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Oxytocin promotes face-sensitive neural responses to infant and adult faces in mothers

Mikko J. Peltola[a,*], Lane Strathearn[b], Kaija Puura[c,d]

[a] Human Information Processing Laboratory, Faculty of Social Sciences, 33014, University of Tampere, Finland
[b] Stead Family Department of Pediatrics, University of Iowa, and the Center for Disabilities and Development, United States
[c] Department of Child Psychiatry, Tampere University Hospital, Finland
[d] Tampere Center for Child Health Research, Faculty of Medicine and Life Sciences, University of Tampere, Finland

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ABSTRACT

Research utilizing intranasal oxytocin (OT) administration has shown that OT may increase attention and sensitivity to social cues, such as faces. Given the pivotal role of OT in parental behaviors across mammals, the paucity of intranasal OT research investigating responses to social cues in parents and particularly mothers of young children is a critical limitation. In the current study, we recorded cortical event-related potentials (ERPs) to investigate whether intranasal OT affects the early neural responses to emotional faces in mothers of 1-year-old infants. Using a double-blind, within-subjects design, mothers (n = 38) were administered intranasal OT and placebo on separate sessions and presented with happy and sad infant and adult faces while ERP components reflecting face-sensitive brain activation and attention allocation were measured. We hypothesized that ERP responses to faces would be larger in the OT condition and that the effects of OT on ERP responses would be more pronounced for infant faces. The amplitudes of the face-sensitive N170 ERP component were larger in the OT condition to infant and adult faces, but no clear support was found for the hypothesis that the responses to infant faces would be more susceptible to OT effects than the responses to adult faces. The attention-sensitive late positive potential (LPP) component was not modulated by intranasal substance condition. The results are in line with the view that OT acts to enhance the perceptual salience of social and emotional stimuli. Demonstrating such effects in mothers of young children encourages further investigation of the potential of intranasal OT to affect the perception of social cues relevant for parent-child interaction.

1. Introduction

Research investigating the impact of intranasal oxytocin (OT) administration has provided support for a view that OT is a critical neuropeptide affecting how we respond to social signals. Compared to placebo (PL), single-dose OT administration has been shown to increase attention to the eye region (Guastella et al., 2008), improve the recognition of subtle emotions from faces (Domes et al., 2007; Leknes et al., 2013), heighten arousal responses to faces indicated by pupil dilation (Leknes et al., 2013; Prehn et al., 2013), and increase electrocortical activity in response to faces (Huffmeijer et al., 2013). Such findings converge in a model suggesting that a general function of OT is to modulate the perceptual salience of social signals by enhancing attention orienting to social cues through interactions with the dopaminergic system (Shamay-Tsoory and Abu-Akel, 2016; Strathearn, 2011).

The current study sought to investigate whether intranasally administered OT affects cortical brain responses to faces in mothers of 1-year-old infants. Given that OT has been critically implicated in activating parenting behaviors in response to salient infant signals across mammals (Carter, 1998), the paucity of intranasal OT administration studies on the perception of social signals in parents and particularly mothers of young children is striking (see Mah et al., 2017; Rupp et al., 2013, for examples). Correlational studies indicate that peripheral OT concentrations (e.g., in plasma, saliva, or urine) are associated with measures of parental behavior, such as interactive synchrony and maternal orienting sensitivity (Feldman et al., 2007; Strathearn et al., 2012), suggesting that OT may be associated with enhanced responsivity to social signals during parent-child interaction. However, it has been questioned whether peripheral levels of OT reliably indicate OT levels in the brain (Kagerbauer et al., 2013; Valstad et al., 2017), making it difficult to ascertain any causal role of OT on responsivity to social signals based on peripheral measures. Furthermore, given that there are even aspirations to utilize intranasal OT as an augmentative treatment for problems in early parent-child interaction due to

* Corresponding author.
E-mail address: mikko.peltola@staff.uta.fi (M.J. Peltola).

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postpartum depression (Kim et al., 2014), it is critically important that the effects of intranasal OT on the perception of social signals in mothers of young children are first investigated in sufficient detail.

While intranasal OT has been generally associated with greater attention and sensitivity to social signals such as emotional faces (e.g., Domes et al., 2007; Guastella et al., 2008; Huffmeijer et al., 2013), the associations of OT with variations in parenting behavior (e.g., Feldman et al., 2007) further suggest that the effects of intranasal OT might be particularly pronounced in response to child and infant social signals. Moreover, viewing infant stimuli preferentially activates dopaminergic reward circuits of the brain (Kringelbach et al., 2008; Strathearn et al., 2008), and considering that OT might exert its effects on modulating perceptual saliency through crosstalk with the dopaminergic system (Shamay-Tsoory and Abu-Akel, 2016), it could be hypothesized that brain responses to infant faces are more susceptible to intranasal OT effects than responses to adult faces. Marsh et al. (2012) provided initial support for this possibility by asking participants to judge the appeal of infant and adult faces, and finding that OT increased such preferences selectively toward infant but not adult faces. Here, we extended this line of research by measuring event-related potentials (ERPs) of the electroencephalogram (EEG) signal in mothers while they were presented with emotional adult and infant faces. ERP measurement is ideally suited for investigating the modulatory role of OT in the perception of faces with superior temporal resolution. ERPs can be utilized to measure neural activation of face-sensitive occipitotemporal areas involved in the initial processing of facial features (i.e., the N170 ERP component; Rossion, 2014) and differential allocation of attention to faces differing in their emotional or motivational significance, as reflected in attention-sensitive ERP components such as the early posterior negativity (EPN), P3, and the late positive potential (LPP) (see Olofsson et al., 2008, for a review). An increasing number of ERP studies probing parental brain responses to infant stimuli have shown that ERP responses to infant faces differ as a function of parental status (i.e., showing enhanced responses to infant faces in parents; Peltola et al., 2014; Proverbio et al., 2006) and indicators of parental sensitivity, such as reflective functioning (Rutherford et al., 2017), and observer ratings of maternal sensitivity (Bernard et al., 2015). However, very few studies have measured ERPs to investigate OT effects on the temporal dynamics of processing social signals (e.g., Huffmeijer et al., 2013; Waller et al., 2015). Huffmeijer et al. (2013) observed that OT administration increased face-sensitive and attention-sensitive ERP responses in the VPP (i.e., a frontocentral counterpart of the N170; Joyce and Rossion, 2005) and LPP components in response to adult facial expression stimuli in nulliparous females, indicating OT-related enhancement in processing salient facial signals.

To date, there have been no studies investigating OT effects on ERPs to infant and adult stimuli in parents. To address this limitation, in the current study, we used a double-blind, within-subjects design to investigate whether OT administration affects the neural responses to infant and adult faces in mothers of 1-year-old infants. The mothers categorized facial expressions according to their emotional valence while ERPs related to processing facial features (N170) and attention allocation (LPP) were measured. Based on available ERP data from nulliparous females (Huffmeijer et al., 2013) and models positing that OT increases the perceptual salience of social signals (Shamay-Tsoory and Abu-Akel, 2016), we expected ERP responses to faces to be larger in the OT condition. As a critical test of the involvement of OT in mothers' neural sensitivity to infant signals, we hypothesized that the effects of OT on ERP responses are more pronounced for infant faces. Regarding the functional properties of the analyzed ERP components, the social salience model (Shamay-Tsoory and Abu-Akel, 2016) proposed that OT exerts its effects on social salience processing primarily by modulating attention orienting to social cues, which suggests that the effects of OT should be more readily observed in the attention-sensitive LPP responses. However, as OT was previously found to impact both perceptual and attentional ERP responses to adult faces (Huffmeijer et al., 2013), we expected to observe the OT-related increase in ERP responses in both the N170 and the LPP components. Finally, research is mixed on whether OT affects responsivity to emotions generally or more specifically to positive (Marsh et al., 2010) vs. negative (Fischer-Shofty et al., 2010) emotions, and in a previous ERP study (Huffmeijer et al., 2013), OT-related increases in ERP responses to faces were not dependent on facial expression. Therefore, we made no specific predictions as to whether the effects of OT would differ depending on the emotional valence of the faces (sad vs. happy).

2. Methods

2.1. Participants

Fifty-two mothers of one-year-old infants (mothers' age $M = 31.92$ years, $SD = 4.98$; infants' age $M = 14.51$ months, $SD = 1.18$) participated in the study. Exclusion criteria included smoking, alcohol and drug abuse, neurological, psychiatric, or cardiac disorders, pregnancy, breastfeeding, and use of medication. All participants were right-handed, Caucasian, and predominantly from an urban, middle-class background (average years of education = 16.33, $SD = 2.81$; annual household income on average within 50,000–69,999 €), and 56% were primiparous. The number of participants included in the ERP analyses was 38. The remaining participants were excluded from the analyses due to excessive artefacts in the EEG data ($n = 3$), technical problems ($n = 3$), experimenter error ($n = 1$), dropping out of the study between assessments ($n = 2$), or oral contraceptive use ($n = 5$), as previous research has indicated that the use of oral contraceptives may critically suppress sensitivity to the effects of OT administration (Montoya and Bos, 2017; Scheele et al., 2016). The excluded participants did not differ from those included in the analyses on available demographic variables (age, years of education, family income, parity) or self-reported depressive symptoms, all $t < 0.77$, all $p > .45$. The study was approved by the ethics committee of Pirkanmaa Hospital District, and an informed written consent was obtained from the participants at the beginning of the experiment.

2.2. Procedure

Using a double-blind, within-subjects design, two laboratory sessions were scheduled to occur approximately 4 weeks apart, during the luteal phase of the menstrual cycle (based on participant self-report of menstrual cycle length and expected date of menstrual period), and approximately at the same time of day. The participants were instructed to abstain from excessive physical activity 24 h before, and from caffeine 4 h before the session. In the beginning of the session, participants completed questionnaire items regarding pregnancy, medication, visual impairments, and current nasal disease or obstruction. Immediately after the intranasal substance administration, participants provided information on socioeconomic status (educational level, income) and current mood (using the Edinburgh Postnatal Depression Scale; Cox et al., 1987). An LMA MAD Nasal™ mucosal atomization device (http://www.lmaco.com) was used to administer 24 IU of OT (Syntocinon, Novartis, Switzerland) or placebo (PL; saline). One puff containing 0.3 ml of the substance was administered by the experimenter to each nostril (i.e., a total of 0.6 ml). Half of the participants received OT on the first visit and PL on the second visit, with the other half receiving the substances in reverse order (within the sample included in the analyses, 18 participants received OT first and 20 participants received PL first). The order randomization of the nasal sprays was conducted by a hospital pharmacist. An awareness check at the end of the second laboratory visit confirmed that the number of participants correctly guessing which substance they had received on the second visit did not differ from chance, $t(48) = 0.14$, $p = .89$. The potential influence of the order of substance administration across the two laboratory visits (i.e., OT-PL vs. PL-OT) was tested by adding administration order as a

between-subjects variable in the main analyses, which showed that the order in which the substances were administered did not have significant main effects or interactions with the variables included in the analyses.

After preparing the electrodes for EEG recording, the participants completed two EEG tasks including measurement of frontal EEG asymmetry (not reported here) and the ERP task measuring neural responses to infant and adult face stimuli. The ERP task was started approximately 55 min after intranasal spray administration. This is well within the time-window shown to be associated with sustained OT-induced activation increases in brain areas important for social cognition and emotion processing (Paloyelis et al., 2016) and also with significantly increased OT levels in saliva following intranasal OT administration (Huffmeijer et al., 2012; Van IJzendoorn et al., 2012).

2.3. ERP measurement

Continuous EEG was recorded from 64 active electrodes mounted in an elastic cap (actiCAP), low-pass filtered at 200 Hz, amplified using a QuickAmp amplifier (Brain Products GmbH, Munich, Germany) with a 1000-Hz sampling rate, and referenced to the common average. Vertical (VEOG) and horizontal (HEOG) electro-oculogram were recorded with bipolar electrodes placed above and below the midpoint of the left eye, and beside the outer canthi of each eye, respectively. Electrode impedances were reduced to under 30 kΩ.

Event-related potentials (ERPs) were measured in response to happy and sad/distressed adult and infant faces, measuring 3.7° and 3.1° vertically and horizontally, respectively, when presented on a 19-inch screen with a 70-cm viewing distance. The adult faces were obtained from the Karolinska Directed Emotional Faces database, (Lundqvist et al., 1998) and the infant faces from an image database of approximately 7-month-old infants collected at Baylor College of Medicine (Strathearn et al., 2008). The infant expressions were still-images extracted from videotaped emotion-eliciting situations, during which happy expressions were elicited by the experimenters interacting with the infant using age-appropriate toys, and the sad/distressed expressions elicited by removing a toy or leaving the infant alone for a short period. Expressions depicting sadness in the adult stimuli were selected for this study as their signal value can be considered to most closely resemble the signal conveyed by the rather unspecific distress facial expressions in infancy (cf. Camras and Shutter, 2010). For both adult and infant stimuli, faces from six individuals (three males and three females, each of Caucasian ethnicity) were included in the ERP task. All faces were cropped along the outer contour of the face, converted into grayscale, matched for size and luminance, and presented against a uniform gray background. An independent group of 11 observers rated the valence of the faces on a scale from 1 (highly negative) to 9 (highly positive). The ratings confirmed that both adult and infant happy and sad faces were perceived as reliably expressing the respective emotions (adult happy $M = 7.4$, $SD = 0.54$, adult sad $M = 2.8$, $SD = 0.54$, infant happy $M = 7.0$, $SD = 0.58$, infant sad $M = 2.2$, $SD = 0.58$). Adult happy faces were rated as more positive than infant happy faces, $t(10) = 2.86$, $p = .017$, while infant sad faces were rated as expressing more negative valence than adult sad faces, $t(10) = 3.32$, $p = .008$.

ERPs were recorded during a task in which a stream of infant and adult faces was presented in random order. To maintain the participants' attention on the faces throughout the recording, the participants were required to categorize each face as expressing positive or negative emotion. Each trial started with the presentation of a fixation stimulus at the center of the screen with a jittered duration between 550 and 850 ms. The face stimulus was then presented for 700 ms, followed by a response prompt until the participant's response, and a blank screen for 750 ms. The participants were instructed to look at each face the whole time it was visible on the screen, and only after its offset to indicate by pressing one of two response buttons whether the face expressed positive or negative emotion. After a practice block of eight trials, each stimulus condition (i.e., adult happy, adult sad, infant happy, infant sad) was presented 60 times, totaling 240 trials presented in four blocks of 60 trials. A self-paced break followed each block. Each individual model within each stimulus condition was repeated 10 times during the task. The emotional valence categorization reaction time data did not yield any effects related to intranasal substance condition, likely due to the task being very simple, as its primary purpose was to maintain the participants' attention on the face stimuli. Therefore, the reaction time data are not discussed further.

2.4. ERP analyses

Using Brain Vision Analyzer 2 software, the continuous EEG signal was first filtered with a 0.5–30 Hz band-pass filter (24 db/octave slope). Individual channels that were bad throughout the recording (due to flat signal or excessive noise resulting from poor contact) were identified on the basis of visual inspection of the continuous EEG signal and if the number of bad channels was not larger than six (i.e., 10% of the recorded channels), these channels were interpolated using spherical spline interpolation. Next, the EEG data were corrected for ocular artifacts (i.e., eye blinks and horizontal eye movements based on signal recorded from the VEOG and HEOG electrodes, respectively) using a semi-automatic independent component analysis (extended infomax ICA) performed in Analyzer 2. The ICA components were visually inspected and selected for deletion only when their topography clearly indicated a blink or a horizontal eye movement. In a majority of EEG files, two components were selected for deletion, with a maximum of four ocular components deleted from the other files. The data were then segmented into 800-ms long epochs including a 100-ms pre-stimulus baseline and the 700-ms face stimulus presentation, and adjusted to the average activity during the pre-stimulus baseline period. To remove residual artifacts, all EEG channels were subjected to an automated artifact detection algorithm which rejected all epochs containing a voltage step exceeding 50 μV/ms, difference between the maximum and minimum activity within the entire segment greater than 150 μV, absolute amplitude values greater than ± 75 μV, or a voltage change smaller than 0.5 μV during an interval of 100 ms from further analyses. Accepted epochs were then averaged for each stimulus type ($M_{\text{infant happy}} = 55.4$, $SD = 3.7$; $M_{\text{infant sad}} = 55.8$, $SD = 3.8$; $M_{\text{adult happy}} = 55.8$, $SD = 4.0$; $M_{\text{adult sad}} = 55.5$, $SD = 4.0$), with no differences in the number of accepted epochs between the OT and PL conditions ($p = .93$).

The N170 ERP component is typically observed as a negative deflection peaking at around 170 ms in occipitotemporal electrode sites (Rossion, 2014). Similarly, in the current data, the N170 peaked on average at 159 ms and was most pronounced on occipitotemporal electrodes. Therefore, the N170 was extracted as the voltage of the minimum amplitude within a time window of 120–220 ms (to ensure that the peak minimum amplitude was extracted in each recording) from a representative set of electrodes averaged over left (P7, PO7, PO9, TP9) and right (P8, PO8, PO10, TP10) occipitotemporal locations in which the N170 waveform was clearly shown. The scalp topographies during the time window of the N170 responses are shown in Fig. 1. Considering the potential attention-related ERP components (i.e., EPN, P3, and LPP), inspection of the grand average waveforms most clearly indicated a parietally distributed sustained positivity starting before 300 ms and returning to preceding levels at around 600 ms, which is characteristic of the LPP component (Olofsson et al., 2008). Therefore, the LPP was selected as the ERP measure of attention allocation to the different stimulus conditions in the current study. The LPP responses were quantified as the mean activity within 300–600 ms averaged over the parietal electrodes Pz, P1, P2, POz, PO3, and PO4, which showed the most prominent LPP waveforms (Fig. 1).

The N170 amplitude data were analyzed with a 2 × 2 × 2 × 2 repeated-measures analysis of variance (ANOVA) with Condition (OT, PL), Hemisphere (left, right), Face Age (infant, adult), and Facial

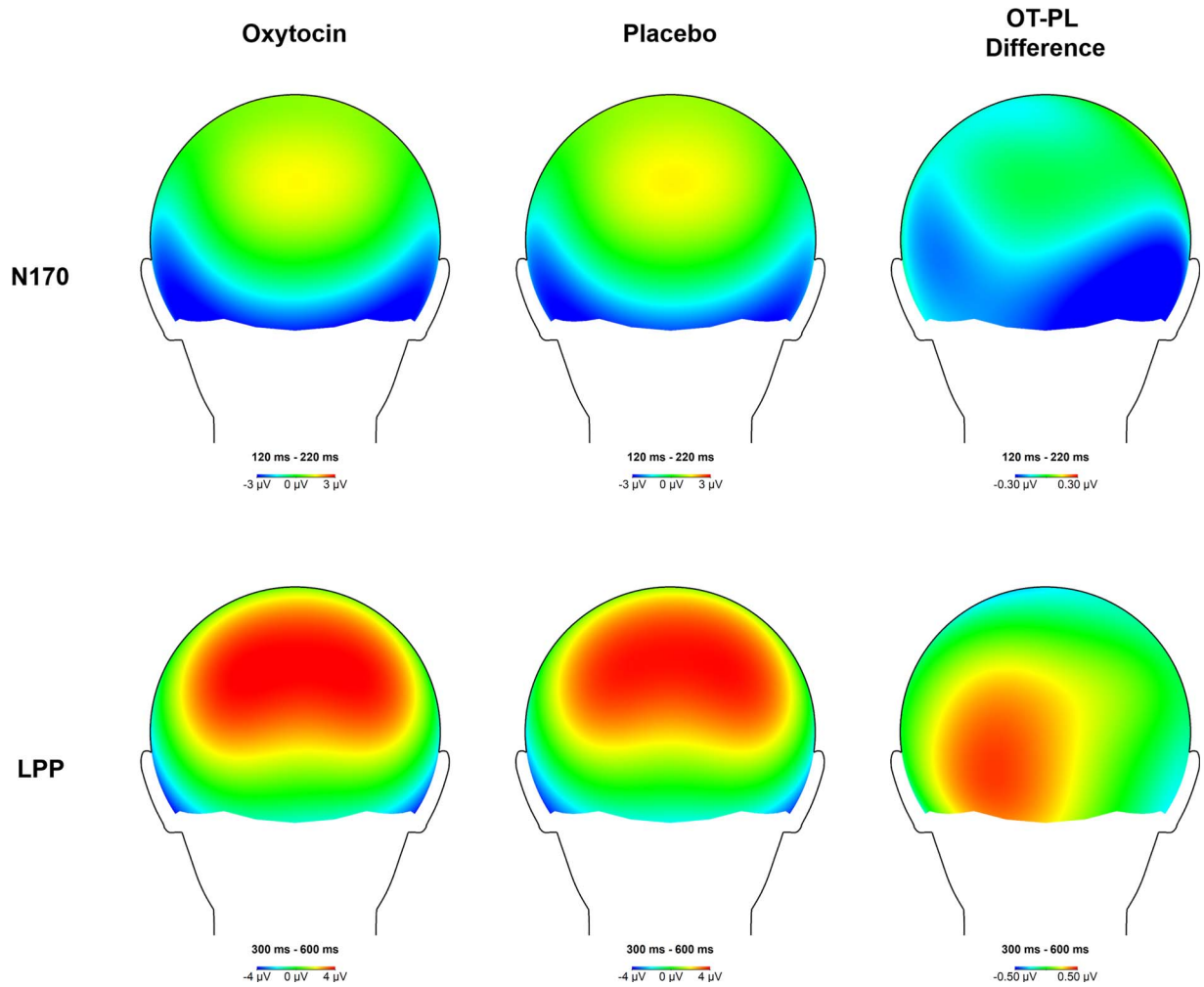

Fig. 1. Scalp topographies of the N170 (top graphs) and the LPP (bottom graphs) responses in the oxytocin (left) and placebo (middle) conditions, and the difference in amplitudes between the oxytocin and placebo conditions (right), averaged across all stimulus categories.

Expression (happy, sad) as within-subjects factors. The LPP data were analyzed with a 2 × 2 × 2 ANOVA with the factors Condition, Face Age, and Facial Expression.

3. Results

3.1. N170

The analysis of N170 amplitudes showed robust main effects of Condition, $F(1,37) = 7.34$, $p = .01$, $\eta_p^2 = .17$, Face Age, $F(1,37) = 38.64$, $p < .001$, $\eta_p^2 = .51$, and Facial Expression, $F(1,37) = 43.21$, $p < .001$, $\eta_p^2 = .54$ (Figs. 1 and 2). These main effects were due to the N170 being larger (i.e., more negative) in the OT ($M = -6.66\,\mu V$, $SD = 3.11$) than the PL ($M = -6.34\,\mu V$, $SD = 3.06$) condition, larger to infant ($M = -6.91\,\mu V$, $SD = 3.13$) than adult faces ($M = -6.09\,\mu V$, $SD = 3.06$), and larger to sad ($M = -6.84\,\mu V$, $SD = 3.12$) than happy faces ($M = -6.15\,\mu V$, $SD = 3.04$). Inspection of Fig. 3 suggests that the effect of Condition was more pronounced in the N170 responses to infant faces. This is also suggested by the mean values showing larger N170 amplitudes to infant faces in the OT ($M = -7.15\,\mu V$, $SD = 3.19$) than the PL ($M = -6.67\,\mu V$, $SD = 3.15$) condition, whereas N170 amplitudes to adult faces showed a smaller difference between the OT ($M = -6.16\,\mu V$, $SD = 3.14$) and PL ($M = -6.01\,\mu V$, $SD = 3.02$) condition. The critical interaction between Condition and Face Age, however, was not significant, $F(1,37) = 3.30$, $p = .077$, $\eta_p^2 = .08$, and, therefore, separate follow-up tests for the infant and adult face data are not justified. No other interactions were observed.

3.2. LPP

For the LPP amplitudes (Fig. 4), the analysis showed a main effect of Face Age, $F(1,37) = 8.25$, $p = .007$, $\eta_p^2 = .18$, while the main effect of Facial Expression was not significant, $F(1,37) = 2.95$, $p = .09$, $\eta_p^2 = .07$. LPP amplitudes were thus larger (i.e., more positive) to infant ($M = 3.92\,\mu V$, $SD = 1.77$) than adult faces ($M = 3.67\,\mu V$, $SD = 1.77$). The main effect of Condition was not significant, $F(1,37) = 0.64$, $p = .43$, $\eta_p^2 = .017$, and no interactions involving Condition were observed in the LPP amplitudes, $ps > .22$.

4. Discussion

This study presented the first investigation of the effects of intranasal oxytocin (OT) on ERP responses to infant and adult faces in mothers of 1-year-old infants. Using a double-blind, within-subjects design, it was shown that intranasal OT administration resulted in increased amplitudes of the early occipitotemporal face-sensitive N170 component to faces. The interaction testing whether the effects of OT differ depending on face age was not significant. Thus, no clear support was found for the hypothesis that the responses to infant faces are more susceptible to OT effects than the responses to adult faces. No effects of OT were observed in the later attention-sensitive LPP responses to

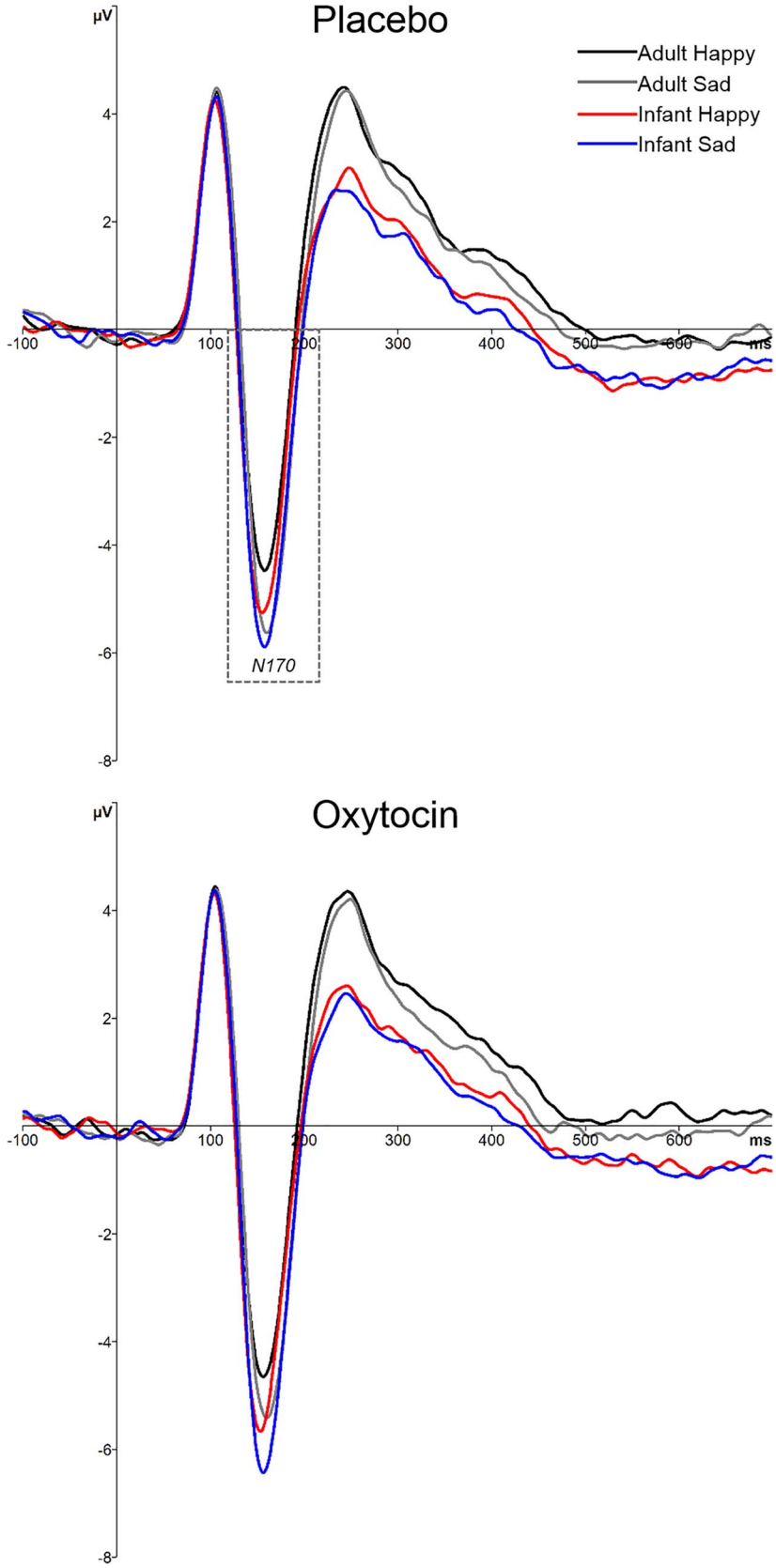

Fig. 2. Occipitotemporal ERP responses to all face stimuli in the placebo and oxytocin conditions, averaged over the left and right hemisphere electrode sets. The dashed area illustrates the N170 component time window.

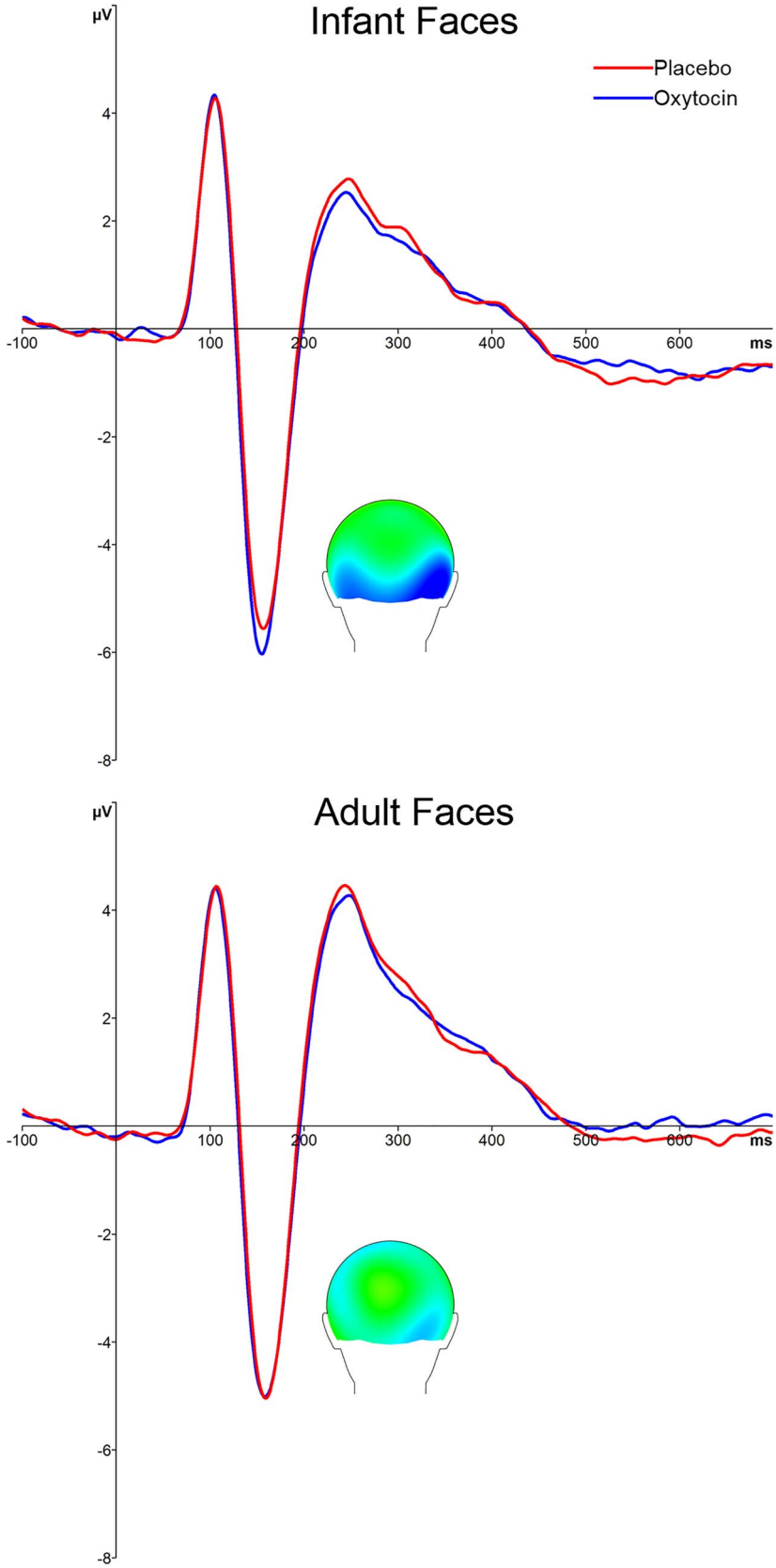

Fig. 3. Occipitotemporal ERP responses to infant faces (top graph) and adult faces (bottom graph) in the placebo and oxytocin conditions, averaged across electrodes and the facial expression categories. The topographic plots illustrate the scalp distribution of the oxytocin effect (i.e., the difference in amplitudes between the oxytocin and placebo conditions) within the N170 time window.

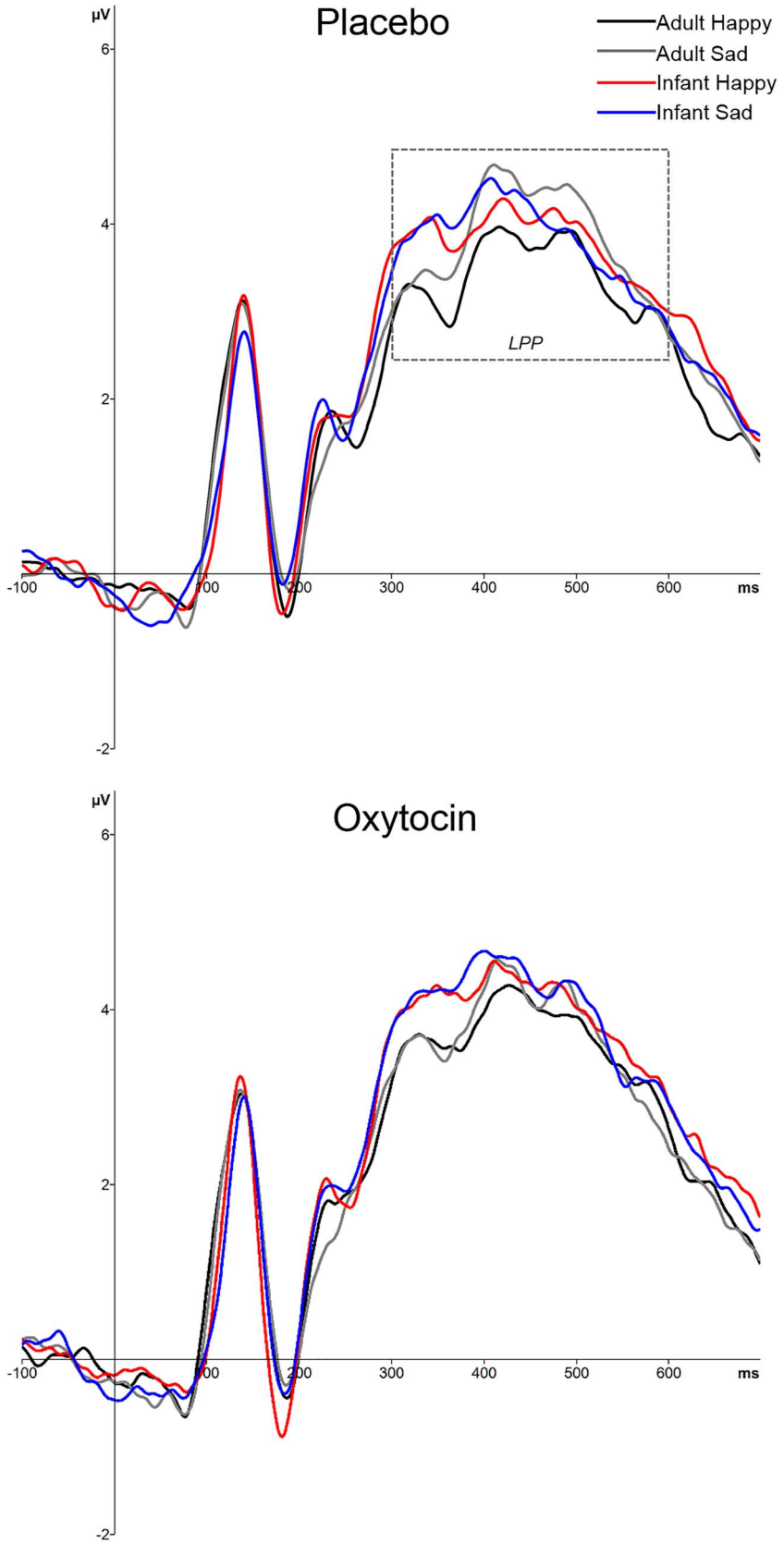

Fig. 4. The ERP graph displaying the LPP waveform to all face stimuli in the placebo and oxytocin conditions, averaged across electrodes Pz, P1, P2, POz, PO3, and PO4. The dashed area illustrates the LPP component time window.

infant and adult faces.

The results are in line with models positing that an important function of OT is to modulate the perceptual salience of social and emotional stimuli (Shamay-Tsoory and Abu-Akel, 2016). Such a function is reflected in findings showing heightened sensitivity to detect subtle emotion signals from faces (Domes et al., 2007; Leknes et al., 2013), increased arousal responses to faces indicated by pupil dilation (Leknes et al., 2013; Prehn et al., 2013), and increased electrocortical activity to faces (Huffmeijer et al., 2013) following intranasal OT administration. The present study extended these findings and made significant contributions to the literature. First, we contributed to the currently very limited amount of research using the ERP method to study the effects of OT on early brain responses to socially relevant stimuli (cf. Huffmeijer et al., 2013; Waller et al., 2015). It was shown that OT specifically affected the N170 ERP response, which reflects activation of key brain structures implicated in processing faces and facial emotions, particularly the face-sensitive areas of the fusiform gyrus and superior temporal sulcus (Rossion, 2014; Sadeh et al., 2010). This finding parallels the ERP results of Huffmeijer et al. (2013) who found that in nulliparous females, OT administration was associated with increased vertex positive potential (VPP) amplitudes to facial expression stimuli, although it should be noted that only adult faces were presented in that study. The VPP bears close similarity to the N170, as it is considered to reflect a frontocentral polarity reversal of the occipitotemporal N170 component (Joyce and Rossion, 2005). These results converge to indicate that intranasal OT administration modulates the activity of brain areas critically implicated in sensitivity to the social and emotional signals conveyed by faces.

In contrast to Huffmeijer et al. (2013) who also found increased LPP amplitudes to adult emotional faces after OT administration, we did not observe any effects of OT on the attention-sensitive LPP responses. Although the results showed robust stimulus-related effects on the LPP (i.e., larger LPP amplitudes to infant vs. adult faces), it is possible that our experimental paradigm was not optimally sensitive to uncover OT-related variation in attentional brain responses. In the current task, participants' attention remained focused on all face stimuli throughout the task, whereas Huffmeijer et al. (2013) measured ERPs to faces that were used as feedback stimuli associated with correct and incorrect button presses, likely triggering greater attentional responses. Future studies should investigate the impact of OT on attention-related ERP components further with paradigms sensitive to variations in attention to faces, such as requiring participants to alternate their attentional focus on separate stimulus categories during the task (cf. Peltola et al., 2014).

This study was also the first to test the effects of OT on electrocortical responses to faces in mothers of young children. The available evidence points to potential sexually dimorphic effects of intranasal OT on neural activation to social stimuli (e.g., Domes et al., 2010; Kirsch et al., 2005; Wigton et al., 2015), indicating that the effects of OT are not universal, and especially in females, OT may function to increase neural responses to social stimuli such as faces (Domes et al., 2010; Huffmeijer et al., 2013; Wigton et al., 2015). Targeting OT research to mothers of young children is particularly important as there have been calls to utilize intranasal OT as an augmentative pharmacotherapeutic tool for conditions affecting early parent-infant interaction, such as postpartum depression (Kim et al., 2014; Kim and Strathearn, 2016; Van IJzendoorn and Bakermans-Kranenburg, 2016). Currently, only one study (Mah et al., 2017) has investigated the effects of intranasal OT on observed mother-infant interaction in depressed mothers of young infants, finding no effects of OT on maternal interaction in this sample. No administration studies with non-depressed mothers of young infants have been published. It is thus vital that the effects of intranasally administered OT on brain functioning, social information processing, and, in particular, responsivity to infant signals are first investigated in sufficient detail in parents and especially mothers to understand whether and how exogenous OT manipulation affects responses to social signals and key parenting phenomena in mothers, such as responsivity to infant emotion signals.

Indeed, as research on whether OT is preferentially associated with responses to infant- or child-related stimuli is currently very limited, a crucial contribution of this study was to directly test whether maternal ERP responses to infant stimuli would be more susceptible to OT effects than the responses to adult stimuli. Although the mean-level changes were suggestive of more pronounced OT effects on infant faces (Fig. 3), the critical statistical interaction testing this hypothesis was not significant, thus providing no clear support for this hypothesis. Clearly, there is a need to replicate the findings with a larger sample to find out with sufficient reliability whether the mean-level changes observed here are indicative of a real (although likely small) effect. Further investigation of the potential infant-specificity of OT effects is also relevant in light of the strong cross-species evidence indicating a pivotal role for OT in mediating parenting behaviors (Carter, 1998; Feldman et al., 2007) and imaging studies showing that infant faces are potent stimuli for activating the brain's dopaminergic circuits (Glocker et al., 2009; Kringelbach et al., 2008) through which OT may exert its effects (Shamay-Tsoory and Abu-Akel, 2016; Strathearn, 2011). A mother's own infant face may be a particularly salient stimulus of the dopamine system, compared to the unknown faces used in the present study (Strathearn et al., 2008). In addition to a larger-scale investigation of any infant-specific effects intranasal OT might have, another important future goal is to assess whether the effects of OT on neural sensitivity to faces are more readily detected in mothers, or whether effects of similar size are detected in fathers or nulliparous adults. Although Huffmeijer et al. (2013) showed OT-related enhancement in cortical responses in nulliparous females, direct comparisons between these studies are complicated by the differences in the experimental paradigms and the fact that only adult faces were used in that study. Finally, although the ERP responses to the happy and sad emotion categories were not modulated by OT in the current study, it will be important to investigate in greater detail whether OT effects are more pronounced in response to certain emotions and whether responses to emotionally neutral stimuli are similarly affected by OT. Meta-analytic results of OT effects on the recognition of basic facial expressions (Leppanen et al., 2017) suggests a small effect in favor of recognizing fearful faces, which supports further investigation of how OT may modulate perceptual and attentional responses to others' distress signals.

While the current study makes important contributions to the literature by investigating the effects of OT on ERP responses to faces in mothers of young children, its limitations are also noteworthy. In addition to the sample size limiting our ability to detect small effects, the current analyses were limited to a highly educated and non-diverse sample of mothers of 1-year-old infants. Thus, it is not known whether exogenous OT would impact responses to faces differently in other caregivers, or in mothers with more variation in the length of caregiving experience, or more diverse backgrounds. Second, reflecting the typical intensity of infant negative emotion expressions, the adult and infant faces were not explicitly matched on emotional intensity. While this is not a critical confound for within-participant analyses testing the main effect of oxytocin vs. placebo on ERPs to the same stimuli across two testing sessions, it would make interpretations of any interactions between face age and facial expression problematic and, thus, equating the emotional intensity of adult and infant stimuli is preferable in future studies. Third, it has also been acknowledged that exogenous OT may not affect all individuals similarly, as participant sex and variation in individual characteristics, such as childhood experiences, may moderate the effects (Bartz et al., 2011). As the current study was the first to investigate neural responses to faces following OT administration in mothers, we considered it appropriate to first explore the potential direct effects OT among this sample and, in the future, potentially extend this line of research to investigate relevant moderating effects in larger samples. Finally, although fairly stringent artifact rejection criteria were applied in the current study to ensure that the data included

in the ERP analyses were of high quality, direct comparisons between separate ERP studies are complicated by variability across studies in how the EEG data are processed. Variability may bring in a degree of subjectivity in the EEG data analysis and, thus, established analysis guidelines are needed to increase comparability across ERP studies and to reduce type I error rates (Keil et al., 2014; Luck and Gaspelin, 2017).

5. Conclusions

In conclusion, the present study showed that single-dose intranasal oxytocin administration increases face-sensitive ERP responses in mothers of 1-year-old infants. The hypothesis that such augmentation is more pronounced to infant faces did not receive sufficient support. The results are in line with the view that OT acts to enhance the perceptual salience of social and emotional stimuli, and contribute to the field by showing such effects in mothers of young children, who are underrepresented in the current literature. Continuing this line of research and thoroughly assessing the potential of intranasal OT to affect the perception of social cues relevant for parent-child interaction should be a major focus of future studies. Important next steps will be to 1) assess the replicability of these findings in larger samples of mothers and other groups of adults (i.e., fathers and nulliparous adults) to more reliably measure whether OT affects the processing of infant and adult stimuli differently, 2) utilize paradigms better suited to test whether OT effects are also found on attention-sensitive brain responses, 3) assess whether the effects of OT would be more pronounced to own infant faces compared to unknown infants (cf. Strathearn et al., 2009, 2008), and 4) when studying parents, incorporate observational assessments of parental interaction to analyze whether the increased neural responses to faces are associated with measurable changes in actual sensitive behavior during interaction with the child.

Conflicts of interest

None.

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