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Specific factors and methodological decisions influencing brain responses to sexual stimuli in women

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ABSTRACT

Most of the neuroimaging studies on sexual behavior have been conducted with male participants, leading to men-based models of sexual arousal. Here, possible factors and methodological decisions that might influence brain responses to sexual stimuli, specifically for the inclusion of women, will be reviewed. Based on this review, we suggest that future studies consider the following factors: menstrual phase, hormonal contraception use, history of sexual or psychiatric disorders or diseases, and medication use. Moreover, when researching sexual arousal, we suggest future studies assess sexual orientation and preferences, that women should select visual sexual stimuli, and a longer duration than commonly used. This review is thought to represent a useful guideline for future research in sexual arousal, which hopefully will lead to a higher inclusion of women and therefore more accurate neurobiological models of sexual arousal.

1. Introduction

During the last twenty years, several studies investigated the cerebral correlates of human sexual behavior, with the majority using external sexual stimuli to evoke sexual arousal (for meta-analyses and reviews, see: Stoléru et al., 2012; Georgiadis and Kringelbach, 2012; Poeppl et al., 2016; Mitricheva et al., 2019). Human sexual arousal refers to a complex set of social, psychological, and biological processes and therefore investigation of sexual arousal requires a multi-method and an inter-disciplinary approach (Woodard and Diamond, 2008).

Sexual arousal can be induced by both internal cues, represented by sexual interest, autobiographical memories, fantasies, or, simply thoughts, and external sexual stimuli. External sexual stimuli, of different sensory modalities, have been considered a reliable tool to study the brain underpinnings of sexual arousal in both men and women. Sexual arousal is usually operationalized through the measurement of genital responses and self-reported (i.e., subjective) sexual arousal. Since both genital responses and subjective sexual arousal are activated, and regulated, by brain circuits responding to internal and external stimuli, sexual arousal has been measured by functional neuroimaging as well. Modalities of functional brain imaging include functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG). EEG and MEG have a considerably lower spatial resolution than fMRI and PET. Since this review will focus on the brain response patterns to sexual stimuli, results of EEG and MEG will not be discussed.

A wide array of brain regions is involved in processing and experiencing sexual arousal, not surprising for a complex task involving multiple sensory modalities and several cognitive functions as focused attention, working and long-term memory, and emotional appraisal (Stoléru et al., 2012; Georgiadis and Kringelbach, 2012). Two recent meta-analyses showed different results regarding the brain regions involved during visual sexual stimulation (VSS) in women and men. A meta-analysis by Poeppl et al. (2016) showed small between-gender differences in brain response in subcortical areas to sexual stimuli, whereas Mitricheva et al. (2019) did not find any differences in brain response to sexual stimuli between men and women. According to Mitricheva et al. (2019), this discrepancy in the meta-analyses results could depend on the inclusion of studies using different sensory modalities sexual stimulation (visual, olfactory, and tactile stimuli).

Although there is a common assumption of large sex differences in brain responses to sexual stimuli, and the evoked sexual arousal, these meta-analyses show small or null between genders differences. However, previous behavioral and psychophysiological studies found a significantly higher level of agreement between self-reported sexual

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arousal and genital response in men than in women (Chivers et al., 2010). Methodological issues, such as differences in devices and procedures used, or fundamental differences, might modulate this. An fMRI study by Parada et al. (2016; 2018) examined both self-reported sexual arousal and genital responses in relation to brain responses in both men and women. Various subregions of the parietal cortex show significant changes in brain responses corresponding to the degree of self-reported sexual arousal, with no gender differences. The strength of the correlation between brain activation and genital response shows that women had a stronger brain-genital relation than men in the insula, amygdala, posterior cingulate cortex, lateral occipital cortex, and bilateral cerebellum. Conversely, in men, no brain regions showed a strong brain-genital correlation. This study presents that fMRI studies can be an important addition to psychophysiological and behavioral research in understanding complex questions, such as the gender differences in concordance between genital response and self-reported sexual arousal.

Previous neuroimaging studies on sexual arousal have predominantly included heterosexual male participants. The recent meta-analysis by Mitricheva et al. (2019) demonstrated the inclusion of 1184 male participants in contrast to 636 female participants. Of these 1184 male participants, 1054 were heterosexual, making it the largest group to be included in neuroimaging studies to sexual arousal. Due to the large inclusion of men, one of the most recent and influential models of brain responses to sexual stimuli is based on data of male participants (Stoléru et al., 2012). The overrepresentation of male participants and overgeneralization of theories and models based on male data is not limited to neurosexology but for instance also present in animal studies (Coiro and Pollak, 2019) or clinical trials (Feldman et al., 2019; Holdcroft, 2007). By including more women, but also more non-heterosexual and non-cis participants, the specificity and clinical utility of future theoretical models could be improved. Besides theoretical reasons, the larger inclusion of women could lead to a better understanding of female-specific sexual disorders and diseases (e.g., female sexual arousal disorder, genito-pelvic pain/penetration disorder).

It is not clear why there is an overrepresentation of men in previous studies. A potential reason might be female-specific factors and methodological decisions, which could be seen as an obstacle. Hence, the present review will examine factors and methodological decisions that could potentially influence brain responses to sexual stimuli when women are included in neuroimaging studies to sexual arousal and genital response. Moreover, we will assess whether previous neuroimaging studies considered these factors.

2. Methods

For this review, participant and methodological factors were selected through an extensive literature review. After that, neuroimaging studies using sexual stimuli, which included women, were selected and we examined whether the selected factors were considered in each study. Previous published studies were selected through an extensive search on the principal databases, like PubMed and Web of Science, with keywords for neuroimaging techniques, for female participants and sexual arousal (e.g., 'fMRI', 'PET', 'women', 'female', 'sexual function', 'sexual arousal') using specific Boolean operators like AND, OR and NOT. Despite the narrative and methodological nature of the present review, our research question was based on the PICO strategy. Specifically, we are interested in analyzing the published literature about studies that involved women (P; Population), to study whole-brain activity (O; Outcome) with the above-mentioned imaging techniques (I; Intervention) in which visual sexual or erotic stimulation (C; Comparison) has been used. Therefore, previous published meta-analyses and narrative or systematic reviews have been retrieved to check the reported bibliographic references. In this way, the studies of interest have been retrieved and the content has been assessed.

3. Results

The published studies included in the present review are reported in Tables 1 and 2. These tables summarize the principal characteristics of the included studies in terms of participants' characteristics (Table 1) and methods used (Table 2). In the following sections, we will report and discuss participant and methodological factors that could potentially influence brain responses to sexual stimuli.

3.1. Participant-related influences on brain responses to sexual stimuli

3.1.1. Hormone levels

Hormone levels in women change physiologically during the menstrual cycle, during pregnancy, after menopause, or induced by oral contraceptive. Before discussing research on brain responses to sexual stimuli in these different hormonal phases, we will first give a general overview of hormones, and neurotransmitters that interact with them, related to sexual arousal.

Both estrogen and testosterone have been proposed to regulate genital response. They might regulate the activity of vasoactive intestinal polypeptide (VIP) and nitric oxide synthase (NOS) during sexual arousal, mediating the vasocongestion of clitoral tissue and subsequent lubrication (Hoyle et al., 1996). Furthermore, bioavailable testosterone can transverse the blood-brain barrier to exert an influence on several brain structures (Clayton and Hamilton, 2010). Prolactin and oxytocin are mainly involved in orgasm, but they might influence genital and/or self-reported sexual arousal indirectly. Exton et al. (2000) present that serum prolactin levels, adrenaline, and cortisol levels were not affected by changes in self-reported sexual arousal, but serum prolactin level increases significantly after a masturbation-induced orgasm. Thus, prolactin may act as a negative feedback signal limiting sexual arousal and decreases the likelihood of continued sexual activity (Exton et al., 2000).

According to a recently published systematic review, the systemic oxytocin in sexual behavior seems to play a complex and relevant role in sexual desire (for a review, see Cera et al., 2021). Most studies collected bodily fluid samples during self-sexual stimulation, in which sexual thoughts and fantasies could trigger arousal and orgasm. Conversely, oxytocin administration affects orgasmic and post-orgasmic intervals and aspects of partner interactions (Behnia et al., 2014). Oxytocin might therefore contribute indirectly to genital and self-reported sexual arousal by a positive feedback loop (Meston and Stanton, 2019). Moreover, according to Robinson (2015), oxytocin plays a role in the stimulation of the nipple-areola-breast complex (breast-sex), considered an erogenous bodily part relevant for sexual arousal (Levin and Meston, 2006), and orgasm (Masters and Johnson, 1966).

Despite animal studies suggesting a role of dopamine in sexual arousal (Pfaus, 2009), few studies investigated the role of dopamine in human sexual arousal. Brom et al. (2016) found no effect of dopamine antagonist administration on conditioned sexual response in women. Conversely, they observed effects of the dopamine antagonist on the unconditional genital response to sexual stimulation in women. Krüger et al. (2018) also found no alteration in subjective and genital response after dopamine agonist administration in women. Moreover, these studies did not consider the levels of dopamine of the participants.

Experimental evidence showed that noradrenaline, cortisol, and serotonin are also involved in sexual arousal. Indeed, plasma noradrenaline in women increased during sexual arousal and orgasm with a rapid fall in plasma levels after orgasm (Wiedeking et al., 1979). Cortisol declines during the presentation of sexual stimuli and elevated cortisol levels decrease self-reported sexual arousal, but not genital response (Hamilton et al., 2008). A review by Frohlich and Meston (2000) showed that serotonin is active in several peripheral mechanisms that are likely to affect female sexual functioning. Serotonin acts as a neurotransmitter in the central nervous system (CNS), but in the periphery acts as a vasoconstrictor and vasodilator. Besides, contractions of smooth

Table 1
Participant information for neuroimaging studies to sexual arousal (sorted by year of publication).

First Author	Year	Number of Healthy Women	Age			Menstrual Phase	Hormonal Contraception Users		Disorders & Diseases			Medication		Sexual Preference		
			M	SD	Range		Users	NonUsers	Sexual	Psychiatric	Neurological	Influence SA	Psychotropic	Heterosexual	Homosexual	Bisexual
Park	2001	6	33	–	25–41	–	–	–	x	–	–	–	–	–	–	–
Karama	2002	20	24	3	–	Non-O	–	–	–	x	–	–	–	–	–	–
Ham	2004	14	25.0	–	–	–	–	–	–	–	–	–	–	x		
Archer	2006	22	42.6	4.2	–	–	–	–	–	x	x	–	–	–	–	–
Gizewski	2006	5	27	–	20–35	Mid-L; M	–	x	–	–	–	–	–	–	–	–
Ponseti	2006	26	23.9	4.45	–	–	–	–	x	x	–	–	–	x	x	
Savie	2008	25	31	4.5	–	–	–	–	–	–	–	–	–	x	x	
Yang	2008	9	40.3	–	23–58	–	–	x	x	x	x	x	x	–	–	–
Arnow	2009	20	29.3	–	18–30	L	x	x	x	x	–	x	–	x		
Georgiadis	2006	12	32	–	21–47	–	–	–	x	x	–	–	–	x		
Zhu	2010	15	26.3	3.8	–	O; M	–	x	–	x	x	–	–	x		
Michels	2010	15	26	–	22–34	–	–	–	–	x	x	x	x	–	–	–
Gillath	2012	20	19.65	–	–	–	–	–	x	x	x	–	–	–	–	–
Komisaruk	2012	11	–	–	26–56	–	–	–	–	x	–	–	–	–	–	–
Bianchi-Demichelli	2011	15	30.4	7.09	21–44	Day 1–10		x	–	x	x	–	x	x		
Yang	2013	9	40.3	–	23–58	–	–	–	x	x	–	–	x	–	–	–
Abler	2013	24	24	2.0	20–29	F; Non-O; L	x	x	x	x	x	–	–	x		
Kim	2013	23	38.4	10	21–51	–	–	–	x	x	x	–	–	–	–	–
Sylva	2013	22	22.1	3.1	–	–	–	–	–	–	–	–	–	x	x	
Woodard	2013	6	29	4.4	–	–	x	x	x	x	–	x	x	x		
Borg	2014	22	22	2.1	–	F; Non-O	x	x	x	x	x	–	x	x		
Kim	2014	12	22.7	2.9	–	–		x	–	x	–	–	–	–	–	–
Wehrum	2014	50	25.4	4.8	–	F; L	x	x	x	x	x	x	–	x		
Kim	2017	15	39.5	7.1	–	F; L		x	–	x	x	x	–	–	–	–
Safron	2018	76	29.67	–	21–46	–	–	–	–	–	–	–	x	x	x	x
Stark	2019	33	25.7	4.6	19–44	–	–	–	–	x	–	–	x	x		x

Note: SA, sexual arousal, -, not reported, O, ovulatory phase, F, follicular phase, L, luteal phase, M, menstruation.

Table 2
Methodologies used by neuroimaging studies to sexual arousal (sorted by year of publication).

First Author	Year	Sexual Stimuli			Control Stimuli				Neuroimaging method	p-value
		Type	Length (seconds)	Content	Selection	Length (seconds)	Content	Selection		
Park	2001	Film	240	Erotic	–	60	Documentary	–	fMRI 1.5 T	0.05
Karama	2002	Film	30	–	Rated by Women	30	Social Interaction and Human Faces	Rated by Women	fMRI 1.5 T	0.05 & 0.001
Hamann	2004	Film	3.75	Couple Sexual Activity	Rated	3.75	Nudes Opposite Sex Couple Interaction Nonsexual	–	fMRI 1.5 T	0.001
Archer	2006	Film	31	Couple Sexual Activity	Rated by Women	31	Single Person Nonsexual	Rated by Women	fMRI 1.5 T	0.05
Gizewski	2006	Film	60	–	Rated	60	Couple Interaction Nonsexual	Rated by Women	fMRI 1.5 T	0.05 & 0.001
Ponseti	2006	Photo	0.3	Single Nude	Rated by Women	0.3	Nonsexual	Selected by Researchers	fMRI 1.5 T	0.05
Yang	2008	Film	240	Erotic	–	60	Nonsexual Documentary	–	fMRI 1.5 T	0.05
Arnow	2009	Film	180	Couple Sexual Activity	Rated by Women	120 60	Single Person Nonsexual Nature Scenes	Rated by Women	fMRI 3.0 T	0.001
Georgiadis	2006	Tactile	120	Tactile clitoris stimulation					PET	0.001
Zhu	2010	Film	30	Couple Sexual Activity	Rated by Women	30	Multiple People Interaction Nonsexual	Rated by Women	fMRI 3.0 T	0.05
Michels	2010	Tactile	12	Electrical clitoral stimulation		18	Rest	–	fMRI 3.0 T	0.001
Gillath	2012	Photo	2.5	Single Nude	Rated by men and women	2.5	Abstract Images	–	fMRI 1.5 T	0.001
Komisaruk	2012	Tactile	30	Tactile/electrical clitoral, vaginal, cervix and nipple stimulation		30	Tactile Stimulation Thumb or Toe		fMRI 3.0 T	0.05
Bianchi-Demichelli	2011	Photo	1.5	Single Nude	Selected by male and female researcher	1.5	Nonsexual Single Models	Selected by one mail and one female researcher	fMRI 3.0 T	0.001
Yang	2013	Film	240	Erotic	–	60	Nonsexual Documentary	–	fMRI 1.5 T	0.05
Abler	2013	Film Photo	20 4	Couple Sexual Activity Single Nude	–	20 4	Nonsexual Couple Interaction Emotional Nonsexual	–	fMR1 3.0 T	0.001
Kim	2013	Film	540	Couple Sexual Activity	–	30	Nature Documentary	–	fMRI 3.0 T & fMRS	0.001
Sylva	2013	Photo	3.5	Couple Sexual Activity Single Nude	Rated by heteroand homosexual men and women	No control	No control	No control	fMRI 3.0 T	0.05
Woodard	2013	Film	60	Couple Sexual Activity	–	60	Nonsexual Couple Interaction	–	fMR1 3.0 T	0.001
Borg	2014	Photo	1.4	Couple Sexual Activity (Hardcore)	Rated by women	1.4	Single Person Nonsexual	Selected by researchers	fMR1 3.0 T	0.05
Kim	2014	Film	180	Couple Sexual Activity	Selected by two researchers	180	–	–	fMR1 3.0 T	0.05
Wehrum-Osinsky	2014	Photo	3	Couple Sexual Activity	Rated by men and women	3	Neutral: Nonsexual Couple Interaction	–	fMRI 1.5 T	0.001& 0.01 & 0.05
Kim	2017	Film	540	Couple Sexual Activity	Approved by women	30	Positive/Negative: Emotional Nonsexual Nature Documentary	Rated by students	fMR1 3.0 T	0.005
Safron	2018	Film Photo	15 3.5	Single Sexual Activity Single Nude	–	–	Fixation Cross	–	fMR1 3.0 T	0.05
Stark	2019	Film Photo	8 8	Sexually Arousing	Rated by men and women	8	Nonsexual Couple Interaction	–	fMRI 3.0 T	0.05

Note: fMRI, functional magnetic resonance imaging, PET, positron emission tomography, T, tesla.

muscles in the genital urinary systems were detected after administering serotonin.

Thus, many hormones and neurotransmitters and their mutual interaction are involved in sexual arousal in women. A clear integration of all findings and proposed models of hormone interaction with the central nervous system during sexual arousal has not yet been proposed.

3.1.1.1. Menstrual cycle. During the menstrual cycle, estradiol rises with the growth and maturation of the dominant follicle to a height at ovulation. Progesterone appears after ovulation, while luteinizing hormone (LH) surges at ovulation. Testosterone mirrors changes in LH over the menstrual cycle, peaking at ovulation. Most of the research on self-reported sexual arousal throughout the menstrual cycle found an increase in self-reported sexual arousal during the late follicular and ovulatory phases and a decrease during early follicular and luteal phases (Shirazi et al., 2018). A few studies, however, found that external factors may have a stronger influence than the phase in the menstrual cycle. For example, Caruso et al. (2014) demonstrated that the menstrual cycle modulates sexual arousal in single women, but not in women having a relationship. These studies show the importance of considering external factors. Nonetheless, questions regarding the influence of the phases in the menstrual cycle on brain response to sexual stimuli are still interesting.

To date, only three studies have investigated the differences in brain response to sexual stimuli throughout different phases of the menstrual cycle. During VSS, women in the mid-luteal phase, compared to the menstrual phase, showed a higher BOLD response in the ACC, left insula, and orbitofrontal cortex (Gizewski et al., 2006). In contrast, Abler et al. (2013) found no menstrual cycle effect upon direct and explicit stimulation (i.e., presentation of videos and pictures). They, however, found differences in frontal regions between phases related to the expectation of a sexual stimulus. During the expectation of the stimulus, the luteal phase was associated with higher activation in the ACC, the dorsolateral, and the dorsomedial prefrontal cortex compared to the follicular phase. Comparing the ovulatory and anovulatory phase, significant activation has found in the right inferior frontal gyrus, right lateral occipital cortex, and postcentral gyrus; during the non-ovulatory phases, in bilateral superior parietal lobes (Zhu et al., 2010). Besides visual sexual stimuli, menstrual cycle might also play a role in brain responses to olfactory cues. Graham et al. (2000) demonstrate that the effect of male fragrance on genital response during erotic fantasies was only apparent in the follicular phase but not in the periovulatory phase.

Overall, the these studies indicated an influence of phase during the menstrual cycle on brain responses to visual sexual stimuli, mainly in cortical regions. The exact influence is not clear, and it is therefore recommended to report the phase in the menstrual cycle of the participants. Studies could measure brain response to sexual stimuli in women that are in the same phase. If women in different phases are included, it is wise to check for differences between phase groups. Table 1 shows the phases as collected and reported in the neuroimaging studies included in the present review. Noteworthy, most of the studies did not report the phase in the menstrual cycle.

3.1.1.2. Hormonal contraception. There are several types of hormonal contraception used by women. Hormonal contraceptives suppress ovulation and the estrogen peak that precedes it. In addition, free testosterone in women using hormonal contraceptives is around 61 % lower compared to naturally menstruating women. (Zimmerman et al., 2014). The type of hormonal contraceptives that are used the most are oral contraceptives, used by 100 million women worldwide (Petitti, 2003) and by 16 % of women in the U.S. (Daniels et al., 2014). Twenty-five percent of those starting oral contraceptives discontinued using within the first 12 months (Ali et al., 2012). The main cause for this discontinuation are side effects experienced by women, including sexual side effects (Sanders et al., 2001). The composition of estrogen level and progestin compound differs per type of oral contraceptives. These different types of oral contraceptives seem to have different effects on desire and arousal reports, with some leading to lower (Wallwiener et al., 2010, 2015; Caruso et al., 2004), and others leading to higher scores (Caruso et al., 2011).

To date, only Abler et al. (2013) investigated the brain responses to sexual stimuli in women with and without hormonal oral contraceptive use. They found higher activation in the bilateral inferior precentral gyrus in the non-contraceptive group in the follicular phase compared with the contraceptive group. These results suggest that hormonal oral contraceptive use could affect brain response to sexual stimuli depending on the menstrual phase. The effects of other hormonal contraceptives on brain response to a sexual stimulus remain unclear. Therefore, we suggest reporting hormonal contraceptive use when studying sexual arousal in women with neuroimaging techniques. Studies can choose to exclude women using hormonal contraceptives or only include women using hormonal contraceptives. If both women using and not using hormonal contraceptives are included, hormonal contraceptive use should be considered as a confounding variable. More than half of neuroimaging studies did not report hormonal contraceptive use by participants (Table 1).

3.1.1.3. Menopause. Menopause is defined as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity (World Health Organization, 1996). Menopause is diagnosed after 12 consecutive months of an absence of a menstrual period. After, low estrogen and progesterone levels leads to reduced lubrication of the vagina, decreased clitoral blood flow, and altered sensory perception from peripheral nerves located in the pelvic region during sexual arousal. This can cause vaginal dryness and genito-pelvic pain/penetration disorder (Bruce and Rymer, 2009). Several studies reported changes in subjective sexual arousal in menopausal women. Leiblum et al. (2006), for example, showed a lower partner relationship and sexual satisfaction in menopausal women compared to premenopausal women. Avis et al. (2000) found that menopause was significantly related to lower sexual desire, but a multi regression analysis showed that other factors such as health, marital status, and smoking had a greater negative impact on sexual functioning than menopause status. A national probability sample of 1150 women in the U.S. showed that the overall prevalence of sexual activity after menopausal age declines. Where sexual activity is prevalent in 73 % among respondents who were 57–64 years of age, this is reduced to 53 % for 65–74 years and 26 % for 75–85 years of age (Lindau et al., 2007). These results indicate that menopausal women have different self-reported sexual arousal and genital response than premenopausal women.

Jeong et al. (2005) and Kim and Jeong (2017) compared the brain responses to sexual stimuli between premenopausal and menopausal women. Jeong et al. (2005) found an overall 8 % higher activation ratio of premenopausal women compared to menopausal women. In addition, the limbic, temporal, and parietal lobes showed greater enhancement of signal intensities in premenopausal women. Menopausal women, however, had dominant signal enhancement of the genus of the corpus callosum and superior frontal gyrus. Overall, Kim and Jeong (2017) also found higher activation in premenopausal women compared to menopausal women. In addition, they found higher activation in the thalamus, amygdala, and ACC in premenopausal women. Moreover, the BOLD signal in the amygdala positively correlated with estrogen levels. Functional connectivity analysis during resting state revealed that perimenopausal women (a period of two to eight years before menopause) suffered from aberrant intrinsic functional connectivity in the right medial superior frontal gyrus, between the left posterior insula, right superior frontal gyrus, and the right orbital gyrus (Lu et al., 2019). Prolactin levels were negatively correlated with the functional connectivity between the right orbital gyrus and right superior frontal gyrus, and between the left posterior insula and the right superior frontal

gyrus. Archer et al. (2006) showed that women after menopause have reduced overall signal activations when viewing both erotic and neutral stimuli and limited brain regions that were exclusive to the erotic visual stimulus compared to premenopausal women. After six weeks of estrogen therapy (administration of both estradiol and testosterone), menopausal women showed a global increase in brain activation during VSS. These results suggest a significant effect of estradiol and testosterone in brain response to sexual stimuli.

Hence, inclusion of perimenopausal and menopausal women can thus lead to insight into the effect of hormone levels on sexual arousal. Overall, these studies show a decreased brain response to sexual stimuli in perimenopausal and menopausal women. Sexual activity has been reported to decline with age. It would therefore be interesting to investigate if brain response to sexual stimuli covaries with age within the group of menopausal women.

Overall, studies found a range of different results of brain response to sexual stimuli influenced by menstrual phase, hormonal contraceptives, and menopause. No conclusions about the hormonal influence on sexual arousal can be drawn from these results. Note that pregnancy also has a large influence on hormone levels (O'Leary et al., 1991) and self-reported sexual arousal differs during pregnancy (Aslan et al., 2005; Senkumwong et al., 2006). To date, the effects of pregnancy on sexual brain response have not been studied. Therefore, studies should report the menstrual phase, hormonal contraceptive use, menopausal state, and pregnancy state of participants.

3.1.2. Diseases and disorders

Sexual dysfunctions represent an obvious group of disorders that have a negative impact on sexual arousal. The subtype of female sexual dysfunction that has been studied most in neuroimaging research is hypoactive sexual desire disorder (HSDD), which falls under Female Sexual Interest/Arousal Disorder in the most recent version of the Diagnostic and Statistical Manual of Mental Disorders. HSDD is defined as the persistent or recurrent deficiency or absence of sexual fantasies and desire for sexual activity that causes marked distress or interpersonal difficulty (American Psychiatric Association, 2013). Brain response to sexual stimuli in women with HSDD has been investigated by Arnow et al. (2009), Bianchi-Demicheli et al. (2011), and Woodard et al. (2013). All studies showed a higher self-reported sexual arousal reported by women without HSDD compared to women with HSDD. Arnow et al. (2009) showed increased brain response in the bilateral entorhinal cortex in women without HSDD compared to women with HSDD. Besides, they showed increased brain response in the medial frontal gyrus, right inferior frontal gyrus, and bilateral putamen in women with HSDD compared to women without HSDD. Comparing HSDD women to healthy controls, Bianchi-Demicheli et al. (2011) found involvement in the inferior frontal gyrus, in the inferior parietal lobule, and the posterior medial occipital gyrus. Women without HSDD showed stronger brain responses in the intraparietal sulcus, dorsal ACC, and ento-perirhinal region to sexual stimuli compared to women with HSDD. During sexual stimulation, Woodard et al. (2013) showed stronger involvement of the right thalamus, left insula, left precentral gyrus, and left parahippocampal gyrus in women without HSDD compared to women with HSDD, whereas women with HSDD showed activations in correspondence of the right medial frontal gyrus and left precuneus (Woodard et al., 2013). Despite the heterogeneity, results suggest an altered brain response pattern to sexual stimuli in women with HSDD compared to women without HSDD.

Sexual addiction represents another factor that might affect brain responses to sexual stimuli and has been predominantly studied in men. Different terminologies are used, associated with different assumptions about the underlying mechanisms (e.g., addiction, compulsivity, impulsivity, hypersexuality). Other studies focus on high levels of pornography use and the number of sexual partners, although it remains to be established if these factors are associated with similar etiologies, trajectories, and outcomes (Janssen et al., 2020). Altered brain responses to sexual stimuli have been found in men with hypersexual behavior (Seok and Sohn, 2015), and compulsive sexual behavior (Kowalewska et al., 2018). Also, the strength of association between brain response and sexual arousal ratings was positively related to self-reported pornography use in men (Klein et al., 2020). Although no relationship between brain activations and indicators of problematic pornography use was found, reward-related brain areas were significantly activated by pornographic videos (Markert et al., 2021). Problematic sexuality might be more associated with a perceived lack of personal control over sexuality and moralistic attitudes than with high levels of sexual desire and activity (Carvalho et al., 2015). For example, a large-scale questionnaire showed that women classified as hypersexual, but not with high sexual desire, reported significantly more negative consequences associated with their sexuality (Stulhofer et al., 2016). Therefore, further studies are needed to disentangle the differences in brain responses to sexual stimuli in women with sexual addiction, compulsivity, impulsivity, or hypersexuality.

Altered sexual responses in women have also been related to neurological disorders (e.g., traumatic brain injury), endocrine disorders (e.g., diabetes), cardiovascular illness (e.g., hypertension), pelvic disease (e.g., urinary incontinence), and other diseases (e.g., breast cancer) (Clayton and Ramamurthy, 2008). Unfortunately, studies regarding brain responses to sexual stimuli in women with these disorders have not been conducted. In addition, sexual impairment appears to be a frequently underestimated issue in psychiatric patients and is reported by depressed subjects (Cohen et al., 2007). Yang et al. (2008) compared women with a depression to healthy controls. They found that women with depression had significantly lower self-reported sexual arousal than healthy women. In addition, they found that the level of brain activity in depressive women was more than 50 % lower than in healthy women in the hypothalamus, septal area, ACC, and parahippocampal gyrus.

Sexual impairment has been related to a range of disorders and diseases. Neurological disorders are often excluded in neuroimaging research since abnormalities in the brain are likely to influence data analysis and results. Since sexual dysfunctions and psychiatric disorders might influence the brain response to sexual stimuli, it is recommended to report and, potentially exclude or separate, these disorders from a healthy group of participants when conducting a neuroimaging study to sexual arousal. Table 1 shows the exclusion criteria regarding sexual arousal-related, psychiatric, and neurological disorders, as reported by neuroimaging studies to sexual arousal in women.

3.1.3. Medication

Medications that can contribute to sexual dysfunction include histamine receptor (H2) blockers, narcotics, non-steroidal anti-inflammatory drugs (NSAIDs), thiazide diuretics, non-selective beta antagonists, and psychotropic such as antidepressants, antipsychotics, and benzodiazepines (Clayton and Ramamurthy, 2008). Research regarding the influence of these medications on brain responses to sexual stimuli is limited. A study by Cohen et al. (2007) found that patients receiving antidepressants suffered from more frequent and severe impairment of sexuality compared with depressed patients not using antidepressants, antipsychotics, or opioids. They found these results for all the types of antidepressants, including mirtazapine. Mirtazapine has been reported to be less associated with sexual dysfunction than SSRIs (Koutouvidis et al., 1999). Yang et al. (2013) reported significantly improved self-reported sexual arousal and brain response to sexual stimuli in the hypothalamus, septal area, and parahippocampal gyrus when using mirtazapine in depressed patients. Studies regarding the effects on brain response to sexual stimuli of other antidepressants have been conducted solely in male participants (e.g., Baldwin et al., 2015).

Besides mirtazapine, the influence of medication on the brain response evoked by sexual stimuli remains unknown. In addition, medication can influence other cognitive brain processes as well. Antidepressants, for example, reduce the subcortical-cortical resting-state

functional connectivity in healthy volunteers (McCabe and Mishor, 2011). Since medication can affect brain processes involved in sexual arousal and the exact effects on brain response to sexual stimuli of all medication, except for mirtazapine, remain unknown, it is recommended to report medication use of participants included or to exclude participants that use medication that directly affects sexual arousal. Since symptoms of decreased sexual arousal continue immediately after discontinuation of antidepressant therapy (Bala et al., 2018), it is recommended to report past antidepressant therapy or the duration of washout. Table 1 shows the studies that reported the medications used by participants.

3.1.4. Sexual orientation, gender identity, and sex characteristics

To investigate sexual arousal in the brain, participants must be aroused by the presented stimuli. The presented stimuli should therefore match the sexual orientation of the participants. However, most studies on sexual arousal in women did not report the match between sexual orientation and used stimuli. Table 1 reports the neuroimaging studies that reported the sexual orientation of participants.

Homosexual women are only included in studies when they are compared to heterosexual women, with varying results. Ponseti et al. (2006) compared brain responses to preferred and non-preferred sexual stimuli (i.e., a female couple for homosexual women and a heterosexual couple for heterosexual women). In both groups, they found stronger responses in the ventral striatum, premotor cortex, and central medial thalamus. Using preferred-sexual stimuli, compared to baseline, in homosexual and heterosexual women, Sylva et al. (2013) found small clusters of greater activation in heterosexual women in the left inferior parietal and right middle temporal cortices. In a region of interest (ROI) analysis, they found that occipital cortices, the mediodorsal thalamic nucleus, and left hypothalamus showed a reliable activity for women for preferred-sex stimuli compared to non-preferred sex stimuli. A whole-brain analysis by Safron et al. (2018) presents brain activation for female vs. male sexual pictures in heterosexual women in occipital and occipitotemporal cortices; in bisexual women in occipital cortices, supramarginal and angular gyri, and posterior cingulate; in homosexual in occipital cortices, parietal lobes, and parahippocampal cortex. All groups showed activity in bilateral superior temporal cortices to female compared to male sexual videos, although this effect varied by sexual orientation, with homosexual women showing more activity compared to heterosexual and bisexual women. Heterosexual and bisexual women showed greater responses in occipital cortices to male compared to female erotic videos. All the groups showed greater activity related to male videos in superior parietal cortices.

Besides research on sexual orientation, male to female (MTF) transgenders have also been included in neuroimaging studies of sexual arousal. Gizewski et al. (2009) included MTF transgenders with ten participants showing sexual orientation to women and two to men, heterosexual cis-women, and heterosexual cis-men. None of the transgender participants had received surgical or hormonal therapy. They depicted films presenting heterosexual couples engaged in sexual activity. MTF transgenders had activation patterns almost identical to cis-woman compared to cis-men. Thus, even though the majority of the MTF transgenders had the same sexual orientation as the cis-men included (towards women), their brain response was almost identical to the cis-woman and not to the cis-man. Note that the most recent meta-analysis shows no difference in brain response between heterosexual cis women and men (Mitricheva et al., 2019), which further complicates interpretation of these results. Oh et al. (2012) included MTF transgender, who underwent sex reassignment surgery and received hormone therapy, with sexual orientation to men. They showed that brain response to male sexual stimuli compared to female was stronger in the cerebellum, hippocampus, putamen, anterior cingulate gyrus, amygdala, midbrain, thalamus, insula, and caudate nucleus. Brain response to female sexual stimuli showed a higher response in the hypothalamus and septal area. They found more brain response towards stimuli that matches their sexual orientation. Noteworthy, Gizewski et al. (2009) only included 12 MTF transgenders, and Oh et al. (2012) only 9. In this way, further studies are needed to reveal the brain responses to sexual stimuli of MTF transgenders and the relation to their sexual orientation.

Another group that has been studied is represented by intersex individuals (referred to as Disorders of Sex Development in clinical settings). These individuals have any or several sex characteristics ranging from chromosome patterns, gonads, or genitals that do not fit the binary notion of female and male bodies. For example, women with complete androgen insensitivity syndrome (CAIS) have Y-chromosome, testes, and produce male-typical levels of androgens. They lack functional androgen receptors preventing the receptors to respond to androgens, developing a female physical phenotype, leading to a discrepancy between their genetic sex and genital appearance. Hamann et al. (2014) compared brain responses to images of heterosexual behavior, self-reported by all participants as sexually arousing, of CAIS women, typically developing women, and men. They showed that brain patterns of women with CAIS were highly like typically developing women but differed from brain patterns of men. These results not only present interesting findings for women with CAIS but also give information about the relationship between hormones and sexual arousal in general. For example, the high testosterone levels in women with CAIS are aromatized to estradiol, ruling out the aromatization of testosterone to estradiol as a determinant of gender differences in patterns of brain activation evoked by sexual images.

The above-mentioned studies that included non-hetero, non-cis individuals show the importance of assessment of the sexual orientation of the participants in the sexual stimuli selection. The recently proposed expansion of the lesbian-gay-bisexual-transgender (LGBT) to lesbian-gay-bisexual-transgender-queer-intersex-asexual-pansexual (LGBTQIAP) might lead inclusion of more groups in future brain research. Asexuality, defined as the absence of sexual attraction, for example, seems to be prevalent in 1 % of the population (Bogaert, 2004). Asexual women report lower autonomic arousal, sensuality-sexual attraction, and positive affect during sexual stimuli. However, Brotto and Yule (2011) found no difference in genital and self-reported sexual arousal compared to non-asexual women. Future brain imaging studies might investigate the cerebral pattern underlying the asexuality in women. Including more individuals that do not identify as heterosexual and/or cis will thus not only lead to a better representative sample but can also lead to more insight in for example sexual orientation and hormone-brain interactions.

3.1.5. Additional factors

Brain responses can be influenced by many other factors. When conducting a neuroimaging study, it is important to check for attention during the presentation of a stimulus. It is possible to check for attention by implementing a task during the presentation of sexual stimuli, for example, the oddball task (Ponseti et al., 2006), the one-back task (Bianchi-Demicheli et al., 2011), or questions (Zhu et al., 2010). However, a task might lead to a loss of sexual arousal, since a task might distract the participant from fully immersing in the sexual stimuli. Presenting questions after the stimuli lengthen the entire scan duration, which might lead to less attention at the end of the experiment. The importance of checking for attention might not be as relevant for sexual stimuli as it is for alternate stimuli since sexual stimuli have been linked to heightened general arousal and attention (Walter et al., 2008a, b). However, finding control stimuli that induce the same level of attention and arousal as a sexual stimulus is a very difficult task. When comparing brain response to control stimuli and sexual stimuli, attention and arousal are thus likely to be higher during sexual stimuli. To understand the brain processes of attention and general arousal, it might be interesting to include an extra control stimulus that elicits higher general arousal and attention levels, without sexual content. The overlap between sexual arousal and general arousal stimuli could present brain

processes of arousal, whereas the differences might present attention and arousal specifically for the sexual stimuli.

Factors that have been proposed to influence sexual arousal, not yet discussed, are emotions, stress, mood, and relationship problems. Besides, the novelty of employed stimuli, experimental setting, or procedure could potentially influence brain responses to sexual and control stimuli. To test the significant influences of additional factors, Wehrum-Osinsky et al. (2014) measured brain responses to sexual stimuli at two separate time points, with an interval of 1–1.5 years. At the group level, they found high stability of valence and sexual arousal ratings of sexual stimuli. When looking at interindividual differences, however, arousal rating was not correlated significantly. The brain network associated with the processing of sexual stimuli (OCC, parietal cortex, ACC, OFC, and left insula) was found to be stable at group level at different time points, except for the hypothalamus. However, the interindividual stability showed that in women, significant correlations between time points 1 and 2 for all contrasts of interest were restricted to the parietal cortex. These findings suggest that additional factors, which are difficult to account for, can be different for women at different time points. However, it also shows that when looking at a group level, these differences are likely to be balanced out.

3.1.6. Description of the methods

3.1.6.1. Sensory modality

3.1.6.1.1. Visual sexual stimuli. When investigating sexual arousal with neuroimaging techniques, sexual arousal needs to be induced during a neuroimaging scan. Most of the studies have used visual stimuli to evoke sexual arousal, assessed with subjective ratings, with variable results. The differences in results might be due to the differences in type, intensity, duration, selection method, and content of the visual sexual stimuli. Principally, the two types of stimuli used in the studies are photographs or video clips. Sexual photos might be well suited for assessing the initial appraisal of sexual stimuli but are static and briefly presented. Abler et al. (2013), using both photos and video clips of 20 s, found that static erotic pictures showed the involvement of the same brain regions as activated by video clips. However, the regions involved in processing the photo responded to a considerably smaller spatial extent.

In addition to the type of visual sexual stimulus, the intensity and content of the visual stimulus in both photos and video clips differ between studies. The content of visual stimuli is very important, as already discussed in the section *Sexual Orientation, Gender Identity, and Sex Characteristics*. In addition to matching visual sexual stimuli for sexual orientation and preference, the intensity of the content might affect the results. Using soft stimuli, such as photos of naked individuals, between-group or inter-individual differences might be harder to detect than with more 'hard-core' stimuli. According to the studies of emotional processing, more explicit stimuli, with higher valence and arousal, can induce higher affective responses. However, visual sexual stimuli with higher valence and arousal, do not necessarily induce sexual arousal or evoke higher brain response. Previous studies demonstrate a similar brain activation pattern to 'hard-core penetrative' or sadomasochistic (SM) and disgusting stimuli in women (Borg et al., 2014b). Note that this could be indicative of the relative responsiveness of the brain to 'strong stimuli' regardless of content, underlining the importance of using control stimuli with similar levels of general arousal. Individuals with a sexual preference for SM content demonstrate brain responses like brain responses of non-SM individuals to non-SM sexual stimuli (Stark et al., 2005), stressing the importance of selecting sexual stimuli in line with the sexual preference of the participant in brain imaging research. To assess what facilitates sexual interest, eye tracker during fMRI research can represent a valuable tool, as previously reported in men (Cera et al., 2020; Nummenmaa et al., 2012).

A few studies reported a women's previous experience with watching visual sexual stimuli (Archer et al., 2006; Hamann et al., 2014; Woodard et al., 2013). Although not studied in fMRI research before, it might be interesting to examine whether women experienced with watching visual sexual stimuli are more sexually aroused by explicit sexual stimuli. Hypothetically, women inexperienced with watching visual sexual stimuli might have more negative affective feelings or disgust and soft, or woman-made stimuli might be more suitable to induce high levels of sexual arousal.

The type of visual stimuli and the content are presented in Table 2. The individual differences in eliciting sexual arousal in participants can be challenging. A method to check whether participants experience sexual arousal is with self-reported ratings of sexual arousal. Some studies did not report subjective sexual arousal results (e.g., Archer et al., 2006; Park et al., 2001; Zhu et al., 2010), although the majority assessed self-reported sexual arousal during (e.g., Arnow et al., 2009; Gillath and Canterberry, 2012; Wehrum-Osinsky et al., 2014) or after the neuroimaging scan (e.g., Borg et al., 2014a; Kim and Jeong, 2014; Safron et al., 2018).

Laan et al. (1994) reported that women are less sexually aroused by a man-made sexual film compared to a woman-made film, although they found no differences in genital response. These results show the importance of selecting the optimal stimuli to induce sexual arousal in the participants. Abler et al. (2013) for example selected film clips for a male audience. Their results might have been different if they had selected film clips specifically selected for women. Many studies did not report how the visual sexual stimuli were selected or if women or men selected the stimuli. Table 2 shows the selection method for sexual stimuli.

The length of the presented visual sexual stimuli also differs between studies (Table 2). Kim and Jeong (2017) used the longest duration for a visual sexual stimulus. They analyzed the time course of BOLD response to sexual visual stimuli with a duration of 9 min. They present the largest BOLD signal in 11 ROIs between 2.30 and 3.30 s for the putamen and the insula; between 5.30 and 6.30 for the hippocampus, parahippocampal gyrus, amygdala, septal area, globus pallidus, head of caudate nucleus, thalamus, and hypothalamus; between 7.30 and 8.30 min for the ACC in premenopausal women. The greatest signal change was found between 5.30 and 6.30 min. Menopausal women showed the greatest signal change between 8 and 9 min. Note that this study carries a substantial risk of signal drift, which could over impose the drift to hemodynamic response function and could create a false positive. Still, these findings raise the question about the optimal signal change in all those studies using photos or video clips with a duration below 6.30 s. Besides, these results show differences in the optimal signal change between different groups. Future studies can consider a longer duration of the visual stimuli than commonly used.

Besides the length of the stimuli, studies also vary in their experimental design. For example, some studies use a block design, whereas others use an event-related design. In addition, the order of stimulus presentation and inter-stimulus interval show variability among the studies. Fig. 1 depicts a schematic overview of the different experimental set-ups used by neuroimaging studies. Noteworthy, many studies present the sexual and control stimuli without a long inter-stimulus interval. Continuous presentation, or with a brief inter-stimulus interval, of sexual and control stimuli can induce a crossover effect. Moreover, it is unclear how long sexual arousal effects might persist after a visual sexual stimulus in women, making it difficult to determine the inter-stimulus interval time window.

At last, the duration, selection method, and content of the visual control stimuli show differences among the studies (Table 2). The content of the control stimuli may affect the results. Some studies did not describe the content of the control stimuli. A commonly used control stimulus is a nature documentary, often rated with low valence and general arousal. In this case, the comparison between sexual and control stimuli may allow other cognitive and emotional processing, such as general arousal, face-processing, and affective appraisal. Note that large

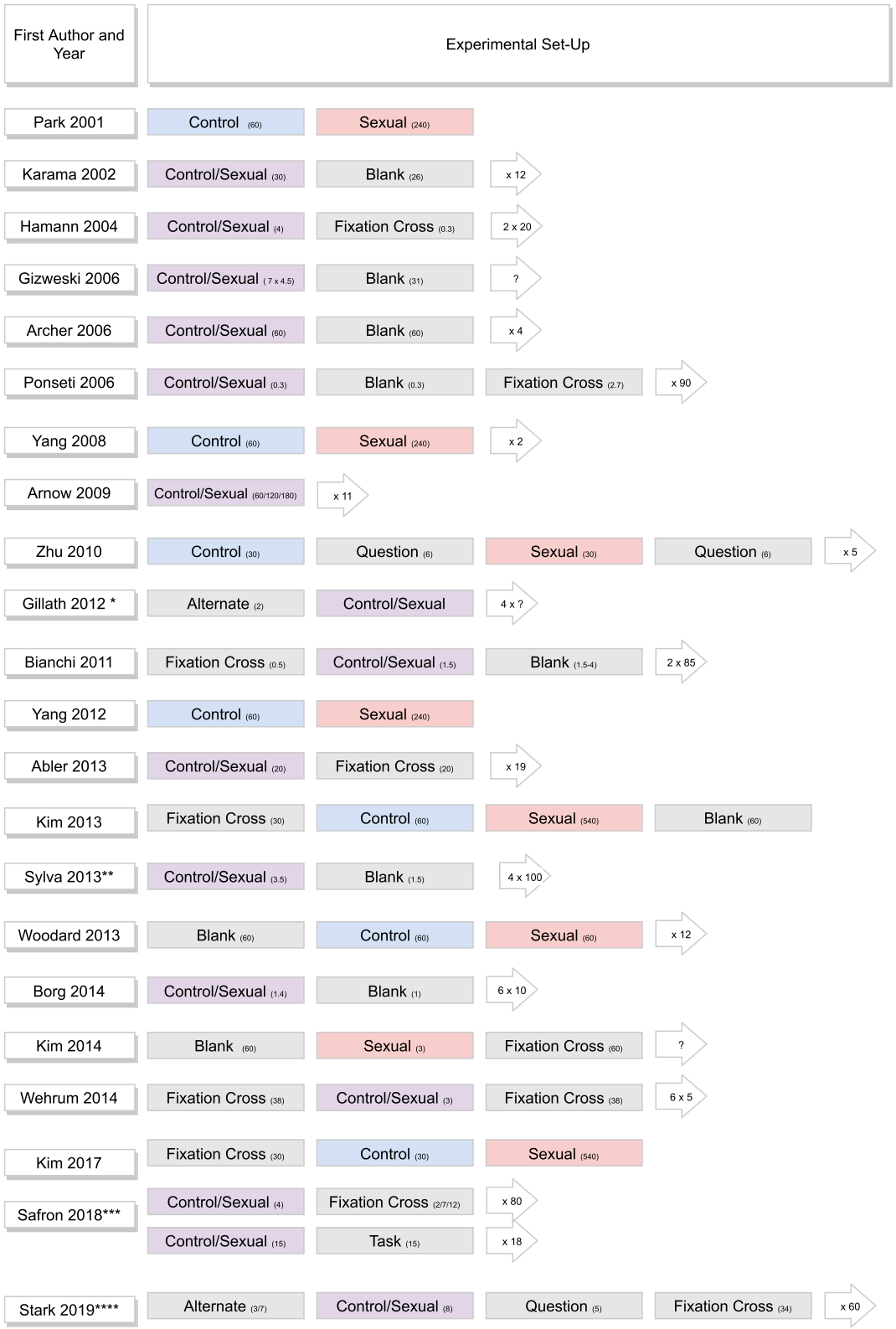

Fig. 1. This image presents a schematic simplified representation of the experimental setups of neuroimaging studies investigating sexual arousal in women. Each block represents the stimulus or interval period, either a blank screen, fixation cross, or question, with the duration in seconds (rounded up). Control (blue) and sexual (pink) stands for the type of stimulus presented, see Table 2 for the content of the stimulus. Control/sexual (purple) means that either a control or a sexual stimulus is presented in a counterbalanced or pseudorandomized order. The amount of repetition is presented in the arrow. A question mark (?) entails that the number of repetitions is not clearly stated in the study. * Gillath and Canterberry (2012) present a cue for 500 milliseconds (ms), followed by a forward mask for 476 ms, a sexual prime for 24 of 524 ms, and a backward mask for 500 ms before presenting the target, ** 50 fixation periods of 5 s pseudorandom interspersed within each run, *** Safron et al. (2018) presented two types of experimental set-ups. First, sexual and control photographs were shown, followed by sexual and control film clips, **** Stark et al. (2019) present a fixation cross for 0 −1550 ms, then a text message announcing the stimulus for 400 ms, followed by a black screen for 3-5 s before presenting the stimulus.

individual differences can be found in attention, valence, and arousal processing of control stimuli. For example, some participants might be very excited watching a documentary about trains, whereas others might be bored. The lack of valence, general arousal, or other types of processing is prevalent during the presentation of abstract drawings or a fixation cross as a control stimulus. On the other hand, control stimuli showing non-erotic clothed couple interactions can be interpreted romantically, inducing sexual arousal or interest. Again, interpretation can differ between individuals. Control stimuli showing people but not couples, for example, a vacuum infomercial, could have low arousal and valence. There is a variety of control stimuli used in neuroimaging studies to sexual arousal. When reviewing results, it is important to consider the processes underlying control stimuli and the impact on the results.

3.1.6.1.2. Fantasy and cognitive sexual stimuli. Fantasy instructions have been used in self-reported and genital sexual arousal assessments. Sexual fantasies play an important role as a trigger for sexual arousal. In men, the self-reported and genital response was higher after visual sexual stimuli compared to sexual fantasy stimuli (Koukounas and Over, 1997) but this has not been shown in women. No studies have implemented sexual fantasies in neuroimaging studies to date. However, Abler et al. (2013) analyzed the expectation period before a sexual picture. In women using or not using hormonal contraceptives and between different menstrual phases, they showed no differences in brain response to both pictures and film clips. Interestingly, they found differences in brain response during the expectation of the sexual pictures between these groups. This result shows that the use of cognitive stimuli, rather than using a passive presentation of visual sexual stimuli, is valuable for detecting between-group differences in sexual arousal.

3.1.6.1.3. Auditive sexual stimuli. Most of the studies did not report the presence of audio during the visual sexual stimuli. The impact of audio during visual sexual stimuli on brain response has not yet been investigated. A study by Polan et al. (2003) demonstrates that self-reported and genital sexual arousal did not differ during the presentation of visual sexual stimuli with or without audio. However, it is plausible that at least the auditory cortex shows a different response to visual sexual stimuli with and without audio. Auditory sexual stimulation has been applied only once in a neuroimaging study. In this fMRI study, authors showed study, happy, angry, fearful, erotic, and neutral prosodies (Ethofer et al., 2007). In response to erotic prosodies in both males and females, they found a significant interaction on brain response in the right superior temporal gyrus. This interaction was stronger for the erotic stimuli than for the other categories of stimuli.

3.1.6.1.4. Olfactory sexual stimuli. Several studies have used pheromones to study sexual behavior. Oliveira-Pinto et al. (2014) found that a progesterone and estrogen type of pheromone activated the anterior hypothalamus in heterosexual women in a gender-differentiated manner. However, Ciumas et al. (2009) found that a progesterone type of pheromone activated the anterior hypothalamus, whereas, the estrogen one activated the amygdala, piriform, and anterior insular cortex in heterosexual women. Olfactory networks, and not the anterior hypothalamus, processed the progesterone pheromone in homosexual women. However, congruently with heterosexual men, the anterior hypothalamus processed the estrogen pheromone in homosexual women (Berglund et al., 2006). Non-homosexual MTF transgenders show a pattern of activation away from their biological sex (Berglund et al., 2008). A group woman with congenital adrenal hyperplasia, a condition that can alter the development of primary and secondary sex characteristics, that rated themselves as heterosexual (8 individuals), bisexual (2 individuals), and homosexual (1 individual), show a brain response and functional connectivity like heterosexual typically developing women and reciprocal to heterosexual typically developing men (Ciumas et al., 2009). Taken together, studies show that olfactory cues might induce a brain response linked to sexual orientation, or to gender identity, but note that this does not necessarily mean that sexual arousal is induced by these olfactory stimuli.

3.1.6.1.5. Tactile sexual stimuli. A stimulus more likely to induce sexual arousal is tactile genital stimulation. The induction of sexual arousal with the genital tactile stimulation depends on the experimental setup in the laboratory. A handful of studies examined brain responses to tactile stimulation of the clitoral, vaginal, or cervical regions. Komisaruk et al. (2011) and Michels et al. (2010) focused on the representation of genital areas in the somatosensory cortex. Michels et al. (2010) used a block design of rest, lasting 18 s, alternating with the electrical stimulation of the clitoris, lasting 12 s. Each block was repeated 10 times. Although stimulation with short intervals might be arousing for some women, the authors reported null values of self-reported sexual arousal in women. These self-reported rating results showed that the electrical stimulation of the clitoris did not induce arousal in women. Komisaruk et al. (2011) also used a block design with a rest period of 30-second and a stimulation lasting 30 s, repeated 5 times. Unfortunately, they did not measure self-reported sexual arousal. These two studies were interested in the representation of genital stimulation on the somatosensory cortex and not exclusively designed to induce sexual arousal.

Georgiadis et al. (2009) presents a study that was designed to induce sexual arousal, in which clitoral tactile stimulation was applied for 2 min, repeated 2–5 times, eventually leading to orgasm. The participants were encouraged to enjoy the stimulation. Self-reported sexual arousal showed to be significantly elevated during stimulation. They found co-joint activation in the left primary and secondary somatosensory cortices and deactivation in the right amygdala, and on the ventral part of the temporal lobe. They found the involvement of the right posterior claustrum, ventral occipitotemporal region, and posterior lobe of the cerebellar vermis in men compared to women. In women compared to men they observed the involvement of the left parietal lobes, posterior parietal cortex, secondary somatosensory cortex, left primary motor cortex, right premotor cortex, and left precuneus. With the proper application of the experimental setup, the use of tactile genital stimuli is a promising method to induce sexual arousal during a neuroimaging scan.

Few studies investigated the role of non-genital visual sexual stimuli and erogenous zones in brain mapping. These zones show paradoxical response properties and can produce erotic feelings and sensations without any connections with genitalia. According to the theory of Ramachandran and Blakeslee (1998), erogenous zones can be mapped in correspondence to the SI cortex. To test this hypothesis, Turnbull et al. (2014) collected data about the Erogenous Zone Questionnaire in which participants assessed the ability of each body area to facilitate sexual arousal. According to the authors, excluding genitalia or perigenital areas, the mouth- lips complex, the neck, the nipple, and the breast were assessed as erogenous by women. According to Levin and Meston (2006), most women report that the stimulation of the nipple-breast complex can facilitate sexual arousal. According to Turnbull et al. (2014), the insula represents one of the best regions in which the elaboration of erogenous zones can be processed to facilitate sexual arousal. Insula is related to affiliative and emotional touch processing (Björnsdotter et al., 2009). Moreover, affective touch and eroticism showed specific gender patterns. Indeed, in women, differences in eroticism ratings between C-tactile fibers (neurons that innervate the human skin) velocities correlated positively with desire for sexual interaction (Bendas et al., 2017). Investigating the preference for the erogenous zones using the above-mentioned questionnaire could be helpful to disentangle the role played by several brain regions, or at least by the insula, in the first stages of sexual arousal in women.

3.1.6.2. Neuroimaging method. The most used neuroimaging method to study human sexual arousal is BOLD fMRI (Blood Oxygen Level Dependent). The fMRI provides a balance between the invasiveness, the spatial and the temporal resolution, becoming the dominant functional imaging modality used in the past decade. It is important to note that BOLD fMRI does not measure neuronal activity directly, but the signal

intensity changes related to blood oxygenation levels. In addition, one study has been conducted using PET (Georgiadis et al., 2006) and one using functional magnetic resonance spectroscopy (fMRS) (Kim et al., 2013).

Studies of brain response to sexual stimuli in women using fMRI have used a magnetic field strength of 1.5 or 3.0 T (Table 2). No studies have been conducted using a field strength of 7.0 T in women. A study with 7.0 T in men shows increased activation in the subnuclei of the thalamus (Walter et al., 2008a, b). However, the field strength differs between studies due to the increased availability of 3.0 T scanners. In the last fifteen years, the increase in the use of 3.0 T scanners for fMRI can find motivation in the improvement of Signal-to-Noise Ratio (SNR) that is proportional to the strength of the field. Indeed, SNR at 3.0 T is the double observed at 1.5 T (Edelstein et al., 1986; Dietrich et al., 2008). Despite this improvement, the effects of susceptibility for different materials, like air, water, and biological tissues, are proportional to the strength of the field and the resulting artifacts are more common at 3.0 T than 1.5 T (Bernstein et al., 2006). Similarly, another consequence of the effect of susceptibility at 3.0 T is the geometric distortion of the collected images in correspondence of the bones and air. Future studies, using a field strength of 7.0 T, might reveal detailed brain responses of subcortical regions, but the SNR and effects of susceptibility are important factors to consider. Besides differences in magnetic field strength, studies also analyze the fMRI data in various ways. For example, some studies show results of a whole-brain analysis with an uncorrected p-value of less than 0.001, whereas others show a corrected p-value of less than 0.01 (for an overview see Table 2).

Note that in the present review, only studies using standard univariate mapping are included. Additional analysis methods could help understand sexual arousal in the brain. For instance, representational similarity analysis (used by e.g., Wehrum-Osinsky et al., 2014) could reveal the synchronization of self-reported sexual arousal with brain activity. Another example is functional connectivity analysis (used by e.g., Lahnakoski et al., 2012) to reveal hubs (i.e., brain centers) for sexual arousal processing. In addition, multivariate methods are upcoming in the neuroimaging field (e.g., Kragel et al., 2018; Pouget et al., 2000; Wager and Lindquist, 2015) and could have a leading role in understanding the complex processing of sexual stimuli. For instance, van 't Hof et al., 2021 present a brain model that can distinguish, based on brain data, whether participants were presented with a sexual or a nonsexual affective stimulus. They present that this distinction is generalizable over participants, both men and women, and for different types of sexual stimuli, suggesting that sexual stimuli processing is a distinct mental brain event from general affective processing.

In addition, several studies do not report significantly lower BOLD response, even though they could be as important as the significantly higher BOLD response (van der Zwaag et al., 2016). Despite the methodological advance in the field of fMRI, studies showed a problem related to replicability and reliability (Zuo and Xing, 2014). Recently, the COBIDAS (Committee on Best Practices in Data Analysis and Sharing) guidelines, also included in a checklist (Nichols et al., 2016) for neuroimaging studies, helped to improve the replicability of the acquisition parameters and data analysis.

3.2. *Methodological considerations and future directions*

The present review showed a list of factors important to consider in neuroimaging studies about sexual stimuli responses in women. For some of the factors discussed, there were no neuroimaging studies in women and our recommendation is based on neuroimaging research in men or other types of research. Other factors have been investigated with neuroimaging in women, but the number of studies per factor is limited to perform a meta-analysis. It is therefore not possible to extract brain areas/networks directly related to every single factor. A summary of all participants' related influences on brain responses to sexual stimuli is presented in Fig. 2.

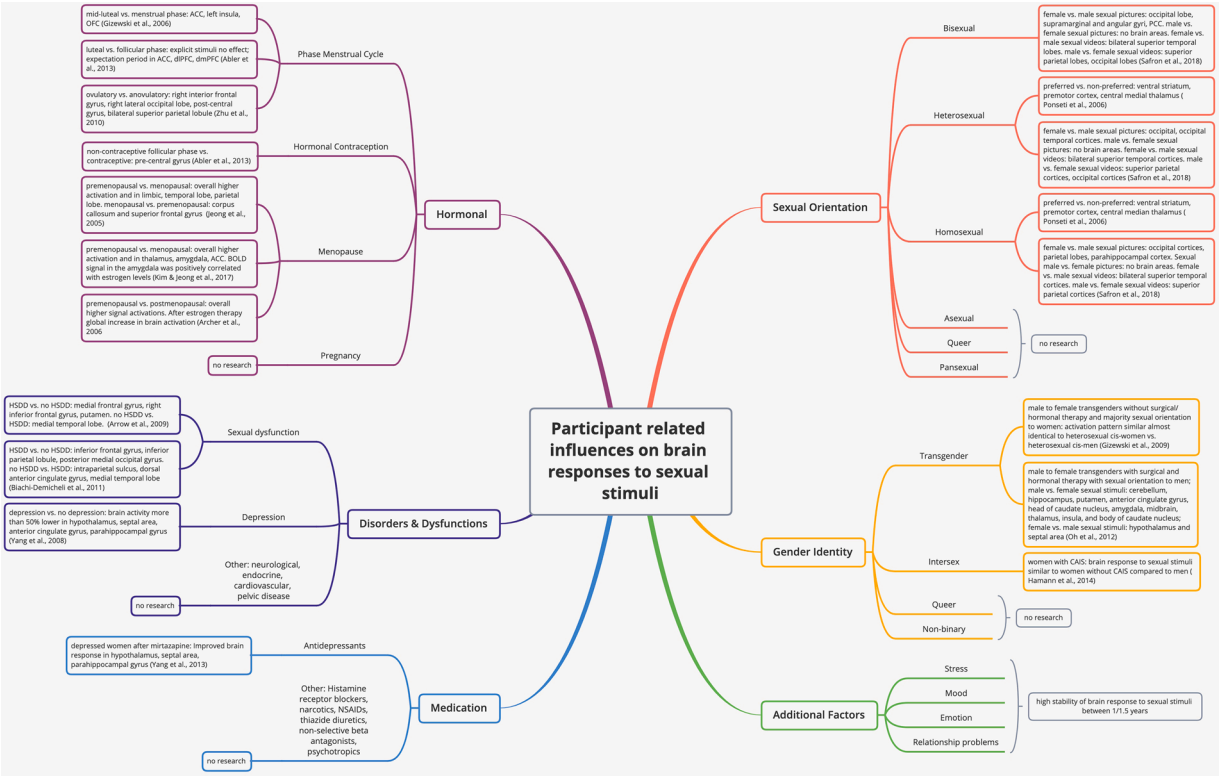

Fig. 2. Overview of participant-related influences on brain responses to sexual stimuli focused on studies that have included female participants. For more information, see the text in this article or the article referenced. ACC = anterior cingulate cortex, OFC = orbitofrontal cortex, dlPFC = dorsolateral prefrontal cortex, dmPFC = dorsomedial prefrontal cortex, PCC = posterior cingulate cortex, HSDD = hypo sexual desire disorder, CAIS = complete androgen insensitivity syndrome.

Despite the interest for the brain correlates of sexual stimuli in women, most of the theoretical models can be conceived as male-based (Stoléru et al., 2012; Georgiadis and Kringelbach, 2012) or clinical-based when their focus is women-specific (Basson, 2000). Disentangling the methodological factors relevant to optimize the brain response to sexual stimuli in women, might improve our knowledge about the "sexual-behavioral-noise" that represents one of the typical features of women's sexuality (Georgiadis, 2015). One of the most salient characteristics of women's sexuality is the cyclical pattern that influences, at several levels, the sexual response. Noteworthy, the male sexual response has been conceived as a linear process, in which the phases, culminating in the ejaculation, represent a set of serial processes.

One of the theoretical models of sexual behavior, based on human neuroimaging data, adheres to the sexual response cycle, and theorizes sexual pleasure as the core of sexual behavior (Georgiadis et al., 2012). Sexual pleasure shows a basic cyclic structure, like other reward-based behaviors, with the presence of motivation-consummation-satiety (or wanting- liking-inhibition, as called by the authors). These three different stages found a corresponding set of underlying brain regions. Given the lack of homogeneous results, it is not possible to infer a consistent brain pattern, or a network, underlying the stages of the sexual pleasure cycle in women. In the same way, it was not possible to perform a meta-analysis to study the contribution of brain regions in the different stages of sexual response. Indeed, the publication bias, as assessed using Egger's test (Egger et al., 1997), is dependent on the number of the studies included in a meta-analysis (Moreno et al., 2009). There are not enough studies for any of the factors discussed in this paper to conduct separate factor-related meta-analyses.

The purpose of the present review is to assess the principal factor that can affect the results of neuroimaging studies of sexual response in women. For this reason, we do not propose a theoretical model, but we aim at highlighting the methodological decisions to lead to a better understanding of the stages of the sexual pleasure cycle. Neuroimaging techniques, like fMRI, allow studying the involvement of subcortical brain structures, relevant for the neuroendocrine and autonomic response. As above described, one of the issues with fMRI studies is the replicability and the control of the artifacts that increase with the strength of the magnetic field. As for the neuroimaging methods, subcortical anatomy is well visualized even at 1.5 T and robust effects can be obtained at 3 T. Although 7 T is more susceptible to artifacts, it also improves the signal-to-noise ratio and therefore increases spatial resolution. It is therefore useful in detecting small subcortical regions. Using Electroencephalography (EEG) or, the less common Magnetoencephalography (MEG- Ziogas et al., 2020) allows studying the temporal pattern of brain response, mainly, limited at cortical level. At the same time, EEG and MEG (Costa et al., 2003) can be helpful tools to study the dynamic involvement of brain districts during the initial stages of sexual stimuli processing and genital response (Ponseti et al., 2009). Noteworthy, a recently published meta-analysis about neuroelectric correlates of human sexual behavior did not consider the specificity of women's response, highlighting only the role played by gender differences (Ziogas et al., 2020).

The selection of participants can affect the results and the level of the conclusion. It is particularly relevant for fMRI studies, which do usually not involve a large sample (Turner et al., 2018). To control for factors that can improve inter-individual variability, we recommend performing a neuropsychiatric interview, a sexual anamnestic interview, to exclude or, at least, include participants. Moreover, we recommend specifying and reporting the use of medication, OCs, and the phase of the menstrual cycle. Although additional factors, like stress or mood, do not seem to affect brain response to sexual stimuli on a group level (Wehrum-Osinsky et al., 2014), it is important to consider these factors when analyzing at an individual level.

The first stage of the "sexual pleasure cycle" is the wanting phase, which appears to be related to sexual desire and sexual interest (Georgiadis and Kringelbach, 2012; Georgiadis et al., 2012). At this point of the cycle, distal sexual stimuli, like auditory or tactile stimuli can induce sexual desire. According to Laan et al. (1994; 1995), it is not possible to separate desire from sexual arousal. In this case, it is conceived as a psychological dimension that is relevant during these stages of sexual response. Sexual desire, assessed by questionnaires or psychometric tests can represent a useful measure to be correlated to fMRI (or other functional techniques) results. To evoke arousal and stimulate sexual interest, it is important to match the sexual orientation and content of the stimuli and consider the duration of the VSS and the interstimulus interval. During the last years, several studies investigated the role played by visual focused attention to sexual stimuli (Carvalho et al., 2017). This has been possible using the collection of eye movements like fixations that showed a specific dwelling pattern for genital, non-genital body regions, as depicted in the stimuli (Cera et al., 2020). The collection of eye movement can be helpful when controlling the sexual interest VSS. Interestingly, using functional connectivity analysis, it is possible to study the role played by regions, like insula or ACC, at the different stages of sexual response. Moreover, these types of data analysis techniques allow at studying, in the case of the seed-based FC, the variation of target regions during VSS.

During the second stage of the "sexual pleasure cycle", (liking- Georgiadis and Kringelbach, 2012), participants can show sustained sexual response. The application of the sexual self-stimulation task, or the genital stimulation performed by the partner, can be helpful to map the genital regions that are stimulated and study the role of brain regions, like insula that play a key role in the processing of intimate touch (Björnsdotter et al., 2009). Therefore, during the sexual self-stimulation task there is a large probability that participants might be involved in sexual fantasies and thoughts, creating prospective sexual memories, or retrieving past autobiographical memories (Nobre and Pinto-Gouveia, 2008).

According to previous studies on male participants (Ferretti et al., 2005; Cera et al., 2020), the cerebral pattern underlying the onset of the genital response is different from the pattern observed during sustained genital response. In the late liking stage, the participant should be able to reach orgasm. Ponseti et al. (2009) collected penile tumescence and EEG to study brain potential related to erection. EEG experimental setup permits the collection of genital psychophysiological measures and allows to control of the genital plateau phase in women. Reaching orgasm during VSS or photo stimuli is less common. Sexual self-stimulation, or the stimulation performed by a partner, can allow reaching the orgasm in women. In this case, it is recommendable to control or limit body movement that might affect fMRI data.

Most studies took into consideration the brain correlates in healthy young women. The average age of participants in neuroimaging studies to sexual arousal discussed in this study is 27.5. As listed above and despite the lack of evidence, a set of studies investigated cerebral correlates of sexual response during the menstrual cycle. The menstrual cycle affects the processing of sexual interest, desire, and arousal. In this way, the brain and behavioral responses of the participant might be affected by the different phases of the menstrual cycle (Abler et al., 2013). Conversely, during menopause, these changes are not present in women, which might allow a change in the pattern of sexual response in women. These changes go together with the behavioral and corresponding alteration in the brain, occurring during normal aging.

After orgasm, the last stage is composed of the refractory period and the learning about the hedonic aspects of the pleasure deriving from the sexual stimulation. This stage occurs also in the incomplete sexual response and could thus follow a sexual stimulus. During the refractory stage, it is possible to question the participant about the experience of the arousal. When self-sexual stimulation has been applied, and the orgasm reached, we can suggest recording cerebral activity during the refractory period and then question the participant about the experience of arousal and the orgasm. An overview recommendation about the methodological decisions related to each stage of the ''sexual pleasure cycle'' can be found in Table 3.

Table 3
Process to control and recommendation about the methodological decisions related to each stage of the sexual response cycle, as described by Georgiadis and Kringelbach (2012).

Stage of sexual cycle	Process to control	Recommendations
Wanting	Sexual desire	Measure the sexual desire using psychometric tests or questionnaire EEG experiment Study of functional connectivity of specific brain regions (i.e., insula, ACC)
	Cognitive appraisal of the sexual stimuli	Matching between the sexual orientation of the participants and the content of the stimulus
	Focused attention to stimuli	Studying the focus attention by means of eye-tracker
Liking	Erogenous zone, as displayed in the stimuli	Measure the preference for the erogenous zones using a questionnaire Eye tracker to study the specific dwelling of fixations
	Sexual arousal elicited by self-sexual stimulation or sexual arousal elicited by genital stimulation performed by partner	Control sexual fantasies and thoughts
	Sexual arousal (genital arousal and self-reported arousal)	Multimodal brain imaging (EEG and genital psychophysiological measures)
	Orgasm	Limit or control body movements
Learning	Refractory period	Control the duration of the refractory period
	Hedonic appraisal and learning	Questionnaire about the experience of arousal /orgasm Study the cerebral dynamics underlying this period

Neuroimaging studies about sexual arousal in women lead to a better insight into the underlying mechanisms of sexual arousal. Understanding the neurophysiological correlates of sexual arousal is important for both clinical as well as theoretical reasons. From a clinical perspective, a better understanding of sexual arousal could lead to better treatment and intervention of sexual disorders and diseases. Including more women is interesting for women-specific sexual disorders, for instance, genito-pelvic pain/penetration disorder. Theoretically, neuroimaging research about sexual arousal in women could lead to a better insight into cognitive knowledge and reproductive behavior, leading to an updated and extensive neuroscientific model of sexual arousal. Hopefully, with the overview of possible factors and methodologies presented here, more women will be included in future neuroimaging studies on sexual arousal, and a brain model of sexual stimuli processing that not solely includes male data will be proposed.

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References

Abler, B., Kumpfmüller, D., Grön, G., Walter, M., Stingl, J., Seeringer, A., 2013. Neural correlates of erotic stimulation under different levels of female sexual hormones. PLoS One 8 (2). https://doi.org/10.1371/journal.pone.0054447.

Ali, M.M., Cleland, J., Shah, I.H., Ali, M., Al, E., 2012. Causes and Consequences of Contraceptive Discontinuation: Evidence from 60 Demographic and Health Surveys WHO Regional Office for the Eastern Mediterranean, Cairo, Egypt WHO Library Cataloguing In-publication Data Causes and Consequences of Contraceptive. World Health Organization.

American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders, 5th. American Psychiatric Press, Arlington, VA.

Archer, J.S., Love-Geffen, T.E., Herbst-Damm, K.L., Swinney, D.A., Chang, J.R., 2006. Effect of estradiol versus estradiol and testosterone on brain-activation patterns in postmenopausal women. Menopause 13 (3), 528–537. https://doi.org/10.1097/01.gme.0000188737.46746.cd.

Arnow, B.A., Millheiser, L., Garrett, A., Lake Polan, M., Glover, G.H., Hill, K.R., et al., 2009. Women with hypoactive sexual desire disorder compared to normal females: a functional magnetic resonance imaging study. Neuroscience 158 (2), 484–502. https://doi.org/10.1016/j.neuroscience.2008.09.044.

Aslan, G., Aslan, D., Kizilyar, A., Ispahi, Ç., Esen, A., 2005. A prospective analysis of sexual functions during pregnancy. Int. J. Impot. Res. 17 (2), 154–157. https://doi.org/10.1038/sj.ijir.3901288.

Avis, N.E., Stellato, R., Crawford, S., Johannes, C., Longcope, C., 2000. Is there an association between menopause status and sexual functioning? Menopause 7 (5), 297–309. https://doi.org/10.1097/00042192-200007050-00004.

Bala, A., Nguyen, H.M.T., Hellstrom, W.J.G., 2018. Post-SSRI sexual dysfunction: a literature review. Sex. Med. Rev. 6 (1), 29–34. https://doi.org/10.1016/j.sxmr.2017.07.002.

Baldwin, D.S., Manson, C., Nowak, M., 2015. Impact of antidepressant drugs on sexual function and satisfaction. CNS Drugs 29 (11), 905–913. https://doi.org/10.1007/s40263-015-02943.

Basson, R., 2000. The female sexual response: a different model. J. Sex Marital Ther. 26 (1), 51–65.

Behnia, B., Heinrichs, M., Bergmann, W., Jung, S., Germann, J., Schedlowski, M., et al., 2014. Differential effects of intranasal oxytocin on sexual experiences and partner interactions in couples. Horm. Behav. 65 (3), 308–318.

Bendas, J., Georgiadis, J.R., Ritschel, G., Olausson, H., Weidner, K., Croy, I., 2017. C-tactile mediated erotic touch perception relates to sexual desire and performance in a gender-specific way. J. Sex. Med. 14 (5), 645–653.

Berglund, H., Lindström, P., Savic, I., 2006. Brain response to putative pheromones in lesbian women. Proc. Natl. Acad. Sci. U. S. A. 103 (21), 8269–8274. https://doi.org/10.1073/pnas.0600331103.

Berglund, H., Lindström, P., Dhejne-Helmy, C., Savic, I., 2008. Male-to-female transsexuals show sex-atypical hypothalamus activation when smelling odorous steroids. Cereb. Cortex 18 (8), 1900–1908. https://doi.org/10.1093/cercor/bhm216.

Bernstein, M.A., Huston III, J., Ward, H.A., 2006. Imaging artifacts at 3.0 T. J. Mag. Resonance Imaging 24 (4), 735–746.

Bianchi-Demicheli, F., Cojan, Y., Waber, L., Recordon, N., Vuilleumier, P., Ortigue, S., 2011. Neural bases of hypoactive sexual desire disorder in women: an event-related fMRI study. J. Sex. Med. 8 (9), 2546–2559. https://doi.org/10.1111/j.1743-6109.2011.02376.x.

Björnsdotter, M., Löken, L., Olausson, H., Vallbo, Å., Wessberg, J., 2009. Somatotopic organization of gentle touch processing in the posterior insular cortex. J. Neurosci. 29 (29), 9314–9320.

Bogaert, A.F., 2004. Asexuality: prevalence and associated factors in a national probability sample. J. Sex Res. 41 (3), 279–287. https://doi.org/10.1080/00224490409552235.

Borg, C., de Jong, P.J., Georgiadis, J.R., 2014a. Subcortical BOLD responses during visual sexual stimulation vary as a function of implicit porn associations in women. Soc. Cogn. Affect. Neurosci. 9 (2), 158–166. https://doi.org/10.1093/scan/nss117.

Borg, C., Georgiadis, J.R., Renken, R.J., Spoelstra, S.K., Schultz, W.W., De Jong, P.J., 2014b. Brain processing of visual stimuli representing sexual penetration versus core and animal-reminder disgust in women with lifelong vaginismus. PLoS One 9 (1). https://doi.org/10.1371/journal.pone.0084882.

Brom, M., Laan, E., Everaerd, W., Spinhoven, P., Trimbos, B., Both, S., 2016. The effect of a dopamine antagonist on conditioning of sexual arousal in women. Psychopharmacology 233 (7), 1179–1189. https://doi.org/10.1007/s00213-015-4201-x.

Brotto, L.A., Yule, M.A., 2011. Physiological and subjective sexual arousal in selfidentified asexual women. Arch. Sex. Behav. 40 (4), 699–712. https://doi.org/10.1007/s10508-010-9671-7.

Bruce, D., Rymer, J., 2009. Symptoms of the menopause. Best Pract. Res. 23 (1), 25–32. https://doi.org/10.1016/j.bpobgyn.2008.10.002.

Caruso, S., Agnello, C., Intelisano, G., Farina, M., Di Mari, L., Cianci, A., 2004. Sexual behavior of women taking low-dose oral contraceptive containing 15 μg ethinylestradiol/60 μg gestodene. Contraception 69 (3), 237–240.

Caruso, S., Sareri, M.I., Agnello, C., Romano, M., Presti, L.L., Malandrino, C., Cianci, A., 2011. Conventional vs. extended-cycle oral contraceptives on the quality of sexual life: comparison between two regimens containing 3 mg drospirenone and 20 μg ethinyl estradiol. J. Sex. Med. 8 (5), 1478–1485.

Caruso, S., Agnello, C., Malandrino, C., Lo Presti, L., Cicero, C., Cianci, S., 2014. Do hormones influence women's sex? Sexual activity over the menstrual cycle. J. Sex. Med. 11 (1), 211–221. https://doi.org/10.1111/jsm.12348.

Carvalho, J., Štulhofer, A., Vieira, A.L., Jurin, T., 2015. Hypersexuality and high sexual desire: exploring the structure of problematic sexuality. J. Sex. Med. 12 (6), 1356–1367.

Carvalho, J., Pereira, R., Barreto, D., Nobre, P.J., 2017. The effects of positive versus negative mood states on attentional processes during exposure to erotica. Arch. Sex. Behav. 46 (8), 2495–2504.

Cera, N., Castelhano, J., Oliveira, C., Carvalho, J., Gomes, A.L.Q., Peixoto, M.M., et al., 2020. The role of anterior and posterior insula in male genital response and in visual attention: an exploratory multimodal fMRI study. Sci. Rep. 10 (1), 1–11.

Cera, N., Vargas-Caceres, S., Oliveira, C., Monteiro, J., Branco, D., Pignatelli, D., Rebelo, S., 2021. How relevant is the systemic oxytocin concentration for human sexual behavior? A systematic review. Sex. Med. 9 (4), 100370.

Chivers, M.L., Seto, M.C., Lalumière, M.L., Laan, E., Grimbos, T., 2010. Agreement of self-reported and genital measures of sexual arousal in men and women: a meta-analysis. Arch. Sex. Behav. 39 (1), 5–56. https://doi.org/10.1007/s10508-009-9556-9.

Ciumas, C., Hirschberg, A.L., Savic, I., 2009. High fetal testosterone and sexually dimorphic cerebral networks in females. Cereb. Cortex 19 (5), 1167–1174. https://doi.org/10.1093/cercor/bhn160.

Clayton, A.H., Hamilton, D.V., 2010. Female sexual dysfunction. Psychiatr. Clin. North Am. 33 (2), 323–338. https://doi.org/10.1016/j.psc.2010.01.011.

Clayton, A., Ramamurthy, S., 2008. The impact of physical illness on sexual dysfunction. Adv. Psychosom. Med. 29, 70–88. https://doi.org/10.1159/000126625.

Cohen, S., Kühn, K.U., Bender, S., Erfurth, A., Gastpar, M., Murafi, A., et al., 2007. Sexual impairment in psychiatric inpatients: focus on depression. Pharmacopsychiatry 40 (2), 58–63. https://doi.org/10.1055/s-2007-970143.

Coiro, P., Pollak, D.D., 2019. Sex and gender bias in the experimental neurosciences: the case of the maternal immune activation model. Transl. Psychiatry 9 (1). https://doi.org/10.1038/s41398-019-0423-8.

Costa, M., Braun, C., Birbaumer, N., 2003. Gender differences in response to pictures of nudes: a magnetoencephalographic study. Biol. Psychol. 63 (2), 129–147.

Daniels, K., Daugherty, J., Jones, J., 2014. Current contraceptive status among women aged 15–44: United States, 2011–2013. NCHS Data Brief 173, 1–8.

Dietrich, O., Reiser, M.F., Schoenberg, S.O., 2008. Artifacts in 3-T MRI: physical background and reduction strategies. Eur. J. Radiol. 65 (1), 29–35.

Edelstein, W.A., Glover, G.H., Hardy, C.J., Redington, R.W., 1986. The intrinsic signal-to-noise ratio in NMR imaging. Magn. Reson. Med. 3 (4), 604–618.

Egger, M., Smith, G.D., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by a simple, graphical test. BMJ 315 (7109), 629–634.

Ethofer, T., Wiethoff, S., Anders, S., Kreifelts, B., Grodd, W., Wildgruber, D., 2007. The voices of seduction: cross-gender effects in processing of erotic prosody. Soc. Cogn. Affect. Neurosci. 2 (4), 334–337.

Exton, N.G., Chau Truong, T., Exton, M.S., Wingenfeld, S.A., Leygraf, N., Saller, B., et al., 2000. Neuroendocrine response to film-induced sexual arousal in men and women. Psychoneuroendocrinology 25 (2), 187–199. https://doi.org/10.1016/S0306-4530(99)00049-9.

Feldman, S., Ammar, W., Lo, K., Trepman, E., Van Zuylen, M., Etzioni, O., 2019. Quantifying sex bias in clinical studies at scale with automated data extraction. JAMA Netw. Open 2 (7), 1–14. https://doi.org/10.1001/jamanetworkopen.2019.6700.

Ferretti, A., Caulo, M., Del Gratta, C., Di Matteo, R., Merla, A., Montorsi, F., et al., 2005. Dynamics of male sexual arousal: distinct components of brain activation revealed by fMRI. Neuroimage 26 (4), 1086–1096.

Frohlich, P.F., Meston, C.M., 2000. Evidence that serotonin affects female sexual functioning via peripheral mechanisms. Physiol. Behav. 71 (3–4), 383–393. https://doi.org/10.1016/S0031-9384(00)00344-9.

Georgiadis, J.R., 2015. Functional neuroanatomy of human cortex cerebri in relation to wanting sex and having it. Clin. Anat. 28 (3), 314–323.

Georgiadis, J.R., Kringelbach, M.L., 2012. Progress in neurobiology the human sexual response cycle: brain imaging evidence linking sex to other pleasures. Prog. Neurobiol. 98 (1), 49–81. https://doi.org/10.1016/j.pneurobio.2012.05.004.

Georgiadis, Janniko R., Kortekaas, R., Kuipers, R., Nieuwenburg, A., Pruim, J., Reinders, A.A.T.S., Holstege, G., 2006. Regional cerebral blood flow changes associated with clitorally induced orgasm in healthy women. Eur. J. Neurosci. 24 (11), 3305–3316. https://doi.org/10.1111/j.1460-9568.2006.05206.x.

Georgiadis, Janniko R., Reinders, A.A.T.S., Paans, A.M.J., Renken, R., Kortekaas, R., 2009. Men versus women on sexual brain function: prominent differences during tactile genital stimulation, but not during orgasm. Hum. Brain Mapp. 30 (10), 3089–3101. https://doi.org/10.1002/hbm.20733.

Georgiadis, J.R., Kringelbach, M.L., Pfaus, J.G., 2012. Sex for fun: a synthesis of human and animal neurobiology. Nat. Rev. Urol. 9 (9), 486–498.

Gillath, O., Canterberry, M., 2012. Neural correlates of exposure to subliminal and supraliminal sexual cues. Soc. Cogn. Affect. Neurosci. 7 (8), 924–936. https://doi.org/10.1093/scan/nsr065.

Gizewski, E.R., Krause, E., Karama, S., Baars, A., Senf, W., Forsting, M., 2006. There are differences in cerebral activation between females in distinct menstrual phases during viewing of erotic stimuli: a fMRI study. Exp. Brain Res. 174 (1), 101–108. https://doi.org/10.1007/s00221-006-0429-3.

Gizewski, E.R., Krause, E., Schlamann, M., Happich, F., Ladd, M.E., Forsting, M., Senf, W., 2009. Specific cerebral activation due to visual erotic stimuli in male-to-female transsexuals compared with male and female controls: an fMRI study. J. Sex. Med. 6 (2), 440–448. https://doi.org/10.1111/j.1743-6109.2008.00981.x.

Graham, C.A., Janssen, E., Sanders, S.A., 2000. Effects of fragrance on female sexual arousal and mood across the menstrual cycle. Psychophysiology 37 (1), 76–84. https://doi.org/10.1017/S0048577200981964.

Hamann, S., Stevens, J., Vick, J.H., Bryk, K., Quigley, C.A., Berenbaum, S.A., Wallen, K., 2014. Brain responses to sexual images in 46, XY women with complete androgen insensitivity syndrome are female-typical. Horm. Behav. 66 (5), 724–730. https://doi.org/10.1016/j.yhbeh.2014.09.013.

Hamilton, L.D., Rellini, A.H., Meston, C.M., 2008. Cortisol, sexual arousal, and affect in response to sexual stimuli. J. Sex. Med. 5 (9), 2111–2118. https://doi.org/10.1111/j.1743-6109.2008.00922.x.

Holdcroft, A., 2007. Gender bias in research: how does it affect evidence-based medicine? J. R. Soc. Med. 100 (1), 2–3. https://doi.org/10.1258/jrsm.100.1.2.

Hoyle, C.H.V., Robson, T., Whitley, K., Burnstock, G., Stones, R.W., 1996. Innervation of vasculature and microvasculature of the human vagina by NOS and neuropeptidecontaining nerves. J. Anat. 188 (3), 633–644.

Janssen, E., Prause, N., Romine, R.S., Raymond, N., MacDonald III, A., Coleman, E., Miner, M.H., 2020. Sexual responsivity and the effects of negative mood on sexual arousal in hypersexual men who have sex with men (MSM). J. Sex. Med. 17 (9), 1751–1760.

Jeong, G.W., Park, K., Youn, G., Kang, H.K., Kim, H.J., Seo, J.J., Ryu, S.B., 2005. Assessment of cerebrocortical regions associated with sexual arousal in premenopausal and menopausal women by using BOLD-based functional MRI. J. Sex. Med. 2 (5), 645–651. https://doi.org/10.1111/j.1743-6109.2005.00134.x.

Kim, G.W., Jeong, G.W., 2014. A comparative study of brain activation patterns associated with sexual arousal between males and females using 3.0-T functional magnetic resonance imaging. Sex. Health 11 (1), 11–16. https://doi.org/10.1071/SH13127.

Kim, G.W., Jeong, G.W., 2017. Menopause-related brain activation patterns during visual sexual arousal in menopausal women: an fMRI pilot study using time-course analysis. Neuroscience 343, 449–458. https://doi.org/10.1016/j.neuroscience.2016.12.010.

Kim, T.H., Kang, H.K., Jeong, G.W., 2013. Assessment of brain metabolites change during visual sexual stimulation in healthy women using functional MR spectroscopy. J. Sex. Med. 10 (4), 1001–1011. https://doi.org/10.1111/jsm.12057.

Klein, S., Kruse, O., Markert, C., León, I.T., Strahler, J., Stark, R., 2020. Subjective reward value of visual sexual stimuli is coded in human striatum and orbitofrontal cortex. Behav. Brain Res. 393, 112792.

Komisaruk, B.R., Wise, N., Frangos, E., Liu, W.-C., Allen, K., Brody, S., 2011. Women's clitoris, vagina, and cervix mapped on the sensory cortex: fMRI evidence. J. Sex. Med. 8 (10), 2822–2830. https://doi.org/10.1111/j.1743-6109.2011.02388.x.

Koukounas, E., Over, R., 1997. Male sexual arousal elicited by film and fantasy matched in content. Aust. J. Psychol. 49 (1), 1–5. https://doi.org/10.1080/00049539708259843.

Koutouvidis, N., Pratikakis, M., Fotiadou, A., 1999. The use of mirtazapine in a group of 11 patients following poor compliance to selective serotonin reuptake inhibitor treatment due to sexual dysfunction. Int. Clin. Psychopharmacol. 14 (4), 253–255.

Kowalewska, E., Grubbs, J.B., Potenza, M.N., Gola, M., Draps, M., Kraus, S.W., 2018. Neurocognitive mechanisms in compulsive sexual behavior disorder. Curr. Sex. Health Rep. 10 (4), 255–264.

Kragel, P.A., Koban, L., Barrett, L.F., Wager, T.D., 2018. Representation, pattern information, and brain signatures: from neurons to neuroimaging. Neuron 99 (2), 257–273. https://doi.org/10.1016/j.neuron.2018.06.009.

Krüger, T.H.C., Keil, L., Jung, S., Kahl, K.G., Wittfoth, M., Leeners, B., Hartmann, U., 2018. Lack of increase in sexual drive and function after dopaminergic stimulation in women. J. Sex Marital Ther. 44 (1), 61–72. https://doi.org/10.1080/0092623X.2017.1318797.

Laan, E., Everaerd, W., Bellen, G., Hanewald, G., 1994. Women's sexual and emotional responses to male- and female-produced erotica. Arch. Sex. Behav. 23 (2), 153–169.

Laan, E., Everaerd, W., van der Velde, J., Geer, J.H., 1995. Determinants of subjective experience of sexual arousal in women: feedback from genital arousal and erotic stimulus content. Psychophysiology 32 (5), 444–451.

Lahnakoski, J.M., Glerean, E., Salmi, J., Jääskeläinen, I.P., Sams, M., Hari, R., Nummenmaa, L., 2012. Frontiers in human neuroscience 6 (233).

Leiblum, S.R., Koochaki, P.E., Rodenberg, C.A., Barton, I.P., Rosen, R.C., 2006. Hypoactive sexual desire disorder in postmenopausal women: US results from the Women's International Study of Health and Sexuality (WISHeS). Menopause 13 (1), 46–56. https://doi.org/10.1097/01.gme.0000172596.76272.06.

Levin, R., Meston, C., 2006. Nipple/breast stimulation and sexual arousal in young men and women. J. Sex. Med. 3 (3), 450–454.

Lindau, S.T., Schumm, L.P., Laumann, E.O., Levinson, W., O'Muircheartaigh, C.A., Waite, L.J., 2007. A study of sexuality and health among older adults in the United States. N. Engl. J. Med. 357 (8), 762–774. https://doi.org/10.1056/NEJMoa067423.

Lu, W., Guo, W., Cui, D., Dong, K., Qiu, J., 2019. Effect of sex hormones on brain connectivity related to sexual function in perimenopausal women: a resting-state fMRI functional connectivity study. J. Sex. Med. 16 (5), 711–720. https://doi.org/10.1016/j.jsxm.2019.03.004.

Markert, C., Klein, S., Strahler, J., Kruse, O., Stark, R., 2021. Sexual incentive delay in the scanner: Sexual cue and reward processing, and links to problematic porn consumption and sexual motivation. Behavioral Addictions 10 (1), 65–76.

Masters, W.H., Johnson, V.E., 1966. Human sexual response. Little, Brown and Company, New York.

McCabe, C., Mishor, Z., 2011. Antidepressant medications reduce subcortical-cortical resting-state functional connectivity in healthy volunteers. NeuroImage 57 (4), 1317–1323. https://doi.org/10.1016/j.neuroimage.2011.05.051.

Meston, C.M., Stanton, A.M., 2019. Understanding sexual arousal and subjective– genital arousal desynchrony in women. Nat. Rev. Urol. 16 (2), 107–120. https://doi.org/10.1038/s41585-018-0142-6.

Michels, L., Mehnert, U., Boy, S., Schurch, B., Kollias, S., 2010. The somatosensory representation of the human clitoris: an fMRI study. NeuroImage 49 (1), 177–184. https://doi.org/10.1016/j.neuroimage.2009.07.024.

Mitricheva, E., Kimura, R., Logothetis, N.K., Noori, H.R., 2019. Neural substrates of sexual arousal are not sex dependent. Proc. Natl. Acad. Sci. 116 (31), 15671–15676. https://doi.org/10.1073/pnas.1904975116.

Moreno, S.G., Sutton, A.J., Ades, A.E., Stanley, T.D., Abrams, K.R., Peters, J.L., Cooper, N.J., 2009. Assessment of regression-based methods to adjust for publication bias through a comprehensive simulation study. BMC Med. Res. Methodol. 9 (1), 2. https://doi.org/10.1186/1471-2288-9-2.

Nichols, T.E., Das, S., Eickhoff, S.B., Evans, A.C., Glatard, T., Hanke, M., Kriegeskorte, N., Milham, M.P., Poldrack, R.A., Poline, J.-B., Proal, E., Thirion, B., Van Essen, D.C., White, T., Yeo, B.T.T., 2016. Best Practices in Data Analysis and Sharing in Neuroimaging Using MRI. bioRxiv. https://doi.org/10.1101/054262.

Nobre, P.J., Pinto-Gouveia, J., 2008. Cognitions, emotions, and sexual response: analysis of the relationship among automatic thoughts, emotional responses, and sexual arousal. Arch. Sex. Behav. 37 (4), 652–661.
Nummenmaa, L., Hietanen, J.K., Santtila, P., Hyönä, J., 2012. Gender and visibility of sexual cues influence eye movements while viewing faces and bodies. Archiv. Sexual Behav. 41 (6), 1439–1451.
O'Leary, P., Boyne, P., Flett, P., Beilby, J., James, I., 1991. Longitudinal assessment of changes in reproductive hormones during normal pregnancy. Clin. Chem. 37 (5), 667–672. https://doi.org/10.1016/B978-0-12-805299-0.00040-3.
Oh, S.K., Kim, G.W., Yang, J.C., Kim, S.K., Kang, H.K., Jeong, G.W., 2012. Brain activation in response to visually evoked sexual arousal in male-to-female transsexuals: 3.0 tesla functional magnetic resonance imaging. Korean J. Radiol. 13 (3), 257–264. https://doi.org/10.3348/kjr.2012.13.3.257.
Oliveira-Pinto, A.V., Santos, R.M., Coutinho, R.A., Oliveira, L.M., Santos, G.B., Alho, A.T. L., et al., 2014. Sexual dimorphism in the human olfactory bulb: females have more neurons and glial cells than males. PLoS One 9 (11). https://doi.org/10.1371/journal.pone.0111733.
Parada, M., Gérard, M., Larcher, K., Dagher, A., Binik, Y.M., 2016. Neural representation of subjective sexual arousal in men and women. J. Sex. Med. 13 (10), 1508–1522. https://doi.org/10.1016/j.jsxm.2016.08.008.
Parada, M., Gérard, M., Larcher, K., Dagher, A., Binik, Y.M., 2018. How hot are they? Neural correlates of genital arousal: an infrared thermographic and functional magnetic resonance imaging study of sexual arousal in men and women. J. Sex. Med. 15 (2), 217–229. https://doi.org/10.1016/j.jsxm.2017.12.006.
Park, K., Kang, H.K., Seo, J.J., Kim, H.J., Ryu, S.B., Jeong, G.W., 2001. Bloodoxygenation-level-dependent functional magnetic resonance imaging for evaluating cerebral regions of female sexual arousal response. Urology 57 (6), 1189–1194. https://doi.org/10.1016/S0090-4295(01)00992-X.
Petitti, D.B., 2003. Combination estrogen – progestin oral contraceptives. N. Engl. J. Med. 349 (15), 1443–1450.
Pfaus, J.G., 2009. Pathways of sexual desire. J. Sex. Med. 6 (6), 1506–1533. https://doi.org/10.1111/j.1743-6109.2009.01309.x.
Poeppl, T.B., Langguth, B., Rupprecht, R., Safron, A., Bzdok, D., Laird, A.R., Eickhoff, S. B., 2016. The neural basis of sex differences in sexual behavior: a quantitative meta-analysis. Front. Neuroendocrinol. 43, 28–43. https://doi.org/10.1016/j.yfrne.2016.10.001.
Polan, M.L., Desmond, J.E., Banner, L.L., Pryor, M.R., McCallum, S.W., Atlas, S.W., et al., 2003. Female sexual arousal: a behavioral analysis. Fertil. Steril. 80 (6), 1480–1487. https://doi.org/10.1016/S0015-0282(03)02210-6.
Ponseti, J., Bosinski, H.A., Wolff, S., Peller, M., Jansen, O., Mehdorn, H.M., et al., 2006. A functional endophenotype for sexual orientation in humans. NeuroImage 33 (3), 825–833. https://doi.org/10.1016/j.neuroimage.2006.08.002.
Ponseti, J., Kropp, P., Bosinski, H.A., 2009. Brain potentials related to the human penile erection. Int. J. Impot. Res. 21 (5), 292–300.
Pouget, A., Dayan, P., Zemel, R., 2000. Information processing with population codes. Nat. Rev. Neurosci. 1 (11), 125–132.
Ramachandran, V.S., Blakeslee, S., 1998. Phantoms in the Brain: Human Nature and the Architecture of the Mind. Fourth Estate.
Robinson, V.C., 2015. Support for the hypothesis that sexual breast stimulation is an ancestral practice and a key to understanding women's health. Med. Hypotheses 85 (6), 976–985.
Safron, A., Klimaj, V., Sylva, D., Rosenthal, A.M., Li, M., Walter, M., Bailey, J.M., 2018. Neural correlates of sexual orientation in heterosexual, bisexual, and homosexual women. Sci. Rep. 8 (1), 1–14. https://doi.org/10.1038/s41598017-18372-0.
Sanders, S.A., Graham, C.A., Bass, J.L., Bancroft, J., 2001. A prospective study of the effects of oral contraceptives on sexuality and well-being and their relationship to discontinuation. Contraception 64 (1), 51–58. https://doi.org/10.1016/S0010-7824(01)00218-9.
Senkumwong, N., Chaovisitsaree, S., Rugpao, S., Chandrawongse, W., Yanunto, S., 2006. The changes of sexuality in Thai women during pregnancy. J. Med. Assoc. Thai. 8 (4), 124–129.
Seok, J.W., Sohn, J.H., 2015. Neural substrates of sexual desire in individuals with problematic hypersexual behavior. Front. Behav. Neurosci. 9, 321.
Shirazi, T.N., Bossio, J.A., Puts, D.A., Chivers, M.L., 2018. Menstrual cycle phase predicts women's hormonal responses to sexual stimuli. Horm. Behav. 103 (6), 45–53. https://doi.org/10.1016/j.yhbeh.2018.05.023.
Stark, R., Schienle, A., Girod, C., Walter, B., Kirsch, P., Blecker, C., et al., 2005. Erotic and disgust-inducing pictures - differences in the hemodynamic responses of the brain. Biol. Psychol. 70 (1), 19–29. https://doi.org/10.1016/j.biopsycho.2004.11.014.
Stark, R., Klein, R.S., Kruse, O., Weygandt, M., Leufgens, L.K., Schweckendiek, J., Strahler, J., 2019. No sex difference found: cues of sexual stimuli activate the reward system in both sexes. Neuroscience 416, 63–73. https://doi.org/10.1016/j.neuroscience.2019.07.049.
Stoléru, S., Fonteille, V., Cornélis, C., Joyal, C., Moulier, V., 2012. Functional neuroimaging studies of sexual arousal and orgasm in healthy men and women: a review and meta-analysis. Neurosci. Biobehav. Rev. 36 (6), 1481–1509. https://doi.org/10.1016/j.neubiorev.2012.03.006.
Stulhofer, A., Bergeron, S., Jurin, T., 2016. Is high sexual desire a risk for women's relationship and sexual wellbeing. J. Sex Res. 53, 882–891.
Sylva, D., Safron, A., Rosenthal, A.M., Reber, P.J., Parrish, T.B., Bailey, J.M., 2013. Neural correlates of sexual arousal in heterosexual and homosexual women and men. Horm. Behav. 64 (4), 673–684. https://doi.org/10.1016/j.yhbeh.2013.08.003.
Turnbull, O.H., Lovett, V.E., Chaldecott, J., Lucas, M.D., 2014. Reports of intimate touch: erogenous zones and somatosensory cortical organization. Cortex 53, 146–154.
Turner, B.O., Paul, E.J., Miller, M.B., Barbey, A.K., 2018. Small sample sizes reduce the replicability of task-based fMRI studies. Commun. Biol. 1 (1), 1–10.
van der Zwaag, W., Schäfer, A., Marques, J.P., Turner, R., Trampel, R., 2016. Recent applications of UHF-MRI in the study of human brain function and structure: a review. NMR Biomed. 29 (9), 1274–1288. https://doi.org/10.1002/nbm.3275.
van 't Hof, S.R., van Oudenhove, L., Klein, S., Reddan, M.C., Kragel, P., Stark, R., Wager, T.D., 2021. The Brain Activation Based Sexual Image Classifier (BASIC): A Sensitive and Specific fMRI Activity-based Pattern for Sexual Images (in revision). Cerebral Cortex. In preparation.
Wager, T.D., Lindquist, M.A., 2015. Principles of fMRI. Leanpub, New York.
Wallwiener, C.W., Wallwiener, L.M., Seeger, H., Mück, A.O., Bitzer, J., Wallwiener, M., 2010. Prevalence of sexual dysfunction and impact of contraception in female German medical students. J. Sex. Med. 7 (6), 2139–2148.
Wallwiener, C.W., Wallwiener, L.M., Seeger, H., Schönfisch, B., Mueck, A.O., Bitzer, J., et al., 2015. Are hormonal components of oral contraceptives associated with impaired female sexual function? A questionnaire-based online survey of medical students in Germany, Austria, and Switzerland. Arch. Gynecol. Obstet. 292 (4), 883–890.
Walter, M., Bermpohl, F., Mouras, H., Schiltz, K., Tempelmann, C., Rotte, M., et al., 2008a. Distinguishing specific sexual and general emotional effects in fMRI: subcortical and cortical arousal during erotic picture viewing. NeuroImage 40 (4), 1482–1494. https://doi.org/10.1016/j.neuroimage.2008.01.040.
Walter, M., Stadler, J., Tempelmann, C., Speck, O., Northoff, G., 2008b. High resolution fMRI of subcortical regions during visual erotic stimulation at 7 T. Magn. Reson. Mater. Phys. Biol. Med. 21 (1–2), 103–111. https://doi.org/10.1007/s10334-007-0103-1.
Wehrum-Osinsky, S., Klucken, T., Kagerer, S., Walter, B., Hermann, A., Stark, R., 2014. At the second glance: stability of neural responses toward visual sexual stimuli. J. Sex. Med. 11 (11), 2720–2737. https://doi.org/10.1111/jsm.12653.
Wiedeking, C., Ziegler, M.G., Raymond Lake, C., 1979. Plasma noradrenaline and dopamine-beta-hydroxylase during human sexual activity. J. Psychiatr. Res. 15 (2), 139–145. https://doi.org/10.1016/0022-3956(79)90025-6.
Woodard, T., Diamond, M., 2008. Contribution of imaging to our understanding of sexual function and dysfunction. Adv. Psychosom. Med. 29, 150–168. https://doi.org/10.1159/000126629.
Woodard, T.L., Nowak, N.T., Balon, R., Tancer, M., Diamond, M.P., 2013. Brain activation patterns in women with acquired hypoactive sexual desire disorder and women with normal sexual function: a cross-sectional pilot study. Fertil. Steril. 100 (4), 1068–1076. https://doi.org/10.1016/j.fertnstert.2013.05.041 e5.
World Health Organization, 1996. Research on the menopause in the 1990s: report of a WHO scientific group. World Health Organization.
Yang, J.C., Park, K., Eun, S.J., Lee, M.S., Yoon, J.S., Shin, I.S., et al., 2008. Assessment of cerebrocortical areas associated with sexual arousal in depressive women using functional MR imaging. J. Sex. Med. 5 (3), 602–609. https://doi.org/10.1111/j.1743-6109.2007.00737.x.
Yang, J.C., Park, J.I., Kim, G.W., Eun, S.J., Lee, M.S., Han, K.L., et al., 2013. Effects of antidepressant treatment on sexual arousal in depressed women: a preliminary fMRI study. Psychiatry Investig. 10 (1), 379–383.
Zhu, X., Wang, X., Parkinson, C., Cai, C., Gao, S., Hu, P., 2010. Brain activation evoked by erotic films varies with different menstrual phases: an fMRI study. Behav. Brain Res. 206 (2), 279–285. https://doi.org/10.1016/j.bbr.2009.09.027.
Zimmerman, Y., Eijkemans, M.J.C., Coelingh Bennink, H.J.T., Blankenstein, M.A., Fauser, B.C.J.M., 2014. The effect of combined oral contraception on testosterone levels in healthy women: a systematic review and meta-analysis. Hum. Reprod. Update 20 (1), 76–105.
Ziogas, A., Habermeyer, E., Santtila, P., Poeppl, T.B., Mokros, A., 2020. Neuroelectric correlates of human sexuality: a review and meta-analysis. Arch. Sex. Behav. 1–100.
Zuo, X.N., Xing, X.X., 2014. Test-retest reliabilities of resting-state FMRI measurements in human brain functional connectomics: a systems neuroscience perspective. Neurosci. Biobehav. Rev. 45, 100–118.