

Effects of intranasal oxytocin on pupil dilation indicate increased salience of socioaffective stimuli

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Abstract

To investigate the mechanisms by which oxytocin improves socioaffective processing, we measured behavioral and pupillometric data during a dynamic facial emotion recognition task. In a double-blind between-subjects design, 47 men received either 24 IU intranasal oxytocin (OXT) or a placebo (PLC). Participants in the OXT group recognized all facial expressions at lower intensity levels than did participants in the PLC group. Improved performance was accompanied by increased task-related pupil dilation, indicating an increased recruitment of attentional resources. We also found increased pupil dilation during the processing of female compared with male faces. This gender-specific stimulus effect diminished in the OXT group, in which pupil size specifically increased for male faces. Results suggest that improved emotion recognition after OXT treatment might be due to an intensified processing of stimuli that usually do not recruit much attention.

Descriptors: Pupillary responses, Oxytocin, Facial emotion recognition, Gender, Social cognition

The neuropeptide oxytocin (OXT) has been found to play a key role in the regulation of social behavior (Bartz, Zaki, Bolger, & Ochsner, 2011; Guastella & Macleod, 2012; Heinrichs, von Dawans, & Domes, 2009; Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011). OXT is synthesized in the hypothalamus and released into both the brain and the bloodstream. Apart from its well-known functions in reproduction, such as stimulating uterine contraction during labor and milk ejection, OXT also acts as a neuromodulator with receptors widely distributed in the brain including the limbic-hypothalamic system, midbrain regions, and the brain stem (Landgraf & Neumann, 2004). Since neuropeptides cross the blood-brain barrier after intranasal administration (Born et al., 2002), a number of studies has been conducted in humans demonstrating, for instance, that OXT promotes prosocial behavior, affiliation, and trust (e.g., Baumgartner, Heinrichs, Vonlanthen,

Fischbacher, & Fehr, 2008; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), improves social cognition and memory (e.g., Guastella, Mitchell, & Mathews, 2008; Rimmele, Hediger, Heinrichs, & Klaver, 2009; Unkelbach, Guastella, & Forgas, 2008), as well as reduces social stress and anxiety (e.g., Heinrichs, Baumgartner, Kirschbaum, & Ehler, 2003; Linnen, Ellenbogen, Cardoso, & Joover, 2011).

In studies specifically investigating effects of OXT on socioaffective information processing, intranasally administered OXT has been consistently found to improve the ability to decode the mental and affective state of others from facial expressions (Di Simplicio, Massey-Chase, Cowen, & Harmer, 2009; Domes, Heinrichs, Michel, Berger, & Herpertz, 2007; Domes et al., 2012; Fischer-Shofty, Shamay-Tsoory, Harari, & Levkovitz, 2010; Guastella et al., 2010; Lischke, Berger et al., 2012; Marsh, Yu, Pine, & Blair, 2010; Schulze et al., 2011). It has been argued that improved emotion recognition might be due to an enhanced exploration of the eye region and that OXT improves emotion recognition by directing attention preferentially to the eyes of a face (Andari et al., 2010; Domes, Steiner, Porges, & Heinrichs, 2012; Gamer, Zurowski, & Büchel, 2010; Guastella et al., 2010; Guastella, Mitchell, & Dadds, 2008). Directly investigating this hypothesis using eye-tracking and a dynamic facial emotion recognition task, Lischke, Gamer et al. (2012) recently replicated the effect of enhanced emotion recognition performance, but did not find any oxytocin-induced alterations with regard to the visual scanning of the faces.

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In the present study, we aimed at further investigating the mechanisms by which OXT might improve the exploration and recognition of socioaffective stimuli by analyzing pupillometric data during the same dynamic facial emotion recognition task. Pupillometric data, such as pupil diameter, can be used as a sensitive and reliable indicator for cognitive resource allocation.

Pupil diameter is controlled by two muscles innervated by the sympathetic and parasympathetic branches of the autonomic nervous system, which get their input from brain structures essential to both affective and cognitive information processing (Granholm & Steinhauer, 2004). Increased sympathetic activity increases the activity of the “dilator muscle,” leading to pupil dilation, whereas decreased parasympathetic activity decreases the activity of the “sphincter muscle,” which also results in pupil dilation. However, as shown by Steinhauer, Siegle, Condray, and Pless (2004), pupil dilation in response to task difficulty specifically occurs as a result of reduced parasympathetic activity innervated by the locus coeruleus (for a more detailed description of the neural basis of pupillary responses, see also Hoeks & Ellenbroek, 1993, or Steinhauer & Hakerem, 1992).

While *tonic changes* in pupil diameter reflect the sensitivity of the cognitive system in general (“exploration mode,” see Aston-Jones & Cohen, 2005; van der Meer et al., 2010), *phasic changes* have been proven to indicate a stimulus-specific and task-related processing load, with larger pupil dilations, reflecting greater processing demands (Beatty, 1982; Loewenfeld, 1993; Steinhauer & Hakerem, 1992). Using a digit span recall task, Kahnemann and Beatty (1966), for instance, demonstrated that pupil diameter proportionally increases as a function of the number of digits that have to be maintained in short-term memory. Pupil diameter increases until individuals reach their limit of cognitive resources available (i.e., until their memory capacity of 7 ± 2 digits; Granholm, Asarnow, Sarkin, & Dykes, 1996). Notably, Just, Carpenter, and Miyake (2003) have demonstrated that pupillary responses reflect an overall aggregate of attentional resource allocation that is not limited to a specific part of the cognitive system. Peak dilation has been found to increase with enhanced processing demand in studies investigating a variety of tasks comprising language comprehension (e.g., Hyönä, Tammola, & Alaja, 1995; Just & Carpenter, 1993), auditory and visual attention (e.g., Karatekin, Couperus, & Marcus, 2004; Kim, Beversdorf, & Heilman, 2000), reasoning and semantic elaboration (e.g., van der Meer, Friedrich, Nuthmann, Stelzel, & Kuchinke, 2003; van der Meer et al., 2010), or emotional valence identification (e.g., Prehn et al., 2008; Prehn, Heekeren, & van der Meer, 2011; Siegle, Granholm, Ingram, & Matt, 2001; Siegle, Steinhauer, Carter, Ramel, & Thase, 2003). With regard to the processing of visual stimuli with emotional content, very early pupillometric studies have shown an increase in pupil size when people view pleasant and attention-getting pictures, such as a picture of a baby, a mother holding her child, or a partially nude man or woman, compared with a neutral landscape (Hess & Polt, 1960). Later studies further showed that pupil size covaries with emotional arousal rather than with the hedonic valence of the pictures (i.e., regardless of whether the pictures were pleasant or unpleasant; see Bradley, Miccoli, Escrig, & Lang, 2008). Recently, Leknes et al. (2012) provided first evidence that OXT treatment leads to greater stimulus-induced pupil dilation during the identification of subtle and hidden emotional expressions. In that study, participants with lower emotional sensitivity and poorer baseline performance showed greater oxytocin-induced improvement in addition to larger task-related pupil dilations.

In summary, pupillometric studies support the view that pupil size represents a general index of attentional resource allocation and reflects whether stimuli are cognitively engaging or emotionally significant. Following these results and a first study on the effects of OXT on task-related pupillary responses during the processing of emotional faces, we hypothesized that improved emotion recognition after OXT administration is accompanied by an increased recruitment of attentional resources (greater “mental work”) indicated by increased pupil dilation. Given that male and female face stimuli are differently appealing for men, we further expected that OXT would affect pupil dilations differentially during the processing of male compared with female faces.

Method

Participants

In a double-blind, placebo-controlled, between-subjects design, 47 healthy men were randomly assigned to receive a nasal spray containing either 24 international units (IU)¹ of OXT ($n = 23$; Syntocinon Spray, Novartis, Basel, Switzerland) or placebo (PLC; $n = 24$) containing all ingredients except for the neuropeptide. All participants were healthy (i.e., they had no current or previous neurological, endocrinological, or psychiatric disease), nonsmokers, and did not take any medication that could influence the pupillary response. Participants reported no ophthalmologic problems other than correctable eyesight.

Groups did not differ with regard to age, $F(1,45) = 0.35, p = .56$ (OXT: $M = 25.78, SD = 3.37$; PLC: $M = 26.38, SD = 3.49$). To control for individual differences in general intelligence, psychopathology, emotion processing, empathy, and alexithymia, participants completed a test battery including Vocabulary Test (WST; Schmidt & Metzler, 1992), Symptom Checklist (SCL-90-R; Franke, 1995), State-Trait Anxiety Inventory (STAI-T; Laux, Glanzmann, Schaffner, & Spielberger, 1981), State-Trait Anger Expression Inventory (STAXI-T; Spielberger, 1991), Positive and Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988), The Twenty-Item Toronto Alexithymia Scale (TAS-20; Bagby, Taylor, & Parker, 1994), and Interpersonal Reactivity Index (IRI, Davis, 1983). No psychometric measure revealed any difference between the two groups of participants (all $ps \geq .11$).

The study was carried out in accordance with the Declaration of Helsinki and was approved by a local ethics committee. All participants gave written informed consent prior to investigation and received payment for participation.

Task and Stimulus Material

To investigate the mechanisms by which OXT might improve the exploration and recognition of socioaffective stimuli, we used a dynamic facial emotion recognition task (Domes et al., 2008; Lischke, Berger et al., 2012). In this task, participants looked at male and female faces gradually and continuously changing from neutral to happy, angry, sad, or fearful expressions. For this task, we selected four pictures of six young male and six young female faces, showing a neutral, happy, angry, sad, and fearful emotion expression from the FACES database (Ebner, Riediger, & Lindenberger, 2010). The colored pictures were converted into grayscale images, equalized in size and cumulative brightness using Adobe Photoshop CS4 (Adobe Systems Inc., CA) and

1. 24 IU equates to about 48 μg of the pure peptide.

MATLAB R2011b (The MathWorks Inc., MA). Then, each image was enclosed within an elliptic mask (411×570 pixels) that showed only the face itself. Finally, we used Winmorph 3.01 (www.debugmode.com/winnormorph) to transform the neutral expressions into all of the emotional ones in 5% steps. This procedure resulted in 48 sets of pictures: 12 (6 male and 6 female) faces \times 4 emotions, each containing 21 pictures with increasing emotion intensity from 0% (neutral) to 100% (emotion).

Each trial of the dynamic facial emotion recognition task started with a black fixation cross appearing for 1 s on a dark gray background (*baseline phase*). Then, the pictures of a set were presented starting with 0% intensity and increasing up to 100% in 5% steps (*emotion recognition phase*). Each image was presented for 0.8 s. Participants were instructed to press a stop button as soon as they recognized the expression the face was beginning to show. Subsequently, participants identified the emotional expression by making a forced choice between four emotion labels (happy, angry, sad, and fearful; *forced-choice phase*). For the choice of the emotion label, no time limit was given.

In total, the experiment contained 48 trials divided into eight conditions (male happy, male anger, male sad, male fearful, female happy, female anger, female sad, female fearful) with six trials each. For each trial, we determined, as indicators of emotion recognition performance, (a) the emotion intensity of the particular picture (0 to 100% in 5% steps) during which the consecutive presentation of the 21 pictures was stopped by the participant, and (b) the emotion label chosen. In trials in which the correct emotion label was chosen, the intensity level indicated the recognition threshold necessary for correctly identifying the emotional expression. For example, a participant could discontinue the presentation of pictures by pressing the stop button during the presentation of picture number 5 of 21 (= 20% happiness), because he or she was recognizing at picture number 5 that the face was beginning to show a happy expression.

Experimental Procedure

Following a standardized protocol (Domes, Heinrichs, Gläscher et al., 2007; Domes, Heinrichs, Michel et al., 2007; Domes et al., 2010), participants self-administered the nasal spray (three puffs per nostril, each containing 4 IU of OXT or PLC) 45 min before the start of the experiment (Born et al., 2002). Self-report after the experiment revealed that participants were not able to discriminate whether they had received OXT or the PLC. Participants also did not report any side effects following drug administration.

As a manipulation check and to potentially identify participants with attenuated OXT resorption, we inserted a venous catheter into the participants' forearm directly after arrival at the laboratory and 30 min before drug application. Blood samples were collected 5 min before and 45 min after substance administration (i.e., directly before the start of the experiment). Immediately after collection, the samples were cooled in ice-chilled water at 4°C, 15 min later centrifuged at 4,000 rpm (for 5 min at 4°C) and finally stored in a freezer at -20°C. After completion of the study, the plasma was shipped on dry ice at -20°C to the Department of Behavioral and Molecular Neuroendocrinology at the University of Regensburg, Germany, where they were extracted and analyzed using a radioimmunoassay (Landgraf, 1981). The assay detection limit was 0.1 pg/sample, and cross-reactivity with other related neuropeptides was < 0.7%. The coefficient of variation for intra-assay precision was 7% to 10%, whereas interassay variation was eliminated by measuring all samples within the same assay.

The experimental session took place in a quiet and slightly dimmed room. Participants were seated comfortably in front of a 20" computer screen (screen size: 30.6 cm \times 40.8 cm; resolution 1,024 \times 768 pixels) at a distance of 55 cm. Picture stimuli were presented in a randomized order using the experimental control software Presentation (Neurobehavioral Systems, Inc., Albany, CA) running on a Microsoft Windows operating system.

As introduced earlier, we measured the intensity levels at which emotional expressions were recognized correctly, error rates, and pupillary responses. In this study, we also recorded eye movements in addition to pupil data. Since the current report specifically focuses on an effect of OXT on pupillary responses, eye tracking data are reported elsewhere (Lischke, Berger et al., 2012).

Pupil Data Acquisition, Cleaning, and Reduction

Pupillary responses as an indicator for attentional resource allocation were continuously recorded using the ViewPoint system (PC-60 Head Fixed, Arrington Research Inc., AZ), including an infrared light source and a video camera sensitive to infrared light. This system was connected to a Presentation computer for transmission of trigger signals marking the beginning of every trial. The participants' head was placed onto a chin rest above which the camera was positioned so that the right eye of the participant could be tracked continuously during the viewing of the picture stimuli. During a trial, participants were asked not to move their head, to maintain fixation, and to restrict eye blinks if possible until the forced-choice phase at the end of the trial.

Pupil size was recorded at 59.5 Hz (i.e., every 17 ms). The ViewPoint system samples pupil diameter in terms of pixels normalized with respect to the width of the camera window. To relate this measure to absolute pupil size, we recorded the size of a black circle of exactly 5 mm in diameter placed on the closed lid of each participant's right eye before the start of the experiment. This calibration procedure made it possible to control for differences in focal length across participants and to convert pupil diameter from pixels to millimeters. Pupil diameter was assessed by the ViewPoint system with an accuracy of 0.03 mm.

Pupillary responses were analyzed only for correctly answered trials. Cleaning and reduction of the pupil data were conducted with MATLAB R2011b (The MathWorks Inc., MA) following standard procedures (Beatty & Lucero-Wagoner, 2000; Granholm et al., 1996; Prehn et al., 2008, 2011; Verney, Granholm, & Dionisio, 2001). Data were smoothed using an unweighted 20-point moving average filter. Blinks, defined as large changes in pupil diameter occurring too rapidly to signify actual pupil dilation or constriction, were replaced by linear interpolation. We determined the baseline pupil diameter for each trial by averaging pupil diameter 0.2 s before presentation of the first picture. This baseline was subtracted from the respective trial (baseline correction). Finally, stimulus-locked pupillary responses for each trial were averaged for each condition and participant.

In our experimental task, in which we presented bright faces on a darker background in a slightly dimmed laboratory, we observed an immediate constriction of the pupil at the beginning of each trial, that is, with the presentation of the first picture stimulus of a set of faces. After 0.8 s, pupil diameter increased again over the course of the trial and with the presentation of the subsequent pictures of the set (see Bradley et al., 2008).

As stated earlier, trials were of variable duration: Each trial ended as soon as the participant recognized the emotional expression and pressed the stop button. On average (across all conditions

and both groups), a trial ended after 7.07 s (range: 1.52–17.76 s; 5th percentile: 3.20 s). To have enough data (i.e., trials) for averaging, we only averaged pupillary responses across a time window (interval of interest) between 0.8 and 3.2 s after the presentation of the first picture of a set of faces, in which at least 95% of trials were included.

When measuring pupillary responses as an index for cognitive and emotional processing, it is important to rule out that changes in pupil diameter were due to changes in lighting conditions (i.e., differences in either illumination of the room or luminance of the stimuli). Therefore, we kept illumination in the laboratory constant for all sessions and compared the cumulative brightness of the pictures between the conditions ensuring that luminance of the picture stimuli did not differ systematically between male and female faces, $F(1,10) = 0.23$, $p = .64$, nor between the different emotional expressions, $F(1.65,16.53) = 0.096$, $p = .88$.

Statistical Analyses

All statistical analyses were performed using SPSS 20 (IBM SPSS, Inc., IL). In particular, we tested whether OXT application had an effect on emotion recognition performance (intensity levels at which emotional expressions were identified correctly and error rates) and pupillary responses (average pupil diameter). Moreover, we investigated effects of emotion category (i.e., whether a happy, angry, sad, or fearful emotion expression appeared) and the gender of the face stimuli (i.e., whether a male or female face was presented). All analyses on intensity levels, error rates, and pupillary responses were conducted with means obtained for each participant and condition. As stated earlier, our design contained eight conditions in total (male happy, male anger, male sad, male fearful, female happy, female anger, female sad, female fearful) with six trials each. Because error trials were excluded prior to the analysis, mean intensity levels and mean pupillary responses for each participant and condition were based on approximately 5.5 trials ($M = 5.46$, $SD = 0.31$).

Repeated measures analyses of variance (ANOVAs) with the factors group (OXT vs. PLC group), emotion category (happy, angry, sad, vs. fearful expressions), and gender of the face stimuli (male vs. female faces) were conducted for each dependent variable. In case of a significant main effect of group, we further calculated exploratory simple effects analyses in order to test for

potential differences within and between the groups with regard to the processing of the four emotional expressions as well as for male and female faces. For significant main and simple effects, we report η_p^2 (partial eta squared). All within-subjects effects were Greenhouse-Geisser corrected whenever the assumption of sphericity was violated ($\epsilon < 1.0$). In those cases, we also report corrected degrees of freedom.

Results

Effect of Intranasal OXT Administration on Peripheral OXT Levels

To test whether participants in the OXT and PLC group differed in peripheral OXT levels before and after substance application, a two-way repeated measures ANOVA (Group \times Time) was conducted. This analysis revealed a significant Group \times Time interaction, $F(1,45) = 26.94$, $p < .001$, $\eta_p^2 = 0.37$, indicating a significant increase in peripheral OXT level (in pg/ml) in the OXT (pre: $M = 24.6$, $SD = 19.0$; post: $M = 39.7$, $SD = 20.1$), but not in the PLC group (pre: $M = 27.2$, $SD = 16.6$; post: $M = 19.1$, $SD = 14.41$) over the time course of substance application.

Behavioral Data

Intensity levels. A three-way repeated measures ANOVA (Group \times Emotion \times Gender) on intensity levels revealed that the application of OXT in general decreased the levels at which the emotional expressions were recognized correctly, $F(1,45) = 4.94$, $p = .031$, $\eta_p^2 = 0.10$ (main effect of group), regardless of the particular type of emotion and whether the face was male or female. That is, we found no Group \times Emotion interaction, $F(3,135) = 1.24$, $p = .299$, and no Group \times Gender interaction, $F(1,45) = 0.01$, $p = .919$. There was a main effect of emotion, $F(3,135) = 75.04$, $p < .001$, $\eta_p^2 = 0.63$, but no main effect of gender, $F(1,45) = 1.80$, $p = .19$. The main effect of emotion indicated that the different emotional expressions were recognized at different intensity levels: All participants recognized happy expressions at low, angry and fearful expressions at intermediate, and sad expressions at high intensity levels (see Table 1 and Figure 1A).

Since we aimed at investigating whether OXT influences the processing of the four emotional expressions differentially, we

Table 1. Mean Intensity Levels and Standard Errors at Which Emotional Expressions Were Recognized Correctly and Mean Error Rates for the Placebo and Oxytocin Group

	Intensity levels Mean (SE)		Error rates Mean (SE)	
	Placebo ($n = 24$)	Oxytocin ($n = 23$)	Placebo ($n = 24$)	Oxytocin ($n = 23$)
Happy expressions				
Male	36.53 (1.64)	32.83 (1.45)	0.00 (0.00)	0.00 (0.00)
Female	34.43 (1.99)	30.99 (1.62)	0.01 (0.01)	0.02 (0.01)
Angry expressions				
Male	43.56 (2.37)	36.84 (1.96)	0.07 (0.02)	0.05 (0.02)
Female	44.22 (2.21)	35.40 (2.36)	0.10 (0.03)	0.16 (0.04)
Sad expressions				
Male	53.23 (2.22)	47.52 (2.46)	0.20 (0.04)	0.30 (0.04)
Female	52.27 (2.52)	48.61 (2.62)	0.18 (0.03)	0.10 (0.03)
Fearful expressions				
Male	46.20 (1.88)	41.06 (1.81)	0.13 (0.03)	0.07 (0.02)
Female	45.22 (2.17)	40.34 (1.52)	0.06 (0.02)	0.02 (0.01)

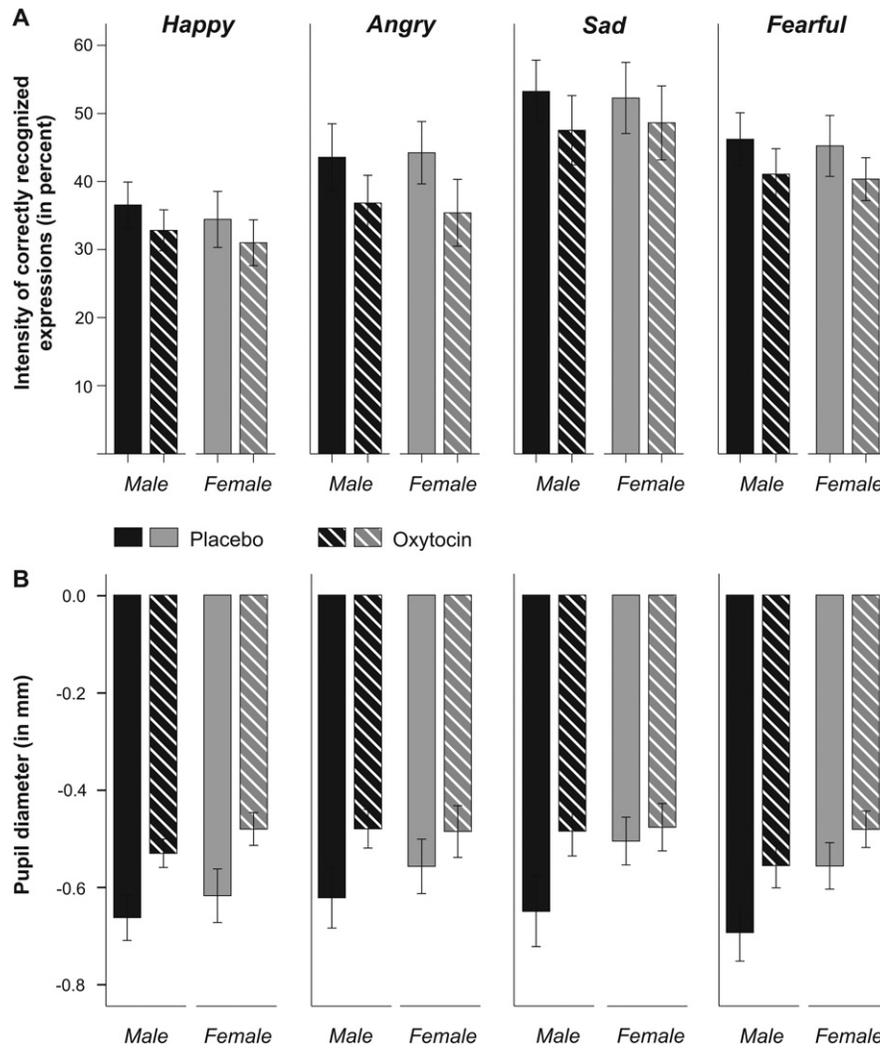


Figure 1. A: Intensity levels (mean and standard error of the mean in percent) by which facial expressions were recognized correctly. B: Task-related pupil diameter averaged across the interval of interest (mean and standard error of the mean in mm) for the placebo and oxytocin group in each of the 8 experimental conditions.

additionally conducted exploratory simple effects analyses. These analyses revealed that OXT specifically lowered the recognition threshold for angry, $F(1,45) = 7.14$, $p = .010$, $\eta_p^2 = 0.14$, but not for happy, sad, and fearful expressions (happy: $F(1,45) = 2.54$, $p = .118$; sad: $F(1,45) = 2.12$, $p = .153$; fearful: $F(1,45) = 3.99$, $p = .052$).

Error rates. Error rates ranged from 0 (male happy condition in both the OXT and PLC group) to 0.30 (male sad condition in the OXT group, see Table 1). A three-way repeated measures ANOVA (Group \times Emotion \times Gender) on error rates showed no effect of OXT application on recognition accuracy, $F(1,45) = 0.15$, $p = .703$. However, we found a main effect of emotion, $F(2.25,101.12) = 34.42$, $p < .001$, $\eta_p^2 = 0.43$, $\epsilon = 0.749$, and also a main effect of gender, $F(1,45) = 4.41$, $p = .041$, $\eta_p^2 = 0.09$. The main effect of emotion indicated, in line with the data on intensity levels, that participants recognized happy expressions best, made more errors when presented with angry and fearful faces, and recognized sad faces worst. The main effect of gender indicated that participants made more errors when presented with male than female faces.

Note that behavioral data without taking the gender of the face stimuli into account were previously reported by Lischke, Berger et al. (2012).

Pupil Data

At the beginning of each trial (i.e., with presentation of the first picture of a set), we observed a constriction of the pupil. After about 0.8 s, pupil diameter increased again in the course of the trial during all conditions, reflecting increased resource allocation during the processing and recognition of the emotional expressions (see Figure 2A and B).

Examination of baseline pupil diameter as a possible confound. To first rule out any influence of baseline pupil diameter on pupillary responses, especially between OXT and PLC group, baseline pupil diameter (i.e., pupil diameter before presentation of the first picture stimulus of a trial) was averaged for each experimental condition and participant (see Table 2) and subjected to a three-way repeated measures ANOVA (Group \times Emotion \times

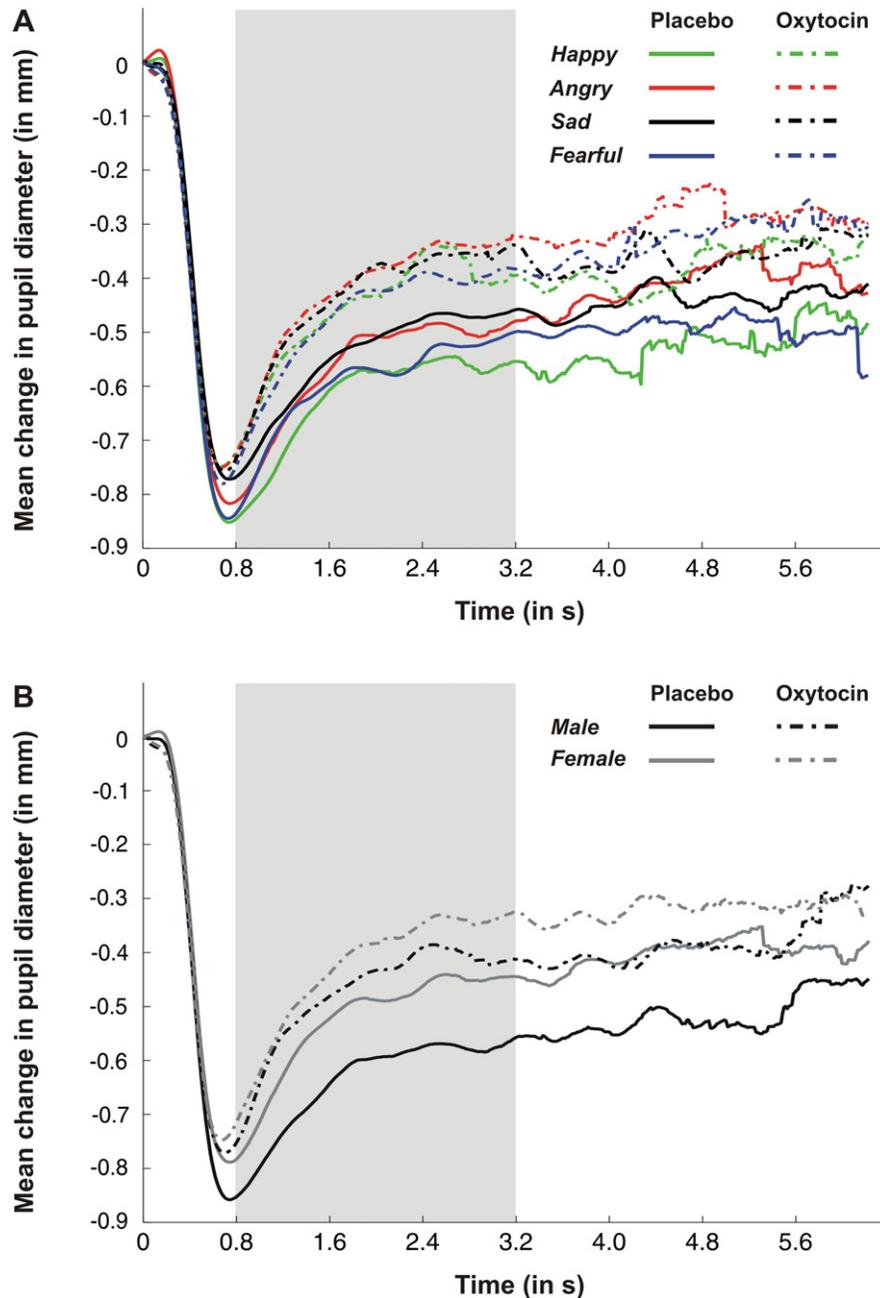


Figure 2. Stimulus-locked averaged pupillary responses (mean change in pupil diameter in mm) in the placebo and in the oxytocin group (A) for the four emotion categories, and (B) for male and female face stimuli. The interval of interest (between 0.8 and 3.2 s) is highlighted in gray.

Gender). There was no main effect of group on baseline pupil diameter, $F(1,45) = 0.71$, $p = .404$; that is, pupil diameter was not affected in general by OXT application. We further found neither an effect of emotion, $F(3,135) = 0.81$, $p = .489$, nor of gender, $F(1,45) = 0.01$, $p = .914$, and thus no evidence for an influence of baseline pupil diameter on the task-related pupil dilations.

Task-related pupillary responses. A three-way repeated measures ANOVA (Group \times Emotion \times Gender) on average pupil diameter in the interval of interest between 0.8 and 3.2 s showed that the application of OXT generally increased pupil diameter, $F(1,45) = 4.15$, $p = .047$, $\eta_p^2 = 0.09$ (see Table 2 and Figure 1B). In contrast to the behavioral data, we did not find a main effect of

emotion, $F(2.48,111.58) = 1.85$, $p = .15$, $\epsilon = 0.826$, but an effect of gender, $F(1,45) = 12.93$, $p = .001$, $\eta_p^2 = 0.22$, as well as a trend for a Group \times Gender interaction, $F(1,45) = 3.35$, $p = .074$, $\eta_p^2 = 0.07$ (see Figure 2A and B). The gender effect showed that pupil diameter was greater during the processing of female than male faces.

Exploratory simple effects analyses revealed that OXT specifically increased pupil diameter during the processing of happy, $F(1,45) = 5.81$, $p = .020$, $\eta_p^2 = 0.11$, but not angry, sad, and fearful expressions (angry: $F(1,45) = 2.89$, $p = .096$; sad: $F(1,45) = 2.13$, $p = .152$; fearful: $F(1,45) = 2.93$, $p = .094$). With regard to potentially different effects of OXT on the processing of male and female faces, we found that OXT increased pupil diameter during the processing of male, $F(1,45) = 5.78$, $p = .020$, $\eta_p^2 = 0.11$, but not

Table 2. Means and Standard Errors for Baseline and Task-Related Pupil Diameter for the Placebo and Oxytocin Group

	Baseline pupil diameter Mean (SE)		Task-related average pupil diameter Mean (SE)	
	Placebo (<i>n</i> = 24)	Oxytocin (<i>n</i> = 23)	Placebo (<i>n</i> = 24)	Oxytocin (<i>n</i> = 23)
Happy expressions				
Male	5.187 (0.334)	4.921 (0.215)	-0.698 (0.049)	-0.559 (0.031)
Female	5.214 (0.335)	4.921 (0.212)	-0.651 (0.058)	-0.507 (0.036)
Angry expressions				
Male	5.185 (0.335)	4.838 (0.201)	-0.655 (0.066)	-0.506 (0.042)
Female	5.254 (0.337)	4.868 (0.208)	-0.587 (0.059)	-0.512 (0.056)
Sad expressions				
Male	5.272 (0.339)	4.862 (0.208)	-0.685 (0.076)	-0.511 (0.053)
Female	5.214 (0.330)	4.867 (0.212)	-0.533 (0.052)	-0.503 (0.051)
Fearful expressions				
Male	5.198 (0.310)	4.876 (0.222)	-0.731 (0.062)	-0.586 (0.048)
Female	5.146 (0.318)	4.872 (0.209)	-0.587 (0.050)	-0.507 (0.039)

Note. Task-related pupil diameter was averaged across the interval of interest (between 0.8 and 3.2 s after presentation of the first stimulus in a trial). Mean change in pupil diameter was measured in mm.

female faces, $F(1,45) = 2.03$, $p = .161$. Interestingly, simple effects analyses also revealed that the significant effect of the gender of the face stimuli, indicating increased pupil diameter for female compared with male faces in the PLC group, diminished in the OXT group, in which no difference could be detected (OXT: $F(1,45) = 1.53$, $p = .223$; PLC: $F(1,45) = 15.04$, $p < .001$, $\eta_p^2 = 0.25$).

Discussion

The aim of the present study was to explore the extent to which OXT might improve the exploration and recognition of socioaffective stimuli. Forty-seven men received either OXT or PLC before performing a dynamic emotion recognition task. During the experiment, we measured behavioral parameters (level of intensity at which emotional expressions were recognized correctly and error rate), as well as the change in pupil diameter during task processing.

The study yielded three main results: First, better emotion recognition after OXT treatment was associated with increased pupil dilation (main effect of group). Second, we found increased pupil dilations during the processing of male compared with female faces (main effect of the gender of the face stimuli), reflecting men's lower interest in male faces. Third, this effect of the gender of the face stimuli was diminished in the OXT group, in which pupil dilation was specifically increased for male faces (trend for a Group \times Gender interaction). In the following, we argue that indicators of task performance (i.e., improved recognition of emotional expressions) in combination with indicators of attentional resource allocation (i.e., increased pupil dilation) provide evidence for the view that OXT increases the salience of socioaffective stimuli, especially for stimuli that usually do not recruit much attention.

Indicators of Emotion Recognition Performance

Intensity levels at which an emotional expression could be recognized correctly showed that emotional expressions were better identified after administration of OXT. Participants who received 24 IU OXT prior to the experiment recognized emotional expressions at lower intensity levels regardless of the specific emotion category (i.e., the specific kind of emotion; see Figure 1A). This result has already been presented in Lischke, Berger et al. (2012) and is in line with other studies showing improved recognition of

emotional expressions and mental states after OXT treatment (e.g., Di Simplicio et al., 2009; Domes, Heinrichs, Michels et al., 2007; Guastella et al., 2010; Marsh et al., 2010; Schulze et al., 2011).

We found no difference in intensity levels with regard to the gender of the face stimuli; however, the gender effect in error rates suggests that male and female faces might be processed differentially. Accuracy in general was quite high in our study, but even better when processing female faces in both groups of participants.

Indicators of Attentional Resource Allocation

Numerous studies have demonstrated that task-related pupil dilations reflect the processing load of a task (e.g., Beatty & Lucero-Wagoner, 2000). Thus, pupillary responses "can be used to index the extent of central nervous system processing allocated to a task" (Granholm & Steinhauer, 2004, p. 2). Increased pupillary responses have been observed in the literature when stimuli are cognitively engaging or emotionally salient.

In our study, pupil size increased in all conditions of the emotion recognition task, after an initial constriction caused by the appearance of the first picture of each trial and the corresponding change in lighting conditions. In line with our hypothesis and consistent with a recent study by Leknes et al. (2012), subsequent pupil (re)dilation was always greater in the OXT than in the PLC group, indicating that improved behavioral performance in the emotion recognition task was associated with greater allocation of attentional resources (see Figure 1B). Since exploratory simple effects analyses revealed that OXT specifically increased the recruitment of attentional resources during the processing of happy faces and not during the processing of sad, angry, and fearful expressions, we interpret that altered attentional resource allocation might also underpin the well-established oxytocin-induced effects with regard to the promotion of prosocial and approach-related behavior.

The effect of the gender of the presented face stimuli showing greater pupil diameter for female than for male faces is in line with early pupillometric studies, such as the seminal Hess study, which reported greater pupil diameter during the viewing of pleasant and attention-demanding pictures (Hess & Polt, 1960). Hess and Polt (1960) also reported differences between the sexes: Men showed greater pupil size in response to a partially nude woman, while women were more interested in baby pictures and the partially

nude man (see also Garrett, Harrison, & Kelly, 1989; Hess, Seltzer, & Shlien, 1965; Libby, Lacey, & Lacey, 1973). Although we used only a very reduced and simplified stimulus material (grayscale, equalized in size, and enclosed within an elliptic mask that showed only the face itself) and no erotica (e.g., pictures with naked individuals), greater pupil dilations for female than for male faces might still indicate men's greater interest in female faces. In contrast to the PLC group, pupil dilations in the OXT group did not differ between female and male faces; that is, an increase in attentional resource allocation affected male more than female faces and was thus reducing the processing advantage of female face stimuli.

Notably, pupil diameter in the baseline phase did not differ between the groups. Thus, there is no evidence for an altered "exploration mode" of the cognitive system after OXT treatment (i.e., no evidence for a general enhanced sensitivity of the cognitive system, see Aston-Jones & Cohen, 2005; van der Meer et al., 2010). Van der Meer et al. (2010), for instance, reported greater pre-experimental pupil baseline diameters in individuals with high fluid intelligence compared with normal controls (i.e., *tonic* changes in pupil diameter). In our study, in contrast, we observed only *phasic* (i.e., task-related) differences in pupil diameter between the groups.

Gamer and Büchel (2012) recently investigated whether OXT modulates sympathetic or parasympathetic activity by measuring skin conductance and heart rate responses during a static emotion recognition task. By showing that OXT differentially enhances the heart rate response to facial expressions, but has no impact on skin conductance, the authors provided evidence that OXT selectively influences parasympathetic activity. Since it has been discussed that changes in pupil diameter might specifically occur as a result of altered parasympathetic activity (Steinhauer et al., 2004), our results are in line with this view.

Limitations

It should be noted that we used only stimuli with both an affective and a social content (i.e., faces that were developing an emotional expression), and pupil diameter was generally increased in all conditions in the OXT group (main effect of group). Therefore, it is presently unclear whether OXT also has an impact on pupillary responses during the processing of other kinds of stimuli. To elucidate this question, we recommend the use of nonsocial stimuli in addition to socioaffective stimuli in further studies to disentangle affective and social aspects of the stimulus material (e.g., by also using pictures of faces with emotional and neutral expressions and pictures of objects).

In our study, the possible impact of the two confounding variables, baseline pupil diameter and luminance of the stimulus mate-

rial, could be excluded. We also controlled for differences in participants' characteristics (e.g., general intelligence, empathy, alexithymia, and psychopathology). However, we did not ask our participants about their sexual orientation. Since we argue that differences in pupil diameter are associated with differences in interest for the stimulus material in question, sexual orientation could be a confound. However, the very unlikely case that more homosexual men would have been in the OXT than in the PLC group cannot fully explain the pattern of results obtained. A two-way repeated measures ANOVA with the factors group and emotion category, while excluding the gender factor, still shows a trend for a main effect of group on pupil diameter, $F(1,45) = 3.87$, $p = .055$, $\eta_p^2 = 0.08$. Nevertheless, we recommend ruling out this possible confound in further studies when measuring pupil dilations in response to male and female faces.

We are aware that the size of our effects is rather small, although comparable with other studies. Therefore, the results should be treated with caution and replicated in further studies.

It also has to be mentioned that we investigated the effect of OXT on pupillary responses only in a sample of men. Since there is considerable evidence that OXT modulates the neural circuitry involved in face processing in men and women differentially, our results might not be generalizable to women. For instance, it has been found that OXT decreases amygdala activity in response to aversive threat-related scenes and fearful/angry faces in men (Domes, Heinrichs, Gläscher et al., 2007; Gamer et al., 2010; Kirsch et al., 2005; Petrovic, Kalisch, Singer, & Dolan, 2008), but increases amygdala activity to similar stimulus material in women (Domes et al., 2010; Lischke, Gamer et al., 2012).

Conclusion

Our finding of increased task-related pupil dilation in combination with improved recognition of emotional expressions provides evidence for an OXT-induced recruitment of supplemental attentional resources during the processing of socioaffective stimuli. Moreover, we found that pupil dilation after OXT treatment was specifically increased during the processing of male and happy faces. These results demonstrate that OXT increases the salience of socioaffective stimuli in general and, in particular, for stimuli that usually do not recruit much attention. Thus, OXT may reduce the processing disadvantage for male and happy faces in men. Finally, our results are consistent with a recent study by Leknes et al. (2012) and provide, in addition, first evidence that OXT promotes the allocation of attentional resources during elaborate conscious processing of emotional facial stimuli during a naturalistic emotion recognition task.

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