Cohen et al., 2000). In particular, it has been suggested that empathy develops much earlier than mentalizing, because it depends on limbic structures that mature early in ontogeny (Singer, 2006).

Previous work has furthered insight into the processes underlying mentalizing (Frith and Frith, 2006a). Especially non-verbal information from the eyes conveys a rich source of social information that is important in mentalizing processes (Blair, 2003). Baron-Cohen et al. (2000) have shown that humans are able to quickly and accurately decode another person's complex mental state based on facial cues.

A means to enhance social cognition including mentalizing is the neuropeptide Oxytocin (OXT; Heinrichs et al., 2009; Campbell, 2010). Previous work suggests that OXT plays an important role in the modulation of human behavior (Meyer-Lindenberg et al., 2011). OXT receptors are found in brain structures that are involved in human social behavior and emotional processing, including the amygdala, striatum, hippocampus, nucleus accumbens and midbrain (Meyer-Lindenberg et al., 2011). The use of intranasal OXT in experiments in humans has led to the promising hypothesis that OXT is capable of modulating a wide range of complex social-cognitive functions. Specifically, previous studies have shown that OXT facilitates social memory (Savaskan et al., 2008; Guastella et al., 2008b; Weigand et al., 2013), reduces fear and anxiety (Heinrichs et al., 2003; Kirsch et al., 2005), and promotes social approach and trust (Kosfeld et al., 2005; Feldman et al., 2007; Baumgartner et al., 2008). OXT administration has also been shown to enhance empathy (Hurlemann et al., 2010).

Regarding the role of facial expressions detection in mentalizing, a number of studies have also provided evidence for the role of OXT in enhancing facial emotion recognition (for a review see Van Ijzendoorn and Bakermans-Kranenburg, 2012). They demonstrate that OXT promotes the identification of happy faces (Guastella et al., 2008b; Di Simplicio et al., 2009; Marsh et al., 2010; Schulze et al., 2011), whereas other studies also show beneficial effects on the recognition of fearful faces (Fischer-Shofty et al., 2010). Some studies indicate that OXT promotes the identification of emotions regardless of valence (Lischke et al., 2012a; Prehn et al., 2013).

Most important for the present study, it has repeatedly been shown that OXT specifically increases mentalizing in healthy participants (Domes et al., 2007; Luminet et al.,

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