

Supplementary Information

The influence of oxytocin on volitional and emotional ambivalence

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Supplementary Experimental Procedures:

1. Study subjects

Forty-eight healthy, non-smoking adult males participated in Experiment 1 (Exp. 1; oxytocin (OXT) group: $n = 25$; mean age \pm S.D. = 25.04 ± 4.69 years; placebo (PLC) group: $n = 23$; age = 24.13 ± 4.48 years). Twenty-three were in a romantic heterosexual relationship and twenty-five were single, all were unmarried and had no children. In Experiment 2 (Exp. 2), 22 non-smoking adult males participated (age = 26.73 ± 3.60 years). All subjects were in a romantic heterosexual relationship for more than 6 months, were unmarried and had no children. Subjects in both studies were free of current and past physical or psychiatric illness, as assessed by medical history and the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan *et al.*, 1998). All participants were recruited by local advertisement at the University Bonn, Germany. They provided written informed consent before study enrollment. All subjects were naïve to prescription-strength psychoactive medication and had not taken any over-the-counter psychoactive medication in the past 4 weeks. Participants were asked to maintain their regular bed and wake times and to abstain from caffeine and alcohol intake on the day of the experiment. All subjects were within a normal range of cognitive performance and there were no a-priori differences between the OXT and PLC groups in Exp. 1 (**Supplementary Tables S1 and S2**). In Exp. 2, the subjects reported to be passionately in love, and the time intervals since they last saw their partners and had intimate contact were comparable between the OXT and PLC sessions (**Supplementary Table S6**). We also controlled whether the subjects had an argument with their partners in the week before both test sessions and if anything important in their relationship changed between the two test sessions. Participants also completed the Positive and Negative Affective Scale (PANAS) (Watson *et al.*, 1988) and the State-Trait Anxiety Inventory (STAI) (Spielberger *et al.*, 1970) immediately before the nasal spray administration and after the experimental task (in Exp. 2), to control for potentially confounding effects of OXT on mood and anxiety. Furthermore, all subjects in Exp 2. completed the d2 Test of Attention (Aufmerksamkeits- und Belastungstest d2) (Brickenkamp and Zillmer, 1998) after the experimental task. There were no differences between the PLC- and OXT-treated participants in either experiment (all P values > 0.05) (**Supplementary Tables S1 and S4**). The estimation of the received treatment was comparable between the OXT and PLC session (Exp.

1: $\chi^2_{(1)} = 1.44$, $P = 0.26$; Exp. 2: $\chi^2_{(1)} = 0.29$, $P = 0.86$), showing that the subjects were unaware of whether they had received OXT or PLC.

Neuropsychological screening. To control for possible pretreatment differences in cognitive performance, all participants completed a comprehensive neuropsychological test battery. Cognitive performance was assessed using the Cambridge Neuropsychological Test Automated Battery (CANTAB), a computerized neurocognitive assessment presented through a touch-screen computer (Sahakian and Owen, 1992). For details of the outcome measure see CANTABeclipse™ Test Administration Guide (CANTABeclipse, 2011). Subjects' speed of response to a visual target (only in Exp. 2), the ability to retain spatial information, and visual memory were measured with the reaction time task (RTI), the spatial working memory task (SWM), and the paired associates learning task (PAL), respectively. All subjects were within a normal range of cognitive performance (**Supplementary Tables S1 and S2**). There were also no differences in ethical ideology between the OXT- and PLC-treated group in Exp. 1 as assessed with the Ethic Position Questionnaire (EPQ) (Forsyth, 1980). Furthermore, all subjects in Exp. 2 completed the Marburg Attitude Scales towards Love Styles (MEIL), which is a German version of Love Styles developed by Lee (1988). It contains three primary styles of love: the first one is Eros, a romantic love that is similar to passionate love and is characterized by a powerful attraction to the beloved individual. The second is Ludus, which describes lovers who view love as a game and often have several partners simultaneously. The third is Storge, a slow developing, friendship-based love. These primary love styles can be combined to form secondary styles of love: Pragma (Storge and Ludus combined; pragmatic view on the relationship), Mania (Eros and Ludus combined; obsessive and possessive lover), and Agape (Storge and Eros combined; altruistic love style). In the German version, each love style is assessed with 10 items.

2. fMRI paradigms

Experiment 1

The stories for all task vignettes were translated into German. Prior to the fMRI experiment, participants were familiarized with the vignettes and the corresponding stories. They were asked to memorize all stories before the fMRI experiment. During the fMRI experiment, the pictures corresponding to the memorized stories were presented in the scanner. Below each picture the words “Yes” and “No” were presented and the participants had to make a decision by pressing a button. The number of correct responses to the non-dilemma conditions was equally high in the OXT ($88.50 \pm 14.40\%$) and PLC group ($85.51 \pm 17.72\%$, $t_{(46)} = 0.65$, $P = 0.52$). To reduce the strong interindividual variance in the reaction times (RT), we excluded all participants ($n = 9$) whose RT differed more than ± 1.5 SDs from the mean. The response buttons for “Yes” and “No” changed depending on the random lateralization of “Yes” and “No” on the screen. The total stimulus interval for each presented illustration was 5 s. After one second, the corresponding dilemma or non-dilemma question and the words “Yes” and “No” were shown below the picture for four seconds. There was a total of 8 blocks (4 non-moral and 4 moral dilemma illustration blocks). The order of blocks was alternated. Each block contained 6 stimulus pictures and lasted for 30 s.

Experiment 2

We adapted an fMRI paradigm used by Takahashi et al. (2006). The participants were confronted with three types of short sentences describing either neutral actions of the partner or sexual and emotional infidelity. The sentences were validated in two pilot studies involving 10 healthy men in Study 1 (age = 25.70 ± 4.11 years) as well as 137 healthy women (age = 21.71 ± 2.66 years) and 69 healthy men (age = 23.20 ± 4.54) in Study 2. None of these women and men participated in the fMRI study. In Study 1, the participants had to classify the sentences twice as being either neutral or as describing emotional or sexual infidelity. After the first evaluation, sentences with a low inter-rater agreement were adjusted. The final set contained only sentences with high concordance (for each sentence $\geq 80\%$ of the participants were in agreement about the category). In Study 2, the participants rated the arousal induced by sentences depicting sexual or emotional infidelity. A repeated measures analysis of variance (ANOVA)

with gender as a between-subject variable, type (sexual vs. emotional infidelity) as within-subject factor, and the arousal ratings as dependent variable yielded a main effect of type ($F_{(1, 204)} = 120.08$, $P < 0.01$, $\eta^2 = 0.37$), with the participants assigning higher arousal ratings to sexual infidelity than to the emotional condition. Importantly, the validity of our sentences is further corroborated by an interaction between type and gender ($F_{(1, 204)} = 5.48$, $P = 0.02$, $\eta^2 = 0.03$). Consistent with previous findings (Buss *et al.*, 1992), female participants (7.90 ± 1.14) rated emotional infidelity as slightly more arousing than male participants (7.65 ± 1.22), while there was no difference in the ratings of sexual infidelity (women: 8.35 ± 1.06 ; men: 8.34 ± 0.88).

An additional analysis of the arousal ratings in the present study did not reveal any difference between the arousal ratings in the first (sexual infidelity: 86.51 ± 16.46 , emotional infidelity: 78.46 ± 18.52 , neutral: 15.87 ± 11.82) and second session (sexual infidelity: 85.17 ± 13.96 , emotional infidelity: 76.94 ± 16.30 , neutral: 14.23 ± 12.50) irrespective of the treatment (all P s > 0.25). Both tasks were programmed in Presentation 14 (Neurobehavioral Systems, Albany, CA) and stimuli were presented via liquid crystal display (LCD) video goggles (Nordic NeuroLab, Bergen, Norway).

3. Statistical analysis

Demographical, neuropsychological, and behavioral data were analyzed using IBM SPSS Statistic 20 (IBM, New York, NY, USA). Quantitative behavioral data were compared using repeated measures ANOVAs and t -tests. Pearson's product-moment correlation was used for correlation analysis. Eta-squared and Cohen's d were calculated as measures of effect size. Pearson's chi-squared tests were used for qualitative variables. All reported P -values are two-tailed, if not otherwise noted, and P -values of $P < 0.05$ were considered significant.

Tables:

Table S1. Demographics and neuropsychological performance Exp. 1

	OXT (<i>n</i> = 25) Mean (\pm SD)	PLC (<i>n</i> = 23) Mean (\pm SD)
Age (years)	25.04 (4.69)	24.13 (4.48)
Education (years)	16.64 (2.62)	16.18 (1.97)
Idealism (EPQ) ^a	61.68 (14.88)	63.59 (13.93)
Realism (EPQ) ^a	51.04 (14.59)	52.36 (12.23)
Positive affect (PANAS) ^b	19.96 (9.59)	22.61 (6.80)
Negative affect (PANAS) ^b	10.72 (1.14)	11.48 (2.47)
State Anxiety (STAI) ^c	43.84 (1.87)	44.65 (2.31)
Trait Anxiety (STAI) ^c	31.92 (7.91)	31.87 (10.9)
PAL ^d		
Total errors	20.88 (13.86)	18.26 (16.69)
Mean errors to success	1.56 (2.26)	1.61 (1.77)
SWM – 6 ^e		
Between errors	5.44 (8.16)	5.65 (8.13)
Strategy score	13.04 (3.43)	12.61 (3.63)

Notes. There were no significant differences between the OXT and PLC group (all *P*s > 0.05). Moral thoughts were measured by using Forsyth's ^aEthics Position Questionnaire (EPQ). Anxiety and mood were assessed before the experiment with the ^bPositive and Negative Affective Schedule (PANAS) and the ^cState Trait Anxiety Inventory (STAI). Visual memory and the ability to retain spatial information were measured with the ^dpaired associates learning task (PAL) and the ^espatial working memory task (SWM). Abbreviations: OXT, oxytocin; PLC, placebo.

Table S2. Demographics and neuropsychological performance Exp. 2

	Mean (\pm SD) ($n = 22$)
Age (years)	26.73 (3.60)
Education (years)	17.32 (2.63)
RTI ^a	
Simple reaction time (ms)	298.26 (30.43)
Simple movement time (ms)	354.70 (61.16)
Five-choice movement time (ms)	316.37 (31.15)
Five-choice reaction time (ms)	365.02 (65.64)
PAL ^b	
Total errors	9.27 (6.51)
Mean errors to success	2.61 (1.91)
SWM – 8 ^c	
Between errors	9.68 (11.15)
Strategy score	14.18 (4.12)
Trait anxiety (STAI) ^d	31.86 (8.60)
Depressive symptoms (BDI) ^e	3.32 (4.91)

Notes. Subjects' speed of response to a visual target, visual memory, and the ability to retain spatial information were measured with the ^a simple and reaction time task (RTI), the ^b paired associates learning task (PAL), and the ^c spatial working memory task (SWM), respectively. Anxiety symptoms were assessed by the ^d State Trait Anxiety Inventory and depressive symptoms by the self-report ^e BDI (Beck's Depression Scale, Version II).

Table S3. Activation table for the GLM analysis in Exp. 1 under PLC

Region	Right/left	Cluster size (voxels)	<i>t</i> -score	<i>MNI-coordinates</i>		
				<i>x</i>	<i>y</i>	<i>z</i>
PLC: Moral > Non-moral						
Medial frontal gyrus*	L	1925	9.39	-27	26	52
Medial frontal gyrus*	L		7.62	-3	53	28
Superior frontal gyrus*	L		7.23	-6	44	49
Precuneus	R	428	8.52	3	-61	37
Cingulate gyrus*	L		6.62	0	-49	34
Precuneus*	L		5.54	-6	52	13
Angular gyrus*	L	139	7.69	-45	-58	25
Superior temporal gyrus*	R	121	6.15	57	-61	19
Angular gyrus*	R		4.77	54	-55	28
Middle temporal gyrus*	R		4.08	45	-73	13
Superior temporal gyrus	L	21	5.44	-45	11	-32
Medial cingulate	R	39	5.20	6	-16	34
Inferior frontal gyrus	L	22	5.20	-42	26	-11
Insula	R	10	4.78	30	17	-14
Middle temporal gyrus	L	15	4.63	-60	-1	-23
Inferior temporal gyrus	R	39	4.55	63	-7	-20
Sub-gyral	R		3.82	48	-4	-23
Cuneus	R	42	4.27	12	-94	7
Calcarine	R		4.12	18	-91	-2

Notes. The whole-brain analysis was thresholded at an uncorrected $P < 0.001$ with a cluster extent threshold of $k = 10$ voxels. Abbreviations: GLM, general linear model; PLC, placebo; *Significant at $P < 0.05$ family-wise error corrected.

Table S4. State measurement of anxiety, mood and attention

	OXT session (<i>n</i> = 22) Mean (\pm SD)	PLC session (<i>n</i> = 22) Mean (\pm SD)	<i>t</i>	<i>P</i>
State Anxiety (STAI) – pre ^a	31.95 (4.74)	31.45 (5.11)	0.43	0.67
State Anxiety (STAI) – post ^a	32.95 (5.32)	32.14 (4.42)	0.95	0.35
Positive affect (PANAS) – pre ^b	28.68 (6.61)	28.41 (5.86)	0.28	0.78
Positive affect (PANAS) – post ^b	27.77 (6.59)	28.14 (7.03)	-0.40	0.69
Negative affect (PANAS) – pre ^b	11.23 (1.57)	12.00 (3.45)	-1.07	0.30
Negative affect (PANAS) – post	11.55 (3.19)	11.09 (2.76)	0.66	0.52
d2 ^c	221.09 (48.14)	218.77 (52.05)	0.29	0.77

Notes. State anxiety before and after the experiment was assessed using the ^aSTAI = State Trait Anxiety Inventory. Mood before and after the experiment was assessed using the ^b PANAS = Positive and Negative Affect Schedule. Attention performance after the experiment was assessed using the ^c D2 = Aufmerksamkeits- und Belastungstest. Abbreviations: OXT, oxytocin; PLC, placebo.

Table S5. Activation table for the GLM analysis in Exp. 2 under PLC

Region	Right/left	Cluster size (voxels)	t-score	MNI-coordinates		
				x	y	z
PLC: Sexual > Neutral						
Medial frontal gyrus*	L	652	7.52	-8	50	14
Medial frontal gyrus*	L		5.95	-4	52	6
Cingulate gyrus*	L		5.52	-2	36	32
Anterior cingulate	R	70	6.13	4	36	8
Fusiform gyrus	L	13	5.71	-38	-50	-10
Inferior parietal lobule*	L	415	5.11	-60	-50	40
Middle temporal gyrus*	L		5.09	-56	-50	4
Superior temporal gyrus*	L		4.80	-60	-54	14
Middle cingulum	R/L	19	4.94	0	-18	40
Superior temporal gyrus	R	57	4.77	50	-48	14
Anterior cingulate	L	35	4.70	-2	38	-4
Medial frontal gyrus	R	58	4.57	12	38	44
Superior frontal gyrus	R		4.22	6	42	50
Middle temporal gyrus	L	116	4.51	-52	-74	20
Middle temporal gyrus	L		4.47	-40	-70	20
Middle temporal gyrus	L		4.38	-46	-80	26
Inferior frontal gyrus	R	19	4.44	42	26	6
Superior frontal gyrus	L	12	4.43	-2	22	58
Supramarginal gyrus	R	51	4.14	64	-48	24
Superior temporal gyrus	R		3.89	62	-50	14
Superior temporal gyrus	R	10	4.14	60	-60	20
Anterior cingulate	L	10	3.87	-2	20	22
Anterior cingulate	L		3.73	-4	26	28
PLC: Neutral > Emotional						
Inferior parietal lobule*	L	1922	6.55	-46	-40	58
Postcentral gyrus*	L		6.27	-52	-32	54
Posterior cingulate cortex*	L	951	6.32	-10	-46	4
Posterior cingulate cortex*	R		5.55	14	-50	4
Posterior cingulate cortex*	R		5.23	12	-56	12
Supramarginal gyrus*	R	212	5.50	64	-20	40
Postcentral gyrus*	R		4.65	52	-30	56
Supramarginal gyrus*	R		4.51	58	-16	28
Superior frontal gyrus	R	108	5.09	30	12	54
Middle frontal gyrus	R		4.02	32	4	58
Middle frontal gyrus	R		3.95	32	-6	58
Postcentral gyrus	R	12	4.60	40	-42	64
Pallidum	L	16	4.58	-24	-14	2
Middle cingulate gyrus	R	20	4.51	6	-38	34
Middle occipital gyrus	L	36	4.50	-28	-78	32

Superior occipital gyrus	L		3.57	-22	-78	38
Middle frontal gyrus	L	24	4.39	-28	12	60
Insula	L	12	4.06	-38	2	-6
Superior frontal gyrus	L	37	3.96	-18	2	60
Precentral gyrus	L	24	3.91	-32	-26	66
Precentral gyrus	L		3.79	-24	-26	64
Middle cingulate gyrus	L	10	3.88	-4	-28	36
Thalamus	L	12	3.84	-16	-30	-2
Middle frontal gyrus	L	42	3.82	-26	-6	64
Middle frontal gyrus	L		3.80	-26	-8	56
Middle frontal gyrus	L		3.12	-26	-12	48
Insula	L	10	3.71	-38	-16	0

Notes. The whole-brain analysis was thresholded at an uncorrected $P < 0.001$ with a cluster extent threshold of $k = 10$ voxels.
 *Significant at $P < 0.05$ family-wise error corrected. Abbreviations: GLM, general linear model; PLC, placebo.

Table S6. Relationship characteristics Exp. 2

Variable	Mean (\pm SD)
Relationship duration (months)	35.68 (25.33)
Age of partner (years)	24.64 (3.40)
Passionate Love Scale (PLS) ^a	6.44 (1.06)
Time (days) since the last time seen OXT ¹	1.73 (3.78)
Time (days) since the last time seen PLC ¹	1.38 (2.54)
Time (days) since the last intimate contact OXT ¹	4.45 (5.36)
Time (days) since the last intimate contact PLC ¹	3.38 (2.94)
Love style Eros ^b	6.86 (1.54)
Love style Ludus ^b	3.08 (0.98)
Love style Storge ^b	5.88 (1.19)
Love style Pragma ^b	4.49 (1.28)
Love style Mania ^b	4.05 (1.41)
Love style Agape ^b	6.95 (0.91)

Notes. Love in the relationship was measured with ^a the Passionate Love Scale (PLS) and different love styles were assessed using a German version of ^b Lee's Love Styles („Marburger Einstellungs-Inventar für Liebesstile (MEIL)“). Abbreviations: OXT, oxytocin; PLC, placebo; ¹There was no significant difference between the OXT and PLC sessions (all *P*s > 0.22).

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