Supporting Information

Effects of exogenous oxytocin and estradiol on resting-state functional connectivity in women and men

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Supplementary Methods

As the study was part of a larger project, methods and results concerning the pharmacokinetic pre-study, power analysis, neuroendocrine parameters, side effects, blinding of treatment, body mass index and hormonal levels, missing values, demographic and psychometric baseline characteristics, and measurements of mood were already described in our previous paper[1], but adapted for the current sample.

Pharmacokinetic pre-study

We conducted a prestudy involving ten healthy participants (5 women; mean age ± SD = 24.10 ± 4.07 years) to examine the pharmacokinetics of estradiol (EST) gel (Estramon 2 mg estradiol, Hexal AG, Holzkirchen, Germany) administration. Blood samples were taken prior to EST administration (i.e. baseline) and in 1-hour intervals after drug application up to five hours post administration. An additional blood sample was taken the next day (after 18 hours). Serum EST levels peaked 3-4 hours after gel administration, but a significant increase relative to baseline was already evident after two hours ($t_{(9)}$ = 2.44, p = 0.04, d = 1.10; **cf.**[2]). EST levels remained significantly elevated throughout the last measurement. A previous study tested the topical administration of a different drug (Divigel, Orion Pharma AG, Zug, Switzerland) containing 2 mg EST and found significantly increased EST serum concentrations as soon as one hour after administration and maximum average levels after two hours[3].

Power analysis

This study was part of a larger project and we used G*Power 3[4] to conduct an a-priori power analysis for the project. We based the power analysis on the effect size obtained in our OXT dose-response study[5]. Regarding the effect of intranasal oxytocin (OXT, 24 IU at a latency of 45 minutes) on the amygdala response to high intensity fearful faces we observed an effect size of dz = 0.56 in a within-subject design. To detect an OXT effect of this size (with α = 0.05 and power = 0.75), we needed to test at least 48 participants in a between-subject design (i.e. 24 male participants in the placebo group (PLC) and 24 male participants in the OXT group). Thus, we planned to include at least 24 participants in each treatment group (1. PLC & PLC; 2. PLC & OXT; 3. EST & PLC; 4. EST & OXT) separately for both sexes (1. female; 2. male). In total, 122 healthy women and 124 healthy men were included in the study to control for drop-outs and exclusions. The final sample for the analyses included 53 participants (26 women) in the PLC_{tra} and PLC_{int} group, 64 participants (33 women) in the PLC_{tra} and OXT_{int} group, 59 participants (27 women) in the EST_{tra} and PLC_{int} group, and 51 participants (25 women) in the EST_{tra} and OXT_{int} group.

Neuroendocrine parameters

EST and other gonadal hormones

Serum EST, testosterone and progesterone were determined by fully automated electrochemiluminescent immunoassays (ECLIA, Elecsys test) on a cobas e801 analyzer (Roche Diagnostics, Mannheim, Germany) according to the manufacturer's instructions (Roche Diagnostics). The coefficients of variation for intra-assay and inter-assay precision were 1.63% and 2.51% for EST, 2.27% and 3.71% for testosterone, and 2.28 % and 2.83 % for progesterone, respectively.

Oxytocin

Plasma samples for the measurement of OXT concentrations were collected with commercial sampling devices (Vacuette, Greiner Bio-One International, Austria) containing ethylenediaminetetraacetic acid (EDTA) and aprotinin. Vacuettes were immediately centrifuged at 3250 rpm for ten minutes, and aliquoted samples were stored at -80°C until assayed. OXT concentrations were 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.

Questionnaires

To characterize the sample, we assessed depressive symptoms (Becks Depression Inventory [BDI][6]), social anxiety (Liebowitz Social Anxiety Scale [LSAS][7]), autistic-like traits (Autism Spectrum Quotient [AQ][8]) and trait anxiety (State Trait Anxiety Inventory [STAI][9]). We used Qualtrics software for the presentation of the questionnaires (Provo, USA).

Supplementary Results

Additional treatment effects in men

To further analyze the significant two-way interactions of the amygdala subregions, and the DMN, we extracted the parameter estimates of the significant peak voxels and employed t-tests to compare the activation between the treatment groups. Analyses of the amygdala subregions showed that under PLC_{int}, EST_{tra} reduced the rsFC between the left centromedial amygdala and the left rolandic operculum (EST_{tra} & PLC_{int} < PLC_{tra} & PLC_{int}: $t_{(57)}$ = -3.36, p_{cor} < 0.01, d = -0.88), whereas the direction of the effect was reversed after the OXT_{int} treatment (EST_{tra} & OXT_{int} > PLC_{tra} & OXT_{int}: $t_{(55)}$ = 4.38, p_{cor} < 0.01, d = 1.17). Likewise, OXT_{int} decreased the rsFC between the left centromedial amygdala and the left rolandic operculum after PLC_{tra} treatment (PLC_{tra} & OXT_{int} < PLC_{tra} & PLC_{int}: $t_{(56)}$ = -4.51, p_{cor} < 0.01, d = -1.19), but significantly increased rsFC after the EST_{tra} treatment (EST_{tra} & OXT_{int} > EST_{tra} & PLC_{int}: $t_{(56)}$ = 3.19, p_{cor} < 0.01, d = 0.84).

Further analyses of the extracted parameter estimates revealed that after the PLC_{int} treatment, EST_{tra} decreased rsFC between the DMN and the right and left superior dorsolateral frontal gyrus (EST_{tra} & PLC_{int} < PLC_{tra} & PLC_{int}: right: $t_{(57)}$ = -3.38, p_{cor} < 0.01, d = -0.88; left: $t_{(57)}$ = -3.13, p_{cor} = 0.01, d = -0.82) and the left Cerebellum Crus 1 (EST_{tra} & PLC_{int} < PLC_{tra} & PLC_{int}: $t_{(57)}$ = -4.13, p_{cor} < 0.01, d = -1.08). However, combined with the OXT_{int} treatment, EST_{tra} increased the rsFC between the DMN and the right and left superior dorsolateral frontal gyrus (EST_{tra} & OXT_{int} > PLC_{tra} & OXT_{int}: right: $t_{(55)}$ = 4.30, p_{cor} < 0.01, d = 1.14; left: $t_{(55)}$ = 4.17, p_{cor} < 0.01, d = 1.11) and the left Cerebellum Crus 1 (EST_{tra} & OXT_{int} > PLC_{tra} & OXT_{int}: $t_{(55)}$ = 2.56, p_{cor} = 0.02, d = 0.68), but reduced rsFC with the right supramarginal gyrus (EST_{tra} & OXT_{int} < PLC_{tra} & OXT_{int}: $t_{(55)}$ = -4.98, p_{cor} < 0.01, d = -1.33). After the PLC_{tra} treatment, OXT_{int} decreased rsFC between the DMN and the right and left superior dorsolateral frontal gyrus (PLC_{tra} & OXT_{int} < PLC_{tra} & PLC_{int}: right: $t_{(56)}$ = -3.33, p_{cor} < 0.01, d = -0.88; left: $t_{(56)}$ = -3.94, p_{cor} < 0.01, d = -1.04) and the left Cerebellum Crus 1 (PLC_{tra} & OXT_{int} < PLC_{tra} & PLC_{int}: $t_{(56)}$ = -3.09, p_{cor} = 0.02, d = -0.81), but increased the rsFC with the right supramarginal gyrus (PLC_{tra} & OXT_{int} > PLC_{tra} & PLC_{int}: $t_{(56)}$ = 3.94, p_{cor} < 0.01, d = 1.04). Again, this pattern was reversed after the combined treatment with EST_{tra} (EST_{tra} & OXT_{int} > EST_{tra} & PLC_{int}: right superior dorsolateral frontal gyrus: $t_{(56)}$ = 4.33, p_{cor} < 0.01, d = 1.14; left superior dorsolateral frontal gyrus: $t_{(56)}$ = 3.39, p_{cor} < 0.01, d = 0.90; left Cerebellum Crus 1: $t_{(56)}$ = 3.61, p_{cor} < 0.01, d = 0.95; EST_{tra} & OXT_{int} < EST_{tra} & PLC_{int}: right supramarginal gyrus: $t_{(56)}$ = -3.02, p_{cor} = 0.02, d = -0.80).

Supraphysiological EST levels

Women exhibited a significantly larger increase in blood EST levels than men. To address that difference, we included the EST increase as a covariate in our analyses. To further probe the impact of this difference, we used a median-dichotomization and excluded EST_{tra}-treated women with large EST

increase (n = 26). In the remaining subsample (n = 200), the treatment-induced increases in EST levels were comparable between women and men within the treatment groups (all $ps > 0.05$). We repeated the main analyses with the parameter estimates of the significant three-way interactions with this subsample and observed a similar pattern of results. In line with our reported main findings, the significant three-way interactions identified in rsFC of the right hippocampus and the left anterior cingulate gyrus remained significant in this subsample ($F_{(1, 192)} = 21.50$, $p < 0.001$, $\eta_p^2 = 0.10$). Further analyses revealed that the significant three-way interactions, which were observed in rsFC of the left amygdala and the right lingual gyrus and the left cuneus remained significant (right lingual gyrus: $F_{(1, 193)} = 15.82$, $p < 0.001$, $\eta_p^2 = 0.08$; left cuneus: $F_{(1, 192)} = 11.48$, $p < 0.01$, $\eta_p^2 = 0.06$). The reported three-way interactions of the rsFC in the amygdala subregions revealed comparable results to our main findings. For the rsFC of the left centromedial amygdala, similar significant three-way interactions with the left cuneus ($F_{(1, 193)} = 18.08$, $p < 0.001$, $\eta_p^2 = 0.09$), the left lingual gyrus ($F_{(1, 193)} = 23.63$, $p < 0.001$, $\eta_p^2 = 0.11$), and the right calcarine gyrus ($F_{(1, 193)} = 19.84$, $p < 0.001$, $\eta_p^2 = 0.09$) were identified. For the right superficial amygdala as a seed region, we still observed a significant three-way interaction with the right frontal lobe ($F_{(1, 193)} = 20.43$, $p < 0.001$, $\eta_p^2 = 0.10$). Therefore, the significantly larger EST increase in women than men has no major impact on the results.

Side effects

Three days following the treatment, the participants were asked to report the side effects of their treatment. No participant experienced severe side effects, but 10.1% of the participants reported side effects consisting of light headache, tiredness, dizziness, sleep disturbance, hilarity, lack of concentration, or circulatory problems. Importantly, the proportion of participants who reported side effects did not significantly differ between the treatment groups (PLC$_{tra}$ & PLC$_{int}$: 13.7%, PLC$_{tra}$ & OXT$_{int}$: 10.0%, EST$_{tra}$ & PLC$_{int}$: 7.0%, EST$_{tra}$ & OXT$_{int}$: 10.0%; $\chi^2_{(3)} = 1.34$, $p = .72$).

Blinding of treatment

Both the participants and the experimenters who conducted the experiment were blinded to treatments. Following the MRI scan, the participants were asked to guess which treatment they received. Out of the 115 participants (109 with available estimates) in the OXT groups (PLC$_{tra}$ & OXT$_{int}$ and EST$_{tra}$ & OXT$_{int}$), 27 (24.8%; 11 men) believed that they had received OXT, while 25 (23.4%; 12 men) subjects in the PLC groups (PLC$_{tra}$ & PLC$_{int}$ and EST$_{tra}$ & PLC$_{int}$; $n = 112$, 107 with available estimates) believed that they had received verum treatment. Out of the 110 participants in the EST groups (EST$_{tra}$ & PLC$_{int}$ and EST$_{tra}$ & OXT$_{int}$ 108 with available estimates), 23 (21.3%; 13 men) estimated that they had received verum treatment, while 22 (20.4%; 4 men) subjects in the PLC groups (PLC$_{tra}$ & PLC$_{int}$ and PLC$_{tra}$ & OXT$_{int}$; $n = 117$, 108 with available estimates) assumed that they had received EST.

In general, the participants who believed in an OXT treatment also guessed an EST treatment ($r_{(214)}$ = 0.41, $p < 0.001$). However, the treatment estimates were not significantly associated with the actual treatments (all ps > 0.05).

Body mass index and hormonal levels

The body mass index (BMI) of the participants did not significantly correlate with the baseline EST or OXT levels in men or women (all ps > 0.05) or with treatment-induced EST_{tra} increases in either sex (all ps > 0.05). Thus, the EST_{tra} treatment did not result in different peripheral levels depending on BMI. While OXT_{int} treatment did not produce different peripheral OXT levels depending on the BMI in men ($p > 0.05$), the BMI positively correlated with the OXT increase in OXT_{int}-treated women (BMI: $r_{(53)}$ = 0.33, $p = 0.02$). Thus, OXT_{int} treatment resulted in higher peripheral OXT levels in women with a higher BMI.

Missing values

The following blood samples were missing due to problems in sample assessment or analysis: baseline (OXT, n = 4; EST, n = 6; progesterone, n = 6; testosterone, n = 7), post-treatment (OXT, n = 2; EST, n = 7; progesterone, n = 3; testosterone, n = 9), and three days after the treatment (EST, n = 15; progesterone, n = 12; testosterone, n = 15). Connection issues and technical errors resulted in the loss of questionnaires evaluating depressive symptoms (n = 9), autistic-like traits (n = 4), alexithymia (n = 4), trait anxiety (n = 5), social anxiety (n = 4), treatment guesses (n = 11), pretreatment negative and positive mood (n = 3), and posttreatment negative and positive mood (n = 10).

Demographic and psychometric baseline characteristics

Demographics and baseline psychometric assessments of the participants are displayed in **Table S3**. There were no significant differences in age, alexithymia, depressive symptoms, social anxiety, and trait anxiety between treatment groups within sexes (all ps$_{cor}$ > 0.05). In men, there were no significant differences in the autistic-like traits between treatment groups, in contrast to the women (main effect of treatment group: $F_{(3, 104)}$ = 117.94, $p = 0.01$, η_p^2 = 0.10). Post-hoc tests revealed that women in the combined treatment group and in the PLC treated group reported higher autistic like traits than the OXT_{int}-treated women (PLC_{tra} & OXT_{int} < EST_{tra} & OXT_{int}: $t_{(33.06)}$ = 2.89, $p_{cor} = 0.03$, $d = 0.83$; PLC_{tra} & OXT_{int} < PLC_{tra} & PLC_{int}: $t_{(33.80)}$ = 2.49, $p_{cor} = 0.03$, $d = 0.71$), while the other treatment groups were not significantly different. Across treatments women reported significantly higher social anxiety (Liebowitz scale, $t_{(221)}$ = -4.18, $p < 0.001$, $d = -0.56$) and increased trait anxiety (STAI Trait, $t_{(220)}$ = -3.17, $p < 0.01$, d = -0.43) than men. Age, alexithymia, depressive symptoms, and autistic-like traits were not significantly different between the sexes (all ps > 0.05). Autistic-like traits and social anxiety were included as

covariates in the main analyses of the significant neural main results (hippocampal and amygdala three- and two-way interactions). All reported effects remained significant and the covariates showed no significant effect (all $ps > 0.05$).

Measurements of mood

A main effect of time was found for the positive ($F_{(1,206)} = 92.98$, $p < 0.001$, $\eta_p^2 = .31$) and negative ($F_{(1,206)} = 9.23$, $p < 0.01$, $\eta_p^2 = .04$) affect measured with the PANAS (the Positive and Negative Affect Schedule) for both sexes (cf. **Table S4**). Positive and negative mood significantly decreased from the beginning of the testing session (mean ± SD positive: 28.84 ± 6.03; negative: 12.15 ± 3.43) to the end (mean ± SD positive: 25.15 ± 6.50; negative: 11.55 ± 2.19), suggesting an increasing fatigue over the time course of the experiment. In addition, we observed a significant main effect of sex for the positive mood. Men reported significantly higher positive mood than women (beginning: $t_{(222)} = 2.18$, $p = 0.03$, $d = 0.29$; end: $t_{(215)} = 3.36$, $p = 0.001$, $d = 0.46$) No further significant main or interaction effects of time and EST_{tra} and OXT_{int} treatments were found for positive or negative mood.

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Table S1. Estradiol, progesterone and testosterone concentrations at baseline, immediately post treatment and three days after the treatment

		Females				Males			
		PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)
Estradiol (pg/ml)	pre	34.80 (26, 19.44)	36.86 (32, 17.94)	45.98 (25, 25.96)	38.51 (24, 16.90)	22.39 (26, 7.86)	25.83 (31, 11.54)	21.90 (32, 11.73)	20.52 (25, 10.33)
	post	40.72 (25, 19.31)	41.44 (32, 17.33)	985.85 (27, 576.68)	990.96 (24, 445.67)	26.88 (27, 10.71)	31.92 (30, 10.36)	587.03 (31, 440.82)	662.38 (24, 419.42)
Progesterone (ng/ml)	pre	1.01 (26, 3.47)	0.26 (32, 0.24)	0.29 (25, 0.27)	0.19 (24, 0.11)	0.16 (26, 0.17)	0.22 (31, 0.14)	0.15 (32, 0.11)	0.13 (25, 0.09)
	post	1.13 (26, 4.31)	0.17 (33, 0.19)	0.19 (27, 0.23)	0.12 (25, 0.09)	0.09 (27, 0.10)	0.12 (31, 0.08)	0.10 (31, 0.11)	0.08 (24, 0.07)
Testosterone (ng/ml)	pre	0.27 (26, 0.15)	0.26 (32, 0.11)	0.23 (25, 0.15)	0.26 (23, 0.14)	4.21 (26, 1.35)	5.33 (31, 1.85)	4.64 (32, 1.45)	4.44 (25, 1.77)
	post	0.23 (26, 0.14)	0.24 (32, 0.10)	0.21 (25, 0.15)	0.23 (22, 0.11)	4.58 (27, 1.67)	5.50 (31, 1.98)	4.39 (31, 1.73)	4.50 (24, 1.61)

Notes. pre; pretreatment; post, 4.5 hours after the gel administration; PLC_{tra} = transdermal placebo gel; PLC_{int} = intranasal placebo; OXT_{int} = intranasal oxytocin; EST_{tra} = transdermal estradiol.

Table S2. Oxytocin baseline and post treatment concentrations

	Females				Males			
	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)
Oxytocin pre (pg/ml)	2.03 (26, 0.72)	1.51 (32, 0.59)	1.65 (26, 0.65)	1.63 (24, 0.52)	1.90 (27, 0.79)	2.02 (31, 0.83)	1.96 (31, 0.68)	1.97 (26, 0.67)
Oxytocin post (pg/ml)	2.14 (26, 0.69)	4.92 (33, 1.71)	1.83 (27, 0.62)	4.84 (24, 1.74)	2.09 (27, 0.89)	6.03 (31, 2.71)	2.25 (31, 0.61)	6.28 (26, 3.18)

Notes. pre; pretreatment; post, 4.5 hours after the gel administration; PLC_{tra} = transdermal placebo gel; PLC_{int} = intranasal placebo; OXT_{int} = intranasal oxytocin; EST_{tra} = transdermal estradiol.

Table S3. Demographic and psychometric baseline characteristics

	Females				Males			
	PLC_{tra} & PLC_{int} Mean (n, ± SD)x	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)
Age (years)	24.31 (26, 5.37)	24.24 (33, 4.95)	24.74 (27, 4.99)	25.28 (25, 5.86)	25.78 (27, 5.47)	24.97 (31, 3.64)	26.69 (32, 4.00)	25.62 (26, 5.29)
Depressive symptoms (BDI[b])	4.00 (25, 3.44)	1.84 (31, 2.33)	3.20 (25, 3.59)	3.40 (25, 3.24)	3.46 (26, 5.62)	1.83 (30, 2.61)	2.00 (32, 2.31)	2.63 (24, 2.90)
Autistic-like traits (AQ[c])	17.32 (25, 6.55)	13.74 (31, 3.32)	14.59 (27, 5.50)	18.04 (25, 6.82)	16.35 (26, 5.05)	14.39 (31, 5.35)	14.66 (32, 4.69)	15.12 (26, 5.74)
Alexithymia (TAS[d])	45.80 (25, 9.79)	42.26 (31, 10.69)	43.67 (27, 12.58)	44.4 (25, 10.21)	41.23 (26, 9.09)	43.52 (31, 9.32)	41.81 (32, 8.23)	39.77 (26, 9.58)
Trait anxiety (STAI[e])	38.52 (25, 8.27)	35.48 (31, 7.65)	33.89 (27, 7.58)	38.08 (25, 9.70)	33.00 (26, 8.39)	33.06 (31, 6.62)	33.94 (32, 6.70)	32.16 (25, 6.82)
Social anxiety (Liebowitz Total[f])	20.88 (25, 10.54)	18.39 (31, 11.97)	17.41 (27, 11.93)	19.80 (25, 11.30)	13.12 (26, 13.09)	11.81 (31, 10.56)	12.09 (32, 10.46)	13.58 (26, 13.32)

Notes. Subjects rated their depressive symptoms with the [b] BDI (Becks Depression Inventory, Beck et al., 1996). Autistic-like traits were measured with the [c] AQ (Autism Spectrum Quotient, Baron-Cohen et al., 2006). Alexithymia was assessed with the [d] TAS (Toronto Alexithymia Scale, Taylor et al., 1985). The [e] STAI-Trait (State-Trait-Anxiety Inventory, Spielberger, 1970) was used to assess trait anxiety and the [f] Liebowitz questionnaire was used to measure social anxiety. PLC_{tra} = transdermal placebo gel; PLC_{int} = intranasal placebo; OXT_{int} = intranasal oxytocin; EST_{tra} = transdermal estradiol.

Table S4. Mood measurements

	Females				Males			
	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)	PLC_{tra} & PLC_{int} Mean (n, ± SD)	PLC_{tra} & OXT_{int} Mean (n, ± SD)	EST_{tra} & PLC_{int} Mean (n, ± SD)	EST_{tra} & OXT_{int} Mean (n, ± SD)
Positive affect pre	27.28 (25, 6.69)	27.44 (32, 6.61)	29.26 (27, 5.54)	27.84 (25, 5.37)	30.00 (26, 5.25)	29.52 (31, 5.99)	28.44 (32, 5.92)	31.12 (26, 6.30)
Positive affect post	23.33 (24, 7.11)	23.29 (31, 6.44)	23.65 (26, 5.32)	24.48 (25, 6.30)	27.72 (25, 5.88)	25.48 (29, 6.12)	25.81 (32, 6.41)	27.64 (25, 7.37)
Negative affect pre	13.36 (25, 5.07)	11.31 (32, 1.45)	12.44 (27, 4.69)	12.64 (25, 4.37)	12.38 (26, 3.10)	11.97 (31, 3.15)	11.66 (32, 2.22)	11.85 (26, 2.48)
Negative affect post	12.42 (24, 2.15)	11.23 (31, 1.76)	11.62 (26, 2.19)	12.28 (25, 2.61)	11.16 (25, 1.57)	11.34 (29, 2.16)	11.19 (32, 1.77)	11.40 (25, 3.03)

Notes. Mood was assessed with the Positive and Negative Affect Schedule (PANAS). Abbreviations: pre; pretreatment; post, 4.5 hours after the gel administration; PLC_{tra} = transdermal placebo gel; PLC_{int} = intranasal placebo; OXT_{int} = intranasal oxytocin; EST_{tra} = transdermal estradiol.