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# Differential effects of intranasal oxytocin on sexual experiences and partner interactions in couples

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ABSTRACT

Knowledge about the effects of the neuropeptide oxytocin (OXT) on human sexual behaviors and partner interactions remains limited. Based on our previous studies, we hypothesize that OXT should be able to positively influence parameters of sexual function and couple interactions.

Employing a naturalistic setting involving 29 healthy heterosexual couples (n = 58 participants), we analyzed the acute effects of intranasally administered OXT (24 IU) on sexual drive, arousal, orgasm and refractory aspects of sexual behavior together with partner interactions. Data were assessed by psychometric instruments (Acute Sexual Experiences Scale, Arizona Sexual Experience Scale) as well as biomarkers, such as cortisol, α-amylase and heart rate.

Intranasal OXT administration did not alter "classical" parameters of sexual function, such as sexual drive, arousal or penile erection and lubrication. However, analysis of variance and a hierarchical linear model (HLM) revealed specific effects related to the orgasmic/post-orgasmic interval as well as parameters of partner interactions. According to HLM analysis, OXT increased the intensity of orgasm, contentment after sexual intercourse and the effect of study participation. According to ANOVA analysis, these effects were more pronounced in men. Men additionally indicated higher levels of sexual satiety after sexual intercourse with OXT administration. Women felt more relaxed and subgroups indicated better abilities to share sexual desires or to empathize with their partners. The effect sizes were small to moderate. Biomarkers indicated moderate psychophysiological activation but were not affected by OXT, gender or method of contraception.

Using a naturalistic setting, intranasal OXT administration in couples exerted differential effects on parameters of sexual function and partner interactions. These results warrant further investigations, including subjects with sexual and relationship problems.



## Introduction

During recent years, the neuropeptide oxytocin (OXT) has exhibited an impressive "scientific career" as revealed by a plethora of neuroscientific investigations in humans (Meyer-Lindenberg et al., 2011). In addition to the well-known physiological effects on parturition and lactation, behavioral human studies have demonstrated that peripheral levels of OXT may be associated with a number of prosocial behavioral aspects, including the stress-protective effects of physical contact (Ditzen et al., 2007), positive physical contact with a partner (Grewen et al., 2005), reduced hormonal responses to a psychosocial stressor (Taylor et al., 2006) and lower levels of anxiety in depressed patients (Scantamburlo et al., 2007). However, the causality of these effects and the relationship between peripheral and central OXT levels remain to be further explored (Heinrichs et al., 2009). The majority of studies in humans have used an intranasal approach of OXT administration, which support the above-mentioned findings comprising a reduced response to social stress (Heinrichs et al., 2003), increased trust (Kosfeld et al., 2005) and an improved ability to infer what another person is thinking or feeling, referred to as "mind-reading" (Domes et al., 2007).

In contrast to these findings on human social cognition and behavior, little is known about the role of OXT in human sexuality, particularly in couple interactions. OXT is released during orgasm in males and females and exhibits a positive correlation with the intensity of muscle contraction of the pelvic floor in women during orgasm (Blaicher et al., 1999; Carmichael et al., 1987; Kruger et al., 1998, 2003a; Murphy et al., 1987). Case studies have reported a facilitating role of OXT on sexual parameters such as accentuated sexual arousal in females, occurrence of an orgasm in anorgasmic males, or improvement in sexual function in a male patient with social anxiety (Anderson-Hunt and Dennerstein, 1994, 1995; Ishak et al., 2008; Macdonald and Feifel, 2012b). However,

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these observations have not been validated in larger controlled trials. More recently, employing an established and well-controlled laboratory paradigm, we were able to demonstrate that intranasal OXT administration triggered the release of plasma catecholamines and altered the perception of arousal during masturbation in healthy males (Burri et al., 2008). However, these OXT-induced perceived changes during sexual activity could not be confirmed with psychometric instruments for the assessment of acute sexual experiences. Moreover, this study was restricted to males and did not elucidate the role of OXT in females. There is evidence that OXT may differentially impact (sexual) behavior depending on gender (Fischer-Shofty et al., 2013). From clinical experience in sexual medicine, one may speculate that males may preferentially recognize changes on a performance level (erectile function, orgasm, sexual satisfaction), whereas many women put more emphasis on the perception of relationship aspects.

With respect to the well-defined prosocial properties of OXT, we hypothesized that OXT may exert behavioral effects predominantly in specific social contacts, such as sexual partner interactions and not in a highly artificial laboratory situation without partner contact. This led us to design and perform a study in a naturalistic field setting with high external validity. Having high prevalence rates of sexual disorders of up to 60% in mind (e.g., sexual desire and arousal disorders, orgasm disorders, problems in couple communication) (Frank et al., 1978; Jha and Thakar, 2010; Laumann et al., 1999), we investigated whether and to what extent a single intranasal OXT administration may affect sexual drive, arousal, orgasm and refractory aspects of sexual behavior as well as couple interactions in healthy heterosexual male and female volunteers. In a double-blind, placebo-controlled, balanced cross-over design, sexual arousal and orgasm were induced by sexual intercourse. Cardiovascular and endocrine parameters were assessed and variables of sexual experience were evaluated using questionnaires especially developed for the assessment of acute sexual experiences (Kruger et al., 2003b; McGahuey et al., 2000). Additionally, a differentiation between couples using hormonal and non-hormonal contraception was necessary. Contraception can affect both female and male mate choice as well as sexual desire by removing or altering the typical endocrine dynamic release pattern and the associated mid-cycle changes in mate preferences, behavior, external appearance and sexual desire ratings (Alvergne and Lummaa, 2010; Burrows et al., 2012).

## Material and methods

### *Participants*

Twenty-nine healthy, heterosexual couples (total n = 58), aged 20–50 years ($mean_{age}$ 29.0 ± 5.75 (standard error of mean, SEM) $mean_{age}$ males 29.76 ± 6.72, $mean_{age}$ females 28.24 ± 6.72) participated in this study after providing written informed consent. Subjects were recruited via advertisements by the Hannover Medical School, Germany. As hormone intake may impact sexual physiology and behavior (Alvergne and Lummaa, 2010; Burrows et al., 2012), couples were grouped according to their method of contraception with n = 15 females using hormonal contraception ($mean_{age}$ 24.53 ± 2.70; $mean_{age}$ of male partner 26.87 ± 2.92) and n = 14 females using non-hormonal contraception ($mean_{age}$ 32.21 ± 7.54. $mean_{age}$ of male partner 32.86 ± 3.98) (Table 1).

Participants were screened by the completion of general medical/health and gynecological questionnaires. The gynecological anamnesis included an assessment of a regular menstrual cycle (25–35 days) of at least 6 months, parity, gravidity, current pregnancy and syndromes such as dysmenorrhea, premenstrual syndrome, polycystic ovary syndrome and virilization. Pregnant subjects and those taking medication, abusing drugs or alcohol, or exhibiting endocrinological or psychological disorders were excluded. To assess the quality of the partnership, the Partnership Questionnaire (PFB) (Hahlweg, 1996) was given to all subjects before participation. The PFB is a tool that comprises three scales, analyzing patterns of quarrels, communality and tenderness within a couple, individually, as well as giving a total score. Only subjects who were sexually active and who had been in the current partnership for at least 12 months ($mean_{duration}$ 55 months, range 12–238 months) were included into the study to control for confounding factors such as states of romantic love or sexual abstinence (Exton et al., 2001a; Marazziti and Canale, 2004). Subjects were remunerated with 50€ for their participation. The institutional review board of the Hannover Medical School, Germany approved the study. The study was conducted in accordance with the Declaration of Helsinki.

### *Design and procedure*

The investigation was performed using a double-blind, placebo-controlled, crossover design in a home setting (Fig. 1). The experimental paradigm included two sessions identical in performance and only differing in the order of treatment. A repeated measure design was used in which participants were randomly assigned to two groups: 15 couples received OXT in the first session and a placebo in the second session, whereas 14 couples received a placebo in the first session and OXT in the second session. A male and a female constituting a couple received treatment in the same order without their knowledge. With regard to the female menstrual cycle (as assessed by gynecological anamnesis), all sessions took place during the midfollicular phase as conducted earlier (Exton et al., 1999, 2001b), being separated by an interval of 72 h, representing a wash-out period in the case of OXT administration. Subjects were asked to abstain from intensified smoking, caffeine and alcohol consumption 24 h prior to and during the sessions to avoid any interference with physiological or endocrine measures. Furthermore, subjects were asked to conduct the sessions in the evening hours between 6 and 11 pm to allow comparability of data (e.g., cortisol levels). Prior to the sessions, couples were asked to an appointment in the laboratory where an instructor gave information on specific aspects of the study design and procedure, including a flow chart depicting the entire procedure (in analogy to Fig. 1). Thereafter, participants provided written informed consent. The experimenters were not present in the homes of participants.

A session comprised a baseline phase, a sexually active phase and a post-sexual phase in the respective home setting. The session began with the couple putting on a heart rate measuring device for the assessment of autonomic nervous system activity. Subsequently, subjects administered 24 IU (three puffs in each nostril) of OXT (Syntocinon® Spray, Novartis, Basel, Switzerland) or a placebo. The methodology of the administration used has been described in detail previously (Burri et al., 2008; Heinrichs et al. 2003). Participants were asked to relax and refrain from any sexual activity for 35 min after drug administration to

**Table 1**
**Methods of contraception used by the respective couples.** IUS: levonorgestrel releasing intrauterine system; COCP: combined oral contraceptive pill; IUD: copper containing intrauterine device.

| Hormonal contraception | Vaginal ring | IUS | COCP | Oral contraception, not further specified | Total |
|---|---|---|---|---|---|
| n | 1 | 1 | 5 | 8 | 14 |
| Non-hormonal contraception | Condom | IUD | No contraception | Not further specified | |
| n | 9 | 2 | 2 | 1 | 15 |

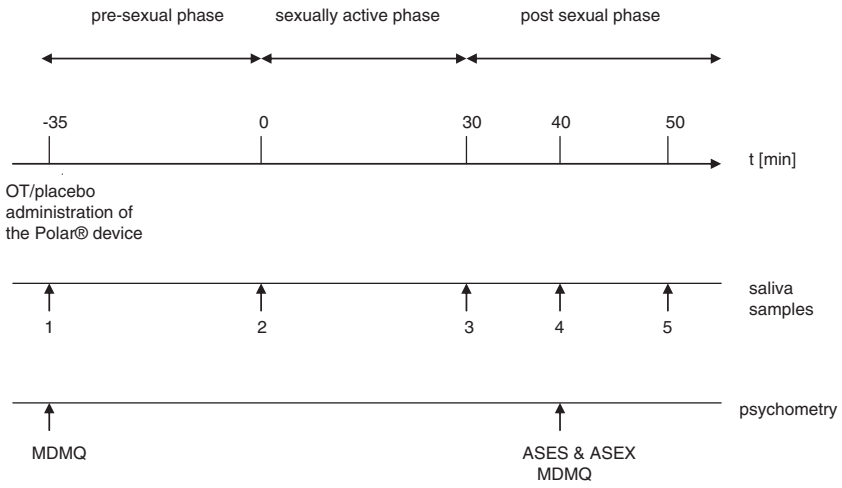


**Fig. 1. Experimental paradigm.** The paradigm consisted of two experimental sessions, each lasting approximately 85 min. Each subject completed two sessions in a balanced cross-over design, with continuous assessment of endocrine, psychometric and cardiovascular parameters throughout each session. For details, see Methods section. OXT, oxytocin; S, saliva sample; HR, heart rate in beats per minute; ASES, Acute Sexual Experiences Scale Questionnaire; MDMQ, Multidimensional Mood State Questionnaire.

allow OXT to reach relevant concentrations in the central nervous system (Born et al., 2002) and periphery (Burri et al., 2008). The sexually active phase consisted of foreplay and sexual intercourse as desired by the participants and was restricted to a maximal length of 30 min to allow a certain degree of standardization and comparability of data. No instruction was given regarding the occurrence of an orgasm. Following a ten-minute interval of rest after sexual intercourse, subjects were asked to complete the questionnaires. After completion, subjects were allowed to remove the heart rate measuring device.

Participants were instructed to identify the different phases of each session by putting marks on the Polar wristwatch, resulting in a total of five marks. Specifically, mark 1 represented the start of the session, mark 2 represented the initiation of sexual activity, mark 3 represented the orgasm or the finish of sexual intercourse, mark 4 represented the time at which the subjects began to complete the questionnaires and mark 5 represented the end of the session. Additionally, subjects were asked to collect saliva samples corresponding to the marks for endocrinological analyses.

## Measures

### *Psychological measures*

Similar to our previous studies (Burri et al., 2008; Kruger et al., 2003b), we assessed sexual function using specific items selected from the Acute Sexual Experience Scale (ASES, Braunert and Kaiser, 2010; Kruger et al., 2003a) together with the Arizona Sexual Experience Scale (ASEX). The ASEX consists of 5 items in total and aims at assessing changes of sexual function in response to pharmacological treatment or psychotherapy using 6-level Likert scales ("not at all" to "extremely") (McGahuey et al., 2000). Reliability (Cronbach's alpha: .90; test–rest reliability: .89) and validity (convergent validity males/females: −.52 to .18/−.69 to −.14; divergent validity males/females: .03 to .29/.05 to .40) for healthy controls are good to excellent. This questionnaire was adapted for the current study by reversing the response options (1–6, from "not at all" to "extremely") to achieve homogeneity with the ASES. The ASEX was used after initial translation into German, followed by back-translation into English, for validation purposes by a native speaking person. The ASEX quantifies sexual drive, arousal, vaginal lubrication/penile erection, ability to reach orgasm and satisfaction from orgasm (Table 3a). To complement the ASEX, specific items from the ASES questionnaire were used to more specifically assess orgasmic and post-orgasmic parameters. The ASES was initially developed in German to measure different qualities of appetitive, consummatory and refractory aspects of sexual behavior in men, containing six subscales of 52 items (Kruger et al., 2003b). For the current study, we used five selected items from a revised and improved version of the ASES, which is applicable to both males and females (Braunert and Kaiser, 2010) (Table 3b). The questionnaire comprises self-reporting sexual functioning ratings using 6-level Likert scales (1–6, from "not at all" to "extremely"). Subjects who did not experience an orgasm were instructed to ignore questions regarding orgasm. For the current study, we included four additional items aimed at assessing specific features of partner interaction during sexual intercourse, such as intimacy and empathy (Table 3c). These items were developed and validated in a previous study in a sample of n = 1154 (online survey) and n = 168 participants (paper and pencil survey) (Braunert and Kaiser, 2010). The reliability for the ASES items/partner interaction items was acceptable (Cronbach's alpha: .72/.76) and the validity was good (e.g., convergent validity for partner interaction: .60).

Additionally, participants were instructed to complete the Multidimensional Mood State Questionnaire (MDMQ) at the beginning and at the end of each session, allowing registration of significant mood, wakefulness and restfulness alterations (Steyer et al., 1997), leading to a total

**Table 2**
**Subjects characteristics.** Values are depicted as means (±standard deviation); NHC = non-hormonal contraception (n = 14); HC = hormonal contraception (n = 15); ns = no statistical significance; PFB = partnership questionnaire.

| | Women | | p | Men | | p | Couples | | p |
|---|---|---|---|---|---|---|---|---|---|
| | NHC | HC | | NHC | HC | | NHC | HC | |
| Age [years] | 32.2 (7.5) | 24.5 (2.7) | .002 | 32.9 (4.0) | 26.9 (2.9) | <.001 | 32.2 (7.5) | 24.5 (2.7) | .002 |
| Duration of partnership [months] | | | | | | | 80.6 (63.9) | 31.2 (17.1) | .013 |
| PFB | 71.9 (8.5) | 69.9 (4.1) | ns | 70.6 (8.4) | 65.8 (7.9) | ns | 51.0 (7.8) | 51.7 (6.0) | ns |

**Table 3a**
**Arizona Sexual Experience Scale (ASEX).** Items assessing sexual drive, function and satisfaction. Depicted are means ± standard deviation (SD) as well as main effects derived from two factorial ANOVA analysis. Post-hoc t-tests are shown in cases of significant treatment effects or where large differences between the respective means were apparent with # $p = .059$. Effect sizes for ANOVA analysis are depicted as partial eta square values ($\eta^2$_p) and Cohen's d where appropriate. NHC, non-hormonal contraception; HC, hormonal contraception; OXT, oxytocin; PLA, placebo.

| Item | Description | Gender | Contraception | Mean OXT (±SD) | Mean PLA (±SD) | ANOVA treatment (within-subject) | ANOVA contraception (between-subject) |
|---|---|---|---|---|---|---|---|
| ASEX 1 | How strong was your sex drive? | Male | NHC | 5.5 (.65) | 5.5 (.65) | n.s. | $F(1, 27) = 4.655$, $p = .040$, $\eta^2$_p = .147 |
| | | | HC | 5.13 (.92) | 4.87 (.83) | | |
| | | Female | NHC | 5.14 (.77)# | 4.36 (1.45)# | n.s. | n.s. |
| | | | HC | 4.80 (1.21) | 4.60 (.99) | | |
| ASEX 2 | How easily were you sexually aroused? | Male | NHC | 4.64 (1.01) | 4.36 (1.15) | n.s. | n.s. |
| | | | HC | 3.87 (1.50) | 4.07 (1.39) | | |
| | | Female | NHC | 4.64 (1.28) | 4.14 (1.41) | n.s. | n.s. |
| | | | HC | 4.13 (1.13) | 3.67 (1.76) | | |
| ASEX 3 | How easily did you get and keep an erection/did your vagina become moist or wet? | Male | NHC | 5.21 (.89) | 5.29 (.91) | m | n.s. |
| | | | HC | 5.13 (.83) | 5.07 (1.03) | | |
| | | Female | NHC | 4.71 (1.20) | 4.36 (1.45) | n.s. | n.s. |
| | | | HC | 4.60 (1.06) | 4.13 (1.51) | | |
| ASEX 4 | How easily did you reach an orgasm? | Male | NHC | 4.71 (1.20) | 4.79 (.89) | n.s. | n.s. |
| | | | HC | 5.08 (2.29) | 5.15 (.90) | | |
| | | Female | NHC | 4.63 (1.06) | 4.63 (.74) | n.s. | n.s. |
| | | | HC | 4.33 (1.23) | 4.22 (.83) | | |
| ASEX 5 | Was your orgasm satisfying? | Male | NHC | 4.93 (.77) | 4.71 (1.07) | n.s. | n.s. |
| | | | HC | 4.53 (.92) | 4.40 (1.12) | | |
| | | Female | NHC | 4.93 (.73) | 4.21 (1.25) | n.s. | n.s. |
| | | | HC | 4.20 (1.08) | 4.00 (1.25) | | |

of four completed MDMQ questionnaires per subject. Subjects were asked to fill out the questionnaires without communicating answers with their respective partner to avoid an influence on the results.

*Endocrine measures*

Salivary free cortisol is a valid indicator of the biologically active fraction of cortisol and depicts hypothalamic–pituitary–adrenal (HPA) axis function (Kirschbaum and Hellhammer, 1989, 1994; Vining et al., 1983). OXT has been shown to decrease basal cortisol levels following systemic administration in humans (Legros et al., 1984, 1988). Alpha-Amylase has been identified as a useful saliva-based marker sensitive stress-induced sympathetic activity (Schumacher et al., 2013). The two parameters were analyzed to detect changes in HPA-axis function and autonomic nervous system function in response to sexual activity and OXT or placebo administration. We hypothesized that in cases of mild or moderate stress or psychophysiological activation, OXT might lower cortisol and/or alpha-amylase levels as well as heart rate. Saliva samples were taken at five time points in accordance with the five marks mentioned above and as indicated in Fig. 1.

Both cortisol and alpha-amylase samples were obtained by using a Salivette®, a standard sampling product (Sarstedt, Nürnberg, Germany). Participants were instructed to suck or chew on the supplied cotton roll until it was saturated and to put the Salivette® into a freezer immediately after completion of a session until the next meeting with the experimenter (generally within 48 h after completion of the experiment). The Salivette® tubes were then centrifuged at 3000 rpm for 7 min to obtain .05–1.0 ml of clear saliva with low viscosity and then stored in the laboratory at −20 °C until required for biochemical analysis. Salivary cortisol levels were measured using a commercial enzyme-linked immunosorbent assay (Cortisol ELISA, IBL International, Hamburg, Germany) according to the manufacturer's instructions.

**Table 3b**
**Acute Sexual Experiences Scale (ASES).** Selected items assessing intensity of orgasm and post-orgasmic aspects such as contentment, lust for reinitiating sex, tension and overall impression of sexual experience. Depicted are means ± standard deviation (SD) as well as main effects deriving from two factorial ANOVA analysis. Post-hoc t-tests are indicated in cases of significant treatment effects or where large differences between the respective means were apparent with **$p < .01$. Effect sizes for ANOVA analysis are depicted as partial eta square values ($\eta^2$_p) and Cohen's d where appropriate. NHC, non-hormonal contraception; HC, hormonal contraception; OXT, oxytocin; PLA, placebo.

| Item | Description | Gender | Contraception | Mean OXT (±SD) | Mean PLA (±SD) | ANOVA treatment (within-subject) | ANOVA contraception (between-subject) |
|---|---|---|---|---|---|---|---|
| ASES 1 | How intense was your orgasm? | Male | NHC | 4.93 (.62) | 4.64 (.75) | $F(1, 25) = 4.571$, $p = .042$, | $F(1, 25) = 4.219$, |
| | | | HC | 4.62 (1.04) | 4.00 (.82) | $\eta^2$_p = .155, d = .415 | $p = .051$, $\eta^2$_p = .144 |
| | | Female | NHC | 4.50 (.27) | 4.25 (.41) | n.s. | n.s. |
| | | | HC | 4.78 (1.09) | 4.33 (1.50) | | |
| ASES 2 | How strong was your contentment after sexual intercourse? | Male | NHC | 5.14 (.77)** | 4.71 (.73)** | $F(1, 27) = 4.624$, $p = .041$, | $F(1, 27) = 4.953$, |
| | | | HC | 4.60 (.51) | 4.20 (1.15) | $\eta^2$_p = .146, d = .414 | $p = .035$, $\eta^2$_p = .155 |
| | | Female | NHC | 5.07 (.73) | 4.50 (1.29) | n.s. | n.s. |
| | | | HC | 4.73 (.88) | 4.40 (1.24) | | |
| ASES 3 | How strong was your lust for new sexual stimulation after sex. intercourse? | Male | NHC | 2.43 (1.16) | 2.86 (1.23) | $F(1, 27) = 4.450$, $p = .044$, | n.s. |
| | | | HC | 2.40 (1.24) | 4.40 (5.05) | $\eta^2$_p = .141, d = −.407 | |
| | | Female | NHC | 2.43 (1.45) | 2.21 (1.63) | n.s. | n.s. |
| | | | HC | 3.27 (1.16) | 2.47 (1.36) | | |
| ASES 4 | What was the effect of participation in this study on your sex. experience? | Male | NHC | 4.18 (.82)** | 3.50 (1.23)** | $F(1, 27) = 7.794$, $p = .010$, | n.s. |
| | | | HC | 3.33 (.72) | 3.20 (.86) | $\eta^2$_p = .224, d = .499 | |
| | | Female | NHC | 3.39 (.63) | 3.29 (1.07) | n.s. | n.s. |
| | | | HC | 3.50 (.98) | 2.93 (1.10) | | |
| ASES 5 | How tense were you after sexual intercourse? | Male | NHC | 1.43 (.65) | 1.79 (1.05) | n.s. | n.s. |
| | | | HC | 2.07 (1.53) | 1.53 (.92) | | |
| | | Female | NHC | 1.14 (.36) | 1.29 (.47) | $F(1, 27) = 4.628$, $p = .041$, | $F(1, 27) = 3.997$, |
| | | | HC | 1.33 (.49) | 1.93 (1.22) | $\eta^2$_p = .146, d = −.456 | $p = .056$, $\eta^2$_p = .129 |

**Table 3c**
**Aspects of partner interaction.** Depicted are means ± standard deviation (SD). t-Tests are presented in cases of significant treatment effects or where huge differences between the respective means were apparent with *p < .05, + p = .05. Effect sizes for ANOVA analysis are depicted as partial eta square values ($\eta^2$_p) and Cohen's d where appropriate. NHC, non-hormonal contraception; HC, hormonal contraception; OXT, oxytocin; PLA, placebo.

| Item | Description | Gender | Contraception | Mean OXT (±SD) | Mean PLA (±SD) | ANOVA treatment (within-subject) | ANOVA contraception (between-subject) |
|---|---|---|---|---|---|---|---|
| Partner interaction 1 | "I felt emotionally close to my partner" | Male | NHC | 5.31 (.63) | 5.23 (.60) | n.s. | $F(1, 27) = 7.966$, $p = .009$, $\eta^2$_$p = .235$ |
| | | | HC | 4.60 (.83) | 4.93 (.70) | | |
| | | Female | NHC | 5.29 (.47) | 5.14 (.95) | n.s. | n.s. |
| | | | HC | 4.87 (1.13) | 4.73 (1.22) | | |
| Partner interaction 2 | "I was able to share my sexual desires" | Male | NHC | 4.69 (1.23) | 5.08 (1.17) | n.s. | n.s. |
| | | | HC | 4.80 (1.27) | 4.80 (1.32) | | |
| | | Female | NHC | 5.07 (.92) | 5.00 (1.17) | $F(1, 27) = 3.427$, $p = .075$, $\eta^2$_$p = .133$, $d = .358$ | n.s. |
| | | | HC | 5.20 (.68)* | 4.40 (1.19)* | | |
| Partner interaction 3 | "I could empathize with my partner" | Male | NHC | 4.85 (.69) | 4.85 (1.07) | n.s. | n.s. |
| | | | HC | 4.60 (1.12) | 4.67 (.62) | | |
| | | Female | NHC | 5.07 (.62)* | 4.57 (.94)* | n.s. | n.s. |
| | | | HC | 4.33 (1.18) | 4.60 (.97) | | |
| Partner interaction 4 | "My partner felt secure" | Male | NHC | 5.15 (.90) | 4.77 (1.09) | n.s. | n.s. |
| | | | HC | 4.93 (.92) | 4.57 (1.09) | | |
| | | Female | NHC | 5.29 (.61)+ | 4.86 (1.17)+ | n.s. | n.s. |
| | | | HC | 4.67 (.72) | 4.60 (.83) | | |

Cross-reactivities of the anti-cortisol antibody with other relevant steroids were 7.0% (11-deoxycortisol), 4.2% (cortisone), 1.4% (corticosterone), 0.35% (progesterone) and <0.01% (testosterone, estrone, estradiol, estriol). Intra- and interassay variances were 4.8% and 5.9%, respectively.

Salivary alpha-amylase activity was determined using a commercially available enzymatic assay (Salivary Alpha-Amylase Assay Kit, Salimetrics, State College, PA, USA) according to the manufacturer's instructions. Briefly, diluted saliva (1:200) was mixed with a prewarmed (37 °C) solution of 2-chloro-p-nitrophenol linked to maltotriose. The enzymatic conversion of this substrate by alpha-amylase yields 2-chloro-p-nitrophenol, which can be spectrophotometrically measured at 405 nm. The increase in absorbance at 405 nm over a period of 2 min is directly proportional to the amount of alpha-amylase activity present in the sample. Intra- and interassay variances were 2.4% and 3.5%, respectively.

*Cardiovascular measures*

Heart rate was continuously monitored with a Polar® heart rate measuring device. The Polar S810i (Polar Electro Oy, Finland) is composed of a belt, which is worn around the chest and a wristwatch, which is used as a receiver and storage device for the data sent by wireless transmission from the belt. Heart rate was measured beat to beat and then averaged over four intervals according to the phases described above. Moreover, we averaged the first 5 min of participants' heart rates to an additional interval to allow a more accurate measurement of baseline heart rate, leading to a total of five heart rate intervals (HR 1–HR 5). Specifically, HR 1 and HR 2 represent heart rate data of the pre-sexual phase (HR 1 represents the first 5 min of the session, HR 2 represents minute 6 to minute 35 of the session), HR 3 represents the sexually active phase, lasting as long as 30 min, HR 4 represents a 10-minute interval between the termination of sexual intercourse and the beginning of filling in the questionnaires and HR 5 represents another ten-minute interval until the end of the session.

The heart rate measures of two subjects were incomplete due to technical problems and were excluded from statistical analyses, resulting in 112 complete heart rate files available for analysis (males on the OXT condition: n = 28, males on the placebo condition: n = 28, females on the OXT condition: n = 28, females on the placebo condition: n = 28).

*Statistical analyses*

Data were analyzed using SPSS Statistics 19 (IBM® Corporation, Amonk, NY, USA). Deviations from normal distributions were tested with the Kolmogorov–Smirnov test ($p > 0.1$ for all variables). Levene's test was used to verify the assumption that the samples were equal in variances.

Endocrine and cardiovascular data were analyzed using repeated measures ANOVA: treatment [two conditions: OXT and placebo] by time [repeated factor: 5 for endocrine and cardiovascular data]. Covariates such as the duration of the relationship and age were controlled for in all analyses. Gender and the method of contraception were included in all analyses as between-subject factors. We verified repeated measures results using Greenhouse–Geisser corrections where appropriate, reflected by the degrees of freedom with decimal values.

Psychological data were first analyzed using repeated measures ANOVA (grouped [two groups: couples using hormonal contraception and couples using non-hormonal contraception] by treatment [two conditions: OXT and placebo]). Effect sizes are reported as partial eta square values ($\eta^2$_p) or eta square values ($\eta^2$), and Cohen's d where appropriate. Post-hoc paired sample t-tests were conducted in cases of significant effects in the ANOVA and for selected items for direct comparison of the two treatment conditions (OXT and placebo). With respect to the exploratory nature of the study, corrections for multiple comparisons were not performed at this point of analysis. Additionally, with respect to the exploratory nature and the naturalistic setting of this study, we sometimes report and interpret borderline effects ($p < 0.06$). To account for covariates that may affect the results, such as relationship duration, sex and age, we conducted a repeated measures multivariate analysis of variance (MANOVA/MANCOVA).

Taking into account the dyadic nature of the psychometric data, additional statistical analyses were conducted. First, inter-couple correlations were calculated. Only a minor proportion (6 out of 28, i.e. 21.4%) of correlations (14 variables of interest, 2 conditions: oxytocin and placebo) yielded significance which was low to moderate ($.38 \leq r \geq .66$). The 6 items included ASEX 2, 3 and 5, ASES 4 and partner interactions 1 and 2 (see also Tables 3a–3c for brief description of items). Hence, the outcome variables appeared to be widely independent within couples. However, because it is possible that more undetected correlations existed in the data and with respect to the nested data structure, a hierarchical linear (mixed) model (HLM) was conducted. Hierarchical linear models are a group of multivariate methods that are implemented when the data set is hierarchically structured and/or nested (Tabachnick and Linda, 2007). With an adequate sample size of 29 couples, detection of effects was ensured (de Leeuw and Kreft, 1998). Each outcome variable was measured at the individual level. The model involved the levels "subject", "couple" and "time" to account for the dyadic data in a repeated measures design. The independent variable "condition", which involved oxytocin vs. placebo and the covariates

"age", "sex", "relationship duration" and "method of contraception" were integrated as fixed effects, whereas the individuals nested in couples were modeled as random effects. We chose the restricted maximum likelihood estimator (REML) over the maximum likelihood estimator (ML), as the estimated variance components of the REML are less likely to be biased (Albright and Marinova, 2010). Significant effects are reported according to APA style together with effect sizes as Cohen's d.

Raw data are presented as the mean ± standard deviation of the mean (SD). All analyses were two-tailed with the level of significance set at $p < .05$.

## Results

### *Subject characteristics*

We assessed 15 couples using hormonal contraception and 14 using non-hormonal contraception (Table 1). Women taking hormonal contraception and their partners were significantly younger and reported a shorter partnership in comparison to women taking non-hormonal contraception and their partners, respectively. However, the PFB revealed no significant difference in partnership happiness (Table 2). The factors age, sex and relationship duration have been accounted for in a MANOVA as reported below.

Females taking *non-hormonal contraception* were aged 20–50 years ($mean_{age}$ 32.2 ± 2.0). Evaluation of the PFB revealed that all of female subjects in this subgroup considered themselves to be in a happy partnership (cutoff score for happiness = 54; mean score 71.9 ± 2.3 points, range: 57–88). Males were aged 26–38 years ($mean_{age}$ 32.9 ± 1.1) and scored 70.6 ± 2.3 points on the PFB, with no male scoring less than 54 points (range: 57–86). The duration of the partnership of couples using non-hormonal contraception was on average 80.6 ± 11.8 months.

Females using *hormonal contraception* were aged 20–29 years ($mean_{age}$ 24.5 ± .7) and scored 69.9 ± 1.1 points on the PFB, with no subject scoring less than 54 points (range 64–77). Males were aged 21–32 years ($mean_{age}$ 26.9 ± .8) and scored 65.8 ± 2.1 points on the PFB (range 48–79) with one subject failing to reach the cutoff score of 54. The duration of the partnership of couples using hormonal contraception was 31.2 ± 3.1 months.

### *Psychological measures*

A total number of 11 subjects in the OXT condition (9 females and 2 males) and 8 subjects in the placebo condition (7 females and 1 male) did not achieve orgasm. Four of the females of the OXT condition did not achieve orgasm in the PLA condition. There was no statistically significant difference between these conditions. In total, there were 19 "anorgasmic" events out of 116 sexual encounters (58 participants having sexual intercourse twice). This is a prevalence rate for "anorgasmic" events of 16%, which is consistent with epidemiological data in normal populations (Bancroft, 2009; Goldstein et al., 2005).

### *ASEX questionnaire data*

Although the majority of items of the ASEX questionnaire revealed slightly improved values after OXT administration, at first glance, the statistical analysis of the participants' subjective assessment of the "classical" parameters of sexual activity such as sexual drive, sexual arousal and erection/lubrication revealed no significant results in men and women (Table 3a). The only finding here was that men from couples using non-hormonal contraception indicated higher levels of sex drive (ASEX 1) compared with their counterparts (hormonal contraception couples) ($F(1, 27) = 4.655$, $p = .040$, $\eta^2\_p = .147$). Additional analysis using HLM revealed only a borderline effect for sexual drive ($p = .057$, $d = .310$), which was modulated by some of the covariates (data not shown).

### *ASES questionnaire data*

In contrast, in males, specific aspects of sexual experiences such as the intensity of orgasm (ASES 1) ($F(1, 25) = 4.571$, $p = .042$, $\eta^2\_p = .155$, $d = .415$) and contentment after sexual intercourse (ASES 2) ($F(1, 27) = 4.624$, $p = .041$, $\eta^2\_p = .146$, $d = .414$) as assessed by the ASES questionnaire were significantly increased by OXT administration in men (Table 3b, Figs. 2A & B). With respect to these two parameters, the mean values were generally higher in men from couples using non-hormonal contraception, which reached statistical significance only for the factor contentment (ASES 2) (Table 3b). Interestingly, after sexual intercourse, men depicted a significantly lower level of lust for new sexual stimulation (ASES 3), indicating a higher level of sexual satiety after OXT administration ($F(1, 27) = 4.45$, $p = .044$, $\eta^2\_p = .141$, $d = -.407$) (Fig. 2C). Furthermore, the effect of participation on sexual experience (ASES 4) was higher after OXT administration ($F(1, 27) = 7.794$, $p = .010$, $\eta^2\_p = .224$, $d = .499$), with more pronounced effects in non-hormonal contraception men (Table 3b).

Women merely depicted reduced levels of tension after sexual intercourse (ASES 5) ($F(1, 27) = 4.628$, $p = .041$, $\eta^2\_p = .146$, $d = -.456$). Tension levels were generally lower in females taking non-hormonal contraception (Table 3b, Fig. 2D).

These results were largely supported using HLM analysis, where significant effects were observed for the intensity of orgasm (ASES 1) ($p = .015$, $d = .43$), contentment after orgasm (ASES 2) ($p = .015$, $d = .45$) and the effect of participation (ASES 4) ($p = .013$, $d = .38$) regardless of gender. Effect sizes were low to moderate and only the effect of OXT on intensity of orgasms might have been influenced by different covariates (see Tables 4a–4c).

### *Partner interaction data*

Finally, we assessed aspects of partner interaction during sexual intercourse. Marginal effects could be observed on a subgroup level for females using t-test comparisons (Table 3c and Figs. 2E and F), indicating an increased ability to share sexual desires (Partner interaction 2) in women taking hormonal contraception as well as an improved ability to empathize with the partner (Partner interaction 3) and increased ratings of the partner's emotional state (Partner interaction 4) in women using non-hormonal contraception.

Non-hormonal contraception males exhibited generally higher perceptions of feeling emotionally close to their partners as shown by a main effect in the ANOVA ($F(1, 27) = 7.966$, $p = .009$, $\eta^2\_p = .235$).

HLM analysis revealed only borderline effects for ratings of the partner's emotional state (Partner interaction 4) ($p = .058$, $d = .33$; data not shown).

In addition to the HLM (which already included covariates), factors such as age, sex and length of relationship were controlled as covariates using multivariate analysis of variance. Only the factor age revealed an impact on psychometric variables ($F(14, 79) = .754$, $p = .047$, $\eta^2 = .246$). With the exception of item ASES 3 (lust for new sexual stimulation after intercourse), all other items – which included sexual arousal, orgasm, sexual satisfaction and the feeling of emotional closeness – exhibited higher scores in older participants.

In contrast to parameters of sexual experience and couple interaction, the MDMQ did not indicate any significant alterations of mood, wakefulness or restfulness after OXT administration.

### *Cardiovascular measures*

When analyzing cardiovascular data, the progression of heart rate was consistent with the human sexual response cycle (Masters and Johnson, 1966) and as previously described (Exton et al., 1999; Kruger

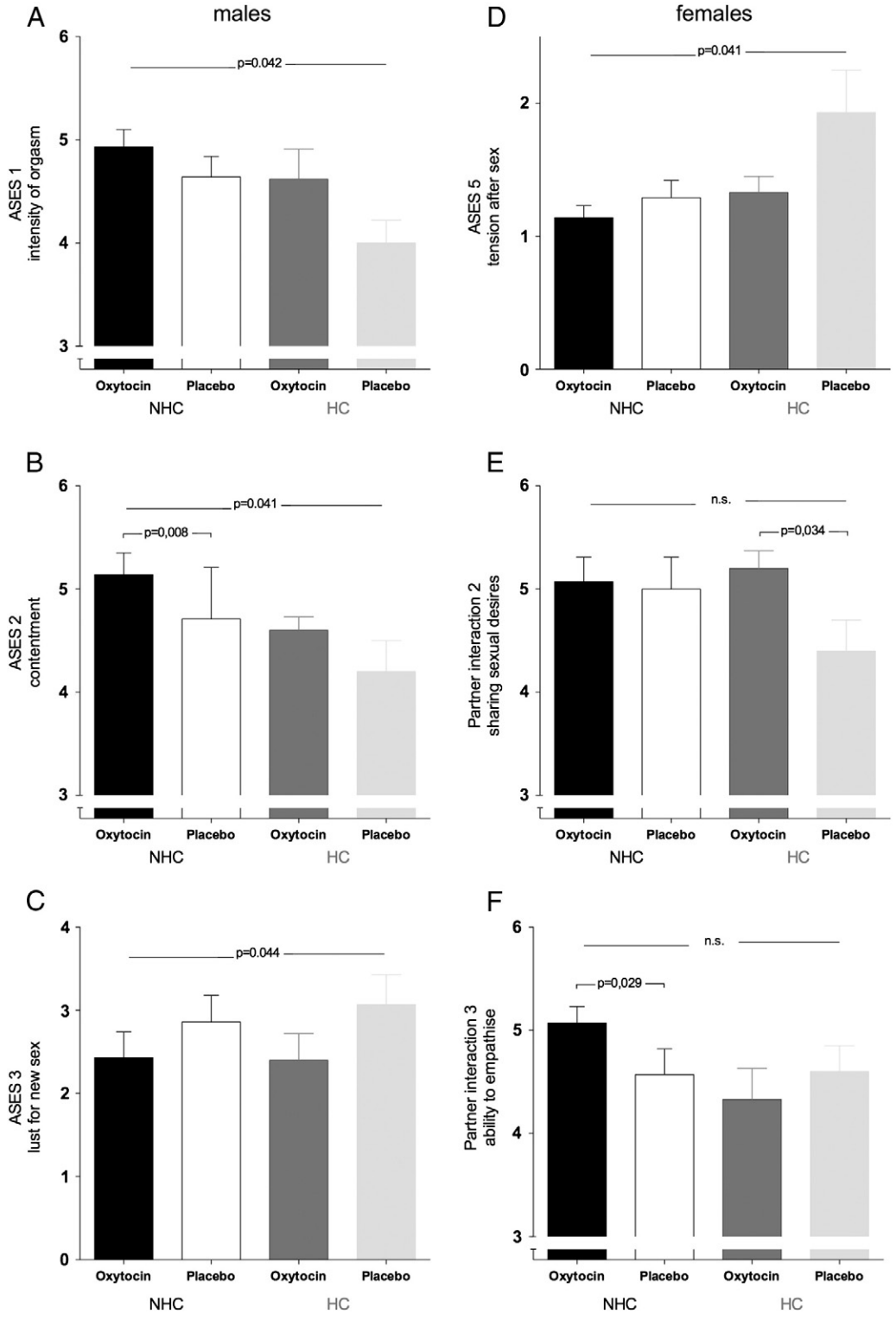


**Fig. 2. Acute sexual experience and partner interactions.** Selected items regarding acute sexual experience (ASES) and partner interactions in males (A–C) and females (D–F), as divided by couples taking non-hormonal contraception (NHC, left of respective panel) and hormonal contraception (HC, right side of respective panel). Two factorial ANOVA and/or post-hoc t-tests are indicated in cases of significant treatment effects. Please also compare with Tables 3a–3c where the entire data set is presented. NHC, non-hormonal contraception; HC, hormonal contraception.

et al., 1998). On average, males and females exhibited a transient increase in heart rate during sexual arousal and orgasm compared with the baseline heart rate (main effect of time in all males: $F(2.71, 70.45) = 26.718$, $p < .001$, $\eta^2 = .072$, main effect of time in all females: $F(2.58, 67.17) = 23{,}344$, $p < .001$, $\eta^2 = .171$) (see Supplementary Table 1 where time effects for subgroups are also shown). There was a significant time by gender effect, partly reflected by higher heart rates in males than in females ($F(2.739, 512.217) = 2.789$, $p = .048$, $\eta^2 = .001$).

**Table 4a**
**Hierarchical linear model (HLM) analysis for item ASES 1 (intensity of orgasm).** Selected items from ASES and partner interaction questionnaires are presented where significant effects were observed for OXT administration. Data are presented according to APA style.

| Parameter | Estimate | Std. error | df | t | Sig. |
|---|---|---|---|---|---|
| Intercept | 4.075528 | 1.627717 | 41.191 | 2.504 | .016 |
| Placebo | −.437389 | .174258 | 46.571 | −2.510 | .016** |
| Oxytocin | 0[a] | 0[a] | | | |
| Age | .033936 | .044617 | 38.575 | .761 | .452 |
| Sex | −.509648 | 3.911912 | 25.730 | −.130 | .897 |
| Contraception | 10.627382 | 7.053651 | 39.441 | 1.507 | .140 |
| Relationship duration | −.027222 | .028488 | 46.635 | −.956 | .344 |
| Age ∗ sex | .000414 | .112149 | 25.770 | .004 | .997 |
| Age ∗ contraception | −.442374 | .278595 | 39.432 | −1.588 | .120 |
| Age ∗ relationship duration | .000663 | .000836 | 48.233 | .793 | .431 |
| Sex ∗ contraception | −14.767509 | 8.462102 | 35.951 | −1.745 | .090 |
| Sex ∗ relationship duration | .052722 | .044374 | 23.168 | 1.188 | .247 |
| Contraception ∗ relationship duration | −.260492 | .167241 | 36.379 | −1.558 | .128 |
| Age ∗ sex ∗ contraception | .583286 | .317612 | 37.114 | 1.836 | .074 |
| Age ∗ sex ∗ relationship duration | −.001321 | .001268 | 23.610 | −1.041 | .308 |
| Age ∗ contraception ∗ relationship duration | .011337 | .006741 | 36.178 | 1.682 | .101 |
| Sex ∗ contraception ∗ relationship duration | .407014 | .197147 | 34.709 | 2.065 | .047** |
| Age ∗ sex ∗ contraception ∗ relationship duration | −.016483 | .007690 | 34.850 | −2.143 | .039** |

** Results statistically significant on a 5% level.
[a] This parameter is set to zero because it is redundant.

*Endocrine measures*

In accordance to the circadian rhythm in males and females taking hormonal contraception, there was a decline of cortisol levels towards the end of the respective sessions (OXT and placebo), which revealed statistical significance in the factorial analysis only in females (time effect in the OXT condition ($F(1.79, 42.601) = 4.431$, $p = .002$, $\eta^2 = .021$), time effect in the placebo condition ($F(1.746, 32.698) = 3.817$, $p = .034$, $\eta^2 < .001$, Supplementary Table 2 and Fig. 1)). Additionally, there was a significant time by method of contraception by gender effect for cortisol levels ($F(2.071, 38.716) = 3.219$, $p = .042$, $\eta^2 = .010$). Most importantly, OXT administration had no significant impact on cortisol levels in males and females.

There was a decline of alpha-amylase saliva levels immediately after being sexually active, which exhibited a significant time effect in the placebo condition ($F(2.580, 58) = 5.116$, $p = .004$, $\eta^2 = .030$) and OXT condition ($F(3.352, 58) = 5.127$, $p = .001$, $\eta^2 = .027$) independent of gender and method of contraception (Table 2 and Supplementary Fig. 1).

## Discussion

Despite strong efforts in uncovering the importance of OXT for social cognition and behavior, including social exploration, recognition and attachment, only a few studies have explored the significance of OXT for human sexual behavior and related couple interaction. In this first double-blind, placebo-controlled naturalistic study, we detected four major findings: (i) "Classical" aspects of sexual activity, such as sexual drive, sexual arousal and erection/lubrication as assessed by the ASEX questionnaire (McGahuey et al., 2000), were not significantly altered by OXT administration. Accordingly, one may assume that OXT cannot simply be regarded as an "aphrodisiac" — at least not in healthy couples. Further investigations in pathological conditions such as hypoactive sexual desire/arousal disorders (HSDD), erectile dysfunction or premature ejaculation may shed more light on the question how OXT may alter sexual drive and function. In men or women who experience sexual problems or dysfunctions, the anxiety modulating effects of OXT may well have a therapeutic effect as anxiety has long been discussed as a central pathogenic factor. (ii) When employing selected items of

**Table 4b**
**Hierarchical linear model (HLM) analysis for item ASES 2 (contentment after sexual intercourse).** Selected items from ASES and partner interaction questionnaires are presented where significant effects were observed for OXT administration. Data are presented according to APA style.

| Parameter | Estimate | Std. error | df | t | Sig. |
|---|---|---|---|---|---|
| Intercept | 6.163980 | 1.269401 | 42.197 | 4.856 | .000 |
| Placebo | −.431034 | .172368 | 57.000 | −2.501 | .015** |
| Oxytocin | 0[a] | 0[a] | . | . | . |
| Age | −.015089 | .035607 | 42.000 | −.424 | .674 |
| Sex | .060232 | 3.396553 | 42.000 | .018 | .986 |
| Contraception | 3.476211 | 3.393260 | 42.000 | 1.024 | .311 |
| Relationship duration | −.028550 | .018022 | 42.000 | −1.584 | .121 |
| Age ∗ sex | −.013643 | .097746 | 42.000 | −.140 | .890 |
| Age ∗ contraception | −.188232 | .130589 | 42.000 | −1.441 | .157 |
| Age ∗ relationship duration | .000643 | .000521 | 42.000 | 1.234 | .224 |
| Sex ∗ contraception | −7.921546 | 5.335208 | 42.000 | −1.485 | .145 |
| Sex ∗ relationship duration | .016247 | .035623 | 42.000 | .456 | .651 |
| Contraception ∗ relationship duration | −.033539 | .095016 | 42.000 | −.353 | .726 |
| Age ∗ sex ∗ contraception | .321216 | .187020 | 42.000 | 1.718 | .093 |
| Age ∗ sex ∗ relationship duration | −.000321 | .001007 | 42.000 | −.319 | .751 |
| Age ∗ contraception ∗ relationship duration | .002079 | .003856 | 42.000 | .539 | .593 |
| Sex ∗ contraception ∗ relationship duration | .170504 | .131067 | 42.000 | 1.301 | .200 |
| Age ∗ sex ∗ contraception ∗ relationship duration | −.006948 | .005000 | 42.000 | −1.390 | .172 |

** Results statistically significant on a 5% level.
[a] This parameter is set to zero because it is redundant.

**Table 4c**
**Hierarchical linear model (HLM) analysis for item ASES 4 (effect of study participation on sexual experience.** Selected items from ASES and partner interaction questionnaires are presented where significant effects were observed for OXT administration. Data are presented according to APA style. Results of HLM on item ASES 4 (effect of study participation on sexual experience).

| Parameter | Estimate | Std. error | df | t | Sig. |
|---|---|---|---|---|---|
| Intercept | 2.657518 | 1.341640 | 41.091 | 1.981 | .054 |
| Placebo | −.370690 | .144238 | 57.000 | −2.570 | .013** |
| Oxytocin | 0[a] | 0[a] | | | |
| Age | .031968 | .037193 | 39.989 | .860 | .395 |
| Sex | 2.442093 | 2.802337 | 29.539 | .871 | .391 |
| Contraception | −1.320987 | 3.714793 | 42.000 | −.356 | .724 |
| Relationship duration | −.000615 | .020115 | 41.818 | −.031 | .976 |
| Age * sex | −.065534 | .080952 | 29.717 | −.810 | .425 |
| Age * contraception | .050158 | .142598 | 41.999 | .352 | .727 |
| Age * relationship duration | −.000058 | .000580 | 41.872 | −.100 | .921 |
| Sex * contraception | −6.739230 | 4.108355 | 25.362 | −1.640 | .113 |
| Sex * relationship duration | .017127 | .027295 | 25.796 | .627 | .536 |
| Contraception * relationship duration | .061770 | .094395 | 38.663 | .654 | .517 |
| Age * sex * contraception | .218657 | .142557 | 24.810 | 1.534 | .138 |
| Age * sex * relationship duration | −.000416 | .000769 | 25.503 | −.541 | .593 |
| Age * contraception * relationship duration | −.002369 | .003784 | 37.621 | −.626 | .535 |
| Sex * contraception * relationship duration | .056550 | .107485 | 25.023 | .526 | .603 |
| Age * sex * contraception * relationship duration | −.002045 | .004128 | 25.295 | −.495 | .625 |

** Results statistically significant on a 5% level.
[a] This parameter is set to zero because it is redundant.

the ASES questionnaire (Braunert and Kaiser, 2010; Kruger et al., 2003b) focusing on orgasmic and post-orgasmic aspects of sexual behavior, HLM analysis revealed increased intensity of orgasm, contentment after sexual intercourse and effects of study participation after OXT administration. According to ANOVA, these effects were more pronounced in men. Men additionally indicated elevated levels of sexual satiety after sexual contact with OXT administration. Women reported higher levels of relaxation and signs of slightly improved abilities in terms of partner interaction after OXT administration. (iii) Although partnership duration only had an impact on sexual parameters according to the MANOVA, age exhibited effects with predominantly better values of sexual function with increasing age. (iv) Finally, we cannot rule out that the method of contraception may have had an impact on acute sexual experience and couple interactions as revealed by some results but not all (two factorial ANOVA depicted some contraception effects; the MANCOVA did not).

Although limited effects and only small to moderate effect sizes were observed in our study, these findings may be of high scientific and clinical interest and deserve careful discussion when further analyzing the potential use of OXT in individuals and couples with sexual and marital problems. First, the current study demonstrates that in contrast to the lack of OXT effects in a highly controlled laboratory situation using a masturbation paradigm (Burri et al., 2008), OXT may exert sexually relevant effects in socially relevant situations/personal interactions, such as sexual intercourse in a familiar setting at home. Second, despite the fact that these couples reported good physical and mental health as well as a high level of partnership satisfaction, effects were nonetheless detectable and always indicated a benefit of OXT. According to this data set, one might speculate that in females, OXT may predominantly impact parameters of partner interactions in terms of deeper bonding and greater openness, whereas in males, OXT may have more pronounced effects on functional variables, especially on orgasmic and post-orgasmic parameters. This may fit into current psychobiological considerations and findings of gender-specific functions of OXT and vasopressin (Ditzen et al., 2013; Meyer-Lindenberg et al., 2011). In addition, these findings could also reflect typical gender-specific modes of experiencing sexual encounters and perceiving sexual arousal, wherein males primarily focus on sexual function or performance and females more on emotional and relationship aspects (Bancroft, 2009).

An interesting question affects the possible role and impact of contraception methods. Psychometric measures were sometimes higher, especially in males in couples taking non-hormonal contraception. These findings may concur with the theory of mate choice being influenced by the hormonal status of females. With respect to the menstrual cycle, men tend to rate women as most attractive during mid-cycle close to ovulation when their estrogen levels are highest. Recent studies suggest that oral contraceptives might remove the cyclicity of female attractiveness, as these women lack an estrogen peak (Alvergne and Lummaa, 2010). Hence, forthcoming studies may help to explore whether our findings of non-hormonal contraception males experiencing higher sexual pleasure may be related to the hormonal status of their partners or other factors. The effects of OXT treatment appeared to be more pronounced in some cases of non-hormonal contraception as shown by post-hoc t-tests, although the effects were by far not as convincing, as one might deduce from previous anecdotal reports in males (Ishak et al., 2008; MacDonald and Feifel, 2012a). Anyway, this again raises the question of whether OXT may have fewer effects in couples taking hormonal contraception because hormonal contraception represents an altered hormonal state (mimicking a state of pregnancy) and may thus be quite robust against external hormonal manipulations. Such a pregnancy-like hormonal status could also affect the endogenous OXT system itself (Silber et al., 1987; Stock et al., 1989). Under such conditions, additional synthetic OXT might be less effective due to possible alterations in OXT receptor binding and/or central OXT availability (Borrow and Cameron, 2012; Neumann, 2008). In contrast, facilitating effects of OXT were reported in a woman taking a progesterone-containing pill, which was interpreted as a beneficial interaction between OXT and progesterone, leading to improved sexual desire, pleasure and orgasm (Anderson-Hunt and Dennerstein, 1994, 1995). This observation could not be confirmed by the current data set. Although final conclusions cannot be drawn at the present time, the current data set underlines the necessity to control not only the phase of menstrual cycle but also the method of contraception in related studies. The relatively non-specific measurement of the types of hormonal contraception used in this study could also be specified in future studies.

As an alternative explanation for possible differences between the two contraception groups, one might point towards the concomitant differences in age and partnership duration demonstrated in Table 1. According to the MANOVA, only the factor age exhibited a significant impact on some variables, with increasing age leading to better sexual function. This result is somewhat surprising, as one might expect declining sexual drive, activity and satisfaction with increasing age (Klusmann, 2002). At this point, it is important to note that mean ages ranged between 24 and 32 years, which represents a period where age-related alterations of sexual function are usually not expected.

This is underscored by the high quality of partnerships, which did not differ between the groups. Accordingly, other possible factors can be taken into consideration, such as increasing sexual experience and trust within the couples with increasing age (and relationship duration). Again, the measurements of such factors are equally important in future trials.

Another important issue may represent the question of the aforementioned endogenous OXT system during sexual activity and its interaction with exogenous OXT. It has been shown that OXT is released both peripherally (Carmichael et al., 1994; Kruger et al., 2003a) and centrally during or after mating or sexual intercourse (see Borrow and Cameron, 2012 for review). Endogenous oxytocin and/or prolactin have been discussed as indicators or mediators of sexual satiation (Brody and Kruger, 2006; Kruger et al., 2002) and mating-induced anxiolysis (Waldherr and Neumann, 2007). Thus, high endogenous levels of brain OXT during sexual encounters may also explain why in general the effects of (additional) exogenous OXT were rather small in the current study.

The assessment of psychobiological markers such as cortisol and α-amylase, as well as recordings of heart rate, revealed a slight psychophysiological activation pattern with increased heart rate during sexual activity and a decline of saliva α-amylase levels thereafter. A down-regulation of the HPA-axis function by OXT as observed previously in stress and partner-conflict studies (Ditzen et al., 2009; Heinrichs et al., 2003) was not observed in this study. This relationship may differ in subjects with high levels of stress, anxiety, sexual disorders and/or marital problems.

We can summarize that this is the first attempt to study the effects of a single OXT administration on parameters of sexual function and partner communication. By using a naturalistic field setting, our study has the advantage of a high external validity while accepting lower control of confounding factors such as the length of sexual intercourse or degree of physical activity. We only used a single pharmacological intervention, which might have masked effects that would only occur after repeated administration of OXT. Some of our subjects may have been disturbed by the participation in the study. Again, this factor may be sufficiently accounted for when subjects repeatedly take OXT. Due to economic reasons, only one experimental condition during which both partners received OXT was compared to a placebo condition. Although taken into account in the HLM and correlational analysis, future trials may further examine this issue by administering OXT to only one person of a respective couple. Also, the impact of gender, method of contraception and environmental setting (laboratory versus naturalistic) definitely needs special attention in the future studies in order to better answer the questions raised here.

## Conclusion

This field study demonstrates that OXT may alter specific aspects of sexual experience and partner interactions in healthy couples. This study encourages further research on OXT incorporating longer treatment periods and different types of sexual, mental and partnership problems.

## Conflict of interest

The authors declare that they have no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yhbeh.2014.01.009.

## References

Albright, J.J., Marinova, D.M., 2010. Estimating Multilevel Models using SPSS, Stata, SAS, and R.
Alvergne, A., Lummaa, V., 2010. Does the contraceptive pill alter mate choice in humans? Trends Ecol Evol 25, 171–179.
Anderson-Hunt, M., Dennerstein, L., 1994. Increased female sexual response after oxytocin. BMJ 309, 929.
Anderson-Hunt, M., Dennerstein, L., 1995. Oxytocin and female sexuality. Gynecol Obstet Invest 40, 217–221.
Bancroft, J., 2009. Human Sexuality and Its Problems, 3rd ed. Churchill Livingston Elsevier.
Blaicher, W., Gruber, D., Bieglmayer, C., Blaicher, A.M., Knogler, W., Huber, J.C., 1999. The role of oxytocin in relation to female sexual arousal. Gynecol Obstet Invest 47, 125–126.
Born, J., Lange, T., Kern, W., McGregor, G.P., Bickel, U., Fehm, H.L., 2002. Sniffing neuropeptides: a transnasal approach to the human brain. Nat Neurosci 5, 514–516.
Borrow, A.P., Cameron, N.M., 2012. The role of oxytocin in mating and pregnancy. Horm Behav 61, 266–276.
Braunert, S., Kaiser, D., 2010. Acute Sexual Experiences Scale. Weiterentwicklung und psychometrische Überprüfung eines Fragebogens zum sexuellen Erleben. Abteilung für Klinische Psychologie, Psychotherapie und Diagnostik. Technischen Universität Carolo-Wilhelmina zu Braunschweig, Braunschweig 86.
Brody, S., Kruger, T.H., 2006. The post-orgasmic prolactin increase following intercourse is greater than following masturbation and suggests greater satiety. Biol Psychol 71, 312–315.
Burri, A., Heinrichs, M., Schedlowski, M., Kruger, T.H., 2008. The acute effects of intranasal oxytocin administration on endocrine and sexual function in males. Psychoneuroendocrinology 33, 591–600.
Burrows, L.J., Basha, M., Goldstein, A.T., 2012. The effects of hormonal contraceptives on female sexuality: a review. The journal of sexual medicine 9, 2213–2223.
Carmichael, M.S., Humbert, R., Dixen, J., Palmisano, G., Greenleaf, W., Davidson, J.M., 1987. Plasma oxytocin increases in the human sexual response. J Clin Endocrinol Metab 64, 27–31.
Carmichael, M.S., Warburton, V.L., Dixen, J., Davidson, J.M., 1994. Relationships among cardiovascular, muscular, and oxytocin responses during human sexual activity. Arch Sex Behav 23, 59–79.
de Leeuw, J., Kreft, I.G.G., 1998. Introducing Multilevel Modeling. Sage Publications Ltd, London.
Ditzen, B., Neumann, I.D., Bodenmann, G., von Dawans, B., Turner, R.A., Ehlert, U., Heinrichs, M., 2007. Effects of different kinds of couple interaction on cortisol and heart rate responses to stress in women. Psychoneuroendocrinology 32, 565–574.
Ditzen, B., Schaer, M., Gabriel, B., Bodenmann, G., Ehlert, U., Heinrichs, M., 2009. Intranasal oxytocin increases positive communication and reduces cortisol levels during couple conflict. Biol Psychiatry 65, 728–731.
Ditzen, B., Nater, U.M., Schaer, M., La Marca, R., Bodenmann, G., Ehlert, U., Heinrichs, M., 2013. Sex-specific effects of intranasal oxytocin on autonomic nervous system and emotional responses to couple conflict. Social cognitive and affective neuroscience 8, 897–902.
Domes, G., Heinrichs, M., Michel, A., Berger, C., Herpertz, S.C., 2007. Oxytocin improves "mind-reading" in humans. Biol Psychiatry 61, 731–733.
Exton, M.S., Bindert, A., Kruger, T., Scheller, F., Hartmann, U., Schedlowski, M., 1999. Cardiovascular and endocrine alterations after masturbation-induced orgasm in women. Psychosom Med 61, 280–289.
Exton, M.S., Kruger, T.H., Bursch, N., Haake, P., Knapp, W., Schedlowski, M., Hartmann, U., 2001a. Endocrine response to masturbation-induced orgasm in healthy men following a 3-week sexual abstinence. World J Urol 19, 377–382.
Exton, M.S., Kruger, T.H., Koch, M., Paulson, E., Knapp, W., Hartmann, U., Schedlowski, M., 2001b. Coitus-induced orgasm stimulates prolactin secretion in healthy subjects. Psychoneuroendocrinology 26, 287–294.
Fischer-Shofty, M., Levkovitz, Y., Shamay-Tsoory, S.G., 2013. Oxytocin facilitates accurate perception of competition in men and kinship in women. Soc Cogn Affect Neurosci 8, 313–317.
Frank, E., Anderson, C., Rubinstein, D., 1978. Frequency of sexual dysfunction in "normal" couples. N Engl J Med 299, 111–115.
Goldstein, I., Meston, C.M., Davis, S., Traish, A., 2005. Women's Sexual Function and Dysfunction. Study, Diagnosis and Treatment. Taylor & Francis.
Grewen, K.M., Girdler, S.S., Amico, J., Light, K.C., 2005. Effects of partner support on resting oxytocin, cortisol, norepinephrine, and blood pressure before and after warm partner contact. Psychosom Med 67, 531–538.
Hahlweg, K., 1996. Fragebogen zur Partnerschaftsdiagnostik (FPD). Partnerschaftsfragebogen PFB, Problemliste PL und Fragebogen zur Lebensgeschichte und Partnerschaft FLP. Hogrefe, Göttingen.
Heinrichs, M., Baumgartner, T., Kirschbaum, C., Ehlert, U., 2003. Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. Biol Psychiatry 54, 1389–1398.
Heinrichs, M., von Dawans, B., Domes, G., 2009. Oxytocin, vasopressin, and human social behavior. Front Neuroendocrinol 30, 548–557.
Ishak, W.W., Berman, D.S., Peters, A., 2008. Male anorgasmia treated with oxytocin. The journal of sexual medicine 5, 1022–1024.

Jha, S., Thakar, R., 2010. Female sexual dysfunction. Eur J Obstet Gynecol Reprod Biol 153, 117–123.
Kirschbaum, C., Hellhammer, D.H., 1989. Salivary cortisol in psychobiological research: an overview. Neuropsychobiology 22, 150–169.
Kirschbaum, C., Hellhammer, D.H., 1994. Salivary cortisol in psychoneuroendocrine research: recent developments and applications. Psychoneuroendocrinology 19, 313–333.
Klusmann, D., 2002. Sexual motivation and the duration of partnership. Arch Sex Behav 31, 275–287.
Kosfeld, M., Heinrichs, M., Zak, P.J., Fischbacher, U., Fehr, E., 2005. Oxytocin increases trust in humans. Nature 435, 673–676.
Kruger, T., Exton, M.S., Pawlak, C., von zur Muhlen, A., Hartmann, U., Schedlowski, M., 1998. Neuroendocrine and cardiovascular response to sexual arousal and orgasm in men. Psychoneuroendocrinology 23, 401–411.
Kruger, T.H., Haake, P., Hartmann, U., Schedlowski, M., Exton, M.S., 2002. Orgasm-induced prolactin secretion: feedback control of sexual drive? Neurosci Biobehav Rev 26, 31–44.
Kruger, T.H., Haake, P., Chereath, D., Knapp, W., Janssen, O.E., Exton, M.S., Schedlowski, M., Hartmann, U., 2003a. Specificity of the neuroendocrine response to orgasm during sexual arousal in men. J Endocrinol 177, 57–64.
Kruger, T.H., Haake, P., Haverkamp, J., Kramer, M., Exton, M.S., Saller, B., Leygraf, N., Hartmann, U., Schedlowski, M., 2003b. Effects of acute prolactin manipulation on sexual drive and function in males. J Endocrinol 179, 357–365.
Laumann, E.O., Paik, A., Rosen, R.C., 1999. Sexual dysfunction in the United States: prevalence and predictors. Jama 281, 537–544.
Legros, J.J., Chiodera, P., Geenen, V., Smitz, S., von Frenckell, R., 1984. Dose–response relationship between plasma oxytocin and cortisol and adrenocorticotropin concentrations during oxytocin infusion in normal men. J Clin Endocrinol Metab 58, 105–109.
Legros, J.J., Chiodera, P., Geenen, V., 1988. Inhibitory action of exogenous oxytocin on plasma cortisol in normal human subjects: evidence of action at the adrenal level. Neuroendocrinology 48, 204–206.
MacDonald, K., Feifel, D., 2012a. Dramatic improvement in sexual function induced by intranasal oxytocin. The journal of sexual medicine 9, 1407–1410.
Macdonald, K., Feifel, D., 2012b. Dramatic improvement in sexual function induced by intranasal oxytocin. J Sex Med 9, 1407–1410.
Marazziti, D., Canale, D., 2004. Hormonal changes when falling in love. Psychoneuroendocrinology 29, 931–936.
Masters, W.H., Johnson, V.E., 1966. Reproductive Biology Research Foundation (U.S.). Human sexual response, Little, Brown, Boston.
McGahuey, C.A., Gelenberg, A.J., Laukes, C.A., Moreno, F.A., Delgado, P.L., McKnight, K.M., Manber, R., 2000. The Arizona Sexual Experience Scale (ASEX): reliability and validity. Journal of sex & marital therapy 26, 25–40.
Meyer-Lindenberg, A., Domes, G., Kirsch, P., Heinrichs, M., 2011. Oxytocin and vasopressin in the human brain: social neuropeptides for translational medicine. Nat Rev Neurosci 12, 524–538.
Murphy, M.R., Seckl, J.R., Burton, S., Checkley, S.A., Lightman, S.L., 1987. Changes in oxytocin and vasopressin secretion during sexual activity in men. J Clin Endocrinol Metab 65, 738–741.
Neumann, I.D., 2008. Brain oxytocin: a key regulator of emotional and social behaviours in both females and males. J Neuroendocrinol 20, 858–865.
Scantamburlo, G., Hansenne, M., Fuchs, S., Pitchot, W., Marechal, P., Pequeux, C., Ansseau, M., Legros, J.J., 2007. Plasma oxytocin levels and anxiety in patients with major depression. Psychoneuroendocrinology 32, 407–410.
Schumacher, S., Kirschbaum, C., Fydrich, T., Strohle, A., 2013. Is salivary alpha-amylase an indicator of autonomic nervous system dysregulations in mental disorders?—a review of preliminary findings and the interactions with cortisol. Psychoneuroendocrinology 38, 729–743.
Silber, M., Almkvist, O., Larsson, B., Stock, S., Uvnas-Moberg, K., 1987. The effect of oral contraceptive pills on levels of oxytocin in plasma and on cognitive functions. Contraception 36, 641–650.
Steyer, R., Schwenkmezger, P., Notz, P., Eid, M., 1997. Der Mehrdimensionale Befindlichkeitsfragebogen (MDBF). Handanweisung, Hogrefe, Göttingen.
Stock, S., Silber, M., Uvnas-Moberg, K., 1989. Elevated plasma levels of oxytocin in women taking low-dose oral contraceptives. Identification of the plasma oxytocin with high performance liquid chromatography. Acta Obstet Gynecol Scand 68, 75–78.
Tabachnick, B.G., Linda, S., 2007. Using Multivariate Statistics, 5th ed. Pearson/A & B, Boston, Montreal.
Taylor, S.E., Gonzaga, G.C., Klein, L.C., Hu, P., Greendale, G.A., Seeman, T.E., 2006. Relation of oxytocin to psychological stress responses and hypothalamic–pituitary–adrenocortical axis activity in older women. Psychosom Med 68, 238–245.
Vining, R.F., McGinley, R.A., Maksvytis, J.J., Ho, K.Y., 1983. Salivary cortisol: a better measure of adrenal cortical function than serum cortisol. Ann Clin Biochem 20 (Pt 6), 329–335.
Waldherr, M., Neumann, I.D., 2007. Centrally released oxytocin mediates mating-induced anxiolysis in male rats. Proc Natl Acad Sci U S A 104, 16681–16684.