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How the Brain Codes Intimacy: The Neurobiological Substrates of Romantic Touch

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Abstract: Humans belong to a minority of mammalian species that exhibit monogamous pair-bonds, thereby enabling biparental care of offspring. The high reward value of interpersonal closeness and touch in couples is a key proximate mechanism facilitating the maintenance of enduring romantic bonds. However, surprisingly, the neurobiological underpinnings mediating the unique experience of a romantic partner's touch remain unknown. In this randomized placebo (PLC)-controlled, between-group, pharmacofunctional magnetic resonance imaging (fMRI) study involving 192 healthy volunteers (96 heterosexual couples), we intranasally administered 24 IU of the hypothalamic peptide oxytocin (OXT) to either the man or the woman. Subsequently, we scanned the subjects while they assumed that they were being touched by their romantic partners or by an unfamiliar person of the opposite sex, although in reality an identical pattern of touch was always given by the same experimenter. Our results show that intranasal OXT compared to PLC selectively enhanced the subjective pleasantness of the partner's touch. Importantly, intranasal OXT selectively increased responses to partner touch in the nucleus accumbens (NAcc) and anterior cingulate cortex. Under OXT, NAcc activations to partner touch positively correlated with the subjects' evaluation of their relationship quality. Collectively, our results suggest that OXT may contribute to the maintenance of monogamous relationships in humans

Additional Supporting Information may be found in the online version of this article.

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by concomitantly increasing the reward value of partner touch and diminishing the hedonic quality of stranger touch. *Hum Brain Mapp 38:4525–4534, 2017.* © 2017 Wiley Periodicals, Inc.

Key words: fidelity; fMRI; oxytocin; pair-bonding; touch

INTRODUCTION

"See how she leans her cheek upon her hand.
O, that I were a glove upon that hand.
That I might touch that cheek!"
—William Shakespeare, Romeo and Juliet

Romantic relationships not only enable biparental care of the offspring but also strengthen the physical and psychological health of the couple [Kiecolt-Glaser and Newton, 2001]. Surprisingly, however, little is known about the proximate neurobiological mechanisms underlying the maintenance of long-term pair-bonds in humans. One of the strongest signals of intimacy and emotional bonding between two individuals is interpersonal touch [van Anders et al., 2013]. Even strangers can accurately decode distinct emotions (e.g., love vs sympathy) when they are touched by another person [Hertenstein et al., 2006], thus supporting the notion that interpersonal touch serves as the primary nonverbal communication channel [Morrison et al., 2010]. The hedonic value of touch is determined by the physical characteristics of the touch, the person's internal emotional status, and the context in which it is applied [Ellingsen et al., 2015]. In romantic relationships, the sensual caress of the partner is experienced as wonderful, while the same touch by an unfamiliar person feels repulsive. The experience of pleasant interpersonal touch is mediated by unmyelinated, C-tactile afferent fibers activated through low-force and slow dynamic touch stimuli [McGlone et al., 2014]. Imaging studies revealed that affective touch elicits activations in a broad neurocircuitry including the insula, orbitofrontal cortex (OFC), and anterior cingulate cortex (ACC) [Gordon et al., 2013; Lindgren et al., 2012; McCabe et al., 2008; Rolls et al., 2003; Voos et al., 2013]. Even the anticipation of a romantic caress resulted in increased neural activity in the insula and was positively associated with the levels of passionate love [Ebisch et al., 2014].

Importantly, we have previously shown that the intranasal administration of the neuropeptide oxytocin (OXT) increases the pleasantness of touch from a female but not a same-sex person, and enhances touch-related activation in the insula, OFC, and pregenual ACC in healthy men [Scheele et al., 2014a]. Furthermore, physical massage [Morhenn et al., 2012] and frequent hugs between romantic partners are associated with higher OXT plasma concentrations [Light et al., 2005].

Several studies also document that the OXT system contributes to parent–offspring bonding [Feldman, 2015]; for example, parents exhibiting high OXT plasma levels touch their infants more frequently [Feldman et al., 2012]. The psychology of parenting and pair-bonding share substantial overlaps, and it has been suggested that maternal attachment is the precursor of monogamous pair-bonding [Ross and Young, 2009]. In fact, in prairie voles, OXT facilitates pair-bond formation through its interaction with dopamine release particularly in the nucleus accumbens (NAcc) [Young and Wang, 2004]. In humans, OXT plasma levels are higher in new lovers than in unattached singles and positively correlate with couples' interactive reciprocity including positive affect and affectionate touch [Schneiderman et al., 2012]. Additionally, intranasal OXT increases NAcc responses to the partner's face compared to an unfamiliar face [Scheele et al., 2013]. Further evidence for the hypothesis that OXT strengthens the maintenance of pair-bonds comes from studies showing that OXT increases positive communication during couple conflicts [Ditzen et al., 2009] and stimulates pair-bonded men to keep a larger social distance from an attractive, unfamiliar woman [Scheele et al., 2012].

While some authors have speculated that the release of OXT due to interpersonal touch may facilitate the formation of long-term relationship bonds [Gallace and Spence, 2010], it remains currently unknown whether OXT also influences the unique experience of partner touch and which neural substrates are involved. Thus, we conducted a randomized placebo-controlled, between-group study involving 96 heterosexual couples. Participants were scanned while they assumed that they would be touched by either their romantic partners or by an unfamiliar experimenter of the opposite sex. In reality, the touch was always applied by the same experimenter. In addition, there was a nontouch control condition (Close) in which the experimenter or the partner would only stand nearby without any physical contact. The fMRI task was designed to carefully control possible confounding factors due to interindividual preferences or habits in partner touch. We hypothesized that the pleasantness of partner touch and touch-induced activation in reward-associated brain areas would increase with levels of passionate love. Furthermore, we predicted that compared to placebo (PLC), intranasal OXT (24 IU) would increase the pleasantness of and neural responses to partner touch relative to stranger touch in both touch-related (insula, OFC, and ACC) and bonding-related neural networks (NAcc).

MATERIALS AND METHODS

Participants

One hundred and ninety-two nonsmoking, heterosexual volunteers with no current or past physical or psychiatric illness participated in this study after giving written

informed consent. OXT or PLC nasal spray was randomly administered to either the man ($n = 67$) (age 25.76 ± 4.41 years) or the woman ($n = 29$) (age 25.48 ± 3.15 years) of the 96 heterosexual couples depending on the inclusion and exclusion criteria (cf. Supporting Information, Methods). For female participants the use of hormonal contraceptives, the birth of a child, or pregnancy during the study were defined as additional exclusion criteria. All women except two were tested in the luteal phase of their menstrual cycle and were premenopausal. Excluding the two women who were tested in the follicular phase did not change the pattern of results. The cycle phase was validated by blood assays (FSH, LSH, estradiol, progesterone, and testosterone concentrations) collected on the testing day (cf. Supporting Information, Table S1). Subjects were free of current and past physical or psychiatric illness, as assessed by medical history and the Mini-International Neuropsychiatric Interview (MINI) [Sheehan et al., 1998]. Screening of the subjects was conducted prior to the test sessions. All heterosexual couples were passionately in love. There were no a priori differences regarding demographical and psychometric variables between the OXT and PLC group (cf. Supporting Information, Table S2).

The study was approved by the institutional review board of the Medical Faculty of the University of Bonn and was in accordance with the Declaration of Helsinki.

Experimental Design

We performed a randomized, double-blind, placebo-controlled, between-group design study. Subjects were randomly assigned to either the intranasal administration of PLC (containing all ingredients except the peptide; $n = 48$) or OXT (24 IU; six puffs per nostril each with 2 IU; $n = 48$; Novartis, Basel, Switzerland). The administration of PLC and OXT was balanced within the male (OXT $n = 34$, PLC $n = 33$) and female (OXT $n = 14$, PLC $n = 15$) subsample. Owing to extreme head movements (>3 mm/°) and technical problems during the fMRI acquisition, six subjects (three men and three women) were eliminated from the fMRI data analysis. Thus, we performed the fMRI data analysis with 46 subjects (32 ♂; 14 ♀) in the PLC group and 44 subjects (32 ♂; 12 ♀) in the OXT group.

The fMRI task began 30 min after the nasal spray administration. To examine potential changes in endogenous OXT levels, two saliva samples of each subject were collected. One sample was collected before the administration of the nasal spray (pre) and another sample immediately after the fMRI task (post). We also collected one saliva sample of the subjects' romantic partners at the beginning of the testing session. Further information regarding the tasks, the fMRI measurement, and the data analysis can be found in the Supporting Information.

fMRI Paradigm

We applied a slightly modified version of a previously used paradigm [Gazzola et al., 2012; Scheele et al., 2014a]. The subjects were informed that either their romantic partner or an unfamiliar male/female experimenter would be in the MRI room during the experiment and would perform the touch. The sex of the experimenter was matched to the partner outside the MRI; that is, if a female participant was lying in the scanner, she assumed that she would be touched either by her male partner or by the male experimenter. Unbeknown to the subjects, the touch was always applied by the same male experimenter thereby keeping the intensity and type of cutaneous stimulation constant across the whole experiment. Furthermore, the romantic partner went into the MRI room before experimental runs with partner touch and shortly talked with the participant.

The subjects were also informed that the romantic partner or the experimenter could be in three different positions (Home, Close, and Touch) during the experiment. In all three conditions, a photograph of the male/female experimenter or the partner was presented to the subject on a screen. No touch was shown on the photographs. The conditions (Home, Touch, and Close) were illustrated via white text next to the photograph. The current experimental condition was highlighted with a white frame surrounding the text. The participants were told that the experimenter and the partner would be in the Home position most of the time. The Home position was precisely described as a position 2 m away from the MRI table and at 45° angle from the junction between the MRI table and the opening of the magnet. In fact, unbeknown to the subject, the partner was outside the MRI room and the unfamiliar experimenter remained in the Close position throughout the experiment. The Close position was defined as the position right at the junction of the MRI table and the opening of the magnet. The subjects were informed that in the Close position, the experimenter or the partner would only stand nearby without any physical contact. In the Touch condition, the touch was applied to the shin and calf of both legs and the direction of the touch was always from the knees toward the ankles. The touch was administered on a 20 cm zone that was marked on the subjects' shins before the fMRI experiment. During the 4 s touch, the complete zone was covered (touch velocity ~5 cm/s). This touch velocity was chosen based on previous studies showing that C-tactile afferents preferentially respond to stroking over the skin within a velocity range of 1–10 cm/s, which is additionally rated as most pleasant [Loken et al., 2009]. The experimenter was trained in keeping the touch velocity and touch pressure as constant as possible. The touch was applied with cotton gloves to equalize temperature differences and to reduce possible differences in the shape of the hands of experimenter and partner. The experimenter who applied the touch was blinded to the drug but not blinded to the

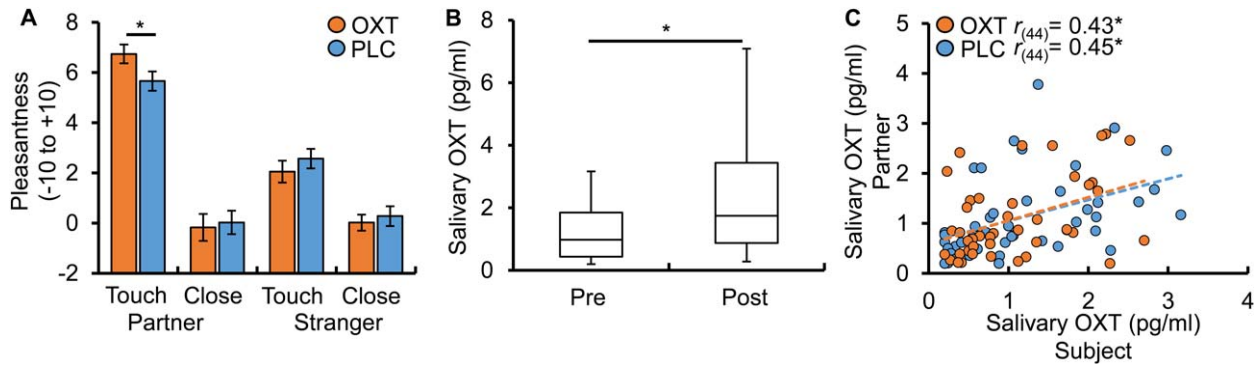

Figure 1.

Intranasal oxytocin (OXT) specifically enhanced the pleasantness of partner touch (**A**; $t_{(94)} = 2.02$, $P < 0.05$). There was no OXT effect on pleasantness ratings of interpersonal touch by an unfamiliar opposite-sex experimenter or the control condition (Close), in which the experimenter or the partner stood at the same distance but did not touch the participant. Salivary OXT concentrations significantly increased in the placebo (PLC) group following interpersonal touch (**B**; $t_{(47)} = 4.09$, $P < 0.01$). Baseline salivary OXT concentrations positively correlated within the romantic couples (subjects and their partners) (**C**; OXT group, $r_{(44)} = 0.43$, $P < 0.01$; PLC group, $r_{(44)} = 0.45$, $P < 0.01$). Error bars indicate the standard error of the mean (SEM). Abbreviations: OXT, oxytocin; PLC, placebo; post, after the touch experiment; pre, before the touch experiment.

condition (Stranger vs Partner). The entire opening of the magnet was covered with a blanket, so the subjects were not able to see their legs, the experimenters, or their partners. In the Close and the Touch conditions, the photographs were presented for 4 s. The order of Touch and Close was randomized and always interleaved with a Home condition. The duration of Home was jittered between 4 and 6 s (mean: 5 s). After each Touch and Close trial, subjects had to rate the pleasantness of the Touch or Close presence on a visual analog scale ranging from −10 (very unpleasant: a sad smiley) to +10 (very pleasant: a happy smiley). The rating scale was presented for 5 s. The experiment consisted of two runs (partner and stranger) and each run entailed 20 Touch, 20 Close, and 40 Home trials. The order of the runs was randomized across gender and treatment groups.

Acquisition of and Analysis of fMRI Data

A 3 T Siemens Trio MRI system (Siemens, Erlangen, Germany) was used to acquire the MRI data, which were preprocessed (cf. Supporting Information) and analyzed using SPM12 software (Wellcome Trust Centre for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm) implemented in Matlab (The MathWorks Inc., Natick, MA). On the second level, the whole-brain analysis was done with a height threshold of $P < 0.001$. The P values were corrected for multiple comparisons (family-wise error (FWE)) and $P < 0.05$ was considered significant.

Our a priori regions of interest (ROI), including the ACC, the insula, the medial OFC, and Nacc, were anatomically defined according to the Wake Forest University Pick Atlas (Version 3.0). The threshold for significance was set to $P < 0.05$, FWE-corrected for multiple comparisons based on the size of the ROI. The Marsbar toolbox was used to extract the parameter estimates from these regions.

RESULTS

Behavioral Results

To investigate the modulatory effect of intranasal OXT, a mixed analysis of variance (ANOVA) with person (Partner, Stranger) and distance (Touch, Close) as within-subject factors, treatment (OXT, PLC) as a between-subject factor, and pleasantness ratings as dependent variable was performed. This ANOVA yielded main effects of person ($F_{(1,94)} = 84.00$, $P < 0.01$, $\eta^2 = 0.47$) and distance ($F_{(1,94)} = 132.86$, $P < 0.01$, $\eta^2 = 0.59$), and a significant interaction between person and distance ($F_{(1,94)} = 98.86$, $P < 0.01$, $\eta^2 = 0.51$, cf. Figure 1A). Touch was rated as significantly more pleasant than the non-touch control condition (Close). As expected, partner touch was perceived as more pleasant than stranger touch, while there was no difference in the control condition. This pattern of results indicates that our experimental design was successful in eliciting different hedonic values of partner and stranger touch despite the touch's sensory properties being identical. Furthermore, we found a significant interaction between person and treatment ($F_{(1,94)} = 4.28$, $P < 0.05$, $\eta^2 = 0.04$) and a trend-to-significant interaction between person, distance, and treatment ($F_{(1,94)} = 3.44$, $P = 0.07$, $\eta^2 = 0.04$). To clarify this three-way interaction, we conducted separate mixed ANOVAs for the Touch and Close condition. Using the pleasantness ratings of touch as a dependent variable, we obtained a significant main effect of person ($F_{(1,94)} = 171.27$, $P < 0.01$, $\eta^2 = 0.65$) and a significant interaction

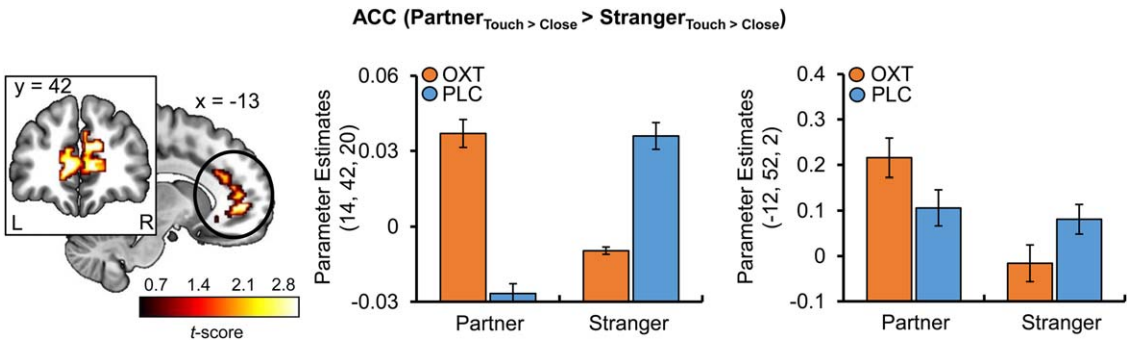

Figure 2.

Intranasal oxytocin (OXT) significantly increased the response to partner touch relative to stranger touch in the bilateral anterior cingulate cortex (peak MNI coordinates *x*, *y*, *z*: 14, 42, 20; $t_{(86)} = 3.73$, $P_{FWE} < 0.05$, display threshold $P < 0.05$ uncorrected; peak MNI coordinates *x*, *y*, *z*: −12, 52, 2; $t_{(86)} = 3.87$, $P_{FWE} < 0.05$, display threshold $P < 0.05$ uncorrected). Error bars indicate the standard error of the mean (SEM). Abbreviations: ACC, anterior cingulate cortex; L, left hemisphere; OXT, oxytocin; PLC, placebo; R, right hemisphere.

between person and treatment ($F_{(1,94)} = 7.20$, $P < 0.01$, $\eta^2 = 0.07$) in the Touch condition. OXT selectively enhanced the pleasantness of partner touch ($t_{(94)} = 2.02$, $P < 0.05$, $d = 0.41$, cf. Figure 1A) but had no significant effect on the pleasantness of stranger touch ($t_{(94)} = 0.88$, $P = 0.38$, $d = 0.18$). This finding replicates our previous observation of context-dependent OXT effects on the processing of interpersonal touch [Scheele et al., 2014a] and provides support for the hypothesis that OXT may contribute to the maintenance of pair-bonds by increasing the hedonic value of partner touch. Moreover, in the control condition (Close), the mixed ANOVA conducted on the pleasantness ratings revealed no main or interaction effects (all Ps > 0.43). An additional mixed ANOVA with gender as a second between-subject factor did not change the reported pattern of the behavioral results (cf. Supporting Information, Results).

Furthermore, the OXT-specific partner effect did not differ between subjects with higher and lower perceived relationship quality, assessed by the Passionate Love Scale (PLS) [Hatfield and Sprecher, 1986] (cf. Supporting Information, Results).

Interestingly, the pleasant tactile contact during the fMRI paradigm caused an increase in the endogenous salivary OXT concentration after the experiment ($t_{(47)} = 4.09$, $P < 0.01$, $d = 0.80$, cf. Figure 1B). An additional correlation analysis revealed a significant positive association between baseline salivary OXT level within the romantic couples (subjects and their partners) in both treatment groups (OXT: $r_{(44)} = 0.43$, $P < 0.01$; PLC; $r_{(44)} = 0.45$, $P < 0.01$, cf. Figure 1C).

fMRI Results

In the PLC group, interpersonal touch relative to the non-touch control condition [Touch > Close] produced widespread activations in touch-processing networks at the whole-brain level [Gazzola et al., 2012; Gordon et al., 2013; Lindgren et al., 2012; McCabe et al., 2008; Rolls et al., 2003; Voos et al., 2013] including in the bilateral insula, somatosensory cortex, precentral gyrus, middle and anterior cingulate cortex, and precuneus (cf. Supporting Information, Tables S3 and S4, and Figures S1 and S2). Partner touch relative to stranger touch elicited increased activation in the OFC, the posterior cingulate cortex, and the somatosensory cortex (cf. Supporting Information, Tables S5 and S6, and Figure S3). The main effect of treatment across all conditions was not significant (all Ps > 0.05), indicating that intranasal OXT did not have unspecific global effects on brain activation. To determine the specific effects of intranasal OXT on the processing of partner touch relative to stranger touch, we compared the responses to the contrast [$\text{Partner}_{\text{Touch > Close}} > \text{Stranger}_{\text{Touch > Close}}$] between the treatment groups.

Intriguingly, OXT compared to PLC enhanced responses to partner relative to stranger touch in the bilateral ACC (peak MNI coordinates *x*, *y*, *z*: −12, 52, 2; $t_{(86)} = 3.87$, $P_{FWE} < 0.05$; 14, 42, 20; $t_{(86)} = 3.73$, $P_{FWE} < 0.05$; cf. Figure 2). Furthermore, OXT elevated responses to partner compared to stranger touch in the left NAcc (−12, 6, −8; $t_{(86)} = 2.69$, $P_{FWE} < 0.05$; cf. Figure 3; see also Supporting Information, Figure S4). We also found a trend-to-significant modulatory effect of OXT on the processing of partner touch relative to stranger touch in the right insula (38, −16, 22; $t_{(86)} = 3.65$, $P_{FWE} = 0.09$) and in the left medial OFC (−10, 54, −2; $t_{(86)} = 3.32$, $P_{FWE} = 0.08$). To explore whether the subjects' relationship quality influenced the specific processing of partner touch, we computed the contrast [$\text{Partner}_{\text{Touch>Close}} > \text{Stranger}_{\text{Touch>Close}}$] and performed a correlation analysis with the PLS scores. Under OXT, participants with higher PLS scores showed increased responses to partner touch relative to stranger touch in the left NAcc (−14, 10, −10; $t_{(41)} = 2.98$; cf. Figure 3).

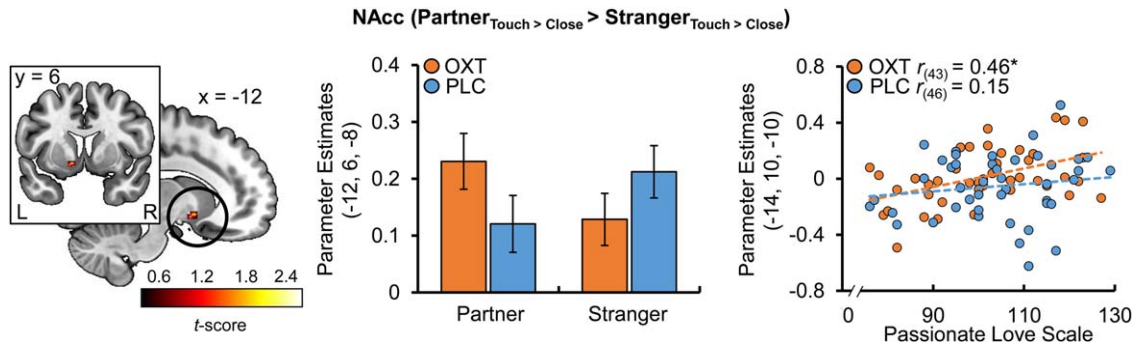

Figure 3.

Intranasal oxytocin (OXT) significantly augmented the response to partner relative to stranger touch in the left nucleus accumbens (NAcc) (peak MNI coordinates *x*, *y*, *z*: −12, 6, −8; $t_{(86)} = 2.69$, $P_{FWE} < 0.05$, display threshold $P < 0.05$ uncorrected). Under OXT, the neural response in the left NAcc to partner touch compared to stranger touch was more pronounced in participants with high scores in the Passionate Love Scale (peak MNI coordinates *x*, *y*, *z*: −14, 10, −10; $t_{(41)} = 2.98$, $P_{FWE} < 0.05$, display threshold $P < 0.05$ uncorrected). There was no significant association in the placebo group. Error bars indicate the standard error of the mean (SEM). Abbreviations: L, left hemisphere; NAcc, nucleus accumbens; OXT, oxytocin; PLC, placebo; R, right hemisphere.

Next, we investigated whether the OXT effect on the neural activation to partner touch relative to stranger touch differed between subjects with higher and lower PLS scores. We detected a trend-to-significant interaction between the PLS score and treatment: The OXT effect on the neural response to the partner's touch in the right NAcc was more pronounced in subjects with higher PLS scores (14, 10, −12; $t_{(85)} = 2.58$, $P_{FWE} = 0.08$).

Finally, we examined potential gender differences in the neural response to the partner's touch relative to the stranger's touch. While there was no difference between female and male participants across treatment groups, our analysis revealed a significant interaction between the subject's gender and treatment. In female participants, the effect of OXT on the neural response to the partner's touch was more pronounced in the right NAcc (12, 6, −8; $t_{(86)} = 3.08$, $P_{FWE} < 0.05$).

DISCUSSION

This study was designed to examine the behavioral and neural correlates of interpersonal touch in romantic couples and to explore the modulatory effects of intranasal OXT on the processing of partner touch. Collectively, our data are in line with our second hypothesis, suggesting that OXT selectively enhances the hedonic value of partner touch by boosting activation in reward-associated brain areas. One of the pivotal findings to emerge from this study is that OXT increased the neural response to partner touch compared to stranger touch not only in touch-related networks, including the ACC, OFC, and insula, but also in the NAcc. This pattern of results is consistent with our previous observations that OXT enhances activation in the ACC, OFC, and insula during pleasant touch [Scheele et al., 2014a]. Clearly, OXT does not induce global changes in the sensitivity to tactile stimulation, but rather produces differential social effects depending on the perceived context [Hurlemann and Scheele, 2016; Marsh et al., 2015; Olff et al., 2013]. The modulatory impact of OXT on NAcc activation may be more pronounced in the context of response to one's partner [Scheele et al., 2013, 2016]. In prairie voles, both a congruent activation of OXT and dopamine D2 receptors and their interaction in the NAcc are necessary for pair-bond formation and partner preference [Numan and Young, 2016; Young and Wang, 2004]. As such, our data support the idea that enhanced endogenous OXT signaling in the brain following intimate contact with the romantic partner increases the hedonic value of this behavior via an interaction with mesolimbic dopamine pathways. This is in line with recent studies suggesting that OXT interacts closely with the neural pathways responsible for processing motivationally relevant stimuli; in particular, OXT appears to impact dopaminergic activity [Love, 2014; Shamay-Tsoory and Abu-Akel, 2016]. However, OXT also modulates the serotonergic system (Mottolese et al., 2014), and thus it is also conceivable that the rewarding properties of social contact are mediated by the coordinated activity of OXT and serotonin in the NAcc (Dolen et al., 2013). Mechanistically, the increase in NAcc activation to partner touch under OXT may have contributed to a positive bias in the attractiveness perception of the partner [Scheele et al., 2013], which may have influenced the perception of touch, because interpersonal touch by a more attractive person is experienced as more pleasant [Novembre et al., 2016]. Importantly, OXT enhanced the NAcc response to partner touch relative to stranger touch, suggesting that OXT increased the hedonic value of partner touch and concomitantly diminished the value of touch by a stranger. By this dual mechanism of action OXT may promote monogamous pair-bonding in humans.

How can these OXT-induced changes in the perception of touch influence romantic relationships? On one hand, stroking touch increases well-being [Uvnäs-Moberg, 2004], reduces anxiety [Field et al., 1996] and pain [Coan et al., 2006], and has beneficial effects on multiple stress-sensitive systems [Holt-Lunstad et al., 2008]. These anti-stress effects may promote relationship stability [Neff and Karney, 2017]. Furthermore, touch in romantic couples enhances positive affect in the partner and improves psychological intimacy [Debrot et al., 2013]. As romantic relationships become more intimate, individuals automatically adopt positively biased perceptions by seeing their partners as more attractive than they really are, and by perceiving their relationships' quality as superior to other relationships [Fletcher and Kerr, 2010]. These cognitive biases operate as effective strategies to suppress mate-search processes and strengthen established pair bonds in both women and men [Fletcher et al., 2015]. On the other hand, a reduced susceptibility to touch by a stranger can be an additional protective factor, because touch in a courtship context increases the acceptance of courtship solicitations [Gueguen, 2007] and may thus facilitate the formation of new relationships. In fact, the likelihood of adultery is greater among individuals whose jobs involve physically touching clients [Tsapelas et al., 2010].

It is noteworthy that our study revealed a more pronounced effect of OXT on NAcc activation to partner touch in female participants. Gender-specific OXT effects have been found in various animal [Kelly and Goodson, 2014; Li et al., 2016; Simpson et al., 2016; Steinman et al., 2016; Young and Wang, 2004] and human [Ditzen et al., 2013; Feng et al., 2015; Hoge et al., 2014; Lischke et al., 2012; Scheele et al., 2014b; Yao et al., 2014] studies. Specifically, intranasal OXT enhanced striatal responses to reciprocated cooperation in a Prisoner's Dilemma Game in men, but not in women [Rilling et al., 2014]. The opposite direction of these findings could be reconciled with our results by taking into account gender differences in the PLC group that were absent in this study. As expected, women in this study displayed higher estradiol levels compared to men (cf. Supporting Information, Table S1). Estradiol enhances the OXT receptor density in the NAcc [de Kloet et al., 1986]. Surprisingly, the gender-specific neural OXT effect was not paralleled by sexual dimorphisms in the OXT effect on behavioral pleasantness ratings. While a ceiling effect in the behavioral ratings could have hindered a stronger OXT modulation in women, behavioral gender differences would possibly have become evident in more subtle aspects of how much a person likes his or her partner than the broad construct of pleasantness [McGlone et al., 2012]. Along these lines, as hypothesized, relationship quality was positively associated with NAcc activation to partner touch under OXT, but there was no significant correlation with behavioral pleasantness ratings. Similarly, the OXT effect on NAcc activation, but not behavioral ratings, was stronger in participants with higher PLS scores, thereby corroborating the idea that OXT modulates self-referential processing and enhances an a priori existing predisposition [Hurlemann and Scheele, 2016]. Given that our sample selectively consisted of participants who were passionately in love, it seems possible that intranasal OXT may produce detrimental outcomes in couples with relationship problems and a less positive experience of partner touch. Thus, future studies are warranted to probe the utility of intranasal OXT as an adjunct to augment latter sessions of couple therapy aimed at consolidating positive couple interactions. The loss of a loved partner is associated with a substantially elevated risk for various psychiatric disorders [Fletcher et al., 2015; Keyes et al., 2014], while a happy and well-functioning relationship can be a catalyst for mental and physical health [Eisenberger and Cole, 2012]. Hence, future studies could test the hypothesis that the stress-buffering effects of touch-based partner support are also mediated by oxytocinergic mechanisms [Uvnäs-Moberg et al., 2014].

Finally, in accordance with previous findings [Holt-Lunstad et al., 2008; Light et al., 2005; Morhenn et al., 2012], this study revealed a heightened concentration of salivary OXT after the application of pleasant interpersonal touch in the PLC session. Considering our observation that OXT increases the pleasantness of partner touch, the interaction between intimate partner contact and OXT may induce a self-reinforcing loop, with touch triggering the release of endogenous OXT and the OXT-mediated pleasantness boosting touch frequency. The amount of tactile physical affection such as stroking, holding hands, and massage is highly correlated with overall relationship and partner satisfaction [Gulledge et al., 2003]. Elevated OXT concentrations may also support the maintenance of romantic bonds by enhancing the intensity of orgasm and the contentment after sexual intercourse [Behnia et al., 2014]. Moreover, the positive correlation between salivary OXT concentrations in couple points to a temporal concordance of the partners' OXT systems, thus supporting the notion that biobehavioral synchrony binds members of social dyads [Feldman, 2012]. Nevertheless, we cannot rule out the possibility that the increased salivary OXT levels after the touch paradigm were driven by other factors such as the MRI setting or the social interaction during the experimental procedure. Additionally, considering the ongoing debate about the most valid method to determine OXT concentrations [McCullough et al., 2013], the salivary OXT data should be interpreted cautiously.

This study has some limitations. First, individual touch differences (e.g., preferences, habits, etc.) were not modeled in our highly controlled fMRI task as the same experimenter applied the touch in all conditions. It seems likely that the differential response to partner and stranger touch would be even more pronounced in a naturalistic setting of a field experiment. Nevertheless, our data suggest that the inner representation of the person being touched is sufficient to elicit differences in the behavioral and neural processing of partner and stranger touch. Second, in our study, the

experimenter was blinded to the drug (OXT vs PLC), but our cover story did not allow blinding of the condition (Partner vs Stranger). Thus, unconscious minimal changes in the application of the touch cannot be entirely excluded. Third, it should be highlighted that differences in the processing of partner and stranger touch could vary with the body region that has been touched. This is in accordance with a previous study showing relationship-specific differences in the bodily areas others are allowed to touch [Suvilehto et al., 2015]. Consequently, it is unclear to what extent the present findings can be extrapolated to other body regions.

Furthermore, we did not detect a significant correlation between relationship duration and behavioral or neural responses to partner touch. However, romantic love may evolve into companionate love over time [Acevedo et al., 2012] and OXT may have different effects in long-term relationships. Considering previous studies [Scheele et al., 2016], the observed OXT effects on the processing of interpersonal touch in female participants without hormonal contraceptives cannot be generalized to women using hormonal contraceptives. Additionally, our results cannot be attributed to unspecific effects of OXT on mood or anxiety (cf. Supporting Information, Table S7), but social desirability may have influenced the positive bias toward the partner. However, as the participants were unaware of the administered treatment (cf. Supporting Information, Methods), it seems unlikely that social desirability would have selectively affected the OXT group.

CONCLUSION

In conclusion, our findings indicate that OXT specifically increases the hedonic value of, and the neural response to, partner touch in reward-related brain circuits. By augmenting the hedonic value of intimate contact with the romantic partner and simultaneously reducing the hedonic value of stranger touch, OXT could contribute to the unique experience of partner touch and facilitate the maintenance of already established romantic relationships.

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The authors report no competing biomedical financial interests or personal affiliations in connection with the content of this manuscript.

AUTHOR CONTRIBUTIONS

A.K. and D.S. contributed equally to this work (shared first authorship). A.K., D.S., and R.H. designed the experiments; A.K., L.W., and M.W. conducted the experiments; A.K., D.S., L.W., and M.W. analyzed the data. All authors contributed to writing the manuscript. All authors read and approved the manuscript in its current form.

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