Effects of Intranasal Oxytocin Administration on Sexual Functions in Healthy Women

A Laboratory Paradigm

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Abstract:

Purpose: The neuropeptide oxytocin (OXT) has a variety of physiological functions in maternal behavior and attachment including sexual behavior. Based on animal research and our previous human studies, we set out to investigate intranasal administration of OXT and hypothesized that OXT should be able to modulate sexual function in women.

Methods: In a double-blind, placebo-controlled, crossover laboratory setting, the acute effects of intranasal administered OXT (24 international units) on sexual drive, arousal, orgasm, and refractory aspects of sexual behavior were analyzed in 27 healthy females (mean age ± SD, 27.52 ± 8.04) together with physiological parameters using vaginal photoplethysmography.

Findings: Oxytocin administration showed no effect on subjective sexual parameters (eg, postorgasmic tension; $P = 0.051$). Physiological parameters (vaginal photoplethysmography amplitude and vaginal blood volume) showed a response pattern towards sexual arousal but were not affected by OXT.

Implications: Using a well-established laboratory paradigm, we did not find that intranasal OXT influences female sexual parameters. Also, sexual drive and other functions were not affected by OXT. These findings indicate that OXT is not able to significantly increase subjective and objective parameters of sexual function in a setting with high internal validity; however, this might be different in a more naturalistic setting.

Key Words: oxytocin, intranasal, females, masturbation, sexual drive, sexual arousal, orgasm

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Over the past few years, the neuropeptide oxytocin (OXT) made it to the top in physiological and psychosocial sciences. Besides its impact on a variety of physiological functions like parturition and lactation in mammalian species (including humans), a growing body of behavioral human studies demonstrates that OXT may be associated with a number of prosocial behavioral aspects.[1,2] However, the big hand for OXT also led to increased criticism of OXT studies and their appraisal, reminding us to carefully evaluate the effects of OXT[3] and to enhance consideration for contextual and interindividual factors, which might moderate the previously demonstrated effects.[4] Moreover, the causality of the effects and the relationship between peripheral and central OXT levels still remain to be further explored.[1]

Although previous experimental work focused on OXT effects on human social cognition and behavior, the role of OXT in human sexuality has not yet been investigated intensely. For now, we know that OXT is released during orgasm in both male and female humans.[5–7] Moreover, OXT seems to be positively related to the intensity of muscle contraction of the pelvic floor in women during orgasm.[5–9] Individual case observations reporting pronounced sexual arousal in females,[10,11] occurrence of an orgasm in anorgasmic males,[12] and improvement in sexual function in a male patient with social anxiety[13] give reason to assume a facilitating role of OXT in terms of sexual experience and function. More generally, it is assumed that OXT has an effect on sexual satiety.[14]

In earlier research, applying an established and well-controlled laboratory paradigm, we could demonstrate that intranasal OXT administration led to alteration of the global perception of arousal during masturbation in healthy males; however, this was not reflected by specific psychometric measurements.[15] In a more recent study, we identified differential effects of intranasal OXT on sexual experiences and partner interactions in couples using a naturalistic setting.[16] Intranasal OXT administration did not alter *classic* parameters of sexual function, such as sexual drive, arousal or penile erection, and lubrication. However, OXT increased the intensity of orgasm and contentment after sexual intercourse. Specifically, men indicated higher levels of sexual satiety after sexual intercourse after OXT administration. Women felt more relaxed and indicated better abilities to share sexual desires or to feel compassion for their partners.

Based on our previous work, the aim of this study was to investigate and confirm the role of intranasal OXT administration on sexual functions in healthy females using a double-blind, placebo-controlled crossover design in a laboratory setting with high internal validity. We hypothesized that OXT should be able to positively influence parameters of sexual function in females.

MATERIALS AND METHODS

Participants

Twenty-seven healthy heterosexual women (n = 27), aged 20 to 59 years (mean age ± SD, 27.52 ± 8.04) participated in this study after being recruited via Hannover Medical School and having provided written informed consent. Screening was performed

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using general medical/health and gynecological questionnaires. For inclusion, the menstrual cycle had to be regular (25–35 days) over the last 6 months. Exclusion criteria were pregnancy, current intake of medication, drug and/or alcohol abuse and any somatic or psychological disorders. Hormonal contraception (HC) was controlled for. Participants had to be sexually active, and their current partnership had to be lasting for at least 12 months.[17,18]

Fifteen women used HC (mean age ± SD, 25.93 ± 9.30), and 12 women used non-HC (mean age ± SD, 29.50 ± 4.97). The responsible institutional review board, Hannover Medical School's ethics committee, approved the study, which was conducted at Hannover Medical School in accordance with the Declaration of Helsinki.

Design and Procedure

The study design incorporated a double-blind, placebo-controlled crossover assessment plan in a laboratory setting, as described in Figure 1 of Burri et al.[15] Participants were randomly assigned to 2 groups: 13 females received OXT in the first session and a placebo in the second session, and 14 females received OXT and placebo vice versa. Study visits were arranged during the midfollicular phase in respect of possible changes of sexual function during the menstrual cycle.[17,19] There was an interval of 1 month between the study visits to ensure OXT wash-out. Also, participants were asked to refrain from intense nicotine, caffeine, and alcohol consumption 24 hours before and during study visits. All appointments were arranged at 4 PM.

In the 2 experimental sessions, a documentary film sequence was shown for 20 minutes, followed by a 20-minute presentation of an erotic film sequence, and a further 20-minute presentation of a documentary film sequence. After the first 10 minutes of the erotic film sequence, subjects were asked to masturbate until orgasm. All visual stimulations were established in previous studies.[9,17,19–22] Subjects completed questionnaires before, in the middle/after orgasm (in retrospect), and immediately after the sessions.

Laboratory characteristics and experimental devices have been described in a previous study.[15] The investigator administered 24 international units OXT (Syntocin spray, Novartis) or an identical appearing placebo spray without OXT, both in the form of a clear nose spray (3 puffs in each nostril). To ensure optimal substance concentration in the central nervous system, OXT was administered 50 minutes before masturbation. The method of administration, safety, and doses of OXT has been described in detail elsewhere.[23]

Psychological Measures

Sexual function was assessed using the Arizona Sexual Experience Scale (ASEX) and single items of interest from the Acute Sexual Experience Scale (ASES[7,24]; and as described earlier[7,15,16]).

Vaginal Photoplethysmograph

Vaginal photoplethysmography (VPG) is widely used to measure genital sexual arousal in women. Participants were instructed to put the VPG device in the vagina before watching the film clips. The alternating current signal is a measure of the vaginal pulse amplitude (VPA) and reflects the pressure change within the blood vessels of the vaginal wall associated with each heart beat.[25] Changes in VPA occur in response to sexual stimuli.[26,27]

Statistical Analyses

Data were analyzed using SPSS Statistics 22 (IBM Corporation, Amonk, NY). For confirmatory data analysis, a particularly suitable approach for crossover-design data was chosen,[28,29] as a crossover-design might lead to time effects and confounding factors (eg, carryover effects, habituation). Instead of pre/post comparisons, intraindividual differences between the 2 measurements (OXT, A and placebo, B condition) as well as sum scores of the 2 measurements were calculated and sequence group (A-B, B-A) differences were analyzed. Vaginal photoplethysmograph data were analyzed using repeated measures analysis of variance. Covariates such as duration of current relationship and age were controlled for in all analyses. Hormonal contraception was included as a covariant factor in all analyses. All analyses were 2-tailed with the level of significance set at $P < 0.05$ (Supplementary Table, Supplemental Digital Content, http://links.lww.com/JCP/A494).

RESULTS

Psychological Measures

A total number of 25 subjects in the OXT condition and 27 subjects in the placebo condition achieved orgasm (no significant differences between conditions).

Confirmatory analysis of treatment differences yielded no significant effect of OXT on postorgasmic tension (ASES 5), sexual desire (ASEX 1), sexual arousal (ASEX 2), physical arousal (erection/lubrication) (ASEX 3), ability to reach orgasm (ASEX 4), satisfaction of orgasm (ASEX 5), intensity of orgasm (ASES 1), contentment after sex (ASES 2), lust for new sexual stimulation after sexual activity (ASES 3), and overall impression of sexual experience (Tables 1 and 2). Moreover, no difference could be seen between HC and non-HC.

TABLE 1. Means and Standard Deviations for ASEX and ASES

	Mean (SD) OXT	Mean (SD) Placebo
How strong was your sex drive? (ASEX 1)	57.81 (27.51)	51.07 (24.26)
How easily were you sexually aroused? (ASEX 2)	62.41 (20.86)	61.41 (18.80)
How easily did you get and keep an erection/did your vagina become moist or wet? (ASEX 3)	59.15 (21.56)	48.67 (21.43)
How easily did you reach an orgasm? (ASEX 4)	69.96 (25.20)	59.15 (20.98)
Was your orgasm satisfying? (ASEX 5)	57.69 (23.58)	55.96 (20.22)
How intense was your orgasm? (ASES 1)	57.27 (22.13)	57.96 (24.61)
How strong was your contentment after sexual intercourse? (ASES 2)	62.92 (20.00)	56.69 (17.12)
How strong was your lust for new sexual stimulation after sexual intercourse? (ASES 3)	43.27 (25.79)	45.69 (24.67)
What was the effect of participation in this study on your sex experience? (ASES 4)	51.07 (15.40)	50.52 (12.30)
How tense were you after sexual intercourse? (ASES 5)	16.85 (16.05)	14.15 (16.63)

TABLE 2. Statistics for Mean Difference (OXT/Placebo) Differences Between Group 1 and Group 2 of ASEX and ASES

Item	Statistics	*Z* values	*P*
ASEX 1	$t(25) = -0.81$	n.a.	$P = 0.423$
ASEX 2	$U(df) = 78.00$	$z = -.637$	$P = 0.524$
ASEX 3	$U(df) = 85.50$	$z = -.268$	$P = 0.789$
ASEX 4	$t(24) = .56$	n.a.	$P = 0.582$
ASEX 5	$t(23) = .99$	n.a.	$P = 0.335$
ASES 1	$t(19.46) = .64$	n.a.	$P = 0.528$
ASES 2	$t(23) = .70$	n.a.	$P = 0.492$
ASES 3	$t(23) = -.69$	n.a.	$P = 0.499$
ASES 4	$t(25) = -.43$	n.a.	$P = 0.673$
ASES 5	$U(df) = 51.00$	$z = -1.948$	$P = 0.051$

Note: *t* test statistics were applied where normal distribution was given. Mann-Whitney *U* test statistics were calculated where normal distribution was not given.

n.a. indicates not available.

VPG Measures

On average, females exhibited a transient increase in VPA of 50% on average during sexual arousal and orgasm compared with baseline (main effect of time in all women: $F_{5,156} = 16.64$, $P < 0.001$). There was no significant effect in interaction between time and condition ($F_{5,156} = 0.53$, $P = 0.75$). With regard to vaginal blood volume, neither time effects ($F_{5,156} = 1.24$, $P = 0.29$) nor time × condition effects ($F_{5,156} = 1.05$, $P = 0.35$) were observed during sexual activity compared with baseline.

DISCUSSION

Although there is evidence from experimental animal studies, case reports, and one study in humans reporting effects of OXT on sexual behavior,[11,16] the role of OXT administration in women's sexuality still remains unclear. The current study demonstrates that a single intranasal administration of OXT (24 international units) may impact postorgasmic tension in healthy females. Women did not indicate alterations of sexual drive and arousal. Physiological parameters as assessed by VPG were not altered by OXT, and the use of HC had no impact on the parameters analyzed in this study.

Our findings indicate no effects of intranasal OXT administration on sexual function in healthy females, at least when using a laboratory setting. Endogenous OXT and/or prolactin have been discussed as indicators or mediators of sexual satiation[30,31] and mating-induced anxiolysis.[32] During sexual arousal, OXT plasma levels increase[6,20] to reach peak levels at the moment of orgasm in multiorgasmic women and OXT levels were positively correlated with subjective reports of orgasm intensity,[33] indicating an involvement in sexual experience. Notably, as there were no differences regarding vaginal pulse amplitude as measured by VPG between OXT and placebo, the minor effect of intranasal OXT seems to be induced via the central nervous system and less likely via peripheral uterine effects. Regarding the arousal and orgasm-induced elevated levels of OXT, it seems to be "still unclear whether OXT increases sexual arousal or is a natural by-product of it."[14] On the one hand, the presence of OXT receptors in multiple organs, especially in male and female genital organs, suggests a possible "preparatory role" of OXT for the later and final phases of copulatory process, like ejaculation and orgasm, "preparing" all necessary muscular contractions and lubrication effects.[34] On the other hand, it has been suggested that the high levels of OXT play a role in "sexual satiety" and pair bond formation after orgasm by flooding the OXT receptors and producing desensitization.[35,36] A number of studies documented the importance of OXT for social cognition and behavior, including social exploration, recognition, and attachment.[37–39] Our previous study on intranasal OXT and sexual functions in couples suggested that in females OXT may predominantly affect parameters of partner interaction.[16] In males, however, OXT administration might rather affect functional variables, especially orgasmic and postorgasmic parameters.[16] These findings might fit well with regard to gender-specific functions of OXT in experiencing sexual encounters and perceiving sexual arousal.[2,40] Thus, males may primarily focus on sexual functions or performance, whereas females put more focus on emotional and relationship aspects.[41] However, effects were not very strong and some of them do not hold in the current laboratory study.

In conclusion, this is the first attempt to study the effects of a single OXT administration on parameters of sexual function in females. This study failed to detect altered sexual function and experience after intranasal administration of OXT. One limitation was not applying a naturalistic field setting to the masturbation paradigm. Naturalistic field studies offer high external validity on the one hand, but on the other hand, they make controlling confounding factors (eg, length of sexual intercourse or degree of physical activity) very difficult. Also, in this study, OXT was only administered once. Effects that might occur after repeated administration of OXT therefore could not have been detected. Moreover, the number of participants was very small and future research would profit from bigger sample sizes.

Thus, more research is needed to further delineate the complex organization of the OXT neural networks involved in reproductive and sexual behavior in males and females. Further investigations in men or women with sexual dysfunctions may shed more light on the question how OXT may alter sexual drive and function.

AUTHOR DISCLOSURE INFORMATION

The authors declare no conflicts of interest.

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