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Reviews and perspectives

Toward an understanding of the cerebral substrates of woman's orgasm

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Abstract

The way women experience orgasm is of interest to scientists, clinicians, and laypeople. Whereas the origin and the function of a woman's orgasm remains controversial, the current models of sexual function acknowledge a combined role of central (spinal and cerebral) and peripheral processes during orgasm experience. At the central level, although it is accepted that the spinal cord drives orgasm, the cerebral involvement and cognitive representation of a woman's orgasm has not been extensively investigated. Important gaps in our knowledge remain. Recently, the astonishing advances of neuroimaging techniques applied in parallel with a neuropsychological approach allowed the unravelling of specific functional neuroanatomy of a woman's orgasm. Here, clinical and experimental findings on the cortico-subcortical pathway of a woman's orgasm are reviewed and compared with the neural basis of a man's orgasm. By defining the specific brain areas that sustain the assumed higher-order representation of a woman's orgasm, this review provides a foundation for future studies. The next challenge of functional imaging and neuropsychological studies is to understand the hierarchical interactions between these multiple cortical areas, not only with a correlation analysis but also with high spatio-temporal resolution techniques demonstrating the causal necessity, the temporal time course and the direction of the causality. Further studies using a multi-disciplinary approach are needed to identify the spatio-temporal dynamic of a woman's orgasm, its dysfunctions and possible new treatments.

Keywords: Social cognitive neuroscience; Women; Sexual function; Orgasm; Functional imaging; Brain; Gender differences; Cognitive functions

Contents

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1. Introduction

Attitudes towards women's sexuality in general, and orgasm in particular, have varied throughout recorded history (Lloyd, 2005; Muchembled, 2005; Symons, 1979). Though repression of both was not uncommon, and continues in some cultures and religions to this day, there have been times when it was viewed positively, and even celebrated (Muchembled, 2005). Even with this complex historical background, several philosophers, anthropologists, writers, anatomists, psychiatrists and sexologists have nevertheless tried to decipher the sense, the mechanisms and the function of a woman's orgasm (e.g., Abraham, 2002; Basson, 2000; Buss, 2003; Hite, 1976; Kaplan, 1974, 1979; Kinsey, Pomeroy, Martin, & Gebbard, 1953; Levin, 1981; Lloyd, 2005; Masters & Johnson, 1966; Meston, Hull, Levin, & Sipski, 2004; Mould, 1980; Symons, 1979; Whipple, 2002). The greatest advances have been made in identifying the anatomy and physiology of the organs that are involved during a woman's orgasm (e.g., Alzate, 1985; Kaplan, 1974; Levin & Wagner, 1985; Masters & Johnson, 1966; Mould, 1980). By highlighting spinal- and cerebral-driven mechanisms on the peripheral response, great insights have been made in understanding the crucial role of the central nervous system during orgasm.

Because the neuropharmacology, neuro-endocrinology and the spinal-driven components of orgasm have been addressed in depth previously (e.g., Argiolas & Melis, 2003; Heaton & Adams, 2003; Levin, 1981; Mah & Binik, 2001; McKenna, 1999, 2002; Meston et al., 2004; Rowland, 2006), we will not review them in the present article. Rather, our article aims to examine and provide a critical review of the current knowledge about the cerebral network of woman's orgasm. To our knowledge, although neurophysiological research focusing on the spinal cord driven mechanisms during orgasm does not exclude the role of higher-order cognitive functions, the cerebral network underlying a woman's orgasm remains poorly known and understood. Indeed, although cerebral correlates of sexual function has been widely investigated and reviewed for a man's orgasm (e.g., Bancroft, 1999; Cohen, Rosen, & Goldstein, 1976; Coolen, 2005; Heath, 1972; Holstege, 2005; Mosovich & Tallaferro, 1954; Tiihonen et al., 1994; Truitt & Coolen, 2002), the functional cerebral organization of a woman's orgasm has been comparatively underrepresented in neuropsychological science. Forty years after Kinsey's and Master's and Johnson's pioneering research, there is still great potential for advancement in the understanding of women's orgasms by studying neuroimaging and neuropsychological data in the framework of current models of sexual function. Thus, our review presents: (i) the definition of a woman's orgasm; (ii) the manifestations of a woman's orgasm; (iii) the inter- and intra-individual variations in the normative response of a woman's orgasm; (iv) the spinal and supra-spinal influences on the mediation of a woman's orgasm; (v) the neuroendocrine influences on a woman's orgasm; (vi) the recent clinical and neuroimaging studies unraveling the neural basis of a woman's orgasm; and (vii) the gender differences in orgasm. This review also informs clinicians about assessing potential orgasm disorders that might occur after brain damage. Finally, we discuss future empirical directions and clinical applications.

2. Definition of a woman's orgasm

A major problem in defining orgasm[1] is the discrepancy between subjective descriptions and objective physiological signs, forcing most researchers to describe only the observed physical changes (e.g., Glenn & Kaplan, 1968; Kaplan, 1974, 1979, 1987; Kinsey et al., 1953; Ladas, Whipple, & Perry, 1982; Levin, 1981; Levin & Wagner, 1985; Mah & Binik, 2001, 2005; Masters & Johnson, 1966; Vance & Wagner, 1976). The change of state of consciousness also makes it difficult for a woman experiencing orgasm to describe the experience with precision until she returns to a "normal" state of consciousness (e.g., Levin, 1981).

Despite all these difficulties, Meston and colleagues recently offered the following effective definition: "A woman's orgasm is a variable transient peak sensation of intense pleasure, creating an altered state of consciousness, usually accompanied by involuntary, rhythmic contractions of the pelvic striated circumvaginal musculature, often with concomitant uterine and anal contractions and myotonia that resolves the sexually-induced vasocongestion, usually with an induction of well-being and contentment" (Meston et al., 2004). This definition is adopted for this paper.

3. Manifestations of a woman's orgasm

There is consensus that a woman's orgasm involves a transient peak of intense sexual pleasure associated with rhythmic contractions of the pelvic circumvaginal musculature, often with concomitant uterine and anal contractions (e.g., Kaplan, 1974, 1979, 1987; Kinsey et al., 1953; Levin, 1981; Mah & Binik, 2001; Masters & Johnson, 1966; Meston et al., 2004; Mould, 1980; Vance & Wagner, 1976). In the tradition of Masters and Johnson, who described a four-stages model of sexual response, orgasm follows the phases of excitement and plateau; and pre-

[1] The word "orgasm" is derived from the Greek word *orgasmos*, from *orgâo* and *organ*, which means: 'to swell up', 'to be excited'. Its fundamental etymological root 'varg' means 'to move', 'to act'. Derived from the Sanskrit *ûrg'as*, from the verbal root urj, orgasm also means strength and energy.

cedes a resolution phase (Masters & Johnson, 1966). In 1979, Kaplan added the concept of desire to the Masters and Johnson's linear model and condensed the sexual response into three phases: desire; arousal; and orgasm (Kaplan, 1979). In brief, a key postulate of Kaplan's model is that these three phases are mediated by *separate* and *interconnected* neurophysiological mechanisms; desire is generated by limbic activation, whereas arousal and orgasm is mostly connected with the stimulation of reflex pathways in the spinal cord (Kaplan, 1974). The orgasmic stage happens when excitement seems to go over the edge and a crescendo is reached (Kaplan, 1974; Masters & Johnson, 1966). A woman's orgasm is accompanied by 3–15 involuntary rhythmic contractions of the pelvic circumvaginal musculature with concomitant uterine and anal contractions (Kaplan, 1974, 1979; Ladas et al., 1982; Levin, 1981; Levin & Wagner, 1985; Mah & Binik, 2001; Masters & Johnson, 1966; Meston et al., 2004).

These contractions usually occur at 0.8-s intervals (Masters & Johnson, 1966). According to Masters and Johnson, "the orgasmic stage is limited to those few seconds during which the vasoconstriction (such as sex flush) and myotonia (such as carpopedal spasm, a spastic contraction of the striated musculature of the hands and the feet) developed from sexual stimuli are experienced" (Masters & Johnson, 1966). More precisely, orgasm may last several seconds (from 3 to 26 s) or longer (~2 mn) (Kaplan, 1974; Kratochvil, 1993; Levin, 1981; Levin & Wagner, 1985; Masters & Johnson, 1966). Other physiological manifestations also occur during orgasm, such as tachycardia, hyperventilation (with an orgasm lasting more than 5 s), blood pressure rise, and involuntary vocalizations (cries, exclamations, screams) and/or involuntary spoken self-report, and perspiratory reaction in the immediately post-orgasmic time sequence (e.g., Kaplan, 1974, 1979, 1987; Kinsey et al., 1953; Levin, 1981; Masters & Johnson, 1966). For instance, according to Masters and Johnson, "tachycardia is a constant accompaniment of orgasmic experience, with cardiac rates running from 110 to beyond 180 beats per minute. Increase of blood pressure also is a constant finding. The systolic pressures are elevated by 30–80 mm and diastolic pressures by 20–40 mmHg (Masters & Johnson, 1966). In addition, a woman's orgasm is also associated with a slight clouding of consciousness (e.g., Levin, 1981; Masters & Johnson, 1966).

4. Inter- and intra-individual differences of a woman's orgasm: a cognitive differentiation?

When women are sexually stimulated, and if the stimulus is maintained and adequate in intensity and duration, it can lead to a culmination of induced sexual arousal that causes a broad variety of mental and physical manifestations that are normally described as the experience of an orgasm. Nevertheless, there is enormous variation in the ease with which women can achieve orgasm (e.g., Kaplan, 1974; Kinsey et al., 1953; Levin, 1981; Masters & Johnson, 1966). For instance, woman's orgasm can be triggered by various erotic stimulations of different genital sites that induce many different types of orgasms (such as clitoral, vaginal, or blended; Alzate, 1985; Glenn & Kaplan, 1968; Ladas et al., 1982; Levin, 1981; Levin & van Berlo, 2004; Masters & Johnson, 1966; O'Hare, 1951). Clitoral stimulation is a primary source of sensory input for triggering woman's orgasm; even during coitus alone, indirect or direct clitoral stimulation may occur (e.g., Kaplan, 1974, 1987; Kinsey et al., 1953; Masters & Johnson, 1966; Meston et al., 2004). Digital stimulations of the upper vaginal wall (which includes the so-called Grafenberg or "G" spot) can also induce orgasm in women who are especially sensitive to such stimulation (e.g., Ladas et al., 1982). Other sources also argue that orgasm may result from a combined clitoral and vaginal stimulation (blended orgasm; Alzate, 1985).

Some women may also experience orgasms after erotic stimulations of non-genital sites (Kaplan, 1974, 1987; Kinsey et al., 1953; Ladas et al., 1982; Levin, 1981; Levin & van Berlo, 2004; Masters & Johnson, 1966; Whipple, Ogden, & Komisaruk, 1992). For instance, different types of tactile stimulation, such as stimulation of the breast/nipple can induce a woman's orgasm (e.g., Kaplan, 1987; Masters & Johnson, 1966). This suggests a general orgasmic principle of building up pleasurable excitation from different parts of the body.

Women may also sometimes achieve orgasm through sexual fantasies, mental imagery or during sleep without any tactile stimulation (Henton, 1976; Kaplan, 1987; Money, 1960; Whipple et al., 1992). For example, Whipple and colleagues observed in 10 women that orgasms after mental imagery induced physiological changes (heart rate, pupil diameter, systolic blood pressure) of a magnitude comparable to those obtained after genital self-stimulation (Whipple et al., 1992). Nevertheless, these results have to be interpreted with caution because the small sample of participants may have limited utility in explaining orgasm in the population of women as a whole. For a better understanding of orgasms without genital stimulation, further studies combining measurements of perineal contractions and self-reports would be useful.

There is great variation in the frequency and type of orgasm (Darling, Davidson, & Jennings, 1991; Kaplan, 1974, 1979; Masters & Johnson, 1966; Whipple, 2002). Five to 10% of women in the United States have never experienced orgasm by any means of self or partner stimulation" (Spector & Carey, 1990). On the other hand, some women can have one orgasm right after another (serial multiple orgasms) and/or a series of orgasms that come close together (2–10 min apart; sequential multiple orgasms), although under other circumstances the same women may be totally satisfied after one orgasm (Darling et al., 1991; Ladas et al., 1982; Mah & Binik, 2001; Masters & Johnson, 1966; Meston et al., 2004). According to Masters and Johnson, women with multiple orgasms return to the plateau phase of excitement after each orgasm, and do not progress into the resolution phase until after the last orgasm (Masters & Johnson, 1966). In order to explain the inter-individual differences of a woman's orgasm, Kaplan also suggested that orgasms, like all reflexes, have a range and distribution of different thresholds (Kaplan, 1974, 1987). According to Kaplan, the female orgasm seems to be distributed more or less along a bell-shaped curve. Near the upper range are women who require only intense genital stimulation to reach orgasm and at the very extreme are women who can achieve an orgasm via fantasy and/or breast stimulation alone (Kaplan, 1987).

Recently, the variation in ability to orgasm has been assumed to be modulated by genetic factors (at 34–45%; Dunn, Cherkas, & Spector, 2005). Whereas this study, investigating mono- and dizygotic twins, does not rule out cultural, environmental or psychological influences on a woman's sexual dysfunction, it does suggest that heredity might influence both masturbation and intercourse outcomes, particularly among identical twins. However, the authors did not look at sex frequency or satisfaction. They also did not examine whether genetic predispositions to certain illnesses or biological disorders and also to certain similar cerebral correlates between twins could be involved. Further studies have to be performed to confirm these results.

Because several inter- and intra-individual differences exist regarding these various physiological manifestations, one might wonder what is the role of cognition during orgasm. Several studies have demonstrated that physiological manifestations of orgasms can be functions of a woman's age, her comfort level (with partner and with surroundings), her energy level (level of stress and fatigue), the context, her partner, her education, her experience, self-esteem, body-image, pleasure, satisfaction, or her culture (e.g., Bancroft, Loftus, & Long, 2003; Basson, 2000, 2001; Kaplan, 1974, 1987; Kinsey et al., 1953; Levin, 1981; Mah & Binik, 2001, 2005; Masters & Johnson, 1966; Meston et al., 2004; Sholty et al., 1984; Whipple & Brash-McGreer, 1997).

For example, in a national survey of 987 women in 1999–2000, Bancroft, Loftus, and Long (2003) found that emotional well-being and the quality of a relationship with a partner had more effects on sexuality than aging. Clinical reports also show that a woman can reach the phase of plateau without having orgasms during intercourse with a specific partner, while she can reach the orgasmic phase without difficulty with another partner with whom she is in love. These inter- and intra-individual differences speak in favor of a critical role of cognition during orgasm.

Although Kaplan's and Masters and Johnson's models remain the currently accepted models of sexual response by acknowledging also a potential role of psychological factors during orgasm ("orgasm is a psychophysiologic experience occurring within, and made meaningful by, a context of psychosocial influence"; Masters & Johnson, 1966; "the thresholds of reflexes are also influenced by other factors such as psychological inhibition, drugs and emotional states"; Kaplan, 1987), these models have been recently called into question for a number of reasons. Notably, many women do not move progressively and sequentially through the phases as described, and some women may not even experience all of the phases—for example, they may move from sexual arousal to orgasm and satisfaction without experiencing sexual desire, or they can experience desire, arousal, and satisfaction but not orgasm (e.g., Basson, 2000, 2001; Levin & van Berlo, 2004; Whipple, 2002). Thus, efforts have been made to further describe orgasm with multidimensional psychological and biological data. For instance, Whipple and Brash-McGreer proposed a circular sexual response pattern demonstrating that pleasure and satisfaction play a crucial role in a woman's sexual experience, especially in the initiation of the seduction phase of the next sexual experience (Bentler & Peeler, 1979; Whipple & Brash-McGreer, 1997). This model suggests that if the orgasm experience was pleasant and satisfying, it would lead to another experience, but if it was not, the woman may not want to repeat the experience. This model of female sexual function highlights that woman's sexual response does not conform to a linear model that describes only one type of sexual response. A woman's sexual experience encompasses different components, such as self-esteem, body image, relationship factors, pleasure, satisfaction (Whipple & Brash-McGreer, 1997).

More recently, Basson also proposed a circular model of female sexual response that incorporates the importance of emotional intimacy, sexual stimuli, and relationship satisfaction in the perception of different sexual stimuli (Basson, 2000, 2001, 2002). This model acknowledges that numerous psychosocial issues, including satisfaction with the relationship, self-image, and past emotional sexual experiences, have a striking impact on female sexual response. It also suggests that female sexual functioning proceeds in a more complex and circuitous manner than male sexual functioning, because the goal of sexual activity for women may not be necessarily orgasm but rather personal satisfaction (Basson, 2000, 2001, 2002). Thus, Basson's model characterizes orgasm as a physical satisfaction (a pleasant feeling due to a combination of various orgasm-related physiological manifestations), a conceptual satisfaction (a feeling of intimacy and connection with a partner), or both (Basson, 2001).

Mah and Binik (2001) proposed another three-dimensional model of the subjective orgasm experience including the sensory, evaluative and affective dimension. According to Mah and Binik, the sensory dimension corresponds to sensations arising from physiological events (such as muscle tension or thermal sensation). The evaluative (nonphysical) dimension ("How does the orgasm feel?) represents the "subjective overall intensity of the orgasm experience" (such as intensity) and appraisals (such as pleasure, satisfaction, or pain). The affective dimension ("How does the person feel during orgasm?") represents both the positive and negative feelings at orgasm and immediately after orgasm (such as, well-being, regrets, intimacy, or love; Mah & Binik, 2001).

5. Spinal and supraspinal influences on the mediation of a woman's orgasm

Female orgasm is mediated by complex interactions of somatic and autonomic nervous systems, operating at a central (spinal and cerebral) and a peripheral level. The neurobiological research of the physiological control of orgasm provides a great opportunity to better understand the interaction between peripheral and central mechanisms of female orgasm in a meaningful way. Because the role of the spinal cord in orgasm and its related neuropharmacology has already been described in depth in previous elegant studies and reviews, we will not review them in the present article (e.g., Mah & Binik, 2001; McKenna, 1999, 2002; Meston et al., 2004; Rowland, 2006). Nevertheless, a brief summary will be provided to highlight the most important findings.

5.1. Modulation of woman's orgasm response by the spinal cord

The crucial role of the spinal cord in woman's orgasm response has been mostly emphasized by studies of spinal-injured women. Findings from these studies demonstrate that female orgasm implicates different neural pathways within a reflexive neuromuscular negative-feedback loop, many of which are similar to those in men (e.g., Komisaruk & Whipple, 1995; Mah & Binik, 2001; Sipski, Alexander, & Rosen, 1995; Sipski & Arenas, 2006). A large body of substantial evidence has demonstrated the impact of specific spinal injuries (mostly lumbosacral) on orgasmic potential (e.g., Sipski et al., 1995; Sipski & Arenas, 2006). On the other hand, there is also a strong level of evidence for the occurrence of orgasm in spinal-injured women (Mah & Binik, 2001; Meston et al., 2004). However, assessment of spinal lesions is typically indirect, and more precise measures of neuropathy and lesion characteristics are desirable. Women with orgasm disorders (such as secondary or primary anorgasmy) without spinal injury would also be appropriate to study.

5.2. Modulation of spinal reflexes by supraspinal sites

The control of the urethrogenital reflex, a spinal sexual reflex consisting of autonomic and somatic nerve activity and vaginal, uterine, and anal sphincter contractions, has been demonstrated to be also modulated by inhibitory and excitatory influence of supraspinal sites (e.g., Mah & Binik, 2001; Meston et al., 2004; Sipski et al., 1995; Sipski & Arenas, 2006). Overall, supraspinal sites of female orgasm have been mainly localized in the nucleus paragigantocellularis and the limbic system (hypothalamus and its paraventricular nucleus, the medial preoptic area, nucleus accumbens, amygdala, hippocampus, etc.; Mah & Binik, 2001 for review). Because both the urethrogenital reflex in rats and orgasm in humans are controlled in part by a spinal pattern generator, studies on animals have provided great insights on the understanding of this supraspinal modulation of female orgasm (Meston et al., 2004). For example, the urethrogenital reflex elicited by mechanical stimulation of the urethra or by electric stimulation of certain brain areas of female rats is characterized by a series of muscle contractions similar to those of orgasm in humans (Mah & Binik, 2001; Meston et al., 2004). Electric stimulations of the medial preoptic area of female rats elicited the urethrogenital reflex even in the absence of genital stimulation (e.g., Giuliano et al., 2001). Other animal studies have also demonstrated that both sympathetic and parasympathetic influences may be produced in female rats by electric stimulations of the medial preoptic area. Interestingly, studies in female rats have identified reciprocal connections between the medial preoptic area/anterior hypothalamus and the lateral septum, bed nucleus of the stria terminalis, the medial amygdala, several hypothalamic nuclei (including the lateral, paraventricular, ventromedial, arcuate), central gray, nucleus paragigantocellularis, raphe nuclei (dorsalis and medianus), ventral tegmental area (area supplying dopamine to the medial preoptic area and in part regulating the reward associated with sexual behavior), and the nucleus of the solitary tract (Mah & Binik, 2001; Meston et al., 2004). Genital reflexes are also under tonic inhibitory control by the neurons originating in the nucleus paragigantocellularis and terminating in the lumbosacral spinal cord neurons, which innerve pelvic viscera.

6. Neuroendocrine influences on a woman's orgasm

The periaqueductal gray matter of the midbrain subserves autonomic functions, and receives input from the medial preoptic area and from the area of the spinal cord in which the pudendal and pelvic nerves terminate, and send outputs reaching, among others area, the clitoris (e.g., McKenna, 1999, 2002; Meston et al., 2004). Interestingly, the paraventricular nucleus is an integrative site of the sympathetic and neuroendocrine systems (e.g., McKenna, 1999, 2002; Meston et al., 2004). For instance, at the level of the paraventricular nucleus, a group of oxytocinergic neurons projecting to extra-hypothalamic brain areas, including the spinal cord (at a lumbosacral level), has been identified to facilitate erectile function, muscle contraction (including those of an orgasm) and copulation. Releases of oxytocin, the peptide hormone known to be involved in psychological bonding, attachment and love, have been also demonstrated to positively correlate with the intensity of the human female orgasmic contractions (Campbell & Petersen, 1953; Carmichael, Warburton, Dixen, & Davidson, 1994; Mah & Binik, 2001; Meston et al., 2004).

Levels of prolactin, another peptide hormone related to attachment, are also consistently raised for 60 min in women after orgasm as a neuro-hormonal index of sexual satiety (Exton et al., 1999; Meston et al., 2004). Nevertheless, changes in prolactin in the circulation are difficult to interpret, although they may be "a useful epiphenomenon acting as a marker of other changes in the neuroendocrine system" (Bancroft, 1999; Meston et al., 2004). Because this central control of prolactin release from the anterior pituitary gland involves dopaminergic and serotoninergic activity, prolactin increases could reflect a decrease of hypothalamic dopamine or an increase in hypothalamic serotonin, either or both of which could explain loss of post-orgasmic arousability. For instance, a growing body of research suggests that neuro-pharmalogical and neuro-endocrinal changes following a woman's orgasm are involved in a loop that serves to decrease arousal through inhibitory central mechanisms (e.g., Bancroft, 1999; Exton et al., 1999; Meston et al., 2004). However, the functional role of prolactin increases remains unclear. If prolactin increases correspond to an "orgasmic linked "off" switch for sexual arousal in men", why do they not induce similar effects in women who do not have a refractory period after one orgasm (Meston et al., 2004)? It might be hypothesized that prolactin increases are just a retrospective indicator that orgasm has indeed taken place (Meston et al., 2004). On the other hand, a recent study in both men and women has demonstrated that the magnitude of prolactin increase following intercourse is 400% greater than that following masturbation (Brody & Kruger, 2006). Thus intercourse may be more physiologically and psychologically satisfying than masturbation (Brody & Kruger, 2006). This supports the

assumption that not only is cognition tightly involved in orgasm, but also that orgasm may play a crucial role in the cognitive ability to maintain healthy interpersonal relationships and healthy psychological boundaries with other people (e.g., Basson, 2001; Carmichael et al., 1994; Lloyd, 2005; Symons, 1979; Whipple & Brash-McGreer, 1997).

Several studies have reviewed the influence of other endocrine factors (such as estradiol) and neurotransmitters on human sexual function, and notably on women orgasm (e.g., Ellison, 1998; Mah & Binik, 2001; Meston et al., 2004; Rowland, 2006). However, the role of particular hormones in orgasm is discussed. For example, a positive association found between testosterone and orgasm in both women and men may be mediated by increased sexual desire and sexual activity (Mah & Binik, 2001). Moreover, female orgasm frequency is not systematically related to fluctuations in androgen levels throughout the menstrual cycle (Mah & Binik, 2001). Increases of orgasm frequencies have been reported just prior to ovulation, but different measures of menstrual phases do not always correspond (Lloyd, 2005; Mah & Binik, 2001). Potential confounds (e.g., mood fluctuations, stress, love intensity) must also be considered in interpreting a pre-ovulatory peak in orgasm frequency (Mah & Binik, 2001).

Research on neurotransmitters has looked at the facilitator role of the cholinergic, adrenergic, and dopaminergic systems. The dopaminergic system facilitates sexual response, and adrenergic, cholinergic, nitrergic, gamma-aminobutyric acidergic (GABA) play important roles as well (Duncan, Blacklaw, Beastall, & Brodie, 1997; Mah & Binik, 2001; Meston et al., 2004). Although some conflicting evidence exists, the central serotoninergic system may play an inhibitory role (McKenna, 1999, 2002; Meston et al., 2004). These findings suggest that any disruption of endocrine, neural, or vascular response – caused by aging, disease, surgery, or medication – has the potential to lead to changes in female sexual responses. Nevertheless, pharmacological data have to be interpreted with caution because most drugs thought to primarily impact one neurotransmitter system more likely affect multiple, interconnected systems through complex, non-linear actions that are not yet completely understood. Although much progress has been made in the past decades to understand the fundamental neurobiology and neuroendocrinology of the nervous system and the complex pathways involved during woman' s orgasm, much remains to be learned.

7. The cortex and limbic system

7.1. Neurological case reports

Although physiological factors are clearly involved during orgasm, emotional, psychosocial and cognitive factors are also strongly implicated as components of sexual motivation that are crucial to sexual behavior. This standpoint has been acknowledged in several studies (e.g., Bancroft et al., 2003; Basson, 2000; Kaplan, 1974, 1979; Mah & Binik, 2001, 2005; Masters & Johnson, 1966; Whipple & Brash-McGreer, 1997). Nevertheless, the specific cerebral network underlying a woman's subjective experience of orgasm is not understood. The systematic study of patients with brain damage has provided critical insights into the cognitive function of relevant brain areas (e.g., Broca, 1861; Corkin, 2002; Penfield & Jaspers, 1954). This approach is of particular interest in the study of orgasm because this phenomenon is difficult to test under laboratory conditions in healthy volunteers (e.g., Levin & Wagner, 1985). The study of the anatomical correlates sustaining the experience of unexpected orgasms in patients without any psychiatric, gynecological, or hormonal disorders has suggested that spontaneous orgasms are associated with cortical discharges, as indicated by monitoring brain waves. [Spontaneous orgasms are mainly caused by epileptic discharges (Janszky et al., 2002, 2004)]. Nevertheless, reports of unexpected orgasms are rare in the clinic. This paucity may be due to the subjective and intimate nature of orgasms that makes spontaneous orgasms delicate to express. Most of the patients are usually hesitant to provide information about the sexual signs that may occur before their epileptic crisis (signs also known as sexual and/or orgasmic aura, or warning; Gastaut & Collomb, 1954; Janszky et al., 2002, 2004).

For a better understanding of this phenomenon, we focused our review on female patients who experienced spontaneous orgasms (Bancaud et al., 1970; Calleja, Carpizo, & Berciano, 1988; Chuang, Lin, Lui, Chen, & Chang, 2004; Crevenna, Homann, Feichtinger, Ott, & Korner, 2000; Currier, Little, Suess, & Andy, 1971; Erickson, 1945; Fadul, Stommel, Dragnev, Eskey, & Dalmau, 2005; Freemon & Nevis, 1969; Gautier-Smith, 1980; Heath, 1972; Janszky et al., 2002, 2004; Reading & Will, 1997; Remillard et al., 1983; Ruff, 1980; Torelli & Bosna, 1958; Table 1). This approach allowed us to find 20 patients, aged 20–57 years, who experienced spontaneous orgasms subsequent to the recruitment of specific brain areas. Using Surface and/or Depth EEG, CT-Scan MRI and/or SPECT techniques, the neuro-anatomical investigation of these patients suggested that 80% of them had a temporal lobe epilepsy (70% focal and 11% non-focal), 16% had an epileptic focus involving the frontal lobe and 21% had some parietal discharges. Moreover we observed that orgasmic aura mostly originated from the right hemisphere (70%) versus the left hemisphere (21%). Note that 11% had epileptic discharges in both hemispheres.

Taken together, these cases illustrate the central role of the brain in a woman's sexual function. Particularly, we found that the temporal lobe plays a crucial role in the generation of an orgasm, even if some parietal, para-sagittal, post-central, and/or frontal activities have also been reported (Table 1). Ictal somatosensory sensations in the genitalia are exceptional and seem to be correlated to epileptic discharges in the centro-parietal region (case#1, case#7, case#10; Table 1). This is congruent with the cortical sensory representation of the genitalia within the paracentral lobule (Allison, McCarthy, Luby, Puce, & Spencer, 1996; Baird, Wilson, Bladin, Saling, & Reutens, 2006; Janszky et al., 2002, 2004).

Phenomenologically, these findings are consistent with the fact that the medial temporal lobe is involved in various aspects of sexuality (Ledoux, 1996; MacLean, 1952, 1990). The present dominant involvement of the medial part of the temporal lobe, including the amygdala, in generating spontaneous woman's

Table 1
Clinical data of the published women with orgasmic auras

Case	Authors	Year of publication	Method	Age of the patient	Seizure types	Symptoms	Symptoms onset	Brain areas specifically involved in the orgasmic sensation	Lateralization
1	Erickson	1945	Histology	55	Simple partial seizures, secondarily generalized tonic-clonic seizures	Paroxysmal vaginal sensation with orgasm-like pleasure	12 years before	Parasaggital post-central hemangioma	Right
2	Torelli and Bosna	1958	Histology	31	Aura, secondarily generalized tonic-clonic seizures	Paroxysmal orgasm	Not reported	Temporo-parieto-occipital glioblastoma	Right
3	Freemon and Nevis	1969	Surface EEG right carotid artheriogram	36	Aura, secondarily generalized tonic-clonic seizures	Orgasmic feeling and verbalization of her sexual needs	4 years before	Temporal	Right
4	Bancaud et al.	1970	Surface EEG, computer tomography (CT), depth electrodes	20	Complex partial seizures	Orgasm with vaginal secretion, epigastric sensation then complex partial seizures	9 years before (with a 16-year history of epilepsy)	Temporal astrocytoma	Right
5	Currier et al.	1971	Surface EEG	52	Nocturnal grand mal seizures	'Sexual' seizures during which she lay on the floor on her back, lifted her skirt, elevated her pelvis rhythmically, made vocalizations	2 years before (with a 37-year history of epilepsy)	Temporal	Left
6	Heath	1972	Depth EEG and surface EEG	34	Aura, complex partial seizures	Euphoria, pleasant feelings, repetitive orgasms (~10–15 mn after injection)	23 years before	Septal region	Bilateral
7	Ruff	1980	CT scan	43	Simple partial seizures	Clitoral warmth, tachycardia, pain, fear with orgasm feeling	Not reported	Parietal post-central malignant glioma	Right
8	Gautier-Smith	1980	CT scan, histology	17 (case 4)	Aura, complex partial seizures, secondarily generalized tonic-clonic seizures	Genital secretion and orgasm occasionally followed by complex partial seizures	Not reported	Temporal oligodendroglioma	Right
9	Remillard et al.	1983	CT scan, histology	22 (case 2)	Complex partial seizures, secondarily generalized tonic-clonic seizures	Orgasm associated with vaginal sensation, followed by complex partial seizures	Not reported	Temporal gliosis	Right
10	Calleja et al.	1988	Surface EEG, CT scan	41	Nocturnal somatosensory seizures	Paresthesia in the right lateral abdominal and pubic regions and about her genitalia, sensation of vaginal dilatation, orgasmic feeling	3 years before	Centro-parietal region	Left
11	Reading and Will	1997	Surface EEG	44	Pure aura, complex partial seizures	Sudden internal and ascending feeling indistinguishable from an orgasm while she was driving	3 years before	Fronto-temporal region	Right

Table 1 (*Continued*)

Case	Authors	Year of publication	Method	Age of the patient	Seizure types	Symptoms	Symptoms onset	Brain areas specifically involved in the orgasmic sensation	Lateralization
12	Crevenna et al.	2000	Surface long-term EEG, MRI, CT scan	37	Complex partial seizures, secondarily generalized tonic-clonic seizures	Epigastric feelings, Déjà-vu, depersonalization, spontaneous orgasms	5 years before (with a 9-year history of epilepsy)	Temporal	Right
13	Janszky et al.	2002	Depth EEG, magnetic resonance imaging (MRI), histology	25	Aura, complex partial seizures	Paroxysmal orgasmic feeling	20-year history of epilepsy (date of the first paroxysmal orgasm unknown)	Hippocampal sclerosis	Right
14	Janszky et al.	2004	Surface EEG, subdural electrodes MRI	37	Aura, complex partial seizures, secondarily generalized tonic-clonic seizures	Orgasmic feeling accompanied by an abdominal sensation	26 years before	Temporal lobe	Right
15	Janszky et al.	2004	Surface EEG, MRI	46	Aura, complex partial seizures, secondarily generalized tonic-clonic seizures	Déjà-vu and orgasm-like euphoric erotic feelings	43 years before	Temporal	Right
16	Janszky et al.	2004	Surface EEG, MRI, single photon emission computed tomography (SPECT)	56	Aura, complex partial seizures, secondarily generalized tonic-clonic seizures	Orgasmic feeling accompanied by an abdominal sensation	31 years before	Temporal	Right
17	Janszky et al.	2004	Surface EEG, MRI	51	Complex partial seizures	Oral and manual automatisms, complex scenic hallucinations, orgasmic feelings	35 years before	Temporal	Bilateral
18	Janszky et al.	2004	Surface EEG, MRI	54	Aura, complex partial seizures	Strange feeling in her vagina accompanied by an orgasmic feeling	42 years before	Temporal	Left
19	Chuang et al.	2004	Surface EEG, MRI, SPECT	41	Aura, complex partial seizures	Sudden feeling of sexual arousal and experienced orgasm-like euphoria very similar to orgasms during coitus, while brushing her teeth	17 years before	Temporal	Right
20	Fadul	2005	Surface EEG	57	Aura	Sudden pleasure provoking feeling described “like an orgasm”	2 months before	Temporal lobe	Left

orgasms corresponds to the well-known "positive" manifestations of sexual function (hypersexuality) that is observed after the removal/damage of bilateral temporal lobes (Kluver–Bucy syndrome; in animals: Kluver & Bucy, 1939; in humans: e.g., Ghika-Schmid, Assal, De Tribolet, & Regli, 1995; Lilly, Cummings, Benson, & Frankel, 1983). However, these results are also inconsistent with some clinical studies including patients with temporal lobe epilepsy that demonstrate "negative" manifestations of sexual function, such as hyposexuality (e.g., Gastaut & Collomb, 1954). Although these discrepancies might be due to the fact that most of the studies studying hypersexuality do not specifically assess orgasm, but rather other phases of woman's sexual response (sexual desire and sexual arousal), one could wonder whether orgasmic aura are related to cerebral changes due to epileptic discharges or to seizure-free status after epilepsy surgery (Janszky et al., 2002). In the future, studies should investigate this issue in the specific framework of orgasm in order to understand whether this phenomenon is related to inhibitory and/or excitatory mechanisms.

Although inter-individual differences for medical and epilepsy history have to be taken into account before drawing any definitive conclusion about the hemispheric lateralization of a woman's orgasm, the present review suggests that orgasmic sensations might be the result of the spread of focal activity within the right hemisphere that might then be generalized to the whole brain. Although orgasm is not a pathological symptom of human sexual response, it can be assumed that epileptic orgasmic aura are caused by electric discharges at the same brain regions, which produce the physiological orgasm in healthy subjects. This assumption is reinforced by the fact that most of the present patients attributed their orgasmic aura to a feeling very similar to one which they experienced during sexual intercourse or masturbation (Bancaud et al., 1970; Calleja et al., 1988; Chuang et al., 2004; Crevenna et al., 2000; Erickson, 1945; Fadul et al., 2005; Freemon & Nevis, 1969; Gautier-Smith, 1980; Heath, 1972; Janszky et al., 2004; Janszky et al., 2002; Reading & Will, 1997; Remillard et al., 1983; Ruff, 1980; Torelli & Bosna, 1958).

On the other hand, because the medial temporal lobe is also known to be involved in a broad variety of cognitive functions, such as autobiographical and semantic memory, perceptual and motivational functioning, facial recognition, emotion, including feeding, fighting, fleeing, fear reactions (e.g., Ledoux, 1996; MacLean, 1952, 1990; Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; Moscovitch et al., 2005), one might also wonder what is the functional role of a woman's orgasm. To elucidate this question, systematic assessment of this phenomenon using neuropsychological assessments and functional neuroimaging techniques might be useful.

7.2. Functional brain imaging in healthy participants

Recently, the first brain imaging studies (PET and BOLD-fMRI) during orgasm in women have been reported (Komisaruk & Whipple, 2005; Komisaruk et al., 2004; Whipple & Komisaruk, 2002). Whipple, Komisaruk et al.'s study was conducted on the basis of a large number of studies demonstrating that a significant number of women with spinal cord injuries are still able to experience orgasm (e.g., Meston et al., 2004; Sipski et al., 1995; Sipski & Arenas, 2006; Whipple & Komisaruk, 2002). Whipple, Komisaruk and colleagues recorded changes in BOLD signal in three women experiencing orgasms (*AP*: 54, 1; *EL*: 40, 2; *ED*: 51, 21; subject identifiers, age in years, number of years since spinal cord injury). For statistical analyses, a contrast differentiating BOLD responses obtained in response to vaginal cervical self stimulations (CSS) with and without orgasm was calculated (Komisaruk et al., 2004). Statistical results revealed higher overall activity during orgasm than during cervical self-stimulation prior to orgasm (Komisaruk et al., 2004). Critically, the orgasmic response activated the following brain regions: insula, limbic system (medial amygdala, hippocampus, cingulate cortex, preoptic area and hypothalamus), nucleus accumbens, basal ganglia (especially putamen), superior parietal cortex (post-central sulcus), dorsolateral prefrontal cortex, and cerebellum, in addition to lower brainstem (central gray, mesencephalic reticular formation, and Nucleus Tractus Solitarus). Interestingly, recordings of brain activity during continuous CSS over an 8–12 min period allowed the authors to show the buildup of activity of these different brain areas involved in orgasm (Fig. 1). First, the medial amygdala, basal ganglia (especially the putamen), and insula showed the earliest

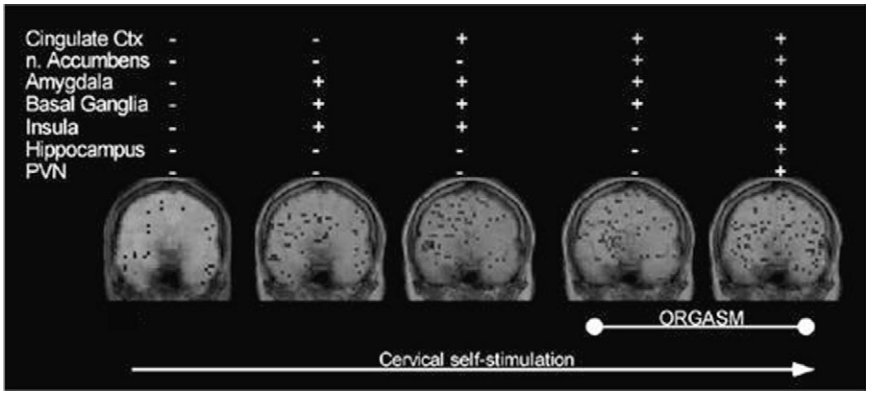

Fig. 1. Chronological increase of BOLD-fMRI signal intensity in brain regions activated during cervical self-stimulation leading up to, and during, orgasm. Data are shown for one woman. At the beginning of the stimulation, none of the seven brain regions showed activation (all "−"), whereas at orgasm each of these seven areas was activated (all "+"). Adapted from Komisaruk et al. (2004).

activation, then the cingulate cortex added to this activation, and at orgasm, the nucleus accumbens, paraventricular nucleus of the hypothalamus, and hippocampus became activated. Finally, the orgasmic response was characterized by an overwhelmingly strong pattern of activation over a broad and distributed neural network (Fig. 1). These findings support the hypothesis that an orgasm results from a spread of neural activation all over the brain, as suggested by the epileptic data we previously described. Nevertheless, whereas these data illustrate the spatio-temporal dynamic of orgasm, it is important to note that BOLD-fMRI does not have a very high temporal resolution as 3D-EEG does with its millisecond temporal resolution. Brain activation observed in BOLD-fMRI data might sum up a succession of several brain activations that occur over tens or hundreds of milliseconds. Future studies should thus specifically address this issue in order to better understand the temporal dynamic of a woman's orgasm.

Despite this temporal limitation, the present high-spatial resolution fMRI results shed some light on the current models of sexual function by specifying the brain areas that are involved during a woman's subjective orgasm experience. Based on previous functional studies, these results highlight the relationship between this orgasm-related cerebral network and some specific cognitive functions. First, the key location of this orgasm-related cerebral network within or near the limbic system, which is known to be crucial in human emotional processing (e.g., Ledoux, 1996; MacLean, 1952, 1990; Papez, 1995), is consistent with the intense emotion felt during orgasm. For instance, the nucleus accumbens is also activated during the intense pleasure felt during the opiate drug or nicotine "rush" induced by an injection of nicotine (e.g., Stein et al., 1998). Furthermore, the nucleus accumbens is involved rather in incentive motivation or reward expectation than in basic affective responses related to reward (e.g., Kampe, Frith, Dolan, & Frith, 2001; O'Doherty et al., 2003). Similarly, the insula recently took a pivotal position in reward processing and especially in prediction of future reward (e.g., O'Doherty, 2004; Tanaka et al., 2004). Thus, modulation of neural activation in these brain areas could explain inter- and intra-individual differences for "motive for sexual intercourse" (Komisaruk et al., 2004). This assumption is in line with current psychosocial models of sexual function, which suggest that women often apprehend a novel sexual experience with a partner as a result of contextual and other reward and motivational factors that are encoded with that partner (Bancroft et al., 2003; Basson, 2000; Mah & Binik, 2001, 2005; Whipple & Brash-McGreer, 1997).

In addition, the present activation of the cingulate cortex and medial amygdala during orgasm corresponds to their well-known activation during various aspects of sexuality (e.g., sexual arousal), regulation of the emotional life, reactivity to emotional stimuli, perceptual and motivational functioning, memory and facial recognition (e.g., Ledoux, 1996; MacLean, 1952, 1990). The activation of cingulate cortex and medial amygdala could also correspond to an oxytocin release, as we described above (e.g., Carmichael et al., 1994). The implication of the amygdala is also consistent with previous clinical studies that showed a positive correlation between the size of the amygdala contralateral to the epileptic focus and the sexual outcome of patients after temporal lobe resection (i.e., larger contralateral amygdala contributing to an increase or improvement of sexual behavior).

The involvement of the amygdala during a woman's orgasm has been recently questioned by Holstege, Georgiadis and colleagues (Georgiadis et al., 2006). In their positron emission tomography (PET) scan study, 12 women 21–47 years of age were submitted to four experimental conditions: a nonsexual resting state, faking an orgasm, having their clitoris stimulated by their partner's fingers (sexual arousal control), and clitoral stimulation to the point of orgasm. Results revealed that there is a 'shut down' of some areas in the brain associated with anxiety and fear, such as the left amygdala. As the women were stimulated, activity rose in the primary somato-sensory cortex, but fell in the amygdala, and hippocampus. During orgasm, activity fell in other areas of the brain, including the ventromedial prefrontal cortex, compared with the resting state. When compared with sexual arousal, orgasm was mainly associated with profound regional cerebral blood flow decreases in the left lateral orbitofrontal cortex, inferior temporal gyrus and anterior temporal pole. The authors propose that decreased blood flow in the left lateral orbitofrontal cortex implies behavioral disinhibition during orgasm, and that deactivation of the temporal lobe is directly related to high sexual arousal (Georgiadis et al., 2006). During faked orgasms, the absence of similar cerebral deactivation led the authors to assume that a basic part of a real orgasm is letting go. In parallel, a salient feature of brain regions activated during orgasm was an activation of the cerebellum, dorsal primary motor cortex, paracentral lobule (when compared with the resting state); and the left deep cerebellar nuclei (when compared with sexual arousal). According to Georgiadis and colleagues, the key to a woman's orgasm seems to be a deep relaxation and a lack of anxiety, with direct sensory input from the genitals playing a less critical role.

On the other hand, the importance of cognition in woman's orgasm is also strengthened in Komisaruk et al.'s study by the activation of other brain areas, such as the hippocampus. The present activation of the hippocampus, an area known to be needed for encoding and re-experiencing detailed episodic and spatial memories and also to contribute to the formation and assimilation of semantic memories (e.g., Moscovitch et al., 2005, 2006), emphasizes that higher-order functional mechanisms take place during woman's orgasm (Bancroft et al., 2003; Basson, 2000; Kaplan, 1974, 1979; Masters & Johnson, 1966; Whipple & Brash-McGreer, 1997). Similarly, the activation of the cingulate cortex and the insula (Komisaruk et al., 2004), two brain areas also known to be implicated in pleasure, pain, empathy, craving, partner selection, recognition of social signal in other people's faces and also both the self's and the other's perspective taking (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Singer et al., 2004; Turk et al., 2004) reinforces the role of cognition during a woman's orgasm (Komisaruk et al., 2004). For instance, the involvement of the insula and the cingulate cortex in human empathy (e.g., Carr et al., 2003; Singer et al., 2004, 2006) may suggest that women having an orgasm imagine how the other perceives the situation and feels as a result.

The importance of higher-order cognitive functions in woman's orgasm is also emphasized in Komisaruk et al.'s study

by the activation of the dorsolateral prefrontal and the superior parietal lobe, which are known to play an important role in a variety of cognitive functions, such as decision making, risk-taking, body image, motor imagery, integration of abstract representations, cognitive time management, and perspective taking (e.g., Jackson, Brunet, Meltzoff, & Decety, 2006; Krain et al., 2006; Rorie & Newsome, 2005; Rubia & Smith, 2004).

Taken together, these results provide additional information towards a better understanding of a woman's orgasm, which is partly a result of context and other cognitive factors, i.e., how they feel about themselves (i.e., body image, abstract representation of the self) and their partner, how safe they feel emotionally and socially, their closeness and their attachment, etc. (e.g., Bancroft et al., 2003; Basson, 2000; Heaton & Adams, 2003; Kaplan, 1974, 1979; Mah & Binik, 2005; Masters & Johnson, 1966; Meston et al., 2004; Whipple & Brash-McGreer, 1997). By specifying the brain areas involved in these mechanisms, contemporary neuroimaging studies throw considerable light on brain activity related to woman's orgasm, as it has been done previously in men (such as Graber, Rohrbaugh, Newlin, Varner, & Ellingson, 1985; Heath, 1972; Heaton & Adams, 2003; Holstege, 2005; Holstege & Georgiardis, 2004; Holstege et al., 2003; McKenna, 1999; Mosovich & Tallaferro, 1954; Rowland, 2006; Tiihonen et al., 1994). This is of particular importance in the field of neuropsychology where patients who suffer from a brain injury may have impaired or affected orgasms. Further studies should keep investigating this issue to reinforce these results.

8. Gender differences in human orgasm

Since the pioneering research of Kinsey and then of Master and Johnson, there has been considerable discussion about the differences between female and male orgasm. While orgasms are physiologically the same in males and females, it has often been assumed that there are two distinct and easily distinguishable kinds of subjective experiences (Vance & Wagner, 1976). This assumption is mostly based on the basic physical disparities between male and female orgasm concerning the orgasm duration. For example, it is agreed that a man's orgasm is often more sudden and explosive in nature while a woman's orgasm is more prolonged and less violent (Meston et al., 2004; Vance & Wagner, 1976). However, a study investigating the basic differences between a man's and a woman's orgasm experience by submitting 48 written descriptions of orgasm (24 men and 24 women) to 70 judges, demonstrated that subjective experience of orgasm do not differ by gender (Vance & Wagner, 1976).

In this study, the judges (obstetrician-gynecologists, psychologists, and medical students) had to sex-identify the descriptions and to discover whether sex differences could be detected. The judges could not correctly identify the sex of the person describing an orgasm. Furthermore, male judges did no better than female judges and vice versa. This suggests that men and women share common mental [cognitive] experiences during orgasm. Whether this is the case at the neurological level is a matter for current neuroimaging data.

Many neurophysiological studies showed that both male and female urethrogenital reflex is controlled in part by the spinal cord, and by inhibitory and excitatory influence of supraspinal sites, including the nucleus paragigantocellularis, the paraventricular nucleus of the hypothalamus, and the medial preoptic area (e.g., Heaton & Adams, 2003; Holstege, 2005; Mah & Binik, 2001; McKenna, 1999; Rowland, 2006). Because there has been very little research on orgasm in female animals, no clear gender differences have been reported in animal models (Giuliano et al., 2001; McKenna, 1999; Meston et al., 2004).

Neuroimaging studies carried out in healthy heterosexual men have demonstrated the significance of brain phenomena in sexual orgasm. Tiihonen et al. (1994), using single photon emission tomography (SPECT), reported ejaculation-related decreased activation in all cortical areas, except for a significant increase in the right prefrontal cortex (Tiihonen et al., 1994). Using positron emission tomography (PET), Holstege et al. (2003) showed ejaculation-related activations in the meso-diencephalic region (including the ventral tegmental area, ventroposterior and intralaminar thalamic nuclei), putamen, insula, and cerebellum. Activations in the right inferior frontal gyrus (Brodmann area (BA) 47), parietal (BA 7 and 40) and inferior temporal (BA 20 and 21) cortex were also observed. Increased activations were also present in the precuneus (BA 23/31). In the left hemisphere, increased regional cerebral blood flow (rCBF) was only found in a small portion of the superior frontal gyrus (BA 6). The visual cortex (BA 18) showed increased rCBF bilaterally despite the fact that the volunteers had their eyes closed. An important decrease of activation was found in the medial amygdala (Holstege et al., 2003). Surprisingly, no increased activation was observed in the male hypothalamus or preoptic area, while activations of these brain structures were observed in females (Komisaruk et al., 2004). The absence of hypothalamic involvement in men may be explained in the following way: the temporal resolution of PET experiment may be too limited (in comparison with other neuroimaging techniques used in women, such as fMRI) to detect short-lasting events occurring in the hypothalamus. This assumption is reinforced by the absence of hypothalamus activation even in women during a recent PET study carried out by the same authors (see above, Georgiadis et al., 2006).

In a more traditional methodology, EEG studies of men have also attempted to register brain activations during ejaculation (e.g., Cohen et al., 1976; Graber et al., 1985; Heath, 1972; Mosovich & Tallaferro, 1954). For example, Mosovich and Tallaferro (1954) recorded EEG activity during the process of masturbation-induced sexual orgasm without conclusive findings, although visual inspection of the EEG records indicated a generalized slowing of electrical activity with concomitant voltage increases. Heath (1972) recorded deep and surface[2] EEG activity in a man with a temporal epilepsy. EEG recordings were obtained at two occasions when the patient's arousal culminated in orgasm: once, as a consequence of masturbation and once through heterosexual intercourse. Deep electrodes were

[2] Surface EEG showed only artifact (Heath, 1972, p. 10).

implanted into a variety of deep sites (i.e., septal region, right hippocampus, bilateral amygdalae, right anterior hypothalamus, right posterior ventral lateral thalamus, left caudate nucleus, two subcortical sites within the left lobe of the cerebellum), and also in bilateral frontal and parietal lobe, and right temporal lobe. During orgasm, deep EEG recordings revealed changes of activity in the septal region (more pronounced in the right than in the left), a brain site most consistently implicated in the pleasure response (Heath, 1972). These changes in the septal region were concomitant with high-amplitude delta waves in the amygdalae (more pronounced in the right than in the left) and similar delta activity in the left caudate nucleus. With onset of orgasm, the septal and thalamic recordings evolved into spike and slow-wave activity. Interestingly, deep EEG recordings in an epileptic woman showed similar changes in the septal region during orgasm (Heath, 1972). However, the presence of result discrepancies found in the EEG literature moderates Heath's findings. Recently, Graber and colleagues showed no remarkable changes in brain activity recorded from four men during orgasm (compared to sexual arousal; Graber et al., 1985), whereas Cohen et al. (1976), who recorded only two parietal derivations on four men, demonstrated changes in left and right parietal EEG activity. These changes were mainly characterized by a large increase in the amplitudes in the right hemisphere (Cohen et al., 1976). Why parietal sites were chosen was not indicated. Interestingly, Cohen et al. found the same pattern of response in two right-handed women and not in a left-handed woman (Cohen et al., 1976). EEG evaluations of rare epileptic men with orgasmic aura showed that paroxysmal orgasmic feelings combined with abdominal aura are predominantly represented in the right hemisphere (Janszky et al., 2002). More precisely, two men have been reported with a right temporal lobe epilepsy and one man with a right parasagittal-postcentral parietal lobe epilepsy (Janszky et al., 2002, 2004).

As it has been shown in EEG studies carried out on women, orgasm in men is characterized by a change of cerebral activity predominantly in the right hemisphere (at least in the initial steps of orgasm). Moreover, both men's and women's orgasms show activations in the septal region, temporal and parietal lobes.

Taken together, the present neuroimaging studies thus suggest that both male and female orgasms implicate a common distributed cerebral network, characterized by activation in the following regions: insula, putamen, temporal, parietal, and prefrontal cortices, septal region and cerebellum. Yet, slight gender differences have also been observed. For example, an activation of the medial amygdala has been reported in female orgasm (Komisaruk et al., 2004) but not in men's (except in Heath's study). However, this gender difference is challenged by a large number of clinical studies demonstrating a clear involvement of the mesial temporal lobe and particularly the amygdala in the mediation of human sexual function (Baird et al., 2006). In addition, other gender differences have been demonstrated in human orgasm. More precisely, a woman's orgasm specifically involves the nucleus accumbens, anterior cingulate, hippocampus, hypothalamus, and preoptic area, although a male orgasm specifically involves the ventral tegmental area (a brain structure connected to the nucleus accumbens via the mesolimbic pathway and involved in a wide variety of rewarding behaviors), thalamus, and visual cortex.

Nevertheless, these gender differences have to be interpreted with caution due to some methodological differences between male and female studies (such as orgasm-related motor confounds that may have been induced during online ejaculation in men but not in women). Understanding the inter-relationships of the brain mechanisms of human orgasm without methodological issues will be an important challenge for future neuroimaging studies that aim to assess this question. As a matter of fact, neuroimaging studies on male orgasm report brain mechanisms sustaining ejaculation as an indicator of orgasm. However, although men usually experience orgasm and ejaculation in conjunction with each other, ejaculation does not always occur at the time of the subjective experience of orgasm. Thus, a new methodological twist is needed in the study of the neural basis of human orgasm based on some reports of men who ejaculate without experiencing any orgasm pleasure during intercourse (orgasmic anhedonia; Ralph & Wylie, 2005), men who subjectively experience orgasm without ejaculation (such as men suffering from spinal cord injury, e.g., McMahon et al., 2004; Ralph & Wylie, 2005; Sipski & Arenas, 2006; or men with retrograde ejaculation, McMahon et al., 2004), and also on numerous reports of women faking orgasm during intercourse with their partner. Further studies should be done to: (i) clarify and better understand gender differences in human orgasms; (ii) and also to discern whether every orgasm-related cerebral activation is a cause or an effect of human orgasm. For instance, further neuroimaging studies (e.g., combined EEG/fMRI studies) using the same experimental set up for both men and women and focusing rather on the subjective pleasurable satisfaction than the peripheral manifestations of orgasm could provide new insights in the understanding of the neural basis of gender differences in orgasm.

9. Conclusions

The discovery of central (spinal- and cerebral-driven) effects during orgasm has implications regarding the mechanisms underlying the physiological responses and also the way to integrate women's orgasm in part as a cognitive function. By demonstrating which brain areas within and outside the limbic system sustain a woman's orgasm, the present review highlights how the heterogeneity of each brain area's architecture and their respective multifaceted functional connections imbue the notable complexity of women's orgasm experience. We hope that the development of neuroimaging techniques applied in parallel with a neuropsychological approach will encourage new work on the neuropsychology of orgasm. This new work can then be integrated into multidimensional models of sexual function. Moving this research forward involves to better understand the hierarchical interactions between the various orgasm components, not only with a correlation analysis but also with combined high spatio-temporal resolution techniques (such as, 3D-EEG, fMRI, Transcranial Magnetic Stimulation, and Diffusion Tensor Imaging) demonstrating the causal necessity, and the direction of the causality of orgasm mechanisms. Mapping each step of

human sexual response with a high spatio-temporal resolution will have also significant clinical benefits aside from making excellent educational material. Further multi-disciplinary studies are thus needed to identify the spatio-temporal dynamic of woman's orgasm, its dysfunctions, and possible new treatments.

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References

Abraham, G. (2002). The psychodynamics of orgasm. *International Journal of Psychoanalysis*, *83*, 325–338.

Allison, T., McCarthy, G., Luby, M., Puce, A., & Spencer, D. D. (1996). Localization of functional regions of human mesial cortex by somatosensory evoked potential recording and by cortical stimulation. *Electroencephalogry and Clinical Neurophysiology*, *100*, 126–140.

Alzate, H. (1985). Vaginal eroticism and female orgasm: A current appraisal. *Journal of Sex and Marital Therapy*, *11*, 271–284.

Argiolas, A., & Melis, M. R. (2003). The neurophysiology of the sexual cycle. *Journal of Endocrinological Investigation*, *26*, 20–22.

Baird, A. D., Wilson, S. J., Bladin, P. F., Saling, M. M., & Reutens, D. C. (2006). Neurological control of human sexual behaviour: Insights from lesions studies. *Journal of Neurology, Neurosurgery, and Psychiatry*, 22.

Bancaud, J., Favel, P., Bonis, A., Bordas-Ferrer, M., Miravet, J., & Talairach, J. (1970). Manifestations sexuelles paroxytiques et epilepsie temporale. *Revue Neurologique*, *123*, 217–230.

Bancroft, J. (1999). Cardiovascular and endocrine changes during sexual arousal and orgasm. *Psychosomatic Medicine*, *199*(61), 290–291.

Bancroft, J., Loftus, J., & Long, J. S. (2003). Distress about sex: A national survey of women in heterosexual relationships. *Archives of Sexual Behavior*, *32*, 193–208.

Basson, R. (2000). The female sexual response: A different model. *Journal of Sex and Marital Therapy*, *26*, 51–65.

Basson, R. (2001). Female sexual response: The role of drugs in the management of sexual dysfunction. *Obstetrics and Gynaecology*, *98*, 350–353.

Basson, R. (2002). A model of women's sexual arousal. *Journal of Sex and Marital Therapy*, *28*, 1–10.

Bentler, P. M., & Peeler, W. H., Jr. (1979). Models of female orgasm. *Archives of Sexual Behavior*, *8*, 405–423.

Broca, P. P. (1861). Perte de la parole; ramolissement chronique et destruction partielle du lobe antérieur gauche de cerveau. *Bulletins de la Société d'Anthropologie de Paris*, *2*, 235–238.

Brody, S., & Kruger, T. H. (2006). The post-orgasmic prolactin increase following intercourse is greater than following masturbation and suggests greater satiety. *Biological Psychology*, *71*, 312–315.

Buss, D. M. (2003). *The evolution of desire*. New York: Basic Books.

Calleja, J., Carpizo, R., & Berciano, J. (1988). Orgasmic epilepsy. *Epilepsia*, *29*, 635–639.

Campbell, B., & Petersen, W. E. (1953). Milk "let-down" and the orgasm in the human female. *Human Biology*, *25*, 165–168.

Carmichael, M. S., Warburton, V. L., Dixen, J., & Davidson, J. M. (1994). Relationships among cardiovascular, muscular, and oxytocin responses during human sexual activity. *Archives of Sexual Behavior*, *23*, 59–79.

Carr, L., Iacoboni, M., Dubeau, M. C., Mazziotta, J. C., & Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *The Proceedings of the National Academy of Sciences of the United States of America*, *100*, 5497–5502.

Chuang, Y. C., Lin, T. K., Lui, C. C., Chen, S. D., & Chang, C. S. (2004). Tooth-brushing epilepsy with ictal orgasms. *Seizure*, *13*, 179–182.

Cohen, H. D., Rosen, R. C., & Goldstein, L. (1976). Electroencephalographic laterality changes during human sexual orgasm. *Archives of Sexual Behavior*, *5*, 189–199.

Coolen, L. M. (2005). Neural control of ejaculation. *Journal of Comparative Neurology*, *493*, 39–45.

Corkin, S. (2002). What's new with the amnesic patient H.M.? *Nature Reviews Neuroscience*, *3*, 153–160.

Crevenna, R., Homann, N., Feichtinger, M., Ott, E., & Korner, E. (2000). Spontaneous orgasm—an epileptic case without structural correlate. *British Journal of Psychiatry*, *176*, 100.

Currier, R. D., Little, S. C., Suess, J. F., & Andy, O. J. (1971). Sexual seizures. *Archives of Neurology*, *25*, 260–264.

Darling, C. A., Davidson, J. K., Sr., & Jennings, D. A. (1991). The female sexual response revisited: Understanding the multiorgasmic experience in women. *Archives of Sexual Behavior*, *20*, 527–540.

Duncan, S., Blacklaw, J., Beastall, G. H., & Brodie, M. J. (1997). Sexual function in women with epilepsy. *Epilepsia*, *38*, 1074–1081.

Dunn, K. M., Cherkas, L. F., & Spector, T. D. (2005). Genetic influences on variation in female orgasmic function: A twin study. *Biology Letters*, *1*, 260–263.

Ellison, J. M. (1998). Antidepressant-induced sexual dysfunction: Review, classification, and suggestions for treatment. *Harvard Review of Psychiatry*, *6*, 177–189.

Erickson, T. C. (1945). Erotomania (nymphomania) as an expression of cortical epileptiform discharge. *Archives of Neurology and Psychiatry*, *53*, 226–231.

Exton, M. S., Bindert, A., Krüger, T., Scheller, F., Hartmann, U., & Schedlowski, M. (1999). Cardiovascular and endocrine alterations after masturbation-induced orgasm in women. *Psychosomatic Medicine*, *61*, 280–289.

Fadul, C. E., Stommel, E. W., Dragnev, K. H., Eskey, C. J., & Dalmau, J. O. (2005). Focal paraneoplastic limbic encephalitis presenting as orgasmic epilepsy. *Journal of Neurooncology*, *72*, 195–198.

Freemon, F. R., & Nevis, A. H. (1969). Temporal lobe sexual seizures. *Neurology*, *19*, 87–90.

Gastaut, H., & Collomb, H. (1954). Etude du comportement sexuel chez les epileptiques psychomoteurs. *Annals of Medicopsychology*, *112*, 657–696.

Gautier-Smith, P. C. (1980). Atteinte des fonctions cécébrales et troubles du comportement sexuel. *Revue Neurologique*, *136*, 311–319.

Georgiadis, J. R., Kortekaas, R., Kulpers, R., Nieuwenburg, A., Pruim, J., Reinders, A. A., et al. (2006). Regional cerebral blood flow changes associated with clitorally induced orgasm in healthy women. *European Journal of Neuroscience*, *24*, 3305–3316.

Ghika-Schmid, F., Assal, G., De Tribolet, N., & Regli, F. (1995). Kluver–Bucy syndrome after left anterior temporal resection. *Neuropsychologia*, *33*, 101–113.

Giuliano, F., Allard, J., Compagnie, S., Alexandre, L., Droupy, S., & Barnabe, J. (2001). Vaginal physiological changes in a model of sexual arousal in anesthesized rats. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *281*, 4140–4149.

Glenn, J., & Kaplan, E. H. (1968). Types of orgasm in women: A critical review and redefinition. *Journal of the American Psychoanalytic Association*, *16*, 549–564.

Graber, B., Rohrbaugh, J. W., Newlin, D. B., Varner, J. L., & Ellingson, R. J. (1985). EEG during masturbation and ejaculation. *Archives of Sexual Behavior*, *14*, 491–503.

Heath, R. G. (1972). Pleasure and brain activity in man. *Journal of Nervous and Mental Disease*, *154*, 3–18.

Heaton, J. P. W., & Adams, M. A. (2003). Update on central function relevant to sex: Remodeling the basis of drug treatments for sex and the brain. *International Journal of Impotence Research*, *15*, S25–S32.

Henton, C. L. (1976). Nocturnal orgasm in college women: Its relation to dreams and anxiety associated with sexual factors. *The Journal of Genetic Psychology*, *129*, 245–251.

Hite, S. (1976). *The Hite report: A nationwide study of female sexuality*. New York: Dell.

Holstege, G. (2005). Central nervous system control of ejaculation. *World Journal of Urology*, *23*, 109–114.

Holstege, G., Geopardis, J. R., Paans, A. M., Meiners, L. C., van der Graaf, F. H., & Reinders, A. A. (2003). Brain activation during human male ejaculation. *Journal of Neuroscience*, *23*, 9185–9193.

Holstege, G., & Georgiardis, J. R. (2004). The emotional brain: Neural correlates of cat sexual behavior and human male ejaculation. *Progress in Brain Research*, *143*, 39–45.

Jackson, P. L., Brunet, E., Meltzoff, A. N., & Decety, J. (2006). Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain. *Neuroimage*, *44*, 752–761.

Janszky, J., Ebner, A., Szupera, Z., Schulz, R., Hollo, A., Szucs, A., et al. (2004). Orgasmic aura—A report of seven cases. *Seizure*, *13*, 441–444.

Janszky, J., Szucs, A., Halasz, P., Borbely, C., Hollo, A., Barsi, P., et al. (2002). Orgasmic aura originates from the right hemisphere. *Neurology*, *58*, 302–304.

Kampe, K. K. W., Frith, C. D., Dolan, R. J., & Frith, U. (2001). Reward value of attractiveness and gaze reinforcing stimuli that serve basic survival. *Nature*, *413*, 589–602.

Kaplan, H. S. (1974). *The new sex therapy: Active treatment of sexual dysfunctions*. New York: Brunner/Mazel.

Kaplan, H. S. (1979). *Disorders of sexual desire and other new concepts and techniques in sex therapy*. New York: Brunner/Hazel.

Kaplan, H. S. (1987). *The illustrated manual of sex therapy*. New York: Brunner-Routledge.

Kinsey, A. C., Pomeroy, W. B., Martin, C. E., & Gebbard, O. H. (1953). *Sexual Behaviour in the human female*. Philadelphia: W.B. Saunders Company.

Kluver, H., & Bucy, P. C. (1939). Preliminary analysis of the functions of the temporal lobes in monkeys. *Archives of Neurology and Psychiatry*, *42*, 979–1000.

Komisaruk, B. R., & Whipple, B. (1995). The suppression of pain by genital stimulation in females. *Annual Review of Sex Research*, *6*, 151–186.

Komisaruk, B. R., & Whipple, B. (2005). Functional MRI of the brain during orgasm in women. *Annual Review of Sex Research*, *16*, 62–86.

Komisaruk, B. R., Whipple, B., Crawford, A., Liu, W. C., Kalnin, A., & Mosier, K. (2004). Brain activation during vaginocervical self-stimulation and orgasm in women with complete spinal cord injury: fMRI evidence of mediation by the vagus nerves. *Brain Research*, *1024*, 77–88.

Krain, A. L., Hefton, S., Pine, D. S., Xavier Castellanos, M., Klein, R. G., & Milham, M. P. (2006). An fMRI examination of developmental differences in the neural correlates of uncertainty and decision-making. *Journal of Child Psychology and Psychiatry*, *47*, 1023–1030.

Kratochvil, S. (1993). The duration of female orgasm. *Cesk Psychiatry*, *89*, 296–299.

Ladas, A., Whipple, B., & Perry, J. D. (1982). *The G spot and other recent discoveries about human sexuality*. New York: Holt, Rinehart, and Winston.

Ledoux, J. E. (1996). *The emotional brain*. New York: Simon & Schuster.

Levin, R. J. (1981). The female orgasm—A current appraisal. *Journal of Psychosomatic Research*, *25*, 119–133.

Levin, R. J., & van Berlo, W. (2004). Sexual arousal and orgasm in subjects who experience forced or non-consensual sexual stimulation—A review. *Journal of Clinical Forensic Medicine*, *11*, 82–88.

Levin, R. J., & Wagner, G. (1985). Orgasm in women in the laboratory—Quantitative studies on duration, intensity, latency, and vaginal blood flow. *Archives of Sexual Behavior*, *14*, 439–449.

Lilly, R., Cummings, J. L., Benson, F., & Frankel, M. (1983). The human Kluver–Bucy syndrome. *Neurology*, *33*, 1141–1145.

Lloyd, E. A. (2005). *The case of the female orgasm: Bias in science of evolution*. Yale: Harvard University Press.

Maclean, P. D. (1952). Some psychiatric implications of physiological studies on frontotemporal portion of limbic system (visceral brain). *Electroencephalography and Clinical Neurophysiology Supplement*, *4*, 407–418.

MacLean, P. (1990). *The triune brain in evolution*. New York: Plenum Press.

Mah, K., & Binik, Y. M. (2001). The nature of human orgasm: A critical review of major trends. *Clinical Psychology Review*, *21*, 823–856.

Mah, K., & Binik, Y. M. (2005). Are orgasms in the mind or the body? Psychosocial versus physiological correlates of orgasmic pleasure and satisfaction. *Journal of Sex and Marital Therapy*, *31*, 187–200.

Masters, W. H., & Johnson, V. (1966). *Human sexual response*. Boston: Little, Brown and Company.

McKenna, K. E. (1999). The brain is the master organ in sexual function: Central nervous system control of male and female sexual function. *International Journal of Impotence Research*, *11*, S48–S55.

McKenna, K. E. (2002). The neurophysiology of female sexual function. *World Journal of Urology*, *20*, 93–100.

McMahon, C. G., Abdo, C., Incrocci, L., Perelman, M., Rowland, D., Waldinger, M., et al. (2004). Disorders of orgasm and ejaculation in men. *The Journal of Sexual Medicine*, *1*, 58–65.

Meston, C. M., Hull, E., Levin, R. J., & Sipski, M. (2004). Women's orgasm. In T. F. Lue, R. Basson, R. Rosen, F. Giuliano, S. Khoury, & F. Montorsi (Eds.), *Sexual medicine: Sexual dysfunctions in men and women* (pp. 783–850). Paris: Health Publications.

Money, J. (1960). Phantom orgasm in the dreams of paraplegic men and women. *Archives of General Psychiatry*, *3*, 372–383.

Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A., & Rosenbaum, R. S. (2006). The cognitive neuroscience of remote episodic, semantic and spatial memories. *Current Opinion in Neurobiology*, *16*, 179–190.

Moscovitch, M., Rosenbaum, R. S., Gilboa, A., Addis, D. R., Westmacott, R., Grady, C., et al. (2005). Functional neuroanatomy of remote episodic, semantic and spatial memory: A unified account based on multiple trace theory. *Journal of Anatomy*, *207*, 35–66.

Mosovich, A., & Tallaferro, A. (1954). Studies of EEG and sex function orgasm. *Diseases of the Nervous System*, *15*, 218–220.

Mould, D. E. (1980). Neuromuscular aspects of women's orgasms. *The Journal of Sex Research*, *16*, 193–201.

Muchembled, R. (2005). *L'orgasme et l'Occident*.

O'Doherty, J., Winston, J., Critchley, H., Perrett, D., Burt, D. M., & Dolan, R. J. (2003). Beauty in a smile: The role of medial orbitofrontal cortex in facial attractiveness. *Neuropsychologia*, *41*, 147–155.

O'Doherty, J. P. (2004). Reward representations and reward-related learning in the human brain: Insights from neuroimaging. *Current Opinion in Neurobiology*, *14*, 769–776.

O'Hare, H. (1951). Vaginal versus clitoral orgasm. *International Journal of Sexology*, *4*, 243–244.

Papez, J. W. (1995). A proposed mechanism of emotion. (Original work in 1937). *Journal of Neuropsychiatry and Clinical Neurosciences*, *7*, 103–112.

Penfield, W., & Jaspers, H. (1954). *The functional anatomy of the brain*.

Ralph, D. J., & Wylie, K. R. (2005). Ejaculatory disorders and sexual function. *BJU International*, *95*, 1181–1186.

Reading, P. J., & Will, R. G. (1997). Unwelcome orgasms. *The Lancet*, *350*, 1746.

Remillard, G. M., Andremann, F., Testa, G. F., Gloor, P., Aube, M., Martin, J. B., et al. (1983). Sexual ictal manifestations predominate in women with temporal lobe epilepsy: A finding suggesting sexual dimorphism in the human brain. *Neurology*, *33*, 323–330.

Rorie, A. E., & Newsome, W. T. (2005). A general mechanism for decision-making in human brain? *Trends in Cognitive Science*, *9*, 41–43.

Rowland, D. L. (2006). Neurobiology of sexual response in men and women. *CNS Spectrums*, *11*, 6–12.

Rubia, K., & Smith, A. (2004). The neural correlates of cognitive time management: A review. *Acta Neurobiologiae Experimentalis (Warsaw)*, *64*, 329–340.

Ruff, R. L. (1980). Orgasmic epilepsy. *Neurology*, *30*, 1252.

Sholty, M. J., Ephross, P. H., Plaut, S. M., Fischman, S. H., Charnas, J. F., & Cody, C. A. (1984). Female orgasmic experience: A subjective study. *Archives of Sexual Behavior*, *13*, 155–164.

Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for pain involves the affective but not sensory components of pain. *Science*, *303*, 1157–1162.

Singer, T., Seymour, B., O'Doherty, J., Stephan, K. E., Dolan, R. J., & Frith, C. D. (2006). Empathic neural responses are modulated by the perceived fairness of others. *Nature*, *439*, 466–469.

Sipski, M. L., Alexander, C. J., & Rosen, R. C. (1995). Orgasm in women with spinal cord injuries: A laboratory-based assessment. *Archives of Physical Medicine and Rehabilitation*, *76*, 1097–1102.

Sipski, M. L., & Arenas, A. (2006). Female sexual function after spinal cord injury. *Progress in Brain Research*, *152*, 441–447.

Spector, I. P., & Carey, M. P. (1990). Incidence and prevalence of the sexual dysfunctions: A critical review of the empirical literature. *Archives of Sexual Behavior*, *19*, 389–408.

Stein, E. A., Pankiewicz, J., Harsch, H. H., Cho, J. K., Fuller, S. A., Hoffmann, R. G., et al. (1998). Nicotine-induced limbic cortical activation in the human brain: A functional MRI study. *American Journal of Psychiatry*, *155*, 1009–1015.

Symons, D. (1979). *The evolution of human sexuality*. New York: Oxford University.

Tanaka, S. C., Doya, K., Okada, G., Ueda, K., Okamoto, Y., & Yamawaki, S. (2004). Prediction of immediate and future rewards differentially recruits cortico-basal ganglia loops. *Nature Neuroscience*, *7*, 887–893.

Tiihonen, J., Kuikka, J., Kupila, J., Partanen, K., Vainio, P., Airaksinen, J., et al. (1994). Increase in cerebral blood flow of right prefrontal cortex in man during orgasm. *Neuroscience Letters*, *170*, 241–243.

Torelli, D., & Bosna, F. (1958). Alterazioni del'erotismo nell'epilessia e nei tumori cerebrali. *Acta Neurologica*, *23*, 154–165.

Truitt, W. A., & Coolen, L. M. (2002). Identification of a potential ejaculation generator in the spinal cord. *Science*, *297*, 1566–1569.

Turk, D. J., Banfield, J. F., Walling, B. R., Heatherton, T. F., Grafton, S. T., Handy, T. C., et al. (2004). From facial cue to dinner for two: The neural substrates of personal choice. *Neuroimage*, *22*, 1281–1290.

Vance, E. B., & Wagner, N. N. (1976). Written descriptions of orgasms: A study of sex differences. *Archives of Sexual Behavior*, *5*, 87–89.

Whipple, B. (2002). Women's sexual pleasure and satisfaction. A new view of female sexual function. *The Female Patient*, *27*, 39–44.

Whipple, B., & Brash-McGreer, K. (1997). Management of female sexual dysfunction. In *Sexual function in people with disability and chronic illness. A health professional's guide*. Gaithersburg, MD: Aspen Publishers, Inc., pp. 509–534.

Whipple, B., & Komisaruk, B. R. (2002). Brain (PET) responses to vaginal-cervical self-stimulation in women with complete spinal cord injury: Preliminary findings. *Journal of Sex and Marital Therapy*, *28*, 79–86.

Whipple, B., Ogden, G., & Komisaruk, B. R. (1992). Physiological correlates of imagery-induced orgasm in women. *Archives of Sexual Behavior*, *21*, 121–133.