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Review article

Meta-analysis of the effects of intranasal oxytocin on interpretation and expression of emotions

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ABSTRACT

Accurate interpretation and appropriate expression of emotions are key aspects of social-cognition. Several mental disorders are characterised by transdiagnostic difficulties in these areas and, recently, there has been increasing interest in exploring the effects of oxytocin on social-emotional functioning.

This review consists of 33 studies. Fifteen of the studies included people with autism spectrum disorder, schizophrenia, borderline personality disorder, frontotemporal dementia, anorexia nervosa, bulimia nervosa, post-traumatic stress disorder, depression, and opioid and alcohol dependence. We conducted ten meta-analyses examining the effects of intranasal oxytocin on expression of emotions, emotional theory of mind, sensitivity to recognise basic emotions, and recognition of basic emotions.

A single dose of intranasal oxytocin significantly improved the recognition of basic emotions, particularly fear, and increased the expression of positive emotions among the healthy individuals. Oxytocin did not significantly influence theory of mind or the expression of negative emotions among the healthy individuals. Finally, intranasal oxytocin did not significantly influence interpretation or expression of emotions among the clinical populations.

1. Introduction

Accurate interpretation of other's emotions, appropriate expression of one's own emotions, and reciprocity within interactions are key aspects of social cognition. In social interaction, emotion expression is believed to be dependent on accurate interpretation of social signals (Hess and Fischer, 2013; Künecke et al., 2014). According to the embodied simulation theory, emotion expression and mimicry, in turn, play an important role in facilitating the interpretation of others' expressions, empathy, and prosocial behaviour in recipients (Gallese, 2005). Indeed, behavioural studies have documented that automatic mimicry of emotions facilitates recognition, whereas blocking mimicry impairs recognition accuracy and sensitivity (Argaud et al., 2016; Duffy and Chartrand, 2015; Künecke et al., 2014; Rychlowska et al., 2014; Schneider et al., 2013). Anomalies in emotion expression also have social and affective consequences, with incongruent emotion expression increasing the desire for greater social distance and negative social evaluation by the recipient (Brown et al., 2015; Szczurek et al., 2012). Similarly, expressive suppression has been found to increase the suppressors' blood pressure, subjective anxiety, and social isolation (Butler et al., 2003; Gross, 2002).

Anomalies in social-emotional functioning are important transdiagnostic features in several psychiatric disorders (Bora and Berk, 2016; Bora and Köse, 2016; Chung et al., 2014; Davies et al., 2016; Henry et al., 2014; Kring and Moran, 2008). Meta-analyses have found that people with eating disorders (EDs), depression, schizophrenia, and autism spectrum disorders (ASD) have similar difficulties in accurate interpretation of emotions, including recognition of basic emotions in faces and tone of voice with small effect sizes and in emotional theory of mind with medium to large effect sizes (Bora and Berk, 2016; Bora and Köse, 2016; Caglar-Nazali et al., 2014; Chung et al., 2014; Uljarevic and Hamilton, 2013). Recent systematic reviews have also found that people with schizophrenia, EDs, depression, ASD, and borderline personality disorder (PBD) display less positive facial affect in response to positive emotional stimuli (Davies et al., 2016; Kring and Moran, 2008). Furthermore, a meta-analysis of 537 task-based fMRI studies in depression, bipolar disorder, schizophrenia, and obsessive-compulsive disorder failed to find significant differences between the disorders in whole brain neural response to social and cognitive tasks (Sprooten et al., 2016). Together these findings suggest that anomalies in social-

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emotional processing in psychiatric disorders may have shared underlying mechanisms. Given social and affective consequences of these difficulties, better understanding of the underlying processes is of interest. One such possible mechanism is the oxytocin system.

Preclinical studies have found that the neuropeptide, oxytocin, may regulate social-emotional functioning (Dölen et al., 2013; Hicks et al., 2012; Lim and Young, 2006; Lukas et al., 2011; Onaka et al., 2012). Endogenous oxytocin has been found to play an important role in the central and medial amygdala, facilitating formation of social bonds, maternal behaviour, and social recognition in rodents (Lim and Young, 2006; Onaka et al., 2012). Additionally, a recent study found that formation of social reward was dependent on coordinated activity between oxytocin and serotonin in the mouse nucleus accumbens (Dölen et al., 2013). In rodents, the administration of oxytocin receptor agonist and exogenous synthetic oxytocin has also been found to increase social place preference and reduce social defeat induced avoidance (Hicks et al., 2012; Lukas et al., 2011). Conversely, the administration of oxytocin receptor antagonist, has been found to increase corticosteroid levels and induce social avoidance in monkeys during times of stress (Cavanaugh et al., 2016).

Recently there has been increasing interest in translating these findings into humans and the effects of intranasal oxytocin on social-emotional function has been widely studied (Bakermans-Kranenburg and van Ijzendoorn, 2013; Bartz et al., 2011; Guastella and MacLeod, 2012; Shahrestani et al., 2013; van Ijzendoorn and Bakermans-Kranenburg, 2012). A few previous meta-analytic reviews have found that intranasal oxytocin improves recognition of anger and happiness, and increases in-group trust among healthy individuals with small effect sizes (Shahrestani et al., 2013; van Ijzendoorn and Bakermans-Kranenburg, 2012). However, to our knowledge no meta-analyses to date have investigated the effects of a single dose of oxytocin on recognition of all six basic emotions, other aspects of emotion interpretation, including theory of mind or sensitivity to recognise basic emotions, or on emotion expression among healthy individuals.

To date, two meta-analytic reviews have investigated the effects of intranasal oxytocin on different aspects of social-emotional functioning in a variety of clinical groups (Bakermans-Kranenburg and van Ijzendoorn, 2013; Ooi et al., 2017). One reported small, but generally positive effect of intranasal oxytocin on social-emotional functioning and psychopathology among people with ASD, anxiety disorders, depression, schizophrenia, and BPD (Bakermans-Kranenburg and van Ijzendoorn, 2013). The other meta-analysis found no significant effects of intranasal oxytocin on social-emotional processing in ASD (Ooi et al., 2017). However, these reviews were quite heterogeneous pooling studies assessing psychopathology and social-emotional processing, or single dose and repeated dose studies into one meta-analysis (Bakermans-Kranenburg and van Ijzendoorn, 2013; Ooi et al., 2017). To our knowledge no previous meta-analyses have investigated the effects of a single dose of intranasal oxytocin separately on different aspects of interpretation and expression of emotions among both healthy and clinical populations. In order to consider the possibility of translating animal studies more widely into treatment for psychiatric disorders it is important to consider various key outcomes and whether there is evidence that they might be modified by oxytocin.

The aim of the current review was to pool studies investigating the effects of a single dose of intranasal oxytocin on various aspects of social-emotional functioning among healthy and clinical populations. Specifically, we aimed to examine the effects of intranasal oxytocin on theory of mind, recognition of basic emotions, sensitivity to recognise basic emotions, and on emotion expression among healthy and clinical populations. We tested the hypothesis that oxytocin would improve all aspects of social-emotional functioning.

2. Methodology

2.1. Literature searches

Electronic databases, including OVID (journals@OVID, PsycINFO, PsycARTICLES, Embase, AGRIS, MEDLINE), PubMed, and Web of Knowledge core collection, were searched for studies published during available years up to February 2017 in accordance with the PRISMA guidelines (Moher et al., 2009). Two separate literature searches were conducted in order to uncover studies investigating the effects of a single dose of intranasal oxytocin on interpretation and expression of emotions in a social context. The first literature search was conducted with the following search terms: *oxytocin AND emotion AND (interpretation OR recognition OR identification OR labelling OR "theory of mind" OR mentalising OR perception OR empath*)*. The second search was conducted with the following search terms: *oxytocin AND emotion AND (expression OR mimicry OR mirroring OR communication OR responsiveness OR expressivity)*. Additionally, to ensure no studies were missed by the initial search, the bibliographies of included studies were searched for additional studies.

2.2. Eligibility criteria

Studies were included if they met the following inclusion criteria: 1) investigated the effects of a single dose of intranasal exogenous oxytocin on interpretation or expression of emotions in a social context among either healthy adult participants or adult clinical populations (18 years old or older); 2) compared the effects of intranasal oxytocin with intranasal placebo spray; 3) investigated short term outcomes; and 4) randomly allocated participants to oxytocin and placebo groups or, in the case of crossover, within subjects studies, randomised the treatment order. Any studies, which used tasks that did not include a social component, such as the bumper car theory of mind task where social context is inferred from the movement of triangles on a computer screen, were excluded. Trials, in which participants either received repeated doses of oxytocin or in which long term outcomes of a single dose of oxytocin were assessed, were excluded. Studies that included only children or adolescents were excluded, because the majority of them were longer trials and the effects of oxytocin on social-emotional processing can be different in adults and children. Full-text articles published in peer reviewed journals and where possible, published conference abstracts were included.

In total, five studies were excluded after further screening because they incorporated tasks that were very different compared to the other included studies despite being otherwise relevant. These studies included a theory of mind task involving infant stimuli, continuously assessing the mood of a target on a video clip on a 9-point Likert scale, manipulating the context in which emotional stimuli was presented, recognising emotions from a point-light-display, and interpreting basic emotions from tone of voice in different languages (Bartz et al., 2010; Bernaerts et al., 2016; De Dreu et al., 2016; Perry et al., 2013; Voorthuis et al., 2014).

2.3. Study selection

The literature searches were conducted by one author (J.L.). The studies yielded from the literature search were then screened based on their titles and abstracts. Full text articles were then assessed for eligibility followed by final screening and assessment by two authors (J.L. and K.W.N.). Where appropriate conference abstracts of studies not yet published were also screened and assessed for eligibility. If deemed eligible the authors were contacted in order to gain access to the data. Only studies that both authors agreed on were included in the final systematic review and meta-analyses. Any cases where eligibility remained in question were brought to the whole team for further discussion and assessment. The study selection processes of the two