

# The Impact of a Single Administration of Intranasal Oxytocin on the Recognition of Basic Emotions in Humans: A Meta-Analysis

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Many studies have highlighted the potential of oxytocin (OT) to enhance facial affect recognition in healthy humans. However, inconsistencies have emerged with regard to the influence of OT on the recognition of specific emotional expressions (happy, angry, fear, surprise, disgust, and sadness). In this study, we conducted a meta-analysis of seven studies comprising 381 research participants (71 females) examining responses to the basic emotion types to assess whether OT enhances the recognition of emotion from human faces and whether this was influenced by the emotion expression and exposure time of the face. Results showed that intranasal OT administration enhances emotion recognition of faces overall, with a Hedges *g* effect size of 0.29. When analysis was restricted to facial expression types, significant effects of OT on recognition accuracy were specifically found for the recognition of happy and fear faces. We also found that effect sizes increased to moderate when exposure time of the photograph was restricted to early phase recognition (<300 ms) for happy and angry faces, or later phase recognition for fear faces (>300 ms). The results of the meta-analysis further suggest that OT has potential as a treatment to improve the recognition of emotion in faces, allowing individuals to improve their insight into the intentions, desires, and mental states of others.

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## INTRODUCTION

Emotion recognition is a universal and central component of social cognition that provides the capacity to understand the intentions, feelings, and reactions of others (Elfenbein and Ambady, 2002). The initial experiments of Ekman *et al* (1969) revealed the capacity for even the most isolated tribes of New Guinea to understand the basic emotions of Western faces. Proficiency in recognizing emotions has been linked to altruistic helping behavior (Marsh *et al*, 2007), higher relationship quality, and a lowered rate of depression (Carton *et al*, 1999). Deficits in emotion recognition have also been associated with increased social anxiety, social avoidance, distress, depression, antisocial behaviors, and psychopathy (McClure and Nowicki, 2001). There is also growing awareness that social cognition is a unique and important neurocognitive domain for human

social function (Shultz and Dunbar, 2012). Social cognitive deficits, including emotion recognition, predict social function in both early psychosis and autism above other tests of neurocognition (Bertrand *et al*, 2007; Losh *et al*, 2009). Thus, enhancement of the ability to recognize emotion in faces has the potential to improve social functioning in healthy humans and across clinical disorders.

Oxytocin (OT), a neuropeptide secreted from the posterior pituitary, has a critical role in mammalian social behavior (Macdonald and Macdonald, 2010). In healthy humans, the impact of OT on social cognition has been evaluated using a single dose of intranasal OT, typically given 30–45 min before the experimental task (see Guastella and Macleod (2012) for a review). Although many studies report that OT improves the perception of happy faces (Marsh *et al*, 2010; Schulze *et al*, 2011), others report that OT improves the recognition of angry, sad, or fear emotions in faces (Fischer-Shofty *et al*, 2010; Ellenbogen *et al*, 2012; Lischke *et al*, 2012). We have previously argued that different methodologies, or samples assessed may contribute to such inconsistent findings (Guastella and Macleod, 2012). For example, recognition performance for faces that are easier to read, such as happy faces (Hess *et al*, 1997), may be at ceiling levels in experiments that use longer exposure intervals (Fischer-Shofty *et al*, 2010).

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A recent meta-analysis performed by Van IJzendoorn and Bakermans-Kranenburg (2012) revealed that OT significantly increased individual's response to facial expressions of emotion and in-group trust. However, their focus was very broad; their meta-analysis included studies on neuroanatomical measures, such as amygdala activation (eg, Domes *et al*, 2007), measures of trustworthiness and attractiveness (Theodoridou *et al*, 2009), and behavioral key presses in response to online social contingency (eg, Alvares *et al*, 2010). Outcomes from these studies were combined with more traditional assessments of facial recognition accuracy to produce the overall effect size of  $d = 0.21$ . This study also did not investigate whether OT differentially impacted the ability to detect specific expressions in faces or other aspects of the experimental design. Thus, the overall effect of OT on the capacity to recognize emotion in faces remains unclear and further research is required to understand factors that may moderate any effect.

The present meta-analysis focuses only on recognition accuracy of full-face, basic expressions of emotion. Here, we focus on studies that recruited healthy controls, and excluded studies on patient populations to avoid biasing results as many clinical conditions display specific deficits in emotion recognition (Marsh and Blair, 2008). Our aim was to determine whether OT improved the accuracy of emotion recognition from faces, and whether this effect was influenced by emotion expression of the face stimuli (happy, sad, angry, fearful, surprised, and disgusted) and exposure time (short < 300 ms; long > 300 ms). Our central hypothesis was that OT would enhance the recognition of emotions overall. We further expected that emotion expressions that are easier to read, such as happy and angry faces, would show effects of OT enhancement at earlier rather than later exposure intervals, where ceiling effects may be more common (Hess *et al*, 1997; Leppänen and Hietanen, 2004; Fox *et al*, 2000).

## MATERIALS AND METHODS

### Criteria for Considering Studies for this Review

All randomized controlled trials of intranasal OT administration *vs* placebo were included (study  $n = 7$ ). All studies examined perception or response in the form of overt choices in the recognition accuracy of both positive and negative emotional stimulus. This allowed us to compare dependent measures across categories of different expression types.

### Inclusion and Exclusion Criteria

Participants included in this review were healthy controls. While many studies have examined individuals with psychopathology, such as autism, schizophrenia, and frontotemporal dementia (Guastella *et al*, 2010; Goldman *et al*, 2011; Jesso *et al*, 2011), the confounding effects of psychopathology were avoided in this study to draw more specific conclusions on the impact of OT on the recognition of differential expressions of facial emotion in healthy controls. Further, papers that used photographs of regions of the face rather than full-face images were not included to

avoid confounding results with region presented (eg, Fischer-Shofty *et al*, 2010).

### Types of Intervention

All doses of OT were administered intranasally; the most common dosage was 24 International Units (IU), with six of the seven studies administering OT at this dosage, and one study administering 40 IU (Leknes *et al*, 2012). Twenty-four International Units is the most common dosage because of historical reasons; however, it is unclear whether other more optimal doses exist or whether someone who does not respond to lower doses will respond to higher ones (see Guastella *et al*, 2013) with respect to the latest recommendations relating to nasal spray administration).

### Primary Outcome Measures

Observable behavioral responses such as recognition accuracy or reaction time are the only scientifically acceptable method of evaluating the veracity of cognitive models (Guastella and Macleod, 2012). In this regard, recognition accuracy was chosen as the primary outcome measure for the present meta-analysis; there was insufficient data available to conduct an analysis on reaction time data. Further, we chose not to combine these different dependent measures as speed of responding will confound accuracy of responding, leading to less meaningful results. Statistics pertaining to intensity thresholds for recognition were also avoided to prevent confounding results.

Recognition accuracy involves identifying specific facial expressions of emotion such as happy, angry, sad, and so on (Marsh *et al*, 2010; Schulze *et al*, 2011). Only full-faced photographs from validated databases of emotional expressions were included in the meta-analysis to standardize the task. Satisfactory reporting of statistics (eg, mean, SD,  $p$ -,  $t$ -,  $r$ -, or F-value, etc) in text or in tables was required for inclusion of a study. The threshold between conscious and nonconscious perception was set at 300 ms on the basis of previous literature (Del Cul *et al*, 2007).

### Search Methods for Identification of Studies

**Initial search.** The search strategy followed guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher *et al*, 2009), previously the QUality Of Reporting Of Meta-analyses (QUORUM) (Moher *et al*, 2000) statement.

Electronic databases including PsycINFO, PubMed/MEDLINE, and EMBASE were searched using combinations of the following: *oxytocin*, *emotion*, *affect*, *face*, and *facial* as per earlier meta-analyses focusing on different, although related research questions (Marsh and Blair, 2008). Databases were searched using the following terms: ('emotions'[MeSH Terms] OR 'emotions'[All Fields] OR 'emotion'[All Fields]) OR ('affect'[MeSH Terms] OR 'affect'[All Fields]) AND ('oxytocin'[MeSH Terms] OR 'oxytocin'[All Fields]) (('face'[MeSH Terms] OR 'face'[All Fields]) OR ('face'[MeSH Terms] OR 'face'[All Fields] OR 'facial'[All Fields])) AND ('oxytocin'[MeSH Terms] OR 'oxytocin'[All Fields]). In addition to these electronic searches, each report's citation list was examined for additional studies.

Reference lists of relevant review papers identified in the literature search were also examined.

**Data collection.** The search strategy involved screening titles and abstracts for duplicates and identifying ineligible studies. Using full copies of the papers, two researchers (SS and JK) independently assessed whether studies met the inclusion criteria, and disagreements were resolved through discussion. Relevant statistics were then extracted from the eligible studies and included in the meta-analysis.

Aspects relating to study quality were assessed, including the extent of blinding, whether groups were randomized and whether the number of participants in the placebo and control conditions was comparable. This information is presented in a table describing features of the included studies (see Table 1).

**Study Characteristics.** Seven articles met our inclusion criteria from a total of 2683 studies (see Figure 1 outlining the number of papers included and excluded at each stage of the meta-analysis). These included seven independent studies comprising 381 research participants (71 females). The average number of participants per study was 54; two studies used The Pictures of Facial Affect Database (Ekman and Friesen, 1976), three used images from the Karolinska Directed Emotional Faces (Calvo and Lundqvist, 2008) series, another used the Dynamic Affect Recognition Evaluation (DARE) from the Cohn-Kanade database, and the remaining study using another validated stimulus set, the FACES database containing facial expressions of younger, middle-aged, and older women and men (Ebner et al, 2010).

### Statistical Analyses

The Comprehensive Meta-Analysis (Borenstein et al, 2005) program was used to transform results of individual studies into the common metric of Hedges  $g$ . Hedges  $g$  is a measure of the standardized difference between intervention and control condition that corrects for biases associated with small sample sizes and can be interpreted in the same way as Cohen's  $d$ ; 0.2 represents a small effect, 0.5 a medium effect, and 0.8 a large effect.

Heterogeneity across studies was assessed using the Q-statistic (Borenstein et al, 2009). A significant Q-statistic indicates dissimilar effect sizes across studies, indicating potential differences in methodology or study population across studies.

To determine whether any publication bias was present, the funnel plot was inspected for asymmetry. This technique determines whether there was a significant risk of bias, and controls for that risk by imputing values to correct for the bias (Begg, 1994).

An initial meta-analysis on the effects of emotional photographs of faces, regardless of expression type, was run to determine an overall effect of OT on emotion recognition, followed by moderator analyses to determine whether OT has an impact on specific expressions. A second moderator analysis was conducted to determine whether OTs impact on the recognition of emotions was moderated by implicit or explicit presentation of stimuli. The threshold between

conscious and nonconscious perception was set at 300 ms on the basis of previous literature (Del Cul et al, 2007).

### RESULTS

OT facilitated emotion recognition regardless of facial expression type ( $g=0.291$ ,  $p<0.001$ , 95% CI: 0.154, 0.429), an effect associated with a small effect size. Inspection of symmetry in the funnel plot of standard error by Hedges'  $g$  revealed no evidence of a significant publication bias, nor was there any indication of study heterogeneity ( $Q(df=13)=15.361$ ,  $p>0.05$ ).

#### Moderation by Emotion Type

A moderator analysis was conducted on facial expression type to determine whether the OT differentially impacts on the recognition of specific facial expressions. OT facilitated the recognition of all facial expressions; however, the effects of happy and fearful faces displayed statistically significant effects relative to placebo, see Figure 2.

Meta-analysis revealed significant effects of OT on emotion recognition of happy faces ( $n=5$ ,  $g=0.290$ ,  $p=0.019$ , 95% CI: 0.047, 0.533) and fearful faces ( $n=1$ ,  $g=0.591$ ,  $p=0.044$ , 95% CI: 0.016, 1.166), while trend level effects of OT were observed for the recognition accuracy of angry ( $n=5$ ,  $g=0.210$ ,  $p=0.059$ , 95% CI:  $-0.008$ , 0.428) and sad ( $n=1$ ,  $g=0.471$ ,  $p=0.075$ , 95% CI:  $-0.048$ , 0.991) facial expressions (see Table 2). The impact of OT on faces in which multiple expressions were presented and emotion type was not differentiated ( $n=2$ ,  $g=0.343$ ,  $p=0.308$ , 95% CI:  $-0.316$ , 1.002) were not significant (see Table 1). Eighty-five percent CIs were overlapping and inspection of heterogeneity Q-statistic for pairwise comparisons of all facial expression categories was nonsignificant ( $p>0.05$ ).

#### Moderation by Implicit or Explicit Presentation

Moderator analyses revealed that emotion recognition in both implicit and explicit presentations were significant ( $n=8$ ,  $g=0.240$ ,  $p=0.007$ , 95% CI: 0.064, 0.415 and  $n=5$ ,  $g=0.459$ ,  $p<0.001$ , 95% CI: 0.227, 0.640, respectively). Furthermore, a significant Q-statistic indicated that these categories did not differ from one another ( $p>0.05$ ). When grouping each of the effect sizes by emotion and further categorizing as explicit or implicit recognition, the implicit recognition of anger ( $n=2$ ,  $g=0.435$ ,  $p=0.002$ , 95% CI: 0.160, 0.710), happiness ( $n=3$ ,  $g=0.447$ ,  $p=0.009$ , 95% CI: 0.114, 0.781), and combined emotions ( $n=1$ ,  $g=0.673$ ,  $p=0.013$ , 95% CI: 0.141, 1.204) were significant along with the explicit recognition of fear ( $n=1$ ,  $g=0.591$ ,  $p=0.044$ , 95% CI: 0.016, 1.166), see Table 3. There were no statistics for the implicit presentation of fear or sadness, so we were not able to conduct these comparisons; however, aside from these, all unmentioned groupings and comparisons were nonsignificant ( $p>0.05$ ).

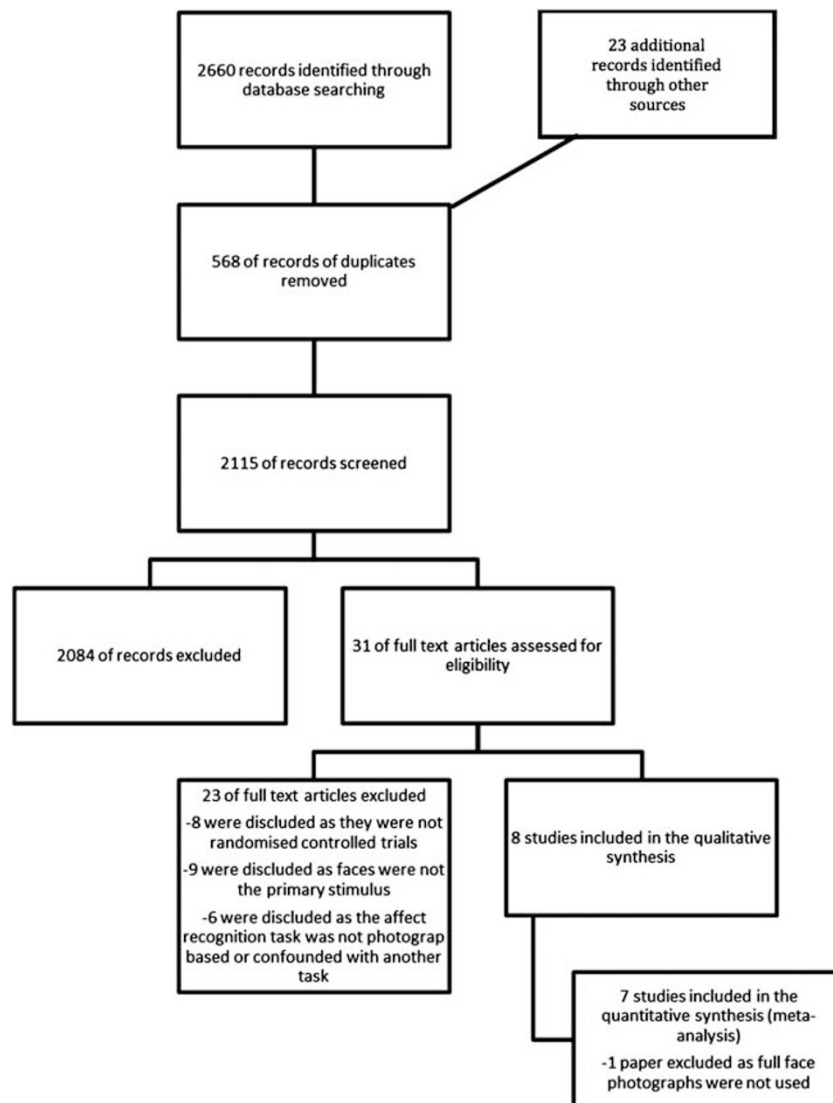
### DISCUSSION

This study demonstrates that OT nasal spray enhances the human capacity to recognize basic facial expressions of

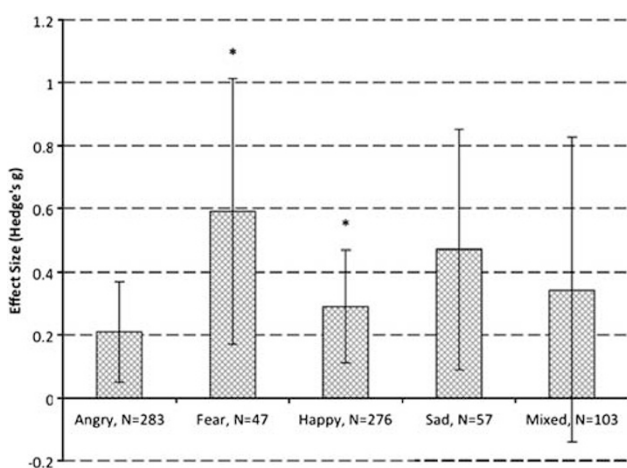
**Table 1** Summary of Studies used in Meta-Analysis

Reference	Sample	Method	Findings	Notes
Domes <i>et al</i> (2012a)	Sixty-nine male participants (mean age = SD: 24.0 ± 3.1 years). Twenty-four International Unit of oxytocin was administered	Dot-probe task was used with angry, happy, and neutral faces from the Karolinska Directed Emotional Faces database. A pair of angry/neutral, happy/neutral, or neutral/neutral facial expressions was presented for 100 ms vs 500 ms. In emotional trials the probe appeared at the location of the emotional (congruent) face and at the location of the neutral (incongruent) face	Oxytocin administration did not enhance recognition at longer exposure durations	
Domes <i>et al</i> (2012b)	Sixty-two healthy male volunteers (mean age = SD: 24.0 ± 2.5 years) participated and were administered 24 IU of oxytocin	The original version of the Dynamic Affect Recognition Evaluation (DARE) using the Cohn-Kanade database of facial expressions. Each trial begins with a neutral facial expression that slowly changed into one of two basic emotions (happiness and anger) over time. Trial duration ranged from 16 to 34 s and participants were asked to detect the emotion of the particular face presented as soon as possible	Oxytocin did not improve overall emotion recognition accuracy and no main effect of group was found for either happiness or anger	Was the task too easy? Were participants given too much time to perform the task?
Ellenbogen <i>et al</i> (2012)	Final sample consisted of 57 participants (15 females and 13 males) administered oxytocin (24 IU) and 29 participants administered placebo (15 females and 14 males). Exclusion criteria included smoking, consuming legal or illegal drugs, being not fluent in English, currently ill, or suffering from a chronic medical condition, major sensory impairment, or lifetime mental disorder	An adapted stimulus detection task was utilized in which subjects fixated on a centrally placed gray '+' sign on a black background. Subjects responded with a single key press as fast as possible when the target (a black dot) appeared in a rectangle on either the left or right. Before the target appeared, a cue picture of a sad, angry, or neutral face from the pictures of facial affect database, signaling the likely location of the target appeared in one of the rectangles. On engagement trials, the cue appeared in the same rectangle as the target. Cue pictures were presented for 750, 200, or 17 ms, followed by a masking stimulus. Images were from the Pictures of Facial Affect Database	Engagement scores consisted of the neutral minus the emotional picture for sad and angry faces presented for 750 ms. One-way ANOVA revealed a significant difference between oxytocin and placebo for valid trials with sad faces but not angry faces	Will the cueing association necessarily be strong enough and will participants have a bias to responding to either side of the screen aside from the cueing. How would presenting images for > 750 ms have affected results compared to 750 ms?
Leknes <i>et al</i> (2012)	Forty healthy right-handed adults were recruited, of which 20 were female. Forty International Unit oxytocin was administered	Participants viewed black and white images of faces displaying explicitly angry faces, implicitly angry faces, neutral faces, implicitly happy faces, and explicitly happy faces. While participants viewed images they received concomitant tactile stimulation; however, only results from visual stimuli were presented in this paper. Perceived mood or facial expression of stimuli was recorded on a binary scale (How happy was the person? Anchors: Not happy-happy and how angry was the person? Anchors: Not angry-angry). Images were from the Karolinska Directed Emotional Faces	Separate ANOVAs confirmed that oxytocin increased ratings of congruent and decreased ratings of incongruent emotional expression, sharpening the perception of emotion	Could the touch or stroking stimulus have confounded results? Why wasn't there a control group for no tactile stimulation?
Lischke <i>et al</i> (2012)	In a double-blind, placebo-controlled between-subjects design, 47 healthy male adults (age: M = 26.09, SD = 3.41) were randomly assigned to receive a nasal spray containing 24 IU of oxytocin or placebo	Computer-manipulated images of faces whose neutral expression was gradually changed into an emotional and consisted of neutral, sad, angry, fearful, or happy expressions. Images were from the FACES database	Oxytocin had no effect on participants' recognition accuracy, which was high for happy expressions, moderate for angry and fearful expressions, and low for sad expressions. Follow-up analysis revealed oxytocin improved specific recognition accuracy for fearful faces but not other expressions	Blood samples collected 45 min after administration of oxytocin and at the same time as emotion detection task. Venipuncture could be perceived as an aversive stimulus, confounding results. Participants were asked to respond when they recognized an emotion but then given time to pick one of four possible emotions (happy, angry, sad, and fearful). This sample space is limited and could allow guessing of responses
Marsh <i>et al</i> (2010)	Fifty healthy volunteers (29 males, 21 females, M age = 26.41 years, range = 20–40 years) participated in this study. Exclusion criteria included current or past major affective disorder, anxiety disorder, psychotic disorder, substance dependence, anorexia nervosa, bulimia, or IQ < 80. All participants were free of psychotropic medications and hormonal supplementation. Twenty-four International Unit of oxytocin was administered	Participant's emotion recognition accuracy in morphed facial expression task was assessed using unbiased hit-rate analysis. Procedure assesses raw accuracy and differential accuracy, then the difference between this and the accuracy that would be expected by chance is computed. The Pictures of Facial Affect set was used	The only emotion for which oxytocin significantly affected recognition rates was happiness. Participants who received oxytocin recognized happiness more quickly (M = 964.1 ms, SD = 248) than participants who received placebo (M = 1096.1 ms, SD = 334; $t(48) = 1.58$ , $p = 0.12$ ). This was nonsignificant	Tasks were completed 35 min after substance administration; however, most papers will wait 50 min. Participants viewed faces for only 500 ms. Does this represent some level of early processing? Were participants making a conscious, informed selection?
Schulze <i>et al</i> (2011)	Fifty-six male participants (mean age = SD: 24.18 ± 3.12) participated in this double-blind, placebo-controlled trial. Twenty-four International Unit of oxytocin was administered	Participants were exposed to an angry, happy, or neutral face was presented for 18, 35, or 53 ms, followed by a 'mask' showing a neutral face. Participants were explicitly informed that two facial stimuli would always appear in each trial, although they might only perceive one. Before each block, an instruction was given regarding the target emotion in the following trials. Following each target-mask pair, participants had 3 s to indicate whether the target emotion was present or absent (four blocks angry present/absent and four blocks happy present/absent). Images were taken from the Karolinska Directed Emotional Faces series	Subjects administered oxytocin showed enhanced recognition memory. Effect of oxytocin on emotion recognition was more pronounced for happy than angry faces	Participants were given only 3 s to respond, is this enough or may pressure have affect their ability to focus?





**Figure 1** Summary of research process for meta-analysis, including numbers of papers included and excluded at each stage.



**Figure 2** Effects of oxytocin on facial emotion recognition: combined effect sizes (g) and 85% confidence intervals. \* $P < 0.05$ , indicating significance.

emotion, an effect associated with small effect size ( $g = 0.291$ ). Additional analyses of specific emotion expressions revealed that OT enhanced the recognition of happy and fearful facial expressions. The impact of OT on the recognition of angry and sad faces was at trend levels for the overall analyses. We then examined whether OT facilitated the recognition of face expressions under implicit ( $< 300$  ms) and explicit ( $> 300$  ms) presentation conditions (Del Cul *et al*, 2007). Results showed that under implicit recognition conditions, OT enhanced recognition of happy and angry expressions. Under longer durations of exposure, OT was found to enhance the recognition of fear expressions only.

The results of this study further support the view that OT nasal spray improves the facial recognition of emotion in humans. We found that OT enhances overall recognition accuracy, with effects for happy and fear faces specifically. The capacity for OT to improve emotion understanding, and the recognition of fear and happiness in particular, may

**Table 2** Moderator Analysis of Emotion Type on Recognition Accuracy Under Oxytocin

Recognition accuracy for different emotions					
Subgroup	No. of data sets	No. of participants under oxytocin	Effect size (95% CI)	SE of summary effect size	Effect size <i>p</i> -value
Anger	5	156	0.210 (−0.008, 0.428)	0.111	0.059
Fear	1	24	0.591 (0.016, 1.166)	0.293	0.044*
Happy	5	158	0.290 (0.047, 0.533)	0.124	0.019*
Mixed	2	52	0.343 (−0.316, 1.002)	0.336	0.308
Sadness	1	23	0.471 (−0.048, 0.991)	0.265	0.075

\* $P < 0.05$ , indicating significance.

**Table 3** Moderator Analysis of Emotion Type and Implicit or Explicit Presentation on Recognition Accuracy Under Oxytocin

Recognition accuracy for different emotions					
Subgroup	Explicit/implicit	No. of data sets	Effect size (95% CI)	SE of summary effect size	Effect size <i>p</i> -value
Anger	Explicit	2	0.000 (−0.345, 0.345)	0.176	1.00
	Implicit	2	0.435 (0.160, 0.710)	0.140	0.002*
Fear	Explicit	1	0.591 (0.016, 1.166)	0.293	0.044*
	Implicit	—			
Happy	Explicit	2	0.225 (−0.260, 0.711)	0.248	0.363
	Implicit	2	0.227 (0.114, 0.781)	0.170	0.009*
Mixed	Explicit	2	0.256 (−0.103, 0.614)	0.183	0.162
	Implicit	1	0.673 (0.141, 1.204)	0.271	0.013*
Sadness	Explicit	1	0.471 (−0.048, 0.991)	0.265	0.075
	Implicit	—			

\* $P < 0.05$ , indicating significance.

have important benefits to social engagement (Kemp and Guastella, 2011). Robust associations have been observed between antisocial behavior and impaired recognition of fearful expressions in particular (Marsh and Blair, 2008). It has been argued that the ability to recognize fear enables one to appreciate the pain and mental experience of others, and is therefore more likely to reduce antisocial tendencies (Marsh and Blair, 2008). This ability has also been linked experimentally to prosocial behavior (Marsh *et al*, 2007; Kirsch *et al*, 2005). Similarly, socially anxious individuals are more likely to interpret facial expressions in a negative manner contributing to both negative self-images and social avoidance (Garner *et al*, 2009; Guastella *et al*, 2009). Further research is now required to determine links between improvements in face recognition from OT and subsequent behavioral outcomes associated with reducing aggressive behavior and anxiety/avoidance in social situations. In light of recent evidence revealing that OT improves social cognition in individuals with frontotemporal dementia relative to baseline (Jesso *et al*, 2011), there may also be implications for the use of OT in disorders of neuropsychological deficit.

The findings from this study also suggest that the previously observed inconsistent results in this field may

be partially associated with stimuli exposure duration. Happy and angry face expressions are more efficiently recognized in humans and require less time for processing (Hess *et al*, 1997; Leppänen and Hietanen, 2004; Fox *et al*, 2000). OT appears to further improve this fast recognition process in humans below the threshold of conscious awareness (Schulze *et al*, 2011). Implicit recognition is associated with the amygdalohippocampal junction, an important part of the limbic system (Critchley *et al*, 2000). Accumulating evidence points to OT as a particularly important hormone within this system (Insel and Young, 2000).

For facial expressions that may require more time to recognize, the facilitating effects of OT administration may be more likely at later stages of recognition processing. The present meta-analysis demonstrated significant effects on fear faces at the longer exposure duration. We note, however, that the weighted effect size obtained for fear was recovered from only one study. Further studies are therefore required across all of the basic emotions of facial expressions at short and long duration intervals to further gather data on this issue.

There is growing recognition for the need to develop robust markers of response to OT nasal spray, to determine when an individual is likely to respond favorably for

longer-term therapeutic purposes (Guastella and Macleod, 2012). The results here support the view that enhanced capacity for face recognition, especially for happy or fearful faces, may provide a useful marker.

To further improve our understanding of the impact of OT on face recognition, we suggest the following directions for future research and recommendations for implementation:

First, we suggest that future studies need to *assess emotion recognition across all basic emotion expressions*. While studies have primarily focused on happy and angry faces as being representative of the positive and negative facial expressions, there is limited data on effects across all basic emotions. The field has now progressed beyond simple positive *vs* negative single expression comparisons. Future research is required employing stimuli across the range of basic emotions of facial expression.

Second, research is needed to *differentiate and assess both fast and longer exposure latencies*. This meta-analysis suggests that exposure latencies of stimuli influence outcome. Timing (eg, pre-conscious, implicit presentations) of exposure needs to be incorporated into designs. Third, researchers need to *use standardized full-faced photographs from established databases of emotion*. Where the aim is to understand the effects on facial emotion recognition, preference could be given to full-faced photos given these stimuli are well validated for this purpose. Consideration also needs to be given to stimuli brightness and contrast, head size, hair cut and color, skin color and the presence of accessories (Gronenschild and Smeets, 2009). *Fourth, more research is needed to assess mechanisms underlying emotion recognition enhancement of OT*. Evaluation of the influence of OT on identity recognition (Calder and Young, 2005), independent of emotion decoding, is required. Studies could explore how OT influence holistic *vs* featural processing Andari *et al*, 2010, recognition of expression intensity, or authentic *vs* posed expressions. In addition, evaluation of emotion recognition in the context of other more traditional neuropsychological measures is required. Factors such as intelligence, attention, verbal ability, and task-specific motivation have all been associated with facial recognition performance (Marsh and Blair, 2008).

Finally, if these tests are to provide reliable markers of response to oxytocin administration, then *systematic evaluation of dose and response to drug is required*. Almost all of the studies testing emotion recognition in healthy samples have administered the standard dose of 24 IU. Systematic evaluation of how response changes according to dose and other measurable factors that influence bioavailability of nasal administration is required (Guastella *et al*, 2013). These changes should be evaluated in the context of a range of other variables thought to mark response to OT, such as heart rate variability (Kemp *et al*, 2012).

There are a number of limitations to the current meta-analysis. First, behavioral measures of rating each emotion differed across studies. Some studies used a multiple-choice format (Lischke *et al*, 2012; Marsh *et al*, 2010), while others used a cue-response format (Ellenbogen *et al*, 2012; Schulze *et al*, 2011), or ratings on a binary scale (Leknes *et al*, 2012). Second, while the meta-analysis weighted the effect size obtained for fear against other extracted effect sizes according to sample size, as discussed above, the effect size

for fear was based on only one study. As such, further research must be conducted to support this obtained result.

Overall the results of this quantitative synthesis indicate that, from the current available data, the enhancement of emotion recognition by OT is driven by improved perception of fearful and happy facial expressions. Findings also point to the need for further research to corroborate findings in the emotions of disgust and surprise. The results of this quantitative synthesis suggest the potential of OT to be an effective treatment for deficits in the recognition of emotions. Specifically, patients with disorders such as schizophrenia, antisocial disorders, and social anxiety may receive some benefit from the improvement in processing of fear and happy emotions in faces following OT administration. Further, improving one's ability to understand emotion in another's face is likely to facilitate understanding of the intentions, desires, and mental states of others.

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## DISCLOSURE

The authors declare no conflict of interest.

## REFERENCES

- Alvares GA, Hickie IB, Guastella AJ (2010). Acute effects of intranasal oxytocin on subjective and behavioral responses to social rejection. *Exp Clin Psychopharmacol* 18: 316–321.
- Andari E, Duhamel JR, Zalla T, Herbrecht E, Leboyer M, Sirigu A (2010). Promoting social behavior with oxytocin in high-functioning autism spectrum disorders. *Proc Natl Acad Sci USA* 107: 4389–4394.
- Begg C (1994). Publication bias. *The Handbook of Research Synthesis*. Sage Publications.
- Bertrand MC, Sutton H, Achim AM, Malla AK, Lepage M (2007). Social cognitive impairments in first episode psychosis. *Schizophr Res* 95: 124–133.
- Borenstein M, Hedges L, Higgins J, Rothstein H (2005). *Comprehensive Meta-analysis Version 2*. Englewood, NJ: Biostat.
- Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009). *Introduction to Meta-Analysis*. Wiley: New York, NY, USA.
- Calder AJ, Young AW (2005). Understanding the recognition of facial identity and facial expression. *Nat Rev Neurosci* 6: 641–652.
- Calvo MG, Lundqvist D (2008). Facial expressions of emotion (KDEF): identification under different display-duration conditions. *Behav Res Methods* 40(1): 109–115.
- Carton J, Kessler E, Pape C (1999). Nonverbal decoding skills and relationship well-being in adults. *J Nonverbal Behav* 23: 91–100.
- Critchley H, Daly E, Phillips M, Brammer M, Bullmore E, Williams S *et al* (2000). Explicit and implicit neural mechanisms for processing of social information from facial expressions: a functional magnetic resonance imaging study. *Hum Brain Mapp* 9: 93–105.

- Del Cul A, Baillet S, Dehaene S (2007). Brain dynamics underlying the nonlinear threshold for access to consciousness. *PLoS Bio* 5: e260.
- Domes G, Heinrichs M, Gläscher J, Büchel C, Braus DF, Herpertz SC (2007). Oxytocin attenuates amygdala responses to emotional faces regardless of valence. *Biol Psychiatry* 62: 1187–1190.
- Domes G, Sibold M, Schulze L, Lischke A, Herpertz SC, Heinrichs M (2012a). Intranasal oxytocin increases covert attention to positive social cues. *Psychol Med* (e-pub ahead of print).
- Domes G, Steiner A, Porges SW, Heinrichs M (2012b). Oxytocin differentially modulates eye gaze to naturalistic social signals of happiness and anger. *Psychoneuroendocrinology* 12: 00337–X.
- Ebner NC, Riediger M, Lindenberger U (2010). FACES—a database of facial expressions in young, middle-aged, and older women and men: development and validation. *Behav Res Methods* 42: 351–362.
- Ekman P, Friesen W (1976). *The Pictures of Facial Affect Database*. Consulting Psychologists Press: Palo Alto, CA, USA.
- Ekman P, Sorenson ER, Friesen WV (1969). Pan-cultural elements in facial displays of emotion. *Science (New York, NY)* 164: 86–88.
- Elfenbein HA, Ambady N (2002). On the universality and cultural specificity of emotion recognition: a meta-analysis. *Psychol Bull* 128: 203–235.
- Ellenbogen MA, Linnen A, Grumet R, Cardoso C (2012). The acute effects of intranasal oxytocin on automatic and effortful attentional shifting to emotional faces. *Psychophysiology* 49: 128–137.
- Fischer-Shofty M, Shamay-Tsoory SG, Harari H, Levkovitz Y (2010). The effect of intranasal administration of oxytocin on fear recognition. *Neuropsychologia* 48: 179–184.
- Fox E, Lester V, Russo R, Bowles RJ, Pichler A, Dutton K (2000). Facial expressions of emotion: are angry faces detected more efficiently? *Cogn Emot* 14: 61–92.
- Garner M, Baldwin DS, Bradley BP, Mogg K (2009). Impaired identification of fearful faces in generalised social phobia. *J Affect Disord* 115: 460–465.
- Goldman MB, Gomes AM, Carter CS, Lee R (2011). Divergent effects of two different doses of intranasal oxytocin on facial affect discrimination in schizophrenic patients with and without polydipsia. *Psychopharmacology* 216: 101–110.
- Gronenschild E, Smeets F (2009). The use of faces as stimuli in neuroimaging and psychological experiments: a procedure to standardize stimulus features. *Behav Res Methods* 41: 1053–1060.
- Guastella AJ, Einfeld SL, Gray KM, Rinehart NJ, Tonge BJ, Lambert TJ et al (2010). Intranasal oxytocin improves emotion recognition for youth with autism spectrum disorders. *Biol Psychiatry* 67: 692–694.
- Guastella AJ, Hickie IB, McGuinness MM, Otis M, Woods E, Disinger H (2013). Recommendations for the standardisation of oxytocin nasal administration and guidelines for its reporting in human research. *Psychoneuroendocrinology* 38: 612–625.
- Guastella AJ, Howard AL, Dadds MR, Mitchell PB, Carson DS (2009). A randomized controlled trial of intranasal oxytocin as an adjunct to exposure therapy for Social Anxiety Disorder. *Psychoneuroendocrinology* 34: 917–923.
- Guastella AJ, Macleod C (2012). A critical review of the influence of oxytocin nasal spray on social cognition in humans: evidence and future directions. *Horm Behav* 61: 773.
- Hess U, Blairy S, Kleck RE (1997). The intensity of emotional facial expressions and decoding accuracy. *J Nonverbal Behav* 21: 241–257.
- Insel T, Young L (2000). Neuropeptides and the evolution of social behavior. *Curr Opin Neurobiol* 10: 784–789.
- Jesso S, Morlog D, Ross S, Pell MD, Pasternak SH, Mitchell DGV et al (2011). The effects of oxytocin on social cognition and behaviour in frontotemporal dementia. *Brain* 134(Part 9): 2493–2501.
- Kemp AH, Quintana DS, Kuhner RL, Griffiths K, Hickie IB, Guastella AJ (2012). Oxytocin increases heart rate variability in humans at rest: implications for social approach-related motivation and capacity for social engagement. *PLoS One* 7: e44014.
- Kemp AH, Guastella AJ (2011). The role of oxytocin in human affect: a novel hypothesis. *Curr Direct Psychol Sci* 20: 222–231.
- Kirsch P, Esslinger C, Chen Q, Mier D, Lis S, Siddhanti S et al (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. *J Neurosci* 25: 11489–11493.
- Leknes S, Wessberg J, Ellingsen DM, Chelnokova O, Olausson H, Laeng B (2012). Oxytocin enhances pupil dilation and sensitivity to ‘hidden’ emotional expressions. *Soc Cogn Affect Neurosci* (e-pub ahead of print).
- Leppänen JM, Hietanen JK (2004). Positive facial expressions are recognized faster than negative facial expressions, but why? *Psychol Res* 69: 22–29.
- Lischke A, Berger C, Prehn K, Heinrichs M, Herpertz S. C., Domes G. (2012). Intranasal oxytocin enhances emotion recognition from dynamic facial expressions and leaves eye-gaze unaffected. *Psychoneuroendocrinology* 37: 475–481.
- Losh M, Adolphs R, Poe MD, Couture S, Penn D, Baranek GT et al (2009). Neuropsychological profile of autism and the broad autism phenotype. *Archiv Gen Psychiatry* 66: 518–26.
- Macdonald K, Macdonald TM (2010). The peptide that binds: a systematic review of oxytocin and its prosocial effects in humans. *Harvard Review Psychiatry* 18: 1–21.
- Marsh AA, Kozak MN, Ambady N (2007). Accurate identification of fear facial expressions predicts prosocial behavior. *Emotion* 7: 239–251.
- Marsh AA, RJR Blair (2008). Deficits in facial affect recognition among antisocial populations: a meta-analysis. *Neurosci Biobehav Rev* 32: 454–465.
- Marsh AA, Yu HH, Pine DS, Blair RJR (2010). Oxytocin improves specific recognition of positive facial expressions. *Psychopharmacology* 209: 225–332.
- McClure EB, Nowicki S (2001). Associations between social anxiety and nonverbal processing skill in preadolescent boys and girls. *J Nonverbal Behav* 25: 3–19.
- Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF (2000). Improving the quality of reports of meta-analyses of randomised controlled trials: The QUOROM Statement. *Onkologie* 23: 597–602.
- Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *PLoS Clin Trials* 6: e1000097.
- Schulze L, Lischke A, Greif J, Herpertz SC, Heinrichs M, Domes G (2011). Oxytocin increases recognition of masked emotional faces. *Psychoneuroendocrinology* 36: 1378–1382.
- Shultz S, Dunbar RI (2012). The social brain hypothesis: an evolutionary perspective on the neurobiology of social behavior. In: Richmond SRees GEdwards S (eds.) *I Know What You're Thinking: Brain Imaging and Mental Privacy*. Oxford University Press.
- Theodoridou A, Rowe AC, Penton-Voak IS, Rogers PJ (2009). Oxytocin and social perception: oxytocin increases perceived facial trustworthiness and attractiveness. *Horm Behav* 56: 128–132.
- Van IJendoorn MH, Bakermans-Kranenburg MJ (2012). A sniff of trust: meta-analysis of the effects of intranasal oxytocin administration on face recognition, trust to in-group, and trust to out-group. *Psychoneuroendocrinology* 37: 438–443.