

How Relevant is the Systemic Oxytocin Concentration for Human Sexual Behavior? A Systematic Review



Nicoletta Cera,^{1,2} Sebastián Vargas-Cáceres,³ Cátia Oliveira,^{1,4,5} Jéssica Monteiro,² David Branco,² Duarte Pignatelli,^{6,7} and Sandra Rebelo,^{6,8,9}

ABSTRACT

Introduction: Despite its role in social cognition and affiliative behavior, less is known about the role played by oxytocin in human sexual behavior.

Aim: In the present systematic review, we aimed to find the levels of oxytocin related to human sexual arousal and orgasm.

Methods: We conducted the study according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We performed a systematic search in the principal databases for studies that reported collection of salivary or plasmatic samples, with dosage of oxytocin in relation to sexual activity during induction of sexual arousal and orgasm.

Results: 414 articles were obtained. After duplicates removal and the application of pre exclusion criteria, 16 articles were considered eligible and 13 articles were included with a Cohen's k of 0.827. Most of the studies used sexual self-stimulation and collected plasmatic or salivary samples to measure oxytocin. The sexual arousal and orgasm were assessed based on subjective reports.

Main Outcome Measure: The primary outcomes were the oxytocin levels collected during the induction of sexual arousal and orgasm.

Conclusions: Several studies collected only subjective reports about the sexual arousal and the orgasm. Most of the studies found higher levels of oxytocin during the orgasm or ejaculation. Given the sexual arousal evoked by self-stimulation in which sexual fantasies play an important role, it should be possible to postulate for a role of the oxytocin in sexual desire. In particular, we hypothesize a complex role of the oxytocin in the modulation of sexual fantasies and thoughts that are relevant in the sexual desire and help to trigger genital and sexual arousal.

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Key Words: Sexual Response; Orgasm; Oxytocin; Sexual Arousal

INTRODUCTION

During the last decades, the oxytocin attracted considerable attention from the scientific community due to its role in several cognitive and emotional functions.¹ Paraventricular and supra optic nuclei of the hypothalamus synthesize the nonapeptide

oxytocin, which is transported in axons to the neurohypophysis, where it is released into the blood circulation to reach remote and peripheral locations.²⁻⁴ Besides its well-known roles in the stimulation of the uterine tone and contractions during labor and in milk ejection during lactation, it also plays an important role in

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¹CPUP- Center for Psychology at University of Porto, University of Porto, Porto, Portugal;

²Faculty of Psychology and Educational Sciences, University of Porto, Porto, Portugal;

³Mental Health Service, Benito Menni CSM, L'Hospitalet de Llobregat, Barcelona, Catalonia, Spain;

⁴Digital Human-Environment Interaction Lab, Lusofona University, Porto, Portugal;

⁵CUF Hospital, Porto, Portugal;

⁶Department of BioMedicine, Faculty of Medicine, University of Porto, Porto, Portugal;

⁷Department of Endocrinology, Centro Hospitalar Universitário de São João, Porto, Portugal;

⁸Department of Clinical Pathology, Centro Hospitalar Universitário de São João, Porto, Portugal;

⁹Instituto de Investigação e Inovação em Saúde (i3S), Universidade do Porto, Porto, Portugal

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the modulation of several cognitive and emotional functions most importantly in creating maternal bonding.⁵⁻⁷ Moreover, oxytocin has been found to be important in the modulation of several aspects of social behavior and in related pathological conditions. It is well documented that oxytocin promotes social cohesion and social contact between the individuals.⁸⁻¹⁰ Indeed, alterations in the level of oxytocin have been observed in borderline disorder, autism spectrum disorders and anxiety.¹¹⁻¹³

As stated by Stolérou et al,¹⁴ sexual behavior is a complex set of components involving, at specific stages, several brain regions. Sexual behavior and, more specifically, sexual arousal involves autonomic, cognitive and emotional components. Among these, the endocrine component is strongly affected by the cognitive appraisal of the sexual stimulation. In this way, according to the Stolérou's hypothesis¹⁴ the cognitive component would be important to stimulate endocrine functions and the release of the sexual and non-sexual hormones.

Evidences from animal studies showed that the administration of oxytocin in the ventral tegmental area of the male rats induced erection and the stimulation of receptors in the meso-limbic dopaminergic pathway was relevant for the reward and drive.¹⁵ Interestingly, IsHak et al¹⁶ tested with good results intranasal oxytocin administration in a case of male treatment-resistant anorgasmia. In the same way, Muin et al,¹⁷ in a Randomized, double-blind, placebo-controlled, crossover trial, involving pre and post —menopausal women, the administration of intranasal oxytocin improved over time sexual function. According to Georgiadis and Kringelback,¹⁸ it is possible to frame the sexual behavior in a continuous process consisting of three stages. The “cycle of pleasure” model conceived sexual behavior as a process starting with the drive, followed by excitation or arousal and orgasm, and inhibited by the refractory periods or dysfunctions. The model relates the stages to the activity in specific brain areas, representing an evolution of the well-known model from Masters and Johnson.¹⁹ The first stage of the cycle implies a motivated, pro-sexual behavior, conceived as a readiness status for sexual behavior. It has a different connotation from the sexual desire, which represents a more complex process relying on the same brain pathways important for sexual arousal and sexual inhibition.²⁰ Moreover, sexual desire is sexual context —independent.²¹⁻²³

Despite the knowledge that sexual development, reproductive life and senescence are under the guidance of hormones, like oxytocin, less is known about their relationship with specific stages of the sexual arousal, desire and orgasm.

Consequently, we performed what we believe to be the first systematic review about the role played by oxytocin levels (plasmatic or salivary) in the male and female sexual behavior. In particular, we were interested in understanding (i) at which stages of sexual behavior previous studies found higher levels of oxytocin. (ii) Which is the best design and the best populations to study the role played by oxytocin in human sexual behavior and (iii) if the levels of oxytocin are related to subjective sexual arousal or to genital sexual arousal.

Table 1. Search strategy used in the current systematic review

Sexual Behavior/VSS	Study Design
1. Sexual Behavior [Mesh]	12. Review [Publication Type]
2. Sexual activity	13. Systematic review [Publication Type]
3. Sexual function [Title/Abstract]	14. OR / 12-13
4. Sexual arousal [Title/Abstract]	
5. Visual sexual stimuli	
6. Orgasm [Title/Abstract]	
7. Ejaculation [Title/Abstract]	
8. OR / 1-7	
Oxytocin	Combined search
9. Oxytocin [Title/Abstract]	15. #8 AND #11 NOT #14
10. Oxytocin [MeSH]	
11. OR / 9-10	

METHODS

We used the approach recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.²⁴

The computer-based literature searches follow the PICO approach with combined terms related to oxytocin, sexual behavior, sexual activity, and sexual function. In particular, our research question was “What is the role played by the oxytocin in sexual behavior as described in the evidence (O) in the healthy population (P)?” The present review was limited to studies that measured the level of oxytocin in body fluids, like saliva or blood (I) during a task involving sexual activities (C). Table 1 shows the search terms have been defined based on the PICO question combined with the Boolean operators like “AND”, “OR” and “NOT”, according to the method that has been previously used in another systematic review.²⁵

We defined the inclusion and exclusion criteria based on the topic, study design and population (Table 2). Most importantly, concerning the population, we decided to exclude the studies in which neuropsychiatric patients have been included (Table 2). Studies about sexual dysfunctions has been included, given the presence of different oxytocin levels in the patients group could allow to disentangle its role in normal sexual behavior.

Table 2. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Experimental studies • Cross over repeated measure studies • Cross sectional studies • Correlational studies	Randomized clinical trial Intranasal oxytocin Animals Neuropsychiatric disease
Human Adults (> 18 yr.) Visual/audio sexual stimulation Self-stimulation Couple sexual activity	

We performed the computer-based literature search in order to retrieve all the published articles in English regarding the above-mentioned topic. The three principal databases: MEDLINE (PubMed), Scopus and Google Scholar were searched.

After the retrieval, all the studies included (see the inclusion criteria) in the present systematic review were screened in order to identify additional relevant bibliographic items. Moreover, the narrative and systematic publications that were retrieved, but considered off the topic for the outcome of the PICO, have also been screened to find relevant studies cited in the reference lists.

After the duplicate removal, the title and abstracts were manually screened to understand if they fulfilled the inclusion and/or exclusion criteria. After the retrieval of potentially relevant studies to be included, we read the full texts in order to confirm the eligibility.

The first and second author performed independently the literature search, screening and methodological evaluation. The consensus about the different stages was reached between the two authors discussing the results and the articles retrieved. If the consensus was not reached, a third opinion was obtained.

To assess the quality of the studies included in the present systematic review, we applied the “NIH/quality assessment tool for before-after (pre-post) studies with no control group” and the “Quality Assessment of Case-Control Studies”, following the instructions (<https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>; National Institutes of Health, 2014).²⁶

Information has been extracted from each included study, following the above-mentioned guidelines. In particular, we extracted the characteristics of the participants, including the exclusion and inclusion criteria.

RESULTS

Flowchart (Figure 1) showed the selection process of the studies. After the consensus was reached, 13 published studies have been included in the systematic review. Following the guidelines from Landis & Koch²⁷ we calculated Cohen's k with the 95 % ($k = 0.827$) indicating almost perfect agreement (<https://idostatistics.com/cohen-kappa-free-calculator/>).

Tables 3 and 4 show the principal characteristics of the studies. We selected studies published from 1969 until 2019. Most of the included studies were conducted in different countries of Europe (61.5%; $n = 8$) and 325 subjects have been enrolled in the included studies. Most of the studies were crossover repeated measure studies, only two were cross sectional, longitudinal case control studies and only one a single case study. For this reason, the quality assessment was based on two different checklists. Tables 1S and 2S (supplementary information) showed the quality assessment of the included studies, by means of “NIH/quality assessment tool for before-after (pre-post) studies with no control group” and the “Quality Assessment of Case-Control Studies”, performed by the two above-mentioned reviewers.²⁶

Radioimmunoassay (RIA) was used to determine the levels of oxytocin in 61.5 % of the studies. In most of the cases, the source of the oxytocin determinations has been plasmatic. Six studies also measured other hormones in the collected samples, namely cortisol, vasopressin and FSH, and LH (Table 4). Six studies (46.5%) used clinical assessment, by means of tests, or clinical interviews to evaluate several dimensions, like personality, anxiety and sexual functions of the participants enrolled. Three studies used a multi-task approach in the same study, in order to control confounding variables.

The studies did not show complete homogeneity and consistency between results. This is congruent with the use of different samples, tasks and experimental designs.

Among the retrieved studies, most of them examined the oxytocin levels during orgasm and ejaculation. In the first published study,²⁸ the authors showed, for the first time, the presence of oxytocin in the plasma before and after an intercourse between man and woman. Since the pioneer studies,²⁹⁻³³ until the most recent published one,³⁴ all of them showed an increase of the oxytocin levels during, or immediately after, the orgasm or ejaculation. The task used has been the sexual self-stimulation that could be associated to visual sexual stimulation.^{30-32,35} Interestingly, most of the studies, assessing orgasm and ejaculation, did not use psychophysiological measures, only based on subjective reports. Carmichael et al^{31,32} assessed pelvic contractions during the arousal and orgasm by means of an anal device containing a photoplethysmograph. Noteworthy, the authors reported^{31,32} in first study no significant differences between men and women and, in the second one, significant positive correlations between the systolic pressure, electromyography levels and oxytocin during the baseline, arousal and orgasm or ejaculation. In the same way, Kruger et al³⁵ assessed cardiovascular parameters (heart rate, systolic and diastolic blood pressure) continuously during the task. In particular, oxytocin showed a significant increase in the orgasm in monorgasmic and multiorgasmic women. In multiorgasmic women, the oxytocin level showed an increase between the first and second orgasm.³¹ Using a different methodological approach, deJong et al³⁴ found an increase in oxytocin salivary levels after 10 minutes of sexual self-stimulation in men and women, without observing a specific gender effect. The studies that used self-stimulation tasks (ie masturbation) showed the highest levels of oxytocin in correspondence or after the orgasm or ejaculation. Interestingly, comparing anorgasmic and orgasmic women, Caruso et al³⁶ found that before and after the sexual intercourse anorgasmic women showed lower oxytocin levels than orgasmic ones. After coital activity, oxytocin levels did not change in anorgasmic women, which experience unpleasant and stressful sexual activity.

Despite the interest for the orgasm, three studies investigated oxytocin levels during sexual arousal. Two of the three studies involved women and used similar tasks. Alley et al,³⁷ studying the oxytocin and cortisol levels during stress and sexual arousal elicited by audio sexual stimulation, found a significant increase

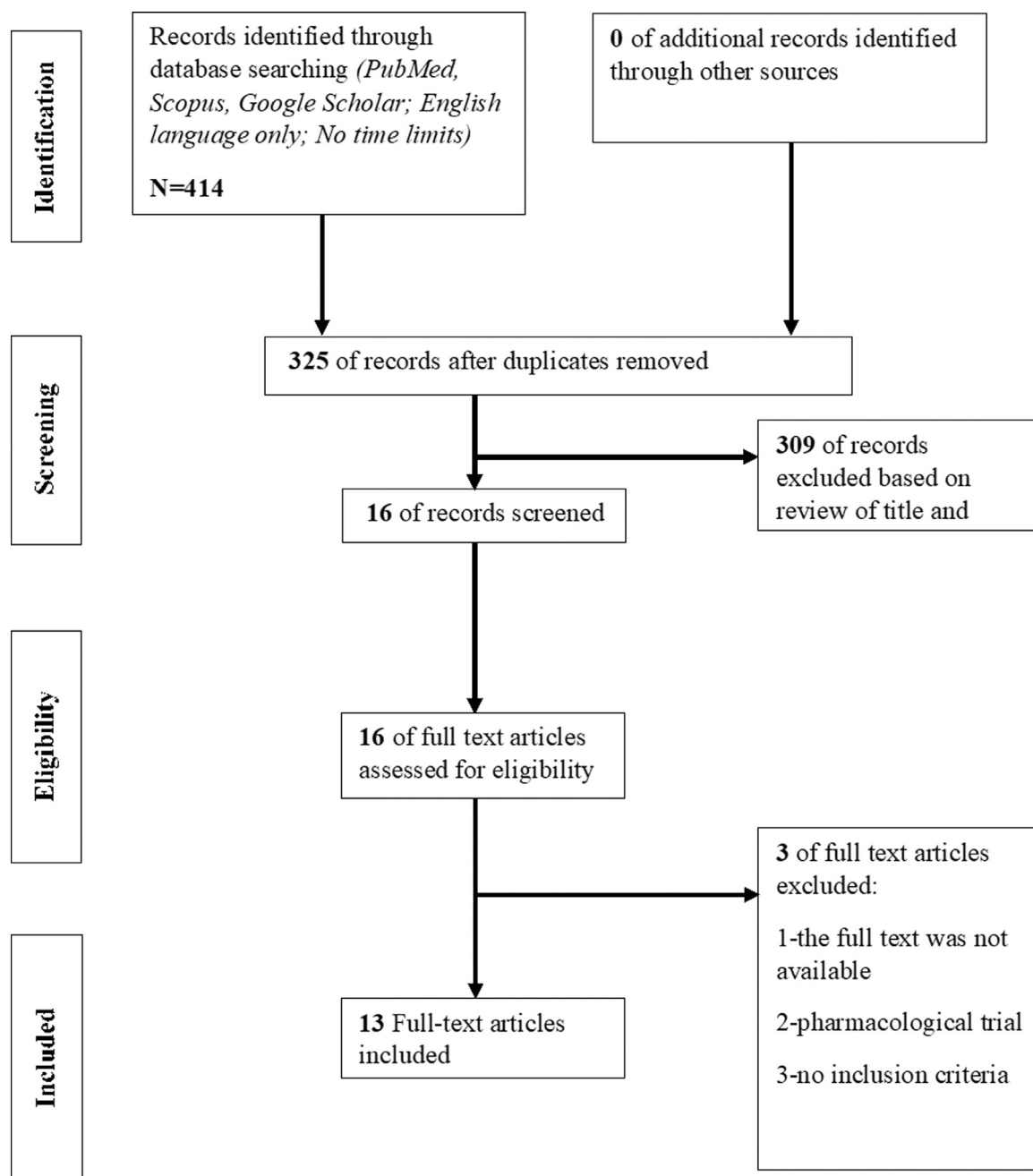


Figure 1. Flow diagram for identifying studies in the systematic review.

in the oxytocin levels from baseline to arousal. Conversely, a second study³⁸ found interesting results about oxytocinergic involvement in the attention related processes of sexual arousal. They found that women who were able to detect attentional shifts and women who reported greater levels of sexual arousal reported decrease in oxytocin in response to mindful breathing and were the only women to report an increase in oxytocin in response to sexual arousal induction. The study from Dickenson et al³⁸ applied the Five-Facet Mindfulness Questionnaire (FFMQ)³⁹

The third study investigated the relationship between genital arousal and oxytocin in men. Moreover, the interest was about the difference in oxytocin concentration in two different sites. Uckert et al⁴⁰ collected the blood samples from cubital vein and corpora cavernosa during the different stages of erection from flaccid to rigidity during visual sexual stimulation and manual stimulation of the gland. From flaccidity, considered as the baseline, to tumescence oxytocin levels increased in both cubital vein and corpora cavernosa, but from tumescent to rigidity, it increased only in the corpora cavernosa. Indeed, the oxytocin

Table 3. Demographic and psychometric tests applied in the included studies

Source	Country	N° subjects	Men (%)	Age (yr)	Design	Psychological assessment
Fox et al., 1969 ²⁸	UK	1	0(0)	N/A	Single case/crossover study	N/A
Ogawa et al., 1980 ²⁹	Japan	17	17(100)	N/A Patients with abnormal spermatogenesis	Crossover study.	N/A
Carmichael et al. 1987 ³⁰	USA	22	9(40.9)	21-40 yr. M: Mean = 28 ± 4 S.D. W: Mean = 27.5 ± 4 SD	Crossover study. correlational study	Psychological Interview MMPI BDI Spielberger Manifest Trait Anxiety Test.
Murphy et al., 1987 ³²	UK	13	13(100)	22-32 yr.	Crossover study.	N/A
Carmichael et al. 1994 ³¹	USA	23	10 (43.5)	21-40 yr. M: Mean = 28 W: Mean = 27.5	Correlational study	Psychological interview MMPI BDI Spielberger Manifest Trait Anxiety Test.
Blaicher et al., 1999 ³³	Austria	12	0 (0)	23-37yr.	Crossover study.	Information from clinical history
Kruger et al., 2003 ³⁵	Germany	10	10 (100)	18-30 yr. (Mean = 25.2 ± 1.21 S.D)	Crossover study.	Semi-structured interview; Physical examination SIS/SES
Uckert et al., 2003 ⁴⁰	Germany	25	25(100)	Mean = 26 yr.	Crossover study	N/A
Salonia et al., 2005 ⁴¹	Italy	30 (G1 = 20; G2 = 10)	0(0)	G1 : 21-43 yr. (Mean = 33.8) G2 : 23-41 yr.(Mean = 32.4)	Cross-sectional study. correlational study	Semi structured interview (sexual function and medical history). G1= normally cycling fertile women G2= monophasic contraceptive pill
Caruso et al., 2018 ³⁶	Italy	31 (G1 = 15; G2 = 16)	0(0)	G1: 25–34yr.; Mean = 28.8 ± 5.7 S.D G2: 24–35; Mean= 27.1 ± 4.4 S.D .	Crossover study.	SHI FSFI; FSDS
de Jong et al., 2017 ³⁴	Germany	17	10(58.8)	M:Median = 28yr., 26-65 yr.; W: Median = 29 yr.; 23-52 yr.	Crossover study	N/A
Alley et al., 2019 ³⁷	USA	63	0(0)	20-35 yr.	Crossover study.	N/A
Dickenson et al., 2019 ³⁸	USA	61	0(0)	20-35 yr.; Mean = 27.2 yr.	Crossover study.	FFMQ

BDI = Beck Depression Inventory; FFMQ = Five Facet Mindfulness Questionnaire; FSDS = Female Sexual Distress Scale; FSFI = Female Sexual Function Index; G = group; M = men; MMPI = Minnesota Multiphasic Personality Inventory; N/A = not available; SHI = sexual history interview; SIS/SES = System Inhibition/System Excitation Scale; W = women; yr=years

levels recorded from the corpora cavernosa returned to the baseline, but the levels of oxytocin recorded in the cubital vein did not return to the baseline. Unfortunately, the authors did not report the time in minutes, but they did only reported that the blood collection was in correspondence of the detumescence.

Moreover, according to Salonia et al.,⁴¹ in normal cycling women, oxytocin varied significantly during the menstrual cycle with significant lower levels during luteal phase and correlated with FSFI lubrication⁴². They found a significant correlation between the oxytocin levels and both the FSFI arousal⁴²

Table 4. Tasks, hormonal assessment and Results described in the studies included in the systematic review

Source	Task	Hormonal assessment	Determination of hormonal levels	Results
Fox et al., 1969 ²⁸	Couple sexual activity	Plasmatic oxytocin and vasopressin	N/A	Oxytocin was found in both cases in the blood sample taken after female orgasm but no activity was found in any of the samples from the male or any of the controls.
Ogawa et al., 1980 ²⁹	Sexual self-stimulation	Plasmatic oxytocin	RIA	Oxytocin levels increased significantly from 3.1 ± 1.9 pg/ml to 7.0 ± 4.5 pg/ml after ejaculation in 17 males ($P < .01$). No correlation with sperm count.
Carmichael et al., 1987 ³⁰	Sexual self-stimulation continuing through orgasm /ejaculation	Plasmatic oxytocin collected 5 min. before starting; 5min post	RIA	Significant levels increase between baseline and orgasm in men and monorgasmic women ($P < .05$). Significant increase in Multiorgasmic W: baseline = 2 pg/ml; 1 st orgasm = 2.7 pg/ml ($P < .03$); 2 nd orgasm = 3.4 pg/ml; post orgasm = 3.4 pg/ml. Oxytocin self-stimulation = W: (3.4 pg/ml) > M: (2.2 pg/ml; $P < .05$). Oxytocin orgasm = W: (4.4 pg/ml) > M: (2.5 pg/ml; $P < .05$)
Murphy et al., 1987 ³²	arousal induction task: using fantasies	Plasmatic oxytocin and vasopressin	RIA	Oxytocin levels increased at the time of arousal (ns) but increased with ejaculation; it increased from a baseline of 1.4 ± 0.3 to 7.3 ± 2.6 pmol/L ($P < .01$). The mean plasma level was still significantly elevated 10 min after ejaculation, reaching baseline in 30 min.
Carmichael et al., 1994 ³¹	Sexual self-stimulation	Plasmatic oxytocin collected at baseline, early SS, mid SS, late SS, orgasm and post orgasm.	RIA	Oxytocin levels increased from baseline through the orgasm.
Blaicher et al., 1999 ³³	Sexual self-stimulation	Plasmatic oxytocin	RIA	Oxytocin level increased in each subject after 1 minute following the orgasm (baseline = 11.53 pg/ml, 1 minutes after orgasm = 14.00 pg/ml; $P = .0033$); Level after 5 Minutes = 12.56 pg/ml.
Kruger et al., 2003 ³⁵	Sexual self-stimulation; visual sexual stimulation	Plasmatic oxytocin, epinephrine, norepinephrine, vasopressin, prolactin, FSH, LH, testosterone and cortisol.	IRMA-oxytocin	Orgasm produced an increase in oxytocin plasma levels, which returned to basal values 10 min after orgasm. However, due to a large interindividual variance these alterations did not reach statistical significance ($F(10,80) = 1.83$, $P = .068$).
Uckert et al., 2003 ⁴⁰	Sexual self-stimulation only in the glans; visual sexual stimulation	Plasmatic oxytocin	RIA	Two subjects feel pain during data collection; Two subjects did not terminate the experiment. Oxytocin plasma levels increased in the systemic and cavernous blood at the beginning of sexual arousal during penile tumescence (Corpus Cavernosum: from 66.7 ± 34 to 75 ± 44 pg/ml; Cubital Vein: from 71 ± 41 to 79 ± 49.5 pg/ml). Level of oxytocin increased during rigidity in the cavernous blood (to 81 ± 58.2 pg/ml), but unaltered in the systemic circulation (to 76.4 ± 44 pg/ml). Increase in the systemic blood (to 94 ± 49 pg/ml).

(continued)

Table 4. Continued

Source	Task	Hormonal assessment	Determination of hormonal levels	Results
Salonia et al., 2005 ⁴¹	N/A	Plasmatic oxytocin and other hormones.	RIA	Oxytocin levels correlated with the FSFI-lubrication subscale during the luteal ($P = .007$; $r = 0.69$) phase. Oxytocin correlated with both the arousal ($P = .04$; $r = 0.72$) and the lubrication ($P = .009$; $r = 0.84$) scales as measured with FSFI during the last week of assumption of the estroprogestinic pill. No significant difference among the mid luteal and mid follicular in FSFI.
Caruso et al., 2018 ³⁶	Couple sexual activity	Plasmatic oxytocin	ELISA	At baseline, anorgasmic women showed lower levels of oxytocin than orgasmic women, 1.8 ± 0.2 pg/mL versus 2.1 ± 0.5 pg/mL, respectively ($P < .04$). At T1, anorgasmic women showed similar baseline levels of oxytocin. Orgasmic women had higher level of oxytocin than anorgasmic women, ($P < .001$).
de Jong et al., 2017 ³⁴	Run, breastfeeding and sex tasks (ROC test): sexual self-stimulation	Salivary oxytocin	RIA	10-min of sexual self-stimulation caused an increase in oxytocin levels ($P < .001$). Post-hoc comparisons revealed a significant increase of oxytocin concentrations 10 min after the start of sexual self-stimulation ($P \leq .001$). No difference after 40 minutes ($P = .438$).
Alley et al., 2019 ³⁷	audio sexual stimulation: arousal induction task	Salivary oxytocin and cortisol	EIA	No differences in oxytocin levels in response to the arousal task (mean difference = 0.18, $t = 0.09$, $P = .94$). Participants showed a significant increase in oxytocin from baseline to task for the arousal assessment ($b = 0.11$, $P = .02$), but no significant change from task to either the first recovery ($b = 0.02$, $P = .87$) or the second recovery ($b = 0.10$, $P = .46$).
Dickenson et al., 2019 ³⁸	audio sexual stimulation: arousal induction task	Salivary oxytocin and cortisol	EIA	Significant random effect ($P < .001$), indicating that women varied in the extent to which oxytocin changed in response to the sexual arousal induction. No significant change in response to the sexual arousal induction ($P > .1$). None of the facets of trait mindfulness (FFMQ) moderated the change in oxytocin in response to the sexual arousal induction ($P > .2$).

EIA= Enzyme immunoassay method; ELISA= Enzyme-linked immunosorbent assay; FSH=Follicle Stimulating Hormone; G= group; IRMA= Immuno radio-metric assay; LH= Luteinizing Hormone; M= Men; RIA= Radioimmunoassay; SS= sexual stimulation; W= Women

($P = .04$; $r = 0.72$) and the lubrication⁴² ($P = .009$; $r = 0.84$) in women under treatment with estroprogestinic oral contraceptives, during the last week of treatment. Carmichael et al,³¹ also reported an increase of oxytocin levels during luteal phase, but they did not observe a relationship between menstrual phases and orgasm for oxytocin.

To check the quality of the selected studies, we assessed how many of them reported the level of oxytocin after the task. This is important from a methodological point of view to know if the baseline is recovered after the task. Moreover, this information can help to establish future practices in studies that aim to collect hormonal data during an experimental session. Most of the studies (ten, 76,9%) reported

the collection of samples to assess the return to the baseline of oxytocin after the tasks. Five (38,5%) studies indicated that blood or salivary samples having been collected after a period of time of 10-20 minutes following the task or the orgasm having been reached by the participants (Table 5).

DISCUSSION

Despite the relevance of the oxytocin in the social cognition and emotions, a limited number of studies investigated the role played by the oxytocin levels in human sexual behavior. The present systematic review took into account only studies that assessed the oxytocin levels without considering the randomized

Table 5. Assessment of oxytocin baseline-recovery after tasks

Source	Time in minutes
Fox et al., 1969 ²⁸	N/A
Ogawa et al., 1980 ²⁹	N/A
Carmichael et al. 1987 ³⁰	5
Murphy et al., 1987 ³²	30
Carmichael et al. 1994 ³¹	5
Blaicher et al, 1999 ³³	5
Kruger et al., 2003 ³⁵	10
Uckert et al., 2003 ⁴⁰	N/A*
Salonia et al., 2005 ⁴¹	N/A**
Caruso et al., 2018 ³⁶	5
de Jong et al., 2017 ³⁴	40**
Alley et al., 2019 ³⁷	20
Dickenson et al., 2019 ³⁸	15-20

*Uckert et al. collected blood samples after detumescence;

correlational study; *40 minutes from the onset of the stimulus and 10 after orgasm.

clinical trials in which the administration of synthetic oxytocin took place. Given the level of invasiveness of the procedure of collection of the oxytocin, several studies collected only subjective reports about the sexual arousal and the orgasm.^{28–38,40,41}

In this way, given the subjective reports, it was not possible to quantify the intensity or the exact moment in which sexual arousal and orgasm occurred. Previous studies used psychophysiological techniques to record the variation of the penile circumference and vasocongestion of the vaginal wall during tasks like visual sexual stimulation.⁴³ Carmichael et al,¹⁰ in their pioneer study, recorded the muscle activity in the pubic area by mean of the recording of the anal blood-pulse amplitude and electromyographic activity that could be conceived as indirect measures of genital arousal but could also be useful to record pelvic contraction during orgasm.

Our first aim concerned the stage of sexual behavior in which the reviewed studies found higher levels of releasing oxytocin. Most of the studies found higher levels, or at least peaks of oxytocin levels during the orgasm or ejaculation.^{28–38} Overall, this seems to be confirmed by indirect evidence about women affected by anorgasmia that showed lower levels than orgasmic women.³⁶ Oxytocin is the hormone responsible for the uterine contractions during the labor^{44,45} and it should be conceivable that a similar contractile mechanism during the orgasm is able to release, at the level of the neurohypophysis, higher amount of oxytocin. The role of oxytocin in the ejaculation has been investigated in pharmacological animal studies,⁴⁶ showing contradictory results in shortening or prolonging the latency of the ejaculation.⁴⁷ Also in a randomized, double-blind, placebo controlled study in men with premature ejaculation, high doses of Cligosiban, an oxytocin receptor antagonist, did not prolong the time of vaginal coitus and the latency of intravaginal intercourse.⁴⁸ In this way, oxytocin might not play a direct role in the latency of the erection needed to a satisfactory intravaginal intercourse.

Importantly, reviewing these studies, we are able to hypothesize that besides to the effect in the orgasm, oxytocin also plays a role in the sexual arousal as confirmed by Alley et al³⁸ who observed a significant change between the baseline and arousal during an audio sexual stimulation task in 63 participants. Similarly, Uckert⁴⁰ found an increase of oxytocin levels in the corpora cavernosa during the tumescence that could reasonably be used as an index of genital arousal. Despite this, the self-stimulation task appears to include a series of sexual fantasies that represent uncontrollable confounding variables, given their level of subjectivity. In this way, responding to our second aim, one of the best options should be the use of a standardized audio and/or visual stimulation task in which it is possible to minimize the effect of uncontrollable confounding variables. At the same time, sexual fantasies, which are considered relevant for sexual desire, can be the trigger for the sexual arousal and orgasm. According to our review and the results obtained in the selected studies, it should be plausible that a mechanism involving empathy and reward could play an important role in these two stages of sexual behavior. Indeed, the studies that used self-stimulation tasks could confirm the hypothesis that sexual desire is a more complex process that goes beyond sexual arousal and orgasm, and it is different from the sexual drive needed to start sexual behavior.²³ Oxytocin is primarily produced in the neurohypophysis and, so, a more central mechanism related to sexual or romantic interaction could be hypothesized. In this way, several studies highlighted its role in prosocial and positive emotions.^{49,50} In particular, oxytocin is important for the neuroendocrine mediation of the romantic love⁵¹ playing a role in the processes related to the initial stages of the romantic passion.⁵² This involvement could be explained in the light of the role played by the oxytocin in empathy, in the reward for positive social interaction^{53–55} and the bonding creation.

Not all the studies, with the exception of Carmichael et al,^{30,31} collected psychophysiological data, but only subjective ratings of sexual arousal (our third aim). Overall, according to the obtained information, the sexual arousal was not assessed with a Likert-like scale, but the participants indicated the exact time in which it occurred. Several studies showed that women' subjective experiences of arousal are not automatically related to genital changes overall when the vaginal pulse amplitude is assessed⁵⁶. Despite the self-detection of the sexual arousal could be easier in the male participants, women showed higher concentration levels of oxytocin than men as described by Marazziti et al.⁵⁷

In summary, the present systematic review was not able to give a definitive response, in particular to determine the contribution of oxytocin in female sexual arousal. Indirectly, Uckert,³⁷ reporting the values of the oxytocin during the penile tumescence allowed a better understanding of the complex role of the oxytocin in male sexual arousal.

CONCLUSIONS

Taking into account the limited number of studies that we were able to collect about the oxytocin levels during the different stages

of human sexual arousal, and the heterogeneity in the tasks and population, our hypotheses have to be considered with caution.

However, the present systematic review highlighted the state of the art of the studies that assessed the role played by the oxytocin levels during the different stages of sexual behavior and, in particular, during sexual arousal and orgasm in men and women. In this way, thanks to the results here reported and described, several hypotheses about the role of oxytocin in the attraction, sexual fantasies and positive thoughts, plausibly regarding sexual interaction and intercourse could play an important role in the sexual arousal and in the genital response. To disentangle the role played by the oxytocin in the sexual desire, arousal and orgasm, further studies will be needed in which it should be important to better control the possible confounding variables, define the genital arousal and obtain a precise self-assessment of the sexual arousal as well as the orgasm timing.

According to our review, the future investigation in the area of the relations between the endocrine and the cognitive components underlying human sexual behavior can be promising.

Corresponding Author: Nicoletta Cera, PhD, Faculty of Psychology and Educational Sciences, University of Porto, Rua Alfredo Allen, 4200-135 Porto, Portugal, Tel: +351 22 607 9700; E-mail: cera.nicoletta@gmail.com

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STATEMENT OF AUTHORSHIP

Conceptualization, N.C. and S.V.C.; Methodology, N.C., S.V.C and C.O.; Investigation, N.C., S.V.C, J.M. and D.B.; Writing – Original Draft, N.C. and S.V.C.; Writing – Review & Editing, D. P. and S.R.; Funding Acquisition, N.C, C.O., J.M. and D.P.; Supervision, D. P. and S.R.

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SUPPLEMENTARY MATERIALS

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