Supplementary Material

How the brain codes intimacy: The neurobiological substrates of romantic touch

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Supplementary Methods

Subjects

All subjects were in a romantic relationship for more than five months. The duration of the romantic relationships was comparable between the oxytocin (OXT) group (43.65 ± 46.83 months) and the placebo (PLC) group (32.17 ± 22.46 months; $t_{(93)}$ = -1.52, P = 0.13, d = -0.31). In a screening session prior to the testing sessions, we assessed social anxiety using a German version (Stangier et al., 1999) of the Social Interaction Anxiety Scale and the Social Phobia Scale (Mattick and Clarke, 1998) and depressive symptoms with the Beck-Depression Inventory (Hautzinger et al., 1995). Autistic-like traits were measured via the Autism Spectrum Quotient questionnaire (Baron-Cohen et al., 2001). The Passionate Love Scale (Hatfield and Sprecher, 1986) was used to measure the subject's relationship quality. Treatment groups did not differ in the above-mentioned questionnaire data (all Ps > 0.13; cf. Supplementary Table S2). All subjects were naive to prescription-strength psychoactive medication. Contraindications for MRI scanning were additional exclusion criteria. For female participants the use of hormonal contraceptives, the birth of a child, and pregnancy were additional exclusion criteria.

In a personal interview on the testing day the subjects were asked if anything of personal significance had changed in their romantic relationships (e.g. moving together). Only one couple mentioned that they had had a dispute 2 days before the MRI session.

The participants were asked to maintain their regular bed and waking times and to abstain from caffeine and alcohol intake on the day of the experiment. To control for potentially confounding effects of OXT on state anxiety and mood, all subjects completed the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970) and the Positive and Negative Affective Scale (PANAS) (Watson et al., 1998) immediately before the administration of the treatment and after the experiment. Three mixed analysis of variance (ANOVA) with Time Point (before the experiment, after the experiment) as a within-subjects factor and Treatment (OXT, PLC) as

between-subjects factor and State Anxiety, Positive Affect, or Negative Affect as dependent variables, revealed no significant main or interaction effects (all *P*s > 0.17; cf. Supplementary Table S7). Thus, OXT did not influence subjective anxiety or mood ratings. After completing the task, subjects were asked to guess whether they had received OXT or PLC. The estimation of the received treatment was comparable between the OXT and PLC group ($\chi^2_{(1)} = 0.31$, $P = 0.58$), showing that the subjects were unaware of whether they had received OXT or PLC. Seven subjects in the PLC group and four subjects in the OXT group reported side effects (headache, slightly dizziness, and fatigue). Finally, the subjects were asked after the experimental paradigm if they had any doubts regarding the task-dependent cover-story. None of the participants mentioned any doubts.

Functional MRI Paradigm

Using Presentation 14 (Neurobehavioral Systems, Albany, CA), stimuli were presented on a 32-inch MRI compatible TFT LCD monitor (NordicNeuroLab, Bergen, Norway) placed at the rear of the magnet bore. In the screening session, standardized photographs were made from all participants who were asked to wear a white t-shirt and dark pants. Brightness and size of the pictures were kept constant. After the touch fMRI task the subjects underwent another unrelated fMRI paradigm (reported elsewhere). The order of the two fMRI-paradigms was fixed across the whole study.

Acquisition of fMRI Data

A Siemens Trio MRI system (Siemens, Erlangen, Germany) operating at 3T and a 32 channel head coil was used to obtain T2*-weighted echoplanar (EPI) images with blood-oxygen-level-dependent contrast (TR = 2500 ms, TE = 30 ms, matrix size: 96 x 96, pixel size: 2 x 2 mm, slice thickness = 3.0 mm, distance factor = 10%, flip angle = 90°, 37 transversal slices). In addition, high-resolution anatomical images were acquired on the same scanner using a T1-weighted 3D

MPRAGE sequence (imaging parameters: TR = 1660 ms, TE = 2.54 ms, matrix size: 320 x 320, pixel size: 0.8 x 0.8 mm, slice thickness = 0.79 mm, flip angle = 9°, 208 sagittal slices).

Analysis of fMRI Data

fMRI data were preprocessed 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). The first five volumes of each functional time series were discarded to allow for T1 equilibration. Images were corrected for head movement between scans by an affine registration. For realignment, a two-pass procedure was used by which images were initially realigned to the first image of the time-series and subsequently re-realigned to the mean of all images.

For normalization, a two-step procedure was applied. Normalization parameters were first determined using the co-registered individual T1 image as source and the multi subject T1-template integrated in SPM12. This step included by default tissue segmentation using tissue probability maps. Next, normalization parameters were applied to normalize the functional images. Finally, these were present in standard anatomical Montreal Neurological Institute (MNI) space and resampled at 2 x 2 x 2 mm^3 voxel size. The normalized images were spatially smoothed using a 6-mm FWHM Gaussian kernel. Raw time series were detrended by the application of a high-pass filter (cut-off period, 128 s). A two-level random effects approach based on the general linear model as implemented in SPM12 was used for statistical analyses. On the first level, four conditions ($Partner_{Touch}$, $Partner_{Close}$, $Stranger_{Touch}$, $Stranger_{Close}$) were modeled by a stick function convolved with a hemodynamic response function (Friston 1995). The movement parameters were included as confounds in the design matrix. Each condition was compared relative to the low level baseline (Home condition) and the non-specific effects of OXT (i.e. the main effect of treatment) were analyzed by comparing all conditions with the low level baseline ([OXT>PLC] and [OXT<PLC]). On the first level, we computed the following

contrasts for each subject: [Touch>Close]; [$Partner_{Touch}$>$Partner_{Close}$]; [$Stranger_{Touch}$>$Stranger_{Close}$]; [$Partner_{Touch}$>$Stranger_{Touch}$]; [$Partner_{Close}$>$Stranger_{Close}$]; [$Partner_{Touch>Close}$>$Stranger_{Touch>Close}$]. On the second level, a full factorial design with treatment and gender as between-subject factors and the BOLD-response of the contrast [$Partner_{Touch>Close}$>$Stranger_{Touch>Close}$] as dependent variable was conducted.

Statistical Analysis

Demographical, neuropsychological, and behavioral data were tested using IBM SPSS Statistic 22 (IBM, New York, NY, USA). Quantitative behavioral data were compared by mixed ANOVA and dependent and independent t-tests. Pearson's product-moment correlation was used for correlation analysis. Consensus between the romantic partners regarding relationship quality was assessed with Lin's concordance correlation coefficient (Lin, 1989). Eta-squared and Cohen's d were calculated as measures of effect size. For qualitative variables, Pearson's chi-squared tests were used. All reported *P*-values are two-tailed and *P*-values of $P < 0.05$ were considered significant.

Hormonal Assessment

Saliva samples were collected using pre-chilled Salivettes (Sarstedt, Rommelsdorf, Germany). One sample was collected before administration of the nasal spray and another sample was collected after the fMRI task. Salivettes were immediately centrifuged at 4180 g for 3 min and aliquoted samples were stored at -80°C until assayed. Saliva OXT was extracted and quantified using a highly sensitive and specific radioimmunoassay (RIAgnosis, Munich, Germany). The limit of detection was 0.1 - 0.5 pg, depending on the age of the tracer. Intra-assay and inter-assay coefficients of variability were < 10%. All samples to be compared were assayed in the same batch, i.e. under intra-assay conditions.

Serum FSH, LH, and estradiol were analyzed by fully automated homogeneous sandwich chemiluminescent immunoassays based on the LOCI™ technology on a Dimension Vista™ System according to the manufacturer´s instructions (Siemens Healthcare Diagnostics, Marburg, Germany). The detection limits of each assay were 0.2 IU/l for LH and FSH and 11 pg/ml for estradiol, respectively. The coefficients of variation for intra-assay and inter-assay precision were <1.8 % and <2.1 % for LH, <1.9 % and <2.2 % for FSH, and <5.5 % and <5.9 % for estradiol, respectively. Serum progesterone was determined by a fully automated solid-phase competitive chemiluminescent enzyme immunoassay on an Immulite™ 2000xpi System according to the manufacturer´s instructions (Siemens Healthcare Diagnostics). The detection limit of the assay was 0.1 ng/ml. The coefficients of variation for intra-assay and inter-assay precision were <4.2 % and <5.5 %. The cross-reactivity of all assays with other related compounds was minimal. Saliva testosterone was determined by a competitive enzyme immunoassay (ELISA) according to the manufacturer´s instructions (IBL International, Hamburg, Germany). The detection limit of the assay was 4.7 pg/ml. The coefficients of variation for intra-assay and inter-assay precision were <7.1 % and <7.7 %.

Supplementary Results

Behavioral Results

We tested whether the OXT-specific partner effect differed between subjects with higher and lower perceived relationship quality, assessed by the Passionate Love Scale (PLS). For this purpose, the PLS score was median dichotomized (PLS high: 114.02 ± 6.59; PLS low: 92.31 ± 8.32). Mixed ANOVAs for the touch and the control condition with treatment (OXT, PLC) and PLS score (Higher, Lower) as between-subject factors and person (Partner, Stranger) as within-subject factor were performed. Using the pleasantness ratings of touch as a dependent variable, we found a significant main effect of person ($F_{(1,91)} = 164.22$, $P < 0.01$, $\eta^2 = 0.64$) and a significant interaction between person and treatment ($F_{(1,91)} = 7.12$, $P < 0.01$, $\eta^2 = 0.07$). The ANOVA yielded no significant main or interaction effects of the PLS score (all Ps > 0.08). Accordingly, the OXT-specific partner effect did not differ between higher and lower PLS scorers. The mixed ANOVA with the pleasantness ratings of the control condition as dependent variable revealed no main or interaction effects (all Ps > 0.38).

To further examine a potential effect of gender on the pleasantness ratings, we performed additional mixed ANOVAs for the touch and control condition with gender (Male, Female) and Treatment (OXT, PLC) as between-subject factors and person (Partner, Stranger) as within-subject factor. Using the pleasantness ratings of touch as dependent variable, we obtained a significant main effect of person ($F_{(1,92)} = 146.54$, $P < 0.01$, $\eta^2 = 0.61$) and a significant interaction between person and treatment ($F_{(1,92)} = 4.96$, $P < 0.05$, $\eta^2 = 0.05$). OXT selectively enhanced the pleasantness of partner touch ($t_{(94)} = -2.02$, $P < 0.05$, $d = -0.41$,) but had no significant effect on the pleasantness of stranger touch ($t_{(94)} = 0.88$, $P = 0.38$, $d = 0.18$). We did not observe a main effect of gender ($F_{(1,92)} = 1.51$, $P = 0.22$, $\eta^2 = 0.02$) and there were no interactions between person and gender ($F_{(1,92)} = 0.24$, $P = 0.53$, $\eta^2 < 0.01$), treatment and gender ($F_{(1,92)} = 0.71$, $P = 0.79$, $\eta^2 < 0.01$), or gender, treatment, and person ($F_{(1,92)} = 0.33$, $P = 0.57$, $\eta^2 = 0.01$). The

mixed ANOVA with the pleasantness ratings of the control condition as dependent variable also revealed no main or interaction effects of gender (all *P*s > 0.52).

Additionally, we examined whether the OXT effect on the pleasantness ratings of partner touch and stranger touch are moderated by autistic-like traits. For this purpose, the AQ scores were median-dichotomized (AQ high= 20.15 ± 4.57; AQ low= 11.16 ± 2.38). A mixed ANOVA for the touch condition with treatment (OXT, PLC) and AQ score (Higher, Lower) as between-subject factors, person (Partner, Stranger) as within-subject factor, and the pleasantness ratings of touch as dependent variable was performed. This analysis revealed a significant main effect of person ($F_{(1,92)}$ = 171.15, P < 0.01, η^2 = 0.65) and a significant interaction between person and treatment ($F_{(1,92)}$ = 27.86, P < 0.01, η^2 = 0.07). The analysis yielded no significant main or interaction effects of the AQ score (all *P*s > 0.13). However, consistent with previous studies (Scheele et al., 2014), an exploratory analysis showed that the partner-specific OXT effect was more pronounced in low AQ scorers ($F_{(1,48)}$ = 7.62, P = 0.08, η^2 = 0.14) than in high scorers ($F_{(1,44)}$ = 0.65, P = 0.42, η^2 = 0.02). The mixed ANOVA with the pleasantness ratings of the control condition as dependent variable also revealed no main or interaction effects of gender (all *P*s > 0.09).

We had predicted a positive correlation between the subjects' relationship quality and the behavioral response to partner touch. Contrary to our a priori hypothesis the relationship quality did not correlate with the pleasantness ratings of partner touch (PLC: P = 0.70; OXT: P = 0.44) or the pleasantness ratings of the other experimental conditions (PLC: $P \geq 0.51$; OXT: $P \geq 0.26$). Furthermore, the concordance correlation coefficients of the romantic partners' PLS scores, indicating the romantic partners' consensus in the evaluation of relationship quality, did not show any significant association with the pleasantness ratings (PLC: all *P*s > 0.23; OXT: all *P*s > 0.08). In an exploratory analysis, potential associations between the pleasantness ratings and BDI scores, SPS scores, and SIAS scores were tested, but revealed no significant correlations in

both treatment groups (PLC: BDI: all *P*s > 0.13, SPS: all *P*s > 0.08, SIAS: all *P*s > 0.28; OXT: BDI: all *P*s > 0.46, SPS: all *P*s > 0.34, SIAS: all *P*s > 0.52).

Finally, we compared the saliva OXT concentrations at baseline and after the touch paradigm between the treatment groups. The mixed-effect ANOVA with treatment (PLC, OXT) as between-subject factor and time point of saliva OXT concentration measurement (Pre, Post) as within-subject factor yielded a significant main effect of treatment ($F_{(1,92)} = 82.58$, $P < 0.01$, $\eta^2 = 0.47$), a significant main effect of time point ($F_{(1,92)} = 93.96$, $P < 0.01$, $\eta^2 = 0.51$), and a significant interaction between treatment and time point ($F_{(1,92)} = 85.38$, $P < 0.01$, $\eta^2 = 0.48$). The salivary OXT concentrations at baseline did not differ significantly between the OXT and PLC groups (OXT: 1.14 ± 0.74 pg/ml; PLC: 1.18 ± 0.86 pg/ml ml; $t_{(93)} = 0.25$, $P = 0.81$, $d = 0.05$). However, following the paradigm, the OXT salivary level was significantly higher under OXT than under PLC (OXT: 46.04 ± 32.51 pg/ml; PLC: 2.24 ± 1.64 pg/ml ml; $t_{(93)} = 9.32$, $P < 0.01$, $d = 1.91$). Post-hoc paired t-tests revealed a strong increase in the saliva OXT concentration after the touch paradigm in both the OXT (pre: 1.12 ± 0.74 pg/ml; post: 45.44 ± 32.61 pg/ml; $t_{(46)} = 9.28$, $P < 0.01$, $d = 1.61$) and the PLC groups (pre: 1.18 ± 0.86 pg/ml; post: 2.24 ± 1.64 pg/ml; $t_{(48)} = 4.09$, $P < 0.01$, $d = 0.80$). In the PLC group, we also tested whether the changes in the salivary OXT levels due to interpersonal touch (post minus pre) were associated with the pleasantness ratings of the different experimental conditions ($Partner_{Touch}$, $Partner_{Close}$, $Stranger_{Touch}$, $Stranger_{Close}$), but found no significant correlations (all *P*s > 0.27).

fMRI results

We have previously found that the modulatory effects of OXT on the processing of interpersonal touch inversely correlated with autistic-like traits (Scheele et al., 2014). Hence, we examined whether the OXT effect on the neural response to partner touch relative to stranger touch differs between subjects with high and low autistic-like traits. The AQ did not moderate the OXT effect on whole brain level or in our priori defined ROIs (all *P*s > 0.05). In a following

exploratory analysis, we tested the modulatory effect of OXT on the neural responses to partner relative to stranger touch separately for AQ high and low scorers. This analysis revealed a trend-to significant effect of OXT on the neural response to partner touch in the left anterior cingulate cortex (ACC) in AQ low scorers (peak MNI coordinates x, y, z: - 6, 32, 24; $t_{(86)} = 3.52$, $P_{FWE} = 0.10$), but not in AQ high scorers ($P_{FWE} = 0.72$).

Furthermore, we observed that under PLC, participants who showed a high consensus with their romantic partner in the evaluation of relationship quality (i.e. high concordance correlation coefficients of the subjects' and their romantic partners' PLS scores) exhibited increased response to partner touch compared to stranger touch in the left medial OFC (peak MNI coordinates x, y, z: - 4, 56,-8; $t_{(44)} = 4.14$, $P_{FWE} < 0.05$). Under OXT this effect was not significant (peak MNI coordinates x, y, z: -6, 44, -6; $t_{(40)} = 3.32$, $P_{FWE} = 0.10$).

Supplementary Tables

Table S1. Baseline measurement of endocrine factors

	OXT group (n = 14) Mean (± SD)	PLC group (n = 15) Mean (± SD)	*t*	*P*
Females				
Baseline Oxytocin (pg/ml)	1.00 (± 0.73)	0.95 (± 0.77)	-0.21	0.84
Estradiol (pg/ml)	151.16 (± 98.57)	111.90 (± 61.24)	-1.30	0.21
FSH (U/l)	6.77 (± 10.29)	4.15 (± 1.54)	-0.98	0.34
LH (U/l)	10.21 (± 10.93)	8.52 (± 5.93)	-0.52	0.61
Progesterone (ng/ml)	6.14 (± 5.51)	4.80 (± 4.20)	-0.74	0.47
Testosterone (pg/ml)	0.23 (± 0.05)	0.26 (± 0.11)	1.16	0.26

	OXT group (n = 34) Mean (± SD)	PLC group (n = 33) Mean (± SD)	*t*	*P*
Males				
Baseline Oxytocin (pg/ml)	1.19 (± 0.75)	1.28 (± 0.89)	0.44	0.66
Estradiol (pg/ml)	25.99 (± 15.59)	26.49 (± 7.30)	-0.16	0.88
FSH (U/l)	3.27 (± 2.04)	3.62 (± 2.15)	0.68	0.50
LH (U/l)	3.63 (± 2.02)	4.37 (± 1.56)	1.67	0.10
Progesterone (ng/ml)	0.32 (± 0.16)	0.35 (± 0.14)	0.62	0.54
Testosterone (pg/ml)	3.42 (± 1.29)	3.72 (± 1.09)	1.01	0.32

Notes. There were no significant differences in any measurements between the OXT and PLC sessions (all *P*s > 0.05). Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; OXT, oxytocin; PLC, placebo.

Table S2. Demographics and psychometric questionnaire data

	OXT group (n = 48) Mean (± SD)	PLC group (n = 48) Mean (± SD)	*t*	*P*
Age (years)	26.42 (± 4.65)	24.94 (± 3.24)	-1.81	0.07
Education (years)	16.70 (± 2.96)	17.06 (± 2.64)	0.63	0.53
Romantic relationship length (months)	43.65 (± 46.83)	32.17 (± 22.46)	-1.52	0.13
BDI [a]	2.40 (± 3.02)	2.31 (± 3.26)	-0.13	0.90
STAI trait [b]	31.31 (± 5.40)	32.35 (± 7.72)	0.77	0.45
SIAS [c]	12.92 (± 7.79)	13.98 (± 7.92)	0.66	0.51
SPS [d]	5.17 (± 3.98)	5.79 (± 4.89)	0.69	0.49
AQ [e]	15.38 (± 6.13)	15.56 (± 5.43)	0.16	0.87
PLS [f]	101.83 (± 13.33)	103.79 (± 13.21)	0.72	0.47

Notes. Depressive symptoms were assessed by the [a] BDI (Beck's Depression Scale, Version II) and trait anxiety symptoms by the [b] STAI (State Trait Anxiety inventory). The attitude towards social distance was measured by the [c] SIAS (Social Interaction Scale) and [d] SPS (Social Phobia Scale). Autistic-like traits were assessed by the [e] AQ (Autism Spectrum Quotient) and relationship quality by the [f] PLS (Passionate Love Scale). Abbreviations: OXT, oxytocin; PLC, placebo.

Table S3. Activation table for GLM analysis under PLC (Touch vs. Close)

Region	Right/left	Cluster size (voxels)	t-score	MNI coordinates		
				x	y	z
PLC: Touch > Close						
Rolandic operculum	L	13601	17.34	-46	-28	20
Insula	L		14.22	-36	-18	12
Postcentral gyrus	R		13.35	60	-16	18
Postcentral gyrus	R	525	12.45	18	-42	68
Postcentral gyrus	R		6.83	34	-38	52
Precuneus	R		6.30	12	-48	56
Precuneus	L	1082	11.89	-14	-48	74
Postcentral gyrus	L		10.64	-20	-44	68
Middle cingulate cortex	L		8.91	-10	-22	44
Middle temporal gyrus	L	325	9.94	-50	-66	10
Middle temporal gyrus	L		8.23	-46	-58	16
Anterior cingulate cortex	L	151	9.94	-4	34	2
Middle cingulate cortex	L	1733	9.06	-12	10	38
Anterior cingulate cortex	L		8.37	-2	26	22
Middle cingulate cortex	R		7.81	2	18	30
Superior medial frontal gyrus	R	111	7.63	6	58	18
Superior medial frontal gyrus	R		6.55	4	54	26
Precuneus	R	42	7.08	8	-52	28
Middle temporal pole	R	50	6.96	48	8	-26
Precentral gyrus	R	75	6.94	46	-2	48
Precentral gyrus	R		6.10	54	4	38
Precentral gyrus	L	25	6.57	-52	0	38
Precentral gyrus	L	11	6.26	-34	-8	50
Inferior frontal gyrus triangularis	R	14	6.16	42	34	2
Inferior temporal gyrus	R	12	6.11	48	-18	-24
Insula	L	6	5.91	-34	20	8
Cerebellum	L	4	5.91	-26	-58	-24
Insula	L	1	5.70	-26	12	16
PLC: Close > Touch						
Inferior orbito-frontal gyrus	L	271	8.74	-46	44	-8
Middle frontal gyrus	L		7.46	-40	48	2
Middle frontal gyrus	L		6.38	-34	56	6
Fusiform gyrus	R	848	8.38	28	-44	-16

Inferior occipital gyrus	R		8.35	42	-64	-12
Parahippocampal gyrus	R		7.78	32	-42	-8
Angular gyrus	L	729	8.15	-38	-68	48
Inferior parietal gyrus	L		8.14	-40	-60	50
Inferior parietal gyrus	L		7.38	-46	-52	50
Middle temporal gyrus	L	256	7.92	-62	-38	-2
Middle temporal gyrus	L		7.08	-60	-48	-4
Superior frontal gyrus	R	43	7.64	30	18	62
Superior frontal gyrus	R		6.32	28	28	56
Middle frontal gyrus	L	187	7.57	-48	24	34
Inferior frontal gyrus triangularis	L		6.94	-52	18	18
Inferior frontal gyrus triangularis	L		5.82	-52	20	28
Middle frontal gyrus	L	180	7.57	-32	14	60
Middle frontal gyrus	L		7.05	-38	8	56
Middle occipital gyrus	R	337	7.24	34	-82	24
Middle occipital gyrus	R		6.54	34	-88	8
Middle occipital gyrus	R		6.51	32	-80	12
Middle occipital gyrus	L	177	7.05	-26	-96	10
Middle occipital gyrus	L		6.31	-24	-96	2
Middle occipital gyrus	L		6.31	-18	-98	8
Angular gyrus	R	137	7.05	44	-60	52
Superior parietal gyrus	R		6.85	32	-70	52
Paracentral lobule	R	17	6.76	10	-26	70
Fusiform gyrus	L	143	6.56	-22	-44	-14
Fusiform gyrus	L		6.56	-32	-44	-14
Cerebelum	L		6.20	-8	-44	-16
Lingual gyrus	L	14	6.38	-18	-68	-8
Inferior frontal gyrus triangularis	L	19	6.19	-54	20	8
Middle frontal gyrus	R	17	6.15	46	30	38
Superior temporal gyrus	R	3	6.11	66	-18	2
Inferior temporal gyrus	R	9	6.03	56	-50	-10
Middle frontal gyrus	L	8	5.93	-38	10	36
Inferior occipital gyrus	L	1	5.79	-38	-58	-6
Middle occipital gyrus	L	4	5.68	-38	-86	0
Lingual gyrus	L	3	5.67	-6	-72	0
Supplementary motor area	R	1	5.56	6	-22	60

Notes. For the whole brain analysis a height threshold of $P < 0.05$ (FWE-corrected) was used. Abbreviations: PLC, placebo.

Table S4. Activation table for GLM analysis under OXT (Touch vs. Close)

Region	Right/left	Cluster size (voxels)	t-score	MNI coordinates		
				x	y	z
OXT: Touch > Close						
Superior temporal gyrus	L	12684	17.36	-46	-32	22
Rolandic operculum	R		16.56	44	-28	24
Insula	L		15.21	-32	-20	12
Superior parietal gyrus	L	713	11.02	-18	-44	74
Superior parietal gyrus	L		9.35	-22	-40	64
Precuneus	L		7.36	-14	-46	56
Middle temporal gyrus	L	448	10.90	-46	-64	10
Middle temporal gyrus	L		8.50	-40	-58	8
Postcentral gyrus	R	549	10.76	18	-44	72
Postcentral gyrus	R		10.76	18	-44	72
Postcentral gyrus	R		10.76	18	-44	72
Middle cingulate cortex	L	2059	8.96	-2	4	40
Anterior cingulate cortex	R		8.96	2	26	18
Middle cingulate cortex	R		8.78	4	12	34
Precentral gyrus	L	15	6.48	-60	6	28
Supplementary motor area	R	11	6.22	6	-4	74
Inferior frontal gyrus triangularis	R	10	6.09	54	32	2
Postcentral gyrus	R	8	6.02	32	-32	36
Anterior cingulate cortex	R	3	6.01	6	28	-6
Postcentral gyrus	R	4	5.92	54	-24	54
Precuneus	R	8	5.92	10	-48	58
Superior medial frontal gyrus	R	3	5.89	8	54	32
Middle cingulate cortex	R	3	5.77	6	-18	38
Postcentral gyrus	L	1	5.74	-54	-30	54
Insula	L	2	5.65	-28	24	12
Anterior cingulate cortex	R	1	5.57	4	32	-2
Middle cingulate cortex	R	1	5.56	14	-24	38
OXT: Close > Touch						
Fusiform gyrus	R	501	8.22	34	-50	-14
Inferior temporal gyrus	R		8.13	40	-62	-10
inferior occipital gyrus	R		6.95	44	-76	-12
Inferior parietal gyrus	L	494	8.14	-36	-70	48
Inferior parietal gyrus	L		7.97	-30	-76	42

Superior parietal gyrus	L		7.75	-22	-78	50
Superior occipital gyrus	R	490	7.73	32	-78	44
Angular gyrus	R		7.54	42	-74	36
Middle occipital gyrus	R		7.53	30	-78	30
Middle frontal gyrus	L	127	6.88	-44	20	36
Inferior frontal gyrus triangularis	L		6.53	-46	22	24
Lingual gyrus	L	73	6.77	-22	-50	-10
Fusiform gyrus	L		8.89	-30	-58	-6
Middle frontal gyrus	L	38	6.75	-32	8	62
Middle frontal gyrus	L		5.98	-38	6	54
Middle frontal gyrus	L		5.97	-32	16	58
Fusiform gyrus	R	14	6.71	36	-36	-10
Middle occipital gyrus	R	84	6.71	32	-90	2
Calcarine sulcus	L	60	6.58	-10	-84	8
Angular gyrus	R	60	6.22	34	-58	48
Fusiform gyrus	L	6	6.17	-36	-60	-8
Inferior parietal gyrus	L	25	6.05	-48	-46	48
Superior frontal gyrus	R	14	6.02	30	16	60
Precentral gyrus	L	7	6.00	-34	6	46
Middle occipital gyrus	L	45	5.98	-30	-84	6
Middle occipital gyrus	L		5.88	-34	-86	14
Precentral gyrus	R	5	5.87	12	-30	72
Middle frontal gyrus	L	7	5.86	-40	54	6
Middle frontal gyrus	L	4	5.81	-44	50	-8
Middle occipital gyrus	L	3	5.75	-28	-80	30
Middle occipital gyrus	R	1	5.75	30	-78	6
Parahippocampal gyrus	L	3	5.70	-30	-44	-6
Middle occipital gyrus	L	2	5.60	-14	-100	4
Lingual gyrus	R	1	5.60	4	-76	-2
Superior occipital gyrus	L	1	5.59	-24	-86	30
Parahippocampal gyrus	R	1	5.57	22	-28	-18

Notes. For the whole brain analysis a height threshold of $P < 0.05$ (FWE-corrected) was used. Abbreviations: OXT, oxytocin.

Table S5. Activation table for GLM analysis under PLC (Partner vs. Stranger)

Region	Right/left	Cluster size (voxels)	t-score	MNI coordinates		
				x	y	z
PLC: Partner$_{Touch}$>Stranger$_{Touch}$						
Medial orbito-frontal gyrus	L	392	5.48	-2	56	-8
Gyrus rectus	L		4.68	-8	44	-16
Medial orbito-frontal gyrus	L		4.64	-12	44	-6
Calcarine sulcus	L	177	4.72	-6	-48	4
Posterior cingulate cortex	L		4.09	-2	-46	16
Vermis	R		3.79	4	-46	4
Postcentral gyrus	L	143	4.68	-38	-20	30
Postcentral gyrus	L		4.42	-50	-20	48
Calcarine sulcus	R	142	4.45	20	-76	6
Superior occipital gyrus	R		4.43	28	-64	18
Calcarine sulcus	R		4.11	28	-72	6
PLC: Stranger$_{Touch}$>Partner$_{Touch}$						
All *Ps* > 0.05						

Notes. For the whole brain analysis a height threshold of $P < 0.001$ was used. Abbreviations: PLC, placebo.

Table S6. Activation table for GLM analysis under OXT (Partner vs. Stranger)

Region	Right/left	Cluster size (voxels)	t-score	MNI coordinates		
				x	y	z
OXT: $Partner_{Touch}$>$Stranger_{Touch}$						
Middle cingulate cortex	L	454	5.91	-14	-20	46
Middle cingulate cortex	L		5.78	-10	-8	50
Middle cingulate cortex	L		4.72	-14	-34	44
Calcarine sulcus	L	116	5.90	-4	-86	-10
Postcentral gyrus	L	654	5.75	-38	-20	48
Postcentral gyrus			4.69	-52	-18	46
Postcentral gyrus			4.53	-30	-24	62
Precuneus	L	875	5.18	0	-54	34
Precuneus			5.12	-2	-74	52
Precuneus	R		4.69	2	-62	20
Anterior cingulate cortex	L	595	5.09	-16	46	0
Medial orbito-frontal gyrus	R		4.74	4	48	-10
Medial orbito-frontal gyrus	L		4.63	0	56	-10
Middle frontal gyrus	L	132	5.01	-28	32	42
Middle frontal gyrus	L		3.92	-24	36	48
Middle frontal gyrus	L		3.63	-30	40	38
Precuneus	L	116	4.98	-10	-62	66
Precuneus	L		4.40	-6	-52	72
Precuneus	L		3.81	-16	-66	62
Superior temporal gyrus	R	112	4.97	58	-30	14
Superior temporal gyrus	R		4.03	54	-38	16
Middle temporal gyrus	L	276	4.96	-54	-64	18
Angular gyrus	L		4.57	-48	-68	30
Middle occipital gyrus	L		3.81	-40	-78	34
Superior medial frontal gyrus	R	154	4.80	16	48	2
Middle frontal gyrus	R		4.47	28	38	8
Middle frontal gyrus	R		4.30	54	-60	16
Middle temporal gyrus	L	186	4.59	-64	-18	-14
Middle temporal gyrus	L		4.56	-56	-6	-18
Middle temporal gyrus	L		4.53	-54	-22	-16
Paracentral lobule	L	113	4.45	-4	-16	76
Paracentral lobule	L		3.96	-12	-22	74
Supplementary motor area	R		3.59	6	-12	74

Middle temporal gyrus	R	256	4.39	46	-58	18
Middle temporal gyrus	R		4.24	60	-52	18
Middle temporal gyrus	R		4.07	54	-60	16
OXT: Stranger$_{Touch}$>Partner$_{Touch}$						
All *Ps* > 0.05						

Notes. For the whole brain analysis a height threshold of $P < 0.001$ was used. Abbreviations: OXT, oxytocin.

Table S7. State measurement of anxiety and attention

	OXT group (n = 48) Mean (± SD)	PLC group (n = 48) Mean (± SD)	t	P
PANAS positive pre [a]	30.42 (5.72)	30.31 (6.07)	-0.09	0.93
PANAS positive post [a]	28.63 (7.56)	27.10 (7.26)	-1.01	0.32
PANAS negative pre [a]	12.02 (2.20)	12.02 (2.65)	0.00	1.00
PANAS negative post [a]	11.21 (1.84)	11.92 (2.98)	1.40	0.17
STAI state pre [b]	33.06 (5.85)	34.33 (7.81)	0.90	0.37
STAI state post [b]	32.96 (5.78)	33.58 (6.79)	0.49	0.63

Notes. Mood before and after the fMRI experiment was assessed using the [a] PANAS = Positive and Negative Affect Schedule. State anxiety before and after the experiment was assessed using the [b] STAI = State Trait Anxiety Inventory. Abbreviations: OXT, oxytocin; PLC, placebo.

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Supplementary Figures

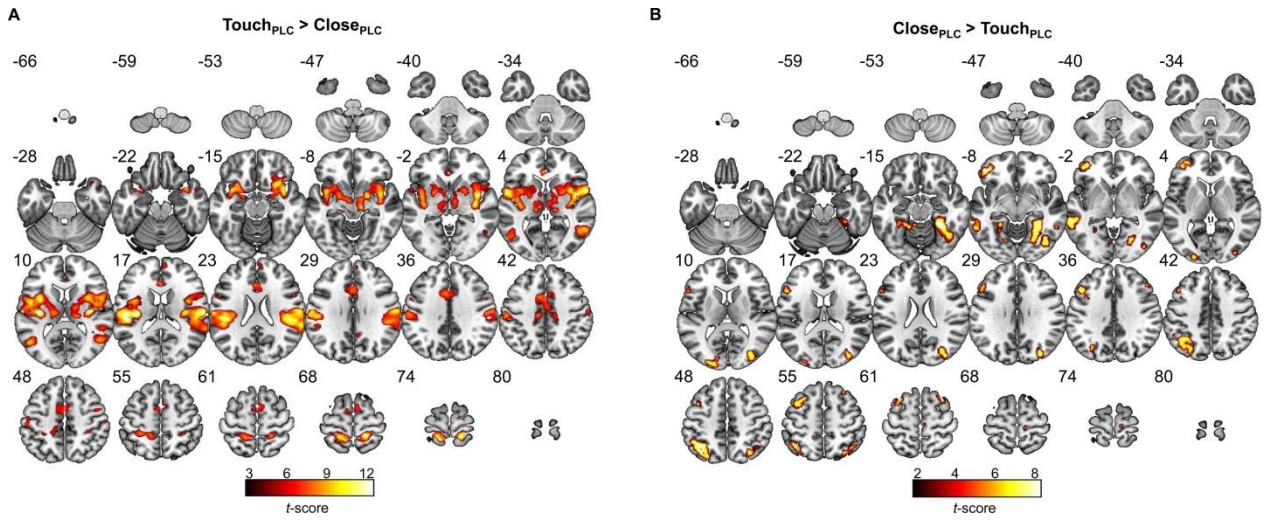

Figure S1. Whole brain activations maps for the contrasts [Touch>Close] (**A**; display threshold $P < 0.05$ FWE-corrected) and [Close<Touch] (**B**; display threshold $P < 0.05$ FWE-corrected) under placebo nasal spray. Abbreviations: PLC, placebo.

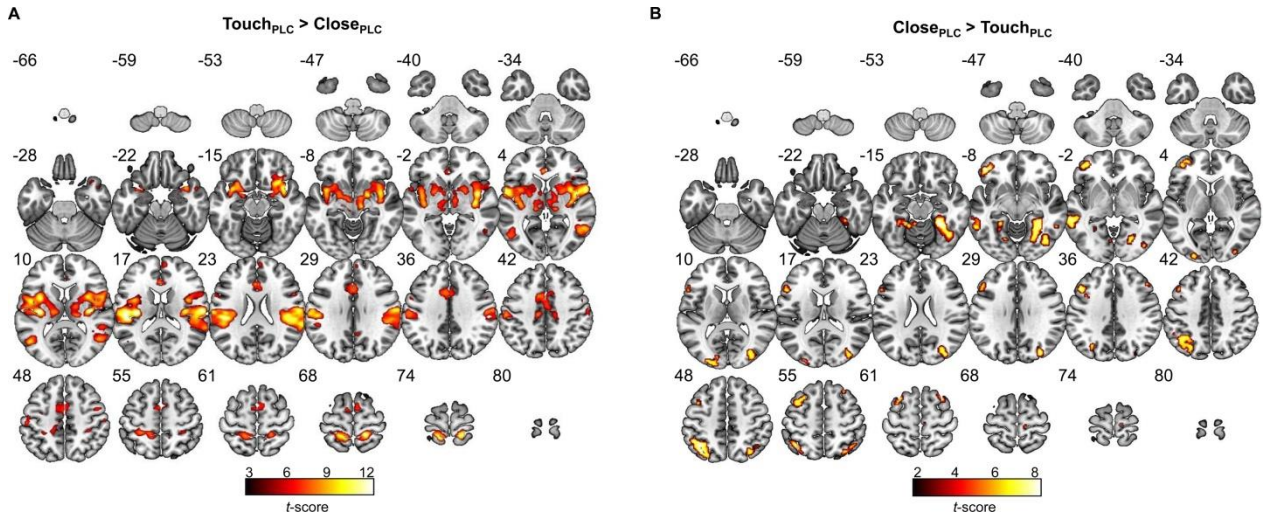

Figure S2. Whole brain activations maps for the contrasts [Touch>Close] (**A**; display threshold $P < 0.05$ FWE-corrected) and [Close<Touch] (**B**; display threshold $P < 0.05$ FWE-corrected) after intranasal administration of oxytocin (display threshold $P < 0.05$ FWE-corrected). Abbreviations: OXT, oxytocin.

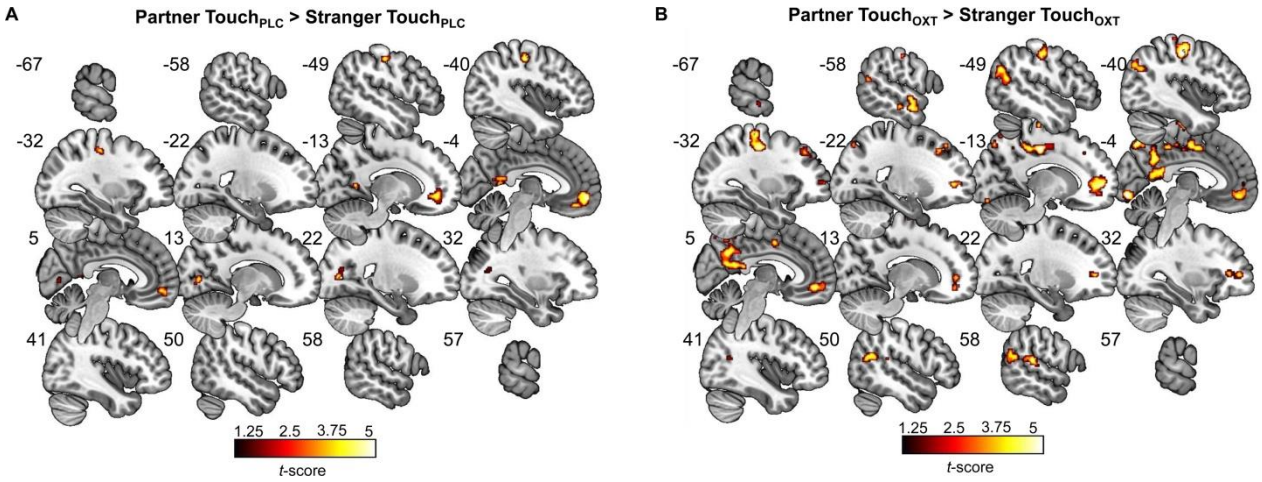

Figure S3. Whole brain responses to partner touch relative to stranger touch under placebo (**A;** display threshold $P < 0.001$ uncorrected) and oxytocin (**B**; display threshold $P < 0.001$ uncorrected). Abbreviations: OXT, oxytocin; PLC, placebo.

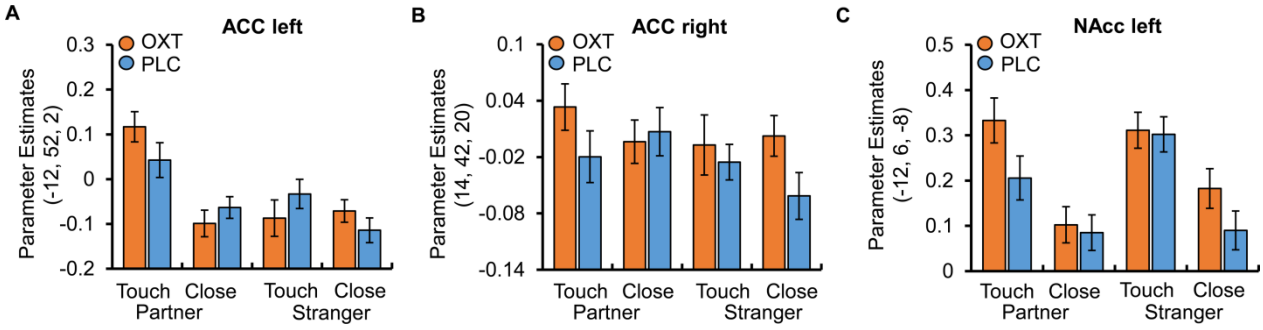

Figure S4. Neural activations to the lower level contrasts [Partner Touch > Baseline], [Partner Close > Baseline], [Stranger Touch > Baseline], and [Stranger Close > Baseline] in the right anterior cingulate cortex (**A**; peak MNI coordinates x, y, z: 14, 42, 20), left anterior cingulate cortex (**B**; peak MNI coordinates x, y, z: -12, 52, 2), and in the left nucleus accumbens (**C**; peak MNI coordinates x, y, z: -12, 6, -8) under placebo and oxytocin. Error bars indicate the standard error of the mean (SEM). Abbreviations: ACC, anterior cingulate cortex; NAcc, nucleus accumbens; OXT, oxytocin; PLC, placebo.