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Attachment Representation modulates Oxytocin Effects on the Processing of Own-Child Faces in Fathers

Running title: Oxytocin and paternal attachment related processing

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Highlights

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- We postulate that oxytocin specifically modulates event-related potentials (ERP)in father-infant-bonds.
- We examine paternal-child visual processing after intranasal oxytocin administration.
- The own child showed differential neural processing under oxytocin compared tofamiliar and unfamiliarchilds.
- Oxytocin induced event-related potential (ERP) modulations in relation to attachment representations in fathers.
- We postulate the existence of a neurophysiological correlate of filial-paternal bond.

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Abstract

Oxytocin (OT) plays a crucial role in parental-infant bonding and attachment. Recent functional imaging studies reveal specific attachment and reward related brain regions in individuals or within the parent-child dyad. However, the time course and functional stage of modulatory effects of OT on attachment-related processing, especially in fathers, are poorly understood. To elucidate the functional and neural mechanisms underlying the role of OT in paternal-child attachment, we performed an event-related potential study in 24 healthy fatherswho received intranasal OT in a double-blind, placebo-controlled, within-subject experimental design. Participants passively viewed pictures of their own child (oC), a familiar (fC) and an unfamiliar child (ufC) while event-related potentials were recorded.

Familiarity of the child's face modulated a broad negativity at occipital and temporo-parietal electrodes within a time window of 300-400 ms, presumably reflecting a modulation of the N250 and N300 ERP components. The oC condition elicited a more negative potential compared to the other familiarity conditions suggesting different activation of perceptual memory representations and assignment of emotional valence. Most importantly, this familiarity effect was only observed under placebo (PL) and was abolished under OT, in particular at left temporo-parietal electrodes. This OT induced attenuation of ERP responses was related to habitual attachment representations in fathers.

In summary, our results demonstrate an OT-specific effect at later stages of attachment-related face processing presumably reflecting both activation of perceptual memory representations and assignment of emotional value.

Key words: oxytocin, father-infant bonds, attachment, event related potentials

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1. Introduction

Parental-infant attachment relationships are crucial for personal development and maturation (Ainsworth and Bell, 1970). During repeated interactions with a supportive and sensitive caregiver, a child develops a stable cognitive schema of the caregiver's availability for reducing stress and providing comfort in potentially threatening situations (Bowlby, 1969).Attachment patterns are associated with different ways to regulate emotions and thus some researchers have actually argued that the attachment system regulates emotions in itself(Vrticka and Vuilleumier, 2012).Interestingly, parental attachment insecurity is associated with higher levels of parenting stress and a lower level of attachment security in the father-child attachment relationship (George et al., 2010).Attachment theory provides a powerful framework for understanding the mental representations of close relationships and their effects on patterns of emotion regulation, psychopathology and clinical intervention (e.g. (Dozier et al., 2008; Westen et al., 2006).Moreover there are indications for different neurophysiological responses inindividuals when the attachment system is activated (e.g. (Diamond and Fagundes, 2010; Gander and Buchheim, 2014).

The neuropeptide oxytocin (OT) and its receptor are essential for bonding and attachment in humans (Buchheim et al., 2009; Heinrichs and Domes, 2008) and other mammals (Lim and Young, 2006; Young and Wang, 2004). Anxiety reduction, affiliative motivation and social salience are potential mechanisms to explain the social effects of OT (Bartz et al., 2010). On the one hand OT has shown anxiolytic effects (Ayers et al., 2011). Other studies report that OT appears to be an indicator of social affiliation (Taylor et al., 2010). A recent report found that intranasal OT increases the salience of certain social stimuli and moderates salience of disgust stimuli (Swain et al., 2014; Theodoridou et al., 2013). Attachment patterns seem to be one of the moderating factors of OT effects (Bartz et al., 2011a). In adults with insecure attachment styles, OT enables to increase the experience of attachment security (Buchheim et al., 2009). In contrast to that, Strathearn and colleagues (2009) found that stimuli that are related to mother-infant bonds resulted in greater activation of both brain-reward regions and OT-associated hypothalamus/pituitary region in securely compared to insecurely attached mothers.

Whereas mother-infant bonds have been widely investigated to better understand the relationship between oxytocin and attachment, OT specific effects on attachment related processing within the domain of father-child interactions have rarely been examined.As

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fathering plays an important role in the development of children's attachment (Owen and Cox, 1997; Tamis-LeMonda et al., 2004), it isimportantto study the effects of OT on the processing of attachment-relevant child stimuli in fathers. Using OT administration is one way to investigate this research question.

A number of functional magnetic resonance imaging (fMRI) studies using exogenous administration of OT suggest an OT sensitive modulatory effect in specific brain regions during attachment sensitive tasks (Bethlehem et al., 2013; Scheele et al., 2013). OT induced an enhancement of activation in limbic regions and augmented the recognition of emotional faces (Van Ijzendoorn and Bakermans-Kranenburg, 2012).Campbell, 2010(Campbell, 2010) stated that one main function of OT is down-regulation of physiological responses to salient cues and reduction of physiological and behavioral responses to stress and pain (Ditzen et al., 2009; Heinrichs et al., 2003; Singer et al., 2008), therefore promoting somatic or psychological well-being. Pathways by which OT facilitates social approach behavior as a basis for social bonds are linked to reduction of aversion or social avoidance on behavioral and neural level (Baumgartner et al., 2008; Kosfeld et al., 2005). Thus OT seems to facilitate approach and affiliative behaviors by an attenuation rather than by enhancement of spontaneous (neuro)physiological responses in emotional brain regions to socially salient cues. This attenuation isprobably also irrespective of the valence of the cues.Correspondingly, we previously found that reward and attachment related brain regions, specifically in the left globus pallidus (GP), are activated when fathers passively view pictures of their own child. Following to OT administration, GP activation and functional connectivity were reduced in response to pictures of their own child (Wittfoth-Schardt et al., 2012). Social effects of OT in humans depend on context and inter-individual differences (Bartz et al., 2011b).

Although fMRI studies have identified the brain areas involved in parent-child attachment, little is known about the time course of attachment processing. The event related potential (ERP) technique allows the investigationof the time course of attachment processing with high temporal resolution in the millisecond range (Luck, 2005). In the present study, we were interested in fast-decaying processes associated with parent-child attachment that take place within time frames too narrow to be captured by functional neuroimaging(Huffmeijer et al., 2013; Noll et al., 2012). In this respect, ERPs are perfectly suited to track the time course of the processing of attachment-related face stimuli and their modulation by OT. In particular, we investigated whether the administration of OT influences early or later stages of stimulus processingafter the sight of attachment-related faces.As scalp ERPs mainly capture cortical activity, it is unlikely to detect OT effects in subcortical emotional brain structures. ERPs may reflect changes in cortical processing that result from changes in subcortical

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signals.Evidence regarding the latency range of the influences of attachment-related facial stimuli is not homogenous, although most studies report relatively late effects in the time range of the P2 and later components (N300, P3/LPP). Some studies found ERP modulations starting as early as the fronto-central N1 when mothers viewed pictures of the faces of their own child (oC) compared to a familiar child(fC)or an unfamiliar child(ufC)(Grasso et al., 2009). Others only found modulations of later ERP components: P2 was modulated by their own child's face compared to faces of other familiar children or faces of unfamiliar children(Caharel et al., 2002); both familiar children and their own child's faces resulted in an increased N300 component (Miyakoshi et al., 2007). Finally, in an even later latency range, P3 and LPP responded to faces of romantic partners (Vico et al., 2010) or to the face of their own child (Weisman et al., 2012). Up to now, ERP studies examining exogenous OT effects are rare and have only been conducted in female participants and with stimuli irrelevant to parent-infant attachment (Huffmeijer et al., 2013; Wu et al., 2013).

Following previous research approaches (Wittfoth-Schardt et al., 2012), a double-blind, placebo-controlled, within–subject experiment with intranasal OT was performed in fathers with stimuli using their own child's face (oC) as the attachment-related stimulus, a familiar child's face (fC) to control for familiarity and an unfamiliar child's face (ufC) to control for novelty. As the majority of studies with attachment-relevant stimuli found familiarity effects at later ERP components such as the N250 and N300, we hypothesized that OT should modulate these later ERP components, which are highly sensitive to familiarity and emotional valence. Familiar faces elicit a larger N250 amplitude(Schweinberger et al., 2004; Tanaka et al., 2006), whereas emotional significance is associated with a larger N300 amplitude (Carretie et al., 1997a; Rossignol et al., 2005). We therefore predicted that fC and, in particular, oC faces would elicit larger N250 and N300 amplitudes than ufC faces. Most importantly, as OT administration reduces neural responses to social stimuli (Domes et al., 2007a; Kirsch et al., 2005; Wittfoth-Schardt et al., 2012), we expected these N250 and N300 familiarity effects only under placebo and reduced under OT. This pattern would suggest that OT primarily modulates mnemonic (Schweinberger et al., 2004; Tanaka et al., 2006) and emotional stages (Carretie et al., 1997a; Rossignol et al., 2005) of attachment-related stimulus processing in fathers. Finally, we hypothesized that the processing of oC faces as the most attachment-relevant stimuli will be modulated by the fathers' attachment styles.

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2. Materials and Methods

2.1. Participants

A total of 32 fathers took part in the ERP experiment. Two participants completed only one session, one was subsequently excluded due to an unknown chronic heart disease, and five participants were not analyzed due to excessive artifacts in the EEG recordings. The final sample thus consisted of 24 healthy, right-handed biological fathers free of medication (mean age ± SD, 39.8 ±5.9 years) having at least one kindergarten child (3-6 years old, **mean age ± SD,**4.9±1.1 years). Eleven fathers were shown pictures of their daughters and other girls, 13 fathers were shown pictures of their sons and other boys. A total of 48 different pictures were used. All of the participating fathers cohabited with their child and its mother. They spent on average 29.7 ± 10.1 hours per week with their child and reported high feelings of closeness with their child (85.1 ± 9.6 on a scale from 0 to 100).

Exclusion criteria included smoking, alcohol and drug abuse, neurological and psychiatric disorders and use of psychotropic drugs, evaluated by self-reports. Written informed consent was obtained before the experiment, and subjects received financial compensation for their participation. The local ethics committee approved the study protocol in accordance with the Declaration of Helsinki.

2.2. Procedures and Stimuli

Initial contact with fathers occurred mainly during pick-up hours in different kindergartens. Written informed consent was obtained before a second contact by telephone. Fathers were asked to name a fC of the same age and sex as their oC. Familiarityof the fC was determined using a self-report questionnaire based on a four-point Likert scale regarding the quality of their acquaintance with the fC. Fathers were asked how well (not well-very well) and how long (<6 months to > 1 year) they know the fC, how they feel while spending time with the fC (pleasant-unpleasant) and how often they spent time with the fC (never-several times / week). All fathers knew the fC for more than one year and reported medium (50%) to good (38%) levels of familiarity. Contact with the fC was rated as neutral (17%), pleasant (50%) or joyous (33%). Informed consent of the parents was obtained to use the oC and fC pictures as stimuli in the ufC condition for other fathers. Unfamiliarity with the ufC for each father was verified by presenting the ufC pictures before starting the EEG sessions.

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Digital pictures were taken within 1-12 weeks prior to the experiments using a 10-megapixel reflex camera (Nikon D80). Pictures were uploaded into Corel Photo-Paint Version x4.Six pictures per condition were chosen in which the child was facing the camera looking straight ahead with a friendly facial expression. We preferred to use friendly facial expressions in the present study over neutral faces for several reasons: Robust modulatory effects in recognition accuracy or reaction time on the processing of facial expression were especially found for happy and angry faces (Shahrestani et al., 2013). Additionally, happy facial expressions are easier to identify than neutral expressions and therefore provide a better experimental control over stimuli in the three familiarity conditions. Friendliness of facial expressions of all pictures were classified (yes/no) by three independent judges and only pictures with 'yes' classification of all three judges were included in the experimental tasks. The pictures were matched for luminance and color temperature, and masked with an oval shape so that only the face of the child was visible. Pictures had a final pixel size of 640x480. In total, 57 different children were photographed (29 ♂, 28 ♀).

Two EEG sessions were performed within 10-29 days at comparable times of day between **0800h – 0900h**a.m. A double-blind placebo-controlled within-subjects design was used. To determine scores for depression, anxiety and alexithymia, participants filled out the Beck Depression Index (BDI), the State-Trait Anxiety scale—Trait version (STAI-T) and a German adaption of the Toronto Alexithymia Scale (TAS-20). At the beginning and at the end of each experimental session, participants completed a multidimensional mood questionnaire (Steyer et al., 1997) and the State-Trait Anxiety Inventory—State version (STAI-S) in order to assess OT-related changes in mood, alertness or calmness.

Thirty minutes before the beginning of the paradigm, participants received an intranasal administration of either 24 IU (international units) of oxytocin (Syntocinon®; Novartis, Basel, Switzerland) or placebo (PL, ingredients equivalent except for the peptide) delivered by three puffs per nostril with 4 IU each (Domes et al., 2007b).**Whereas several studies showed a significant increase of cerebrospinal fluid (CSF) OT levels 30 minutes following intranasal OT (Born et al., 2002), other investigations revealed significant increases in OT CSF levels up to 75 minutes after administration (Striepens et al., 2013).**Our experiment, which lasted about 60 min, began 30 min after spray administration in order to ensure sufficient neuropeptide availability during the whole experimental procedure.The order of administration was counterbalanced across subjects.After each experimental session, fathers rated feelings of closeness to the depicted child for each photo on a visual analogue scale (VAS) from 0 to 100. Ratings were compared across sessions (OT, PL) and familiarity conditions (oC, fC, ufC). Each of the six pictures was presented 10 times over the

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course of the experiment, amounting to a total of 180 experimental trials. The fathers were instructed to attentively view each picture. Similar to our earlier study and other work (Miyakoshi et al., 2007; Wittfoth-Schardt et al., 2012), we used a passive viewing task to probe emotional processing of naturalistic stimuli without any bias originating from overt responses or specific task demands.The stimuli were presented for 2000 ms on a grey background in pseudo-randomized order. After each stimulus, a white fixation cross was presented at the center of the screen for 2000 ms. After 60 and 120 stimuli, a longer fixation of 10 seconds each were included during which participants were instructed to attend the fixation cross and relax. Continuation of stimulus presentation was signaled by visual presentation of the word “Attention” (“Achtung”). Stimulus presentation was controlled using Presentation 13.0 (Neurobehavioral systems, Albany, CA, USA). Total presentation time of each session was 12.26 minutes.

Given the length of each experimental ERP session, assessment of attachment representation using the Adult Attachment Projective Picture System(George and West, 2001)was conducted in a separate visit in 22 fathers.Two fathers were not able to attend due to time constraints. **Attachment classifications were coded by one coauthor (AB), who is a certified trainer of the AAP measure and highly experiencedin coding**(George and West, 2012). In this sample n=9 fathers were classified as being secure and n=13 fathers were classified as being insecure.

2.3. EEG recording and Data Analysis

EEG was recorded (reference at FCz, ground at AFz) with a digitalization rate of 500 Hz (low cutoff filter at 0.3 Hz, high cutoff filter at 70 Hz, impedance 5 kOhm) from 32 scalp sites positioned according to the international 10-20 system using active electrodes (Ag/AgCl) mounted in an elastic cap (actiCAP) with a Brain Amp DC amplifier (Brain Products Gilching, Germany).

EEG data were analyzed with the BrainVision Analyzer (BrainProducts, Gilching, Germany). Data were filtered offline (low cut-off: 0.1 Hz, 12 dB/oct attenuation; high-cut-off: 30 Hz, 24 db/oct attenuation)and segmented in 200 ms pre-stimulus and 600 ms post-stimulus epochs. After baseline correction (-200 ms to 0 ms), trials containing ocular artifacts in the VEOG or HEOG channels (voltages > +/- 40 microV) or other artifacts in the recording channels (voltages > +/- 70 microV) were discarded. For ERP extraction, artifact-free EEG segments were averaged separately for three conditions (ufC, fC, oC) and for the two sessions (OT, PL). On average, the following average number of artifact-free segments were included in the analyses (PL: ufC: 48.1, fC: 51.2, oC: 51.1; OT: ufC: 50.0, fC: 50.1, oC: 49.5). Number of

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segments did not differ significantly across conditions [F(5, 115)=0.91, p=0.48]. Due to the relatively small number of recording electrodes, an average reference transform, which requires at best 64 electrodes or more, was not appropriate (Scherg, 1990). We kept the original recording reference FCz for further data analyses since ERP components at parietal and occipital leads, which were of primary interest in our research, are clearly visible due to their large distance to FCz (Nunez, 1981).

Peak amplitudes of the P1 (voltage maximum within 90-140 ms after stimulus onset), the N170 (voltage minimum within 142-200 ms) and the P2 (voltage maximum within 210-300 ms) were calculated.All amplitudes were calculated as an average of the peaks and the twelve adjacent time points preceding and following the peaks, leading to an amplitude time window of 24 ms. Mean potentials in two further time windows, which might coincide with the N250 and N300 ERP components, were statistically analyzed to capture modulation of an extended negative deflection following the P2 (300-350 ms), possibly N250, and a broad negative peak (350-400 ms), possibly N300. Two scalp regions of interest, in which our ERP components of interest were typically largesteach represented by pairs of contra-lateral electrodes were selected for further statistical analysis. An occipital electrode cluster comprised electrodes O1/O2 and PO9/PO10 and the temporo-parietal electrode cluster the electrodes CP5/CP6, P7/P8, T7/T8. Amplitudes of all ERP components of interests were statistically analyzed within both electrode clusters in order to assess topographic differences. Although the LPP would have been potentially interesting due to its sensitivity to emotional face processing (Vico et al., 2010; Weisman et al., 2012), visual inspection of the ERPs revealed that familiarity effects disappeared in time intervals longer than 400 ms after picture onset. We therefore did not analyze ERPs in the LPP time window.

2.4. Statistical analyses

For each of the ERP components (P100, N170, P200, N250, N300), separate repeated-measures analyses of variance (ANOVA) tests for each of the two electrode clusters with treatment (OT vs. PL) x face familiarity (ufC, fC, oC) x laterality (left vs. right) x electrode site (number of contralateral pairs within each cluster) were computed. In order to reduce complexity of the results section, we only report significant effects involving one of the experimental factors and do not describe effects of purely topographical factors (laterality and electrode site).Significant main effects and interactions were further explored with subsequent two-sided (paired) t-tests (*p* level .05)**which were not corrected for multiple comparisons (Hays, 1994).**Possible relations between ERP responses to face familiarity and attachment representations (securely and insecurely attached fathers) were explored by means of correlation analyses (Spearman) using secure/ insecure attachment

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representations and mean voltage differences between oC and fC/ufC at left or right occipital and temporo-parietal clusters (averaged across electrode sites within each hemisphere of each cluster).

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3. Results

3.1. Behavioural Data

Mood, alertness, calmness and STAI-S were not affected by OT administration at the beginning [t(23)=-1.21, p=0.238, t(23)=-1.53, p=0.140, t(23)=0.48, p=0.639 and t(20)=1.57, p=0.132, respectively] or at the end of the experimental sessions [t(23)=-0.30, p=0.765, t(23)=-0.43, p=0.672, t(23)=0.59, p=0.561 and t(20)=0.00, p=1.000, respectively]. Visual analogue scale (VAS) closeness ratings showed the highest values under PL for oC (97 ± 4), intermediate for fC (60 ± 14) and the lowest for ufC (18 ±19) and were not affected by OT [oC: t(23)=-1.14, p=0.265; fC: t(23)=1.63, p=0.117; ufC: t(23)=0.29, p=0.773]. Fathers with insecure adult attachment reported significantly higher calmness and VAS closeness ratings for the fC during PL compared to OT [t(12)=-2.29, p=0.041, d=0.64 and t(12)=2.19, p=0.049, d=0.61, respectively].

3.2. Electrophysiological Data

3.2.1. Occipital electrodes

The P1 and N1 at occipital electrodes were neither modulated by familiarity nor treatment. However, familiarity significantly affected P2 [F(2, 46)=4.20, p=0.021, η^2=0.155]. Subsequent t-tests showed that the P2 amplitude while looking at fC were more positive compared to the amplitudes while looking at ufC [t(23)=-3.00, p=0.006, d=0.61] and oC [t(23)=2.30, p=0.031, d=0.47] (Figures 1a and 1c).

We found a main effect of familiarity in the time windows of 300-350 and 350-400 ms [F(2, 46) = 6.59, p=0.003, η^2=0.223; F(2, 46) = 4.76, p=0.013, η^2=0.172], indexing more negative potentials in the oC compared to the ufC and fC conditions. Most importantly, we found an interaction of familiarity x treatment x hemisphere at 350-400 ms post stimulus [F(2, 46) =3.34, p=0.044, η^2=0.127]. Subsequent t-tests revealed differences between oC and ufC only in the left hemisphere in both PL and OT conditions. During PL, oC showed a more negative potential compared to ufC [t(23)=2.99, p=0.006, d=0.61]. During OT, the negative potential in the oC condition was less pronounced than during PL, but remained significant compared to ufC [t(23)=2.18, p=0.039, d=0.45] (Figures 1a and 1c).

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3.2.2. Temporo-parietal electrodes

N1, P1 and P2 were neither modulated by familiarity nor by treatment. In the time windows of 300-350 and 350-400 ms, we found main effects of familiarity [$F(2, 46) = 5.68$, $p=0.006$, $\eta^2=0.198$] and treatment [$F(2, 46) = 3.66$, $p=0.034$, $\eta^2=0.137$] indexing more negative ERPs to oC (Figures 1b and 1d).

Most importantly, we also found interactions between treatment and familiarity in the time frame between 300-350 ms [$F(2, 46) = 3.90$, $p=0.027$, $\eta^2=0.145$]. Subsequent t-tests revealed differences between familiarity conditions only in the PL condition with a more negative potential to oC compared to fC [$t (23)=4.70$, $p=0.000$, $d=0.96$] and ufC [$t (23)=3.25$, $p=0.004$, $d=0.66$]. We found no differences between familiarity conditions under OT (Figures 1b and 1d).

In the time window of 350-400 ms, a significant interaction of familiarity x treatment x hemisphere [$F(2, 46) = 5.52$, $p=0.007$, $\eta^2=0.193$] was observed. According to subsequent t-tests, significant potential differences were obtained in the left hemisphere in the PL condition: a more negative potential was obtained in the oC condition compared to ufC [$t (23)=3.83$, $p=0.001$, $d=0.78$] and fC [$t(23)=2.38$, $p=0.026$, $d=0.48$]. Further t-tests for independent samples revealed a significantly enlarged negative potential for oC in PL condition compared to OT [$t (23)=-2.09$, $p=0.048$, $d=43$].Hence, OT treatment specifically modulated ERP of the oC condition in the left hemisphere at 350-400 ms (Figure 2).

3.3. Correlations between Familiarity ERP Effects and Attachment Representations

No correlations between familiarity and attachment representations were found for N1, P1 and P2. In both time windows between 300-400 ms, correlation analyses showed that OT reduced the familiarity effects observed under PL only in secure fathers. At 300-350 ms we found a negative correlation between oC and fC potential differences and attachment at right occipital electrodes [N(22), r=-0.44, p=0.038, CI=(-0.79)-(-0.01)] (Figure 3a). In the time window of 350-400 ms, we observed a negative relationship between oC and fC potential differences and attachment under OT treatment at right temporo-parietal electrodes [N(22), r=-0.59, p=0.004, CI (-0.81)-(-0.24)] (Figure 3b) and occipital electrodes [N(22), r=-0.46, p=0.032, CI=(-0.76)-(0.07)] (Figure 3c). We also found negative correlations between oC and ufC potential differences and attachment at left [N(22), r=-0.49, p=0.021, CI=(-0.77)-(-0.11)] (Figure 3d) and right [N(22), r=-0.65, p=0.001, CI=(-0.83)-(-0.33)] (Figure 3e) occipital electrodes. Correlation analysis was confirmed by subsequent t-tests for independent samples: Under OT mean potential differences between oC and fC were more negative, i.e. larger in insecure compared to secure fathers at right temporo-parietal [t(20)=3.28, p=0.004,

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d=1.42] and occipital electrodes at 300-350 ms [t(20)=2.39, p=0.027, d=1.04] and at 350-400 ms [t(20)=2.85, p=0.010, d=1.23] post stimulus. Potential differences between oC and ufC were also more negative in insecure vs. secure fathers at 350-400 ms in left [t(18.6)=2.57, p=0.019, d=1.11] and right [t(20)=3.27, p=0.004, d=1.42] occipital electrodes clusters.

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4. Discussion

In the present study we used ERPs to elucidate the time course of neuronal processing in fathers in response to an individualized picture of their own child under PL and OT conditions. We found a broad negative deflectionat occipital and temporo-parietal electrode positions in response to oC between 300-400 ms post stimulus, within the time range of the N250 and N300 ERP components. OT abolished this oC-specific negative ERP deflection, with a left lateralized treatment effect at 350-400 ms resulting in comparable potentials across familiarity conditions. This result pattern suggests that OT mainly modulates later stages of processing of attachment-related faces associated with activation of mnemonic and emotional memoryprocesses leaving earlier perceptual stages unaffected. Interestingly, this OT induced modulation of attachment-related stimulus processing may depend, among other things, on attachment representations in fathers.The reduction of the oC specific effect under OT compared with PL was more pronounced in the secure group (over the right hemisphere) whereas insecure attachment resulted in a persistence of the oC effect even under OT.

4.1. ERP components

Recordings of electrical brain activity during passive viewing of face stimuli of differential familiarity allowed us to identify the processing stage at which OT modulates processing of attachment-related stimuli. In the present study, P1 and N170 components were neither modulated by familiarity nor by OT. This indicates that processing of low-level visual features and activation of structural representations did not differ across conditions. The earliest effect was an increased P2 amplitude in fC. Since P2 is known to reflect attentional modulation of higher-order perceptual processing (Luck and Hillyard, 1994),one may speculatethat fC induced more intense attention in comparison to oC and ufC. FC faces exhibit an intermediate degree of familiarity compared with oC und ufC faces that enhances attentional selection. This interpretation is clearly post-hoc and deserves further investigation. However, several studies have identified oC and the novel ufC conditions as more salient cues for reward and attachment related processes (Caharel et al., 2002; Doi and Shinohara, 2012a, 2012b; Leibenluft et al., 2004). In any case, P2 modulation by fC in our study was much smaller compared to the oC specific modulations in subsequent time intervals.

Most importantly, between 300 and 400 ms, we observed a broad negative deflection, which was modulated by familiarity and OT. Regarding the latency range and topography of the potential at 300-350 ms, this negative deflection may be a modulation of the N250 ERP component, indexing activation of perceptual face representation in long-term memory

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(Schweinberger et al., 2004; Schweinberger et al., 2002). The N250 is not specific to faces but can also be elicited by familiar objects and is thought to distinguish personally familiar and generically familiar objects from novel and unfamiliar objects with a left-lateralized potential (Miyakoshi et al., 2007; Tanaka et al., 2006). In line with the known sensitivity of the N250 to familiarity (e.g., the largest amplitude is to ones own face;(Tanaka et al., 2006), the face of the oC elicited the largest negativity. N250 amplitude in the fC condition did not differ from that of the ufC condition, suggesting that the familiarity of the fC was not sufficiently high to have established a face representation in long-term memory (Bentin and Deouell, 2000; Tanaka et al., 2006).

The later portion of this late negativity in the 350-400 ms time window might coincide with the N300, which has been associated with emotional processing of visual stimuli (Carretie et al., 1997b). Under PL, N300 was larger for oC than for fC and ufC suggesting that the face of the oC was assigned with a particular emotional valence. In line with this interpretation, N300 was enhanced for positive emotional trials compared to neutral ones (Carretie et al., 1997a; Rossignol et al., 2005) and distinguished between emotional valences of visual stimuli at left lateralized parietal electrode sites (Carretie et al., 1997b). We acknowledge that the positive emotional expression of the children's faces might be one factor responsible for the emergence of ERP effects of familiarity in later time windows covering the N250 and N300 components similar to earlier work investigating the influence of positive valence(Carretie et al., 1997a; Rossignol et al., 2005). It is therefore an open question to be addressed in future studies whether emotionally negative face stimuli expressing anger or fear, for instance, would give rise to ERP effects of familiarity with an earlier onset.

4.2. OT specific effects

Several lines of evidence suggest that OT facilitates the processing of facial expressions (Domes et al., 2007a; Schulze et al., 2011) and improves recognitionfor faces (Rimmele et al., 2009; Van Ijzendoorn and Bakermans-Kranenburg, 2012). However, only a few studieshave focused on the neural processing of emotional stimuli under OT. Despite the important role of fathers for children's development of attachment (Owen and Cox, 1997; Tamis-LeMonda et al., 2004), our study is the first to investigate the OT effects in attachment-related processing in fathers using personalized face stimuli.Wu et al. (Wu et al., 2013) studied the evaluation of self vs. other owned objects using ERP and revealed an OT specific modulation of affiliative and approach motivations during social interaction. Only one study (Huffmeijer et al., 2013) focused on intranasal OT effects on emotional faces using a performance feedback design. The authors revealed an OT induced attention increase in the feedback stimuli and a better processing of emotional faces due to increased vertex positive

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potential (VPP) and late positive potential (LPP). However, as this earlier study did not use personalized attachment-related face stimuli of children, the results are not comparable with the present work.

An fMRI study of our group revealed that OT reduced activation and functional connectivity of the left globus pallidus (GP) with reward and attachment related regions in response to oC (Wittfoth-Schardt et al., 2012). We have suggested that OT reduces neural reactivity to social cues as a function of social salience. These earlier results are in accordance with the present temporo-parietal and occipital ERP effects, which were reduced after administration of OT. Similarly, recent fMRI studies observed reduced neural activation to emotional stimuli (Domes et al., 2007a; Kirsch et al., 2005) due to OT**.** Therefore, we conclude from the present ERP study that OT may attenuate (neuro)physiological responses to salient social cues which may reflect a more efficient processing and facilitation of social interactions under OT (Domes et al., 2007a; Gordon et al., 2010; Kanat et al., 2015). This OT induced attenuation of neural reactivity may increase approach tendencies and reduce social avoidance in order to form new social bonds and increase the experience of social support. It is particularly consistent with the 'approach-related' behavior model of oxytocin effects proposed by Kemp and Guastella (Kemp and Guastella, 2011).

Similar to the effects in the brain, OT induces a down-regulation of physiological responses to salient cues or stress (Campbell, ; Ditzen et al., 2009). Both, central and peripheral OT effects are directly related to somatic and psychological well-being. Our present study provides information about the time course and the functional stages at which OT modulates attachment related processing: OT influences processing at later stages of attachment-related face processing associated with activation of perceptual memory representation and assignment of emotional value by attenuating the saliency of attachment-related stimuli. Given that activity in subcortical structures is barely reflected in scalp ERPs, we assume that the observed ERP modulations by OT indirectly index modulated activation of reward- or attachment related subcortical structures (Wittfoth-Schardt et al., 2012). Possibly, our scalp ERP modulations index at best consequences of subcortical activity on cortical processing related to face memory and emotional valence assignment.

4.1. Attachment specific effects

The present study identifies some important contextual and interindividual factors that moderate the effects of OT. Correlation analyses of the familiarity effects with fathers' attachment classifications yield an OT induced decrease in N300 amplitude in response to oC over the right temporo-occipital scalp only in secure fathers. This finding indicates that a

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secure attachment style enables OT effects by facilitation of approach and affiliative behaviors to reward and attachment relevant stimuli. OT did not affect the familiarity processing, indicating that for insecure fathers, OT is unable to facilitate attachment-relevant stimuli processing. Our findings are in line with previous studies suggesting less pronounced OT effects in individuals with more unfavorable childhood relationship experiences such as high love withdrawal (Huffmeijer et al., 2013; Van Ijzendoorn et al., 2011). Additionally, Bartz et al. found that OT effects on maternal recollections were critically moderated by individual differences in attachment anxiety (Bartz et al., 2010) and that OT caused detrimental effects on trust and cooperation in patients suffering from borderline personality disorder (Bartz et al., 2011a). From an attachment perspective, longitudinal data indicate that security is associated with high-investment parenting (Van Ijzendoorn et al., 2011), including in fathers (van Ijzendoorn et al., 1992). However, given the relatively small sample size of secure and insecure attached **fathers and the lack of estimations of inter-rater reliability due to only one AAP rater**, these attachment-specific effects should be replicated in a larger sample.

4.2. Conclusions

The present ERP study determines, for the first time, the stage at which exogenous OT in fathers modulates processing of their own child's faces. We observed both, familiarity and attachment related OT effects as potential neurophysiological correlates of a filial-paternal bond. OT modulated ERPs in response to attachment-related faces between 300-400 ms after stimulus onset (N250 and N300 ERP components) indexing activation of face representation in memory and assignment of emotional valence, respectively. Thus, OT primarily modulates functionality of post-perceptual stages of attachment-related face processing. Finally, OT modulation was more pronounced in securely attachedfathers which indicates that OT might depend on a specific attachment style to be effective.

5. Disclosure

The authors declare no conflict of interest. All authors have approved the final article.

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7. Figure Legends

Figures 1 a-d: Grand mean ERPs for oC, fC and ufC in the PL (a, b) and OT (c, d) treatment conditions in occipital and temporo-parietal electrode clusters. OT administration attenuated a broad negative deflection to oC, which was only present under PL, particular over the left hemisphere in a time window between 300-400 ms post stimulus. This modulatory effect of OT on ERPs is highlighted by the black rectangle. Negative potentials are plotted downward. Abbreviations: oC=own child; fC= familiar child; ufC: unfamiliar child; OT=oxytocin; PL=Placebo

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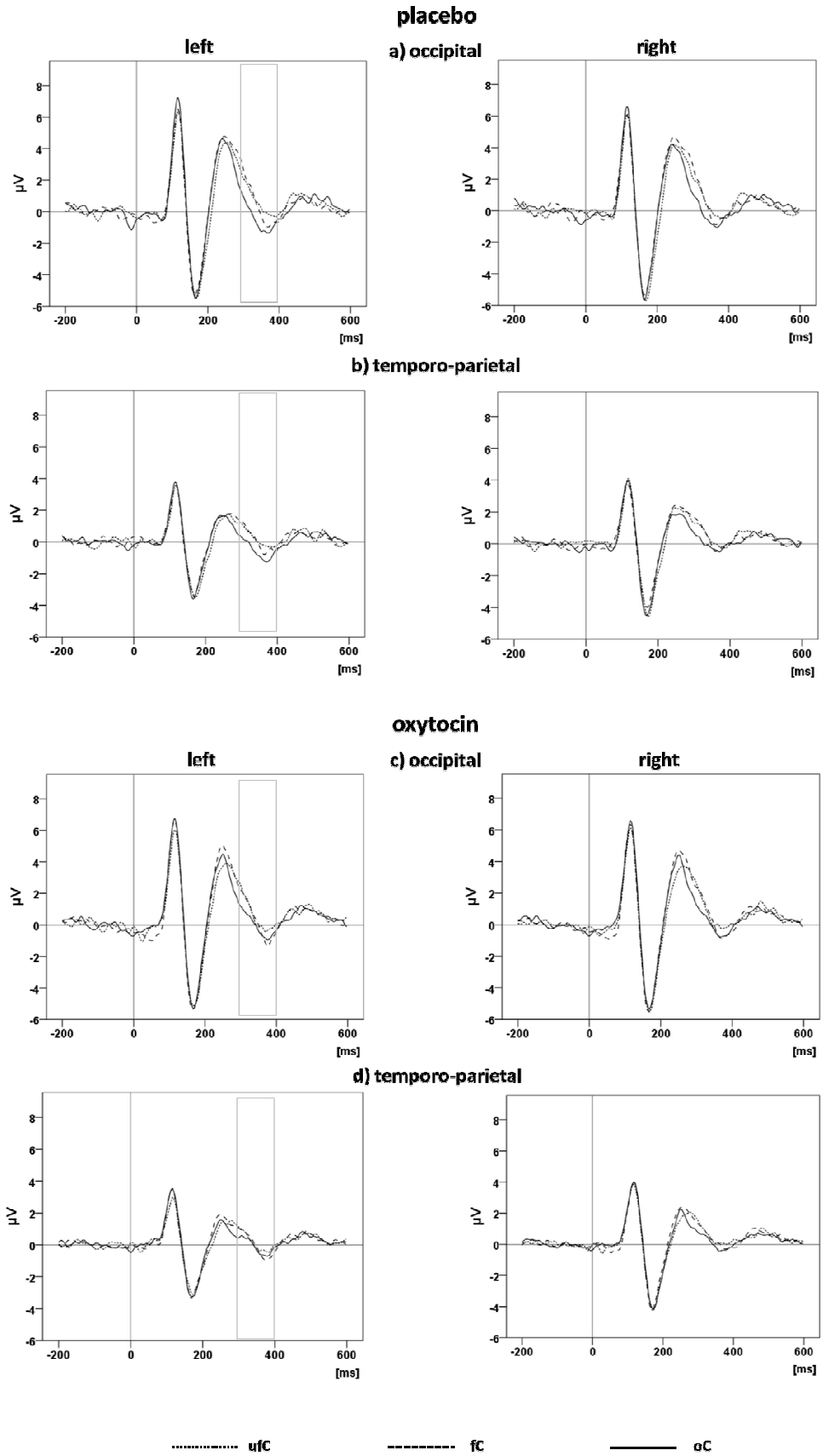

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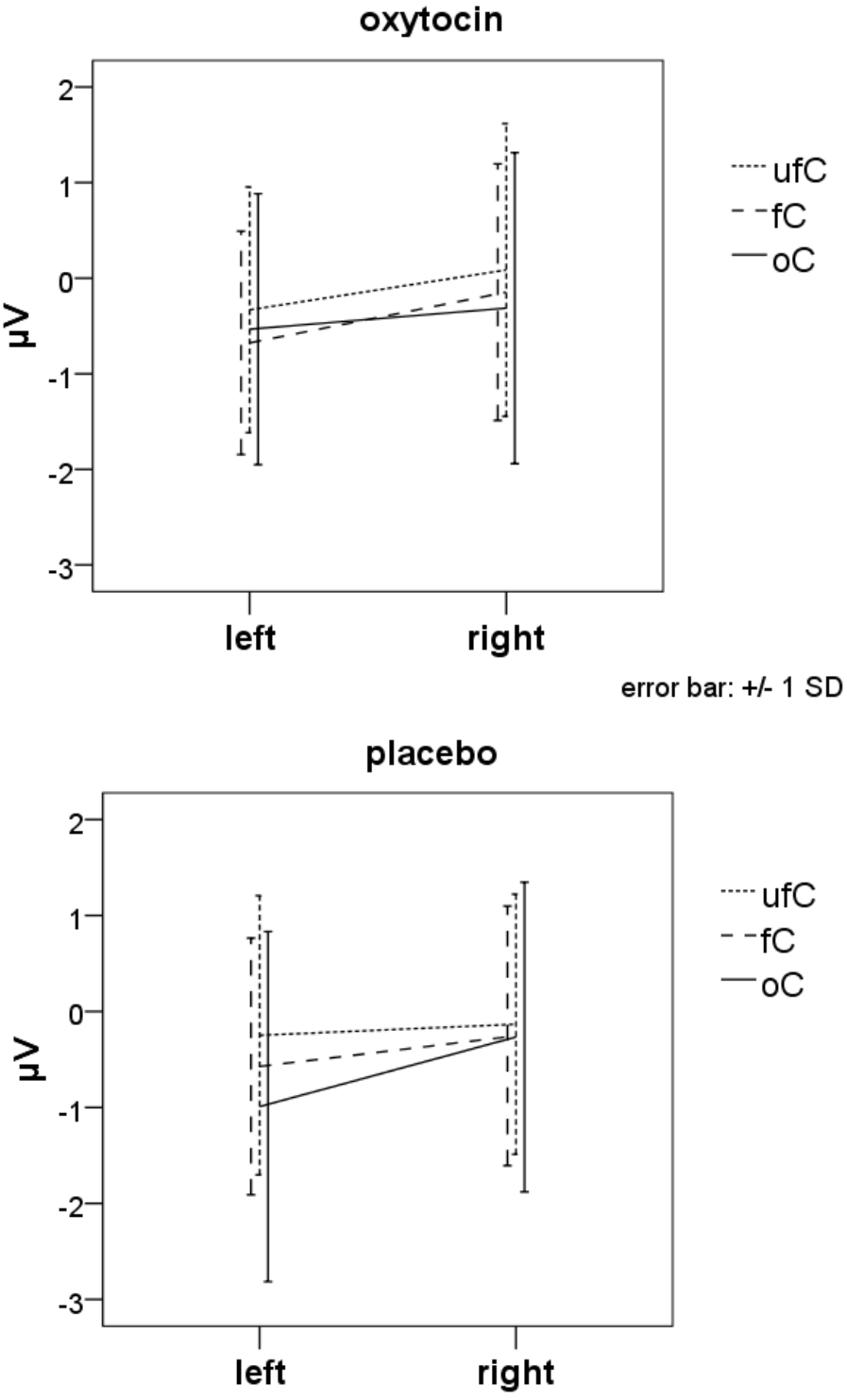
Figure 2: Mean ERPs in the temporo-parietal electrode cluster within the time window of 350-400 ms post stimulus as a function of familiarity and OT treatment. This figure illustrates the condition x treatment x hemisphere interaction: the left lateralized oC ERP effect is present under PL, but abolished after OT treatment.



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Figures 3 a-e: Individual potential differences for oC vs. fC and ufC, respectively, between fathers with secure and insecure attachment representations in both occipital and temporo-parietal electrodes clusters. After OT treatment, insecure attached fathers exhibit a greater negative potential to oC faces compared to the other conditions. Only secure attached fathers show a reduction of the familiarity effect under OT as it was obtained for the entire sample.

