



Sniff and mimic – Intranasal oxytocin increases facial mimicry in a sample of men



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ABSTRACT

The neuropeptide oxytocin (OT) has many potential social benefits. For example, intranasal administration of OT appears to trigger caregiving behavior and to improve the recognition of emotional facial expressions. But the mechanism for these effects is not yet clear. Recent findings relating OT to action imitation and to the visual processing of the eye region of faces point to mimicry as a mechanism through which OT improves processing of emotional expression. To test the hypothesis that increased levels of OT in the brain enhance facial mimicry, 60 healthy male participants were administered, in a double-blind between-subjects design, 24 international units (IUs) of OT or placebo (PLA) through nasal spray. Facial mimicry and emotion judgments were recorded in response to movie clips depicting changing facial expressions. As expected, facial mimicry was increased in the OT group, but effects were strongest for angry infant faces. These findings provide further evidence for the importance of OT in social cognitive skills, and suggest that facial mimicry mediates the effects of OT on improved emotion recognition.

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1. Introduction

Primates, including humans, are highly social creatures, whose brains have evolved to understand and interact with other individuals (Dunbar, 1998). The face is one of the richest means of (nonverbal) social communication (Ekman and Rosenberg, 2005). Therefore, efficient and accurate recognition and interpretation of facial expressions is critical input into our inferences about and reactions to other people's affective states and behavioral intentions, and the achievement of smooth social interactions and successful goal pursuit in society.

A mechanism suggested to play a key role in the fast and accurate recognition of facial expressions is the simulation of that expression on one's own face (Wood et al., 2016). *Facial mimicry* consists of small changes in the activation of facial muscles of the observer, which match the facial movements perceived on another person's face. Seeing somebody smiling, for example, elicits contractions of the smiling muscles in the perceiver (Dimberg, 1982; Korb et al., 2014), which can be measured using electromyography (EMG) (Dimberg, 1982; Tassinari

and Cacioppo, 1992). Information from muscular contractions that comprise facial mimicry reaches somatosensory areas of the brain through facial feedback (Hatfield et al., 1993; Korb et al., 2015), and contributes to the processing of the perceived facial expressions (Barsalou, 2008; Niedenthal et al., 2010). For example, the intensity of smile mimicry predicts judgments of smile authenticity (Korb et al., 2014), and when facial mimicry is blocked recognition of facial expressions becomes slower and poorer (Maringer et al., 2011; Niedenthal et al., 2001; Oberman et al., 2007; Rychlowska et al., 2014; Stel and van Knippenberg, 2008; Wood et al., 2015). When mimicry is inhibited, responses to emotional faces in emotion circuits of the brain, such as the amygdala, are also reduced (Hennenlotter et al., 2009). Facial mimicry is present from early infancy (Field et al., 1982; Meltzoff and Moore, 1977; but see Oostenbroek et al., 2016), is difficult to voluntarily suppress (Korb et al., 2010), and occurs in the absence of conscious perception of the stimulus face (Dimberg et al., 2000; Mathersul et al., 2013; Tamietto et al., 2009).

The important role of facial mimicry for emotion recognition is also illustrated by psychiatric and neurodevelopmental conditions characterized by deficits in social interaction. For example, anomalies in face processing and difficulties in emotion recognition likely contributing to deficits in empathy and social interaction, are one of the hallmarks of autism spectrum disorders (ASD; Rump et al., 2009; but see Tracy et al., 2011). Some of the difficulties in emotion recognition and social

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interaction that accompany ASD are likely caused by a lack of or delay in facial mimicry (Beall et al., 2008; McIntosh et al., 2006; Oberman et al., 2009).

Oxytocin (OT) is both a hormone and a neuropeptide that has been implicated in a number of behaviors, including attachment, exploration, and sexuality (Carter et al., 2008; Donaldson and Young, 2008; Meyer-Lindenberg et al., 2011; Strathearn, 2011). For example, OT released into the brain or cerebro-spinal fluid (CSF), either endogenously from the hypothalamus or through exogenous administration, facilitates parental care and pair bonding, as shown most impressively in voles and other rodents (Johnson and Young, 2015; Young et al., 2008), but more recently also in humans (Campbell, 2008; Kim et al., 2014). In addition to its role in mother-infant bonding, recent studies have suggested that OT is also important for fatherhood, and could modulate father-infant interactions (Weisman et al., 2014). Moreover, administration of OT is being tested as a treatment for some of ASD's most debilitating symptoms, such as avoidance of eye contact, and the inability to understand other people's feelings (Anagnostou et al., 2012; Andari et al., 2010; Dadds et al., 2014; Guastella et al., 2015, 2010; Hollander et al., 2007).

In human studies, 24 to 48 international units (IUs) of OT are typically administered through nasal spray, and compared to placebo (PLA). Although the precise mechanisms through which intranasal OT reaches the brain are not well understood (Churchland and Winkielman, 2012; Leng and Ludwig, 2016; Quintana et al., 2015; Veening and Olivier, 2013), OT is believed to reach its maximum effect in the brain after about 45 min, and to alter resting regional cerebral blood flow for up to at least 78 min after administration (Born et al., 2002; Paloyelis et al., 2014; for an even later peak in CFS see Striepens et al., 2013). Elevated levels of peripheral OT, as measured for example in saliva, can persist for hours after intranasal administration (Van Ijzendoorn et al., 2012), although the relationship between central and peripheral OT levels is uncertain (Churchland and Winkielman, 2012). OT is likely to have widespread and long-lasting effects on the brain, especially on brain regions subserving social skills (Bethlehem et al., 2013).

There is currently great interest in the effects of OT on the perception of social stimuli. Research suggests that OT administration robustly improves the recognition of emotional facial expressions in neurotypical (NT) individuals (Bartz et al., 2011; Domes et al., 2007b; Macdonald and Macdonald, 2010; Meyer-Lindenberg et al., 2011; for a review and estimation of the effect size see Van Ijzendoorn and Bakermans-Kranenburg, 2012). Moreover, intranasal OT increases positive social behavior of macaque infants and modulates activity in face-responsive brain regions of adult macaques (Liu et al., 2015; Simpson et al., 2014). However, whether OT improves the detection and identification of facial expressions in general (Lischke et al., 2012; Schulze et al., 2011), or of specific emotions, such as happiness (Marsh et al., 2010; Schulze et al., 2011) or fear (Fischer-Shofty et al., 2010), remains an open question in the light of mixed evidence.

Studies carried out in people with ASD, often using multi-dose treatments over periods of several weeks, have also led to mixed results (Anagnostou et al., 2014). Some findings point to improvements in emotion recognition and social functioning, for example on the Reading-the-Mind-in-the-Eyes Test (Baron-Cohen et al., 2001), which requires the recognition of emotional and cognitive states based solely on the part of faces including and surrounding the eyes (Anagnostou et al., 2012; Andari et al., 2010; Guastella et al., 2010; Hollander et al., 2007). Others, however, show no evidence of improvements in emotion recognition or interaction skills, even after weeks of daily OT administration (Dadds et al., 2014; Guastella et al., 2015).

Based on several considerations, we hypothesized that improved emotion recognition after OT administration is due in part to an increase in facial mimicry. First, although its effects on facial mimicry remain unknown, OT was recently shown to facilitate automatic imitation¹ of finger movements. In a study by De Coster and colleagues (De Coster et al.,

2014), forty-eight male volunteers received either OT or PLA, and performed a well-established task, in which index or middle finger movements are made while watching either congruent or incongruent movements on a screen. The incongruency effect, defined by slower responses on incongruent trials (e.g. participant moves index finger while observing middle finger movement) compared to congruent trials (participant performs same movement as on the screen), was bigger in the OT group, compared to the PLA group. According to the authors, these results indicate that OT suppresses control over automatic imitative behavior. Second, OT increases visual processing of the eye-region of the face (Guastella et al., 2008). This is relevant because the eye region carries critical information, and people with ASD make reduced eye contact (Dalton et al., 2005; Rutherford et al., 2007). Eye contact has also been proposed as a trigger for facial mimicry, at least in healthy participants (Neufeld et al., 2015; Niedenthal et al., 2010; Schrammel et al., 2009). Third, testosterone, a steroid hormone that under many aspects has effects opposite of OT on perception and behavior, is associated with decreases in mimicry (Hermans et al., 2006). Finally, at the anatomical level, OT binding sites exist at several areas of the human brainstem, possibly including the facial nuclei (Freeman et al., 2016; Loup et al., 1989).

In summary, the effects of the neuropeptide OT are often described as "prosocial", and include increasing trust, empathy, bonding, and caregiving (but depending on the context OT may increase aggression, e.g. see Ne'eman et al., 2016). Based on studies in NT individuals and initial clinical trials in individuals with ASD, OT has been implicated in the accuracy of recognition of emotions in faces. However, it remains unclear to date if improved emotion recognition occurs for all or only specific facial expressions. Most importantly, it is unknown if facial mimicry, which contributes to emotion recognition, and is impaired in ASD, is increased through OT administration.

The current study aimed to investigate the hypothesis that OT administration enhances facial mimicry in healthy adult males. In a double-blind, placebo-controlled, between-subjects design, sixty healthy male participants received as nasal spray 24 IUs of either OT or a PLA. The sample was restricted to male participants to reduce complications linked to the female menstrual cycle. A between-subjects design was chosen to prevent habituation to the stimuli, and because it was shown to lead to larger effect sizes in a recent meta-analysis on the effects of OT on emotion recognition (Van Ijzendoorn and Bakermans-Kranenburg, 2012). Facial mimicry to dynamic happy and angry facial expressions in adult and infant faces was measured, across two tasks, with facial EMG. To rule out an unspecific motor effect of OT, voluntary facial movements were also assessed with EMG. Changes in mood and empathy were assessed by questionnaire.

Due to its prosocial and anxiolytic effects, OT was expected to lead to increased facial mimicry for both happy and angry facial expressions. Due to OT's role in caregiving behavior, including fatherhood (Weisman et al., 2014), we expected the increase in facial mimicry under OT to be more pronounced for infant faces, compared to adult faces. Based on findings by Lischke et al. (Lischke et al., 2012), who used a similar task and stimuli, we expected speed of emotion recognition to be faster under OT. Emotional facial expressions were also expected to be perceived as more intense under OT. Finally, we explored the effects of OT on questionnaire measures of empathy and mood.

2. Methods

2.1. Participants

Sixty healthy male participants (10 left-handed; average age = 24.85 years, $SD = 4.75$, range 18 to 35 years) were recruited through advertisements on campus and gave written informed consent. The study,

¹ For the purpose of the current discussion imitation is used as a synonym of mimicry.

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