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SHORT COMMUNICATION

Oxytocin differentially modulates eye gaze to naturalistic social signals of happiness and anger

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Summary A number of previous studies has shown that oxytocin (OT) promotes facial emotion recognition and enhances eye gaze to facial stimuli in humans. Other studies report valence-specific effects of OT, supporting the proposed prosocial role of OT in social interactions. In the present study, we tested the hypothesis whether OT might selectively enhance eye gaze to positive, approach-related, but not to negative, threat-related social cues. In a placebo-controlled, double-blind, between-subject design, we assessed the effects of intranasal OT administration (24 IU) in 62 healthy male volunteers on eye gaze toward the eyes of neutral, positive (happy) and negative (angry) facial expressions compared with placebo. In order to capture the dynamics of facial expressions, we used video sequences showing neutral faces gradually displaying a specific emotion. In line with previous studies, OT increased eye gaze toward neutral facial expressions. Moreover, under OT treatment, eye gaze remained increased when the face showed a happy facial expression, but in contrast decreased when the face displayed an angry expression. These results support the notion that OT differentially modulates visual attention toward social signals of positive approach and threat and thereby contributes to the modulation of non-verbal interpersonal communication.

1. Introduction

The ability to infer the emotions of others from their facial expressions is critical for functional reciprocal social interactions in humans (Adolphs, 2002). Face perception and facial emotion recognition depends on visual attention to relevant facial features. Eyetracking studies have revealed that healthy adults devote the majority of their overt attention to the eye region during face processing (e.g. Sullivan et al., 2007). Thus, time spent looking at the eyes might indicate social approach and social information processing, depending on how unambiguous the emotional expression appears. Eye gaze to ambiguous faces is initiated to extract social information from the most informative part of the face. As the emotional facial expression becomes more and more obvious, eye gaze might have a different function, regulating the social interaction in terms of approach and avoidance.

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Numerous animal studies have shown that the neuropeptide oxytocin (OT) is involved in the regulation of complex social behavior. OT receptors are distributed in various brain regions including the amygdala, hippocampus, and paraventricular nucleus of the hypothalamus, regions associated with the central regulation of social behaviors (Carter, 1998; Donaldson and Young, 2008). Recent studies report similar effects of OT on human social behavior including interpersonal trust, positive communication, social support, and attachment (Heinrichs et al., 2009). OT improves the ability to infer the mental states of others from subtle social cues (Domes et al., 2007; Schulze et al., 2011) and dynamic facial expressions (Lischke et al., 2012) and increases gaze toward the eyes of neutral faces (Guastella et al., 2008) and briefly presented emotional faces (Gamer et al., 2010). OT modulates brain activity in areas associated with social cognition and thus appears to be an important neuromodulator for interpersonal perception and communication in humans (for reviews, see Ebstein et al., 2010; Meyer-Lindenberg et al., 2011).

In addition, there is some evidence for selectively prosocial effects of OT, since OT specifically enhances the processing of positive social information such as the recognition of happy faces (Di Simplicio et al., 2009; Marsh et al., 2010; Schulze et al., 2011). Since previous studies have demonstrated that visual attention is sensitive to OT treatment, these prosocial effects could be due to specific modulations of visual attention toward positive social cues. However, in a recent study we were not able to demonstrate OT effects on visual scanning to morphed emotional faces (Lischke et al., 2012), a finding probably related to the low ecological validity of the stimuli.

In the present study, we aimed to investigate how OT might modulate visual attention during the viewing of naturalistic dynamic human faces expressing different emotions. We hypothesized that OT given intranasally would enhance visual attention toward the eyes of neutral facial stimuli. In response to obvious emotional stimuli, we expected OT to promote eye gaze to happy faces and decrease eye gaze to angry faces, which would be in accordance to the social regulation hypothesis introduced above.

2. Materials and methods

2.1. Participants

Sixty-two healthy male volunteers (age, mean $\pm$ SD: 24.0 $\pm$ 2.5 years) participated in the present study and were divided in two groups which did not differ in age (mean $\pm$ s.d.: OT: 23.9 $\pm$ 0.4; PL: 24.4 $\pm$ 0.5; $t_{60} = 0.47$; $p = .50$). Exclusion criteria were medical or psychiatric illness, use of medication, substance abuse, and smoking. Psychology students were also excluded. All participants had normal or corrected to normal vision. The study protocol was approved by the institutional review board and all subjects gave written informed consent and were paid for participation.

2.2. Experimental protocol

In a double-blind, placebo-controlled study design, subjects were randomly assigned either to receive 24 IU of OT ($n = 30$, 6 puffs of Syntocinon-Spray; Novartis, Basel, Switzerland) or placebo ($n = 32$) intranasally 40 min before beginning the Dynamic Affect Recognition Evaluation, with the placebo including all ingredients except for the neuropeptide.

2.3. Dynamic Affect Recognition Evaluation (DARE)

The original version of the Dynamic Affect Recognition Evaluation (DARE), which was developed to serve as a naturalistic yet standardized tool for assessing facial emotion recognition (Porges et al., 2007) uses the Cohn–Kanade database of facial expressions (Cohn et al., 1999; Kanade et al., 2000). The original DARE is described in detail elsewhere (Bal et al., 2010). The version employed in the present study consisted of 12 video sequences presenting facial expressions of different male and female actors. Each trial began with a neutral facial expression that slowly changed into one of two basic emotions (happiness or anger) over time. Trial duration ranged from 16 to 34 s. Participants were asked to detect the emotion of the particular face presented as soon as possible. The percentage of correct answers and the response latency for each emotion were calculated.

2.4. Eye movement recordings and analysis

To assess visual attention, we recorded eye movements with a remote infra-red eyetracker (iView X^{TM} RED, SensoMotoric Instruments, Teltow, Germany). Eye movements were recorded at 50 Hz sampling rate with a spatial resolution of $<0.1^{\circ}$ for tracking resolution and $<0.5^{\circ}$ for gaze position accuracy. The DARE stimuli (640 $\times$ 480 pixels) were presented on a 17 in. screen (resolution: 1280 $\times$ 1024 pixels) with a viewing distance of 60 cm. Fixations were coded for a minimum gaze duration of 80 ms within a sphere of approx. 1° visual angle (approx. 28 pixels). The mean number of fixations and the mean fixation time were calculated for the whole face and the eye region of the facial stimuli using stimulus-specific templates. In order to test for specific effects induced by the emotional expression, we divided the whole trial into an early exploratory phase showing the neutral expression (the first 2 s of a trial), and the late emotion recognition phase before a decision about the emotion displayed was made (the last 2 s before button press of a trial). For each individual trial presented, the relative fixation duration for the eye region compared to the whole face for each processing phase was calculated.

2.5. Statistical analyses

In order to explicitly test for the proposed interaction effects, eyetracking data were analyzed using a three-way ANOVA [substance (OT, PL) $\times$ emotion (happy, angry) $\times$ phase (early, late)] and subsequent two-way ANOVAs for each phase (early and late) for both the percentage of time and the number of fixations spent on the eye region relative to the whole face.

Performance in recognizing angry and happy facial expressions was tested using MANOVA for the number of correct responses and the response latency, i.e. the percentage of time elapsed before the button was pressed relative to the

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length of the whole video clip. In case of a significant overall effect, follow-up pair-wise tests were performed.

Statistical analyses were performed with PASW (Version 18.0 for Windows). Statistical significance was set at $p < .05$.

3. Results

3.1. Eye-tracking data

A 2 × 2 × 2 ANOVA on the percentage of time of fixations on the eye region revealed significant main effects of emotion ($F_{1,60} = 36.72$; $p < .001$) and phase ($F_{1,60} = 28.81$; $p < .001$), and 2-way interactions of emotion and substance ($F_{1,60} = 6.22$; $p = .015$) and phase and substance ($F_{1,60} = 15.46$; $p < .001$). In addition, the analysis showed a marginally significant 3-way interaction ($F_{1,60} = 3.73$; $p = .058$) (Fig. 1). The analysis for percentage of the number of fixations revealed similar results: we found main effects of emotion ($F_{1,60} = 14.06$; $p < .001$) and phase ($F_{1,60} = 48.86$; $p < .001$), 2-way interactions of emotion and substance ($F_{1,60} = 7.38$; $p = .009$) and phase and substance ($F_{1,60} = 20.75$; $p < .001$), and a significant 3-way interaction ($F_{1,60} = 4.07$; $p = .048$). Due to the comparable pattern of results, we restricted the follow-up analyses to the time of fixations.

Early exploration phase: A subsequent 2 × 2 ANOVA [substance (OT, PL) × emotion (happy, angry)] for the early exploration phase revealed a significant main effect of substance indicating that subjects who received OT gazed significantly longer ($F_{1,60} = 6.58$; $p = .013$) toward the eyes regardless of the subsequent valence of the facial expression (Fig. 1, upper panel). There was no significant substance × emotion interaction in the early exploration phase ($F_{1,60} = .54$, $p = .47$). Follow-up *t*-tests revealed that during the early exploration phase, the OT group showed a significantly longer fixation time toward the eye region toward both subsequently happy and subsequently angry facial expressions (mean percent ± SD; happy: OT: 54 ± 24; PL: 38 ± 23; $t_{60} = 2.64$; $p = .010$; angry: OT: 66 ± 18; PL: 54 ± 27; $t_{60} = 2.08$; $p = .042$) (Fig. 1, upper panel).

Emotion recognition phase: Results of the 2 × 2 ANOVA for the late emotion recognition phase revealed a significant substance × emotion interaction for fixation duration toward the eyes ($F_{1,59} = 8.08$; $p = .006$); no significant main effect of substance was found ($F_{1,59} = .04$; $p = .85$). Subsequent *t*-tests showed a differential effect of OT for happy vs. angry faces. The OT group still showed a trend toward enhanced eye gaze while recognizing happy facial expressions (mean ± SD: OT: 44 ± 21; PL: 34 ± 20; $t_{60} = 1.84$; $p = .070$), whereas this effect reversed during recognition of angry expressions (mean ± SD: OT: 46 ± 26; PL: 53 ± 24; $t_{59} = -1.21$; $p = .23$) (Fig. 1, lower panel).

3.2. Affect recognition task

Oxytocin did not improve overall emotion recognition accuracy ($F_{2,59} = 0.20$; $p = .82$) and no main effect of group was found with respect to recognition accuracy for either of the basic emotions (anger: $F_{1,60} = 0.39$; $p = .54$; happiness:

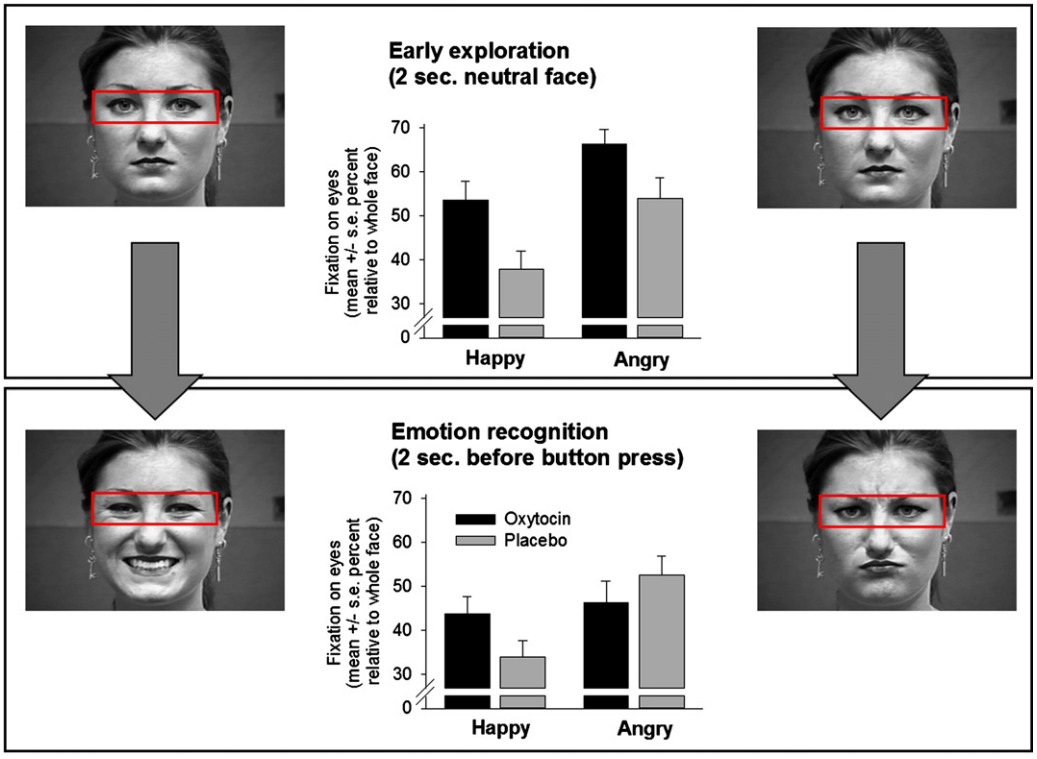

Figure 1 In the early exploration phase, 24 IU of intranasal oxytocin increased gaze duration toward the eyes for both subsequently happy ($t_{60} = 2.64$; $p = .010$; two-sided) and subsequently angry faces ($t_{60} = 2.04$; $p = .042$; two-sided) compared to placebo (upper panel). In the late emotion recognition phase, there was still a trend toward increased eye gaze under oxytocin to happy faces ($t_{60} = 1.84$; $p = .07$; two-sided) but not to angry faces ($t_{60} = -1.21$; $p = .23$; two-sided). Pictures were taken from the Cohn–Kanade database for illustration (Kanade et al., 2000).

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$F_{1,60} = 0.004$; $p = .95$). The MANOVA for response latencies showed an overall main effect of OT ($F_{2,59} = 3.72$; $p = .030$), which was mainly driven by increased response time in the OT group to happy faces ($F_{1,60} = 6.553$; $p = .013$), whereas the univariate effect for angry faces was not significant ($F_{1,60} = 0.093$; $p = .761$).

4. Discussion

In the present study we investigated whether intranasal OT enhances emotion recognition from dynamic naturalistic facial stimuli and influences visual attention toward the eye region of these stimuli. We show a substantial influence of a single dose of intranasal OT on visual attention toward the eye region of neutral and emotional facial expressions. In line with previous studies, which used static pictures of neutral faces or very short presentations of emotional expressions (Gamer et al., 2010; Guastella et al., 2008), OT increased eye gaze during exploration of ambiguous neutral faces in the present study. More importantly, as the facial expression slowly developed an increasingly unambiguous emotional expression, OT differentially modulated eye gaze: OT preserved increased eye gaze to positive social signals (happy faces), and in contrast, it decreased eye gaze to negative social signals (angry faces) — relative to the exploration phase. OT had no effect on emotion recognition accuracy, but seemed to slightly slow down responses to happy facial expressions, which might reflect enhanced engagement in processing positive social signals.

Whereas a previous study showed that OT can enhance reflexive saccades toward the eye region of very briefly presented emotional faces regardless of valence (Gamer et al., 2010), our results seem to reflect a modulation of visual attention depending on the social signal communicated by the presented expression when the stimulus is evaluated for an extended duration. The differential effect of OT on eye gaze for happy vs. angry faces suggests that OT promotes visual attention to signals of positive social approach and thereby might help to regulate the individual's own social interaction behavior. In particular, OT might contribute to the regulation of social interactions by promoting social proximity via increased eye contact with potentially approaching others (displaying positive facial expressions), and by reducing social proximity via decreased eye contact with potentially threatening others (displaying negative facial expressions). In addition, it is also possible that this modulation is influenced by the differential salience of the eye region in positive and negative facial expressions. The observed effect seems to depend on the ecological validity of the stimuli presented, since the modulatory effect was not detected in a previous study using more artificially morphed facial expressions (Lischke et al., 2012). In order to further investigate the role of oxytocin in human social approach and avoidance, future studies could use paradigms specifically tailored to assess approach and avoidance on a behavioral level (cf. Derntl et al., 2011).

Accumulating evidence suggests a crucial role for the amygdala and its cortical and subcortical projections in the mediation of these behavioral effects (for a review, see Meyer-Lindenberg et al., 2011). In particular, a recent study reported differential neural effects of OT in the amygdala during processing of happy versus fearful facial expressions, suggesting that OT differentially modulates the neural circuitry involved in focused attention toward positive vs. negative social signals (Gamer et al., 2010).

In sum, the present results — together with previous studies summarized above — suggest that OT might not only play a role in the understanding of others' emotional states by enhancing emotion recognition, but also contribute to the regulation of social interactions by shaping non-verbal communication on the level of subtle changes in eye contact. Future studies could use even more naturalistic settings to further investigate how OT contributes to the regulation of interpersonal communication in the context of positive and negative social interactions.

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Conflict of interest

The authors declare no conflict of interest.

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