

# Doing it . . . wild? On the role of the cerebral cortex in human sexual activity

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**Background:** We like to think about sexual activity as something fixed, basic and primal. However, this does not seem to fully capture reality. Even when we relish sex, we may be capable of mentalizing, talking, voluntarily postponing orgasm, and much more. This might indicate that the central control mechanisms of sexual activity are quite flexible and susceptible to learning mechanisms, and that cortical brain areas play a critical part.

**Objective:** This study aimed to identify those cortical areas and mechanisms most consistently implicated in sexual activity.

**Design:** A comprehensive review of the human functional neuroimaging literature on sexual activity, i.e. genital stimulation and orgasm, is made.

**Results:** Genital stimulation recruits the classical somatosensory matrix, but also areas far beyond that. The posterior insula may be particularly important for processing input from the engorged penis and coordinating penile responses. Extrastriate visual cortex tracks sexual arousal and responds to genital stimulation even when subjects have their eyes closed. The ventromedial prefrontal cortex is also tightly coupled to sexual arousal, but low activity in this area predicts high sexual arousal.

**Conclusion:** This review has indicated cortical sites where activity is moderated by tactile genital inflow and high sexual arousal. Behavioral implications are discussed and where possible the relevance for learning mechanisms is indicated. Overall, it is clear that the cerebral cortex has something to say about sexual activity.

Keywords: *functional neuroimaging; insula; ventromedial prefrontal cortex; extrastriate visual cortex; penis; clitoris; orgasm*

In the days of phrenology, ‘amativeness’ (sexual arousal) was assigned to the cerebellum and, therefore, to a ‘lower’ part of the brain (Gall, 1822). This is no coincidence. Even today, many people would be inclined to support Gall’s intuition about sexuality being grounded in low-level processes. In a way, the seeds planted in those days came to blossom a century later with an impressive amount of neuroscientific work on sexual behavior that focused primarily on animal models, sexual reflexes, gonadal hormones, and primitive neuronal control systems. The involvement of areas beyond the hypothalamus, or the influence of more complex forms of learning, was often not considered (e.g. Coolen, Allard, Truitt, & McKenna, 2004; McKenna, 2002). Yet, for all its primitive reproductive benefits, human sexuality comes in an astounding variety of behaviors, most of which, by the way, are of a recreative rather than a procreative character.

One way to understand the sheer complexity of human sexual behavior is to look at it from the viewpoint of brain evolution. Central nervous systems

like ours enable us to adapt to unpredictable environmental challenges and to live in complex social structures. In humans, much of the brain’s resources are, therefore, devoted to highly sophisticated, cognitively taxing functions, like introspection, self-other relations, empathy, inhibitory control, planning, and foresight (Forbes & Grafman, 2010). The evolution of these functions has proven to be highly successful with respect to the survival of the human species, which is perhaps mainly due to the fact that they enable strong top-down control over primal drives and reflexes. However, homeostatic signals, if strong enough, will reach consciousness for behavior to adapt. Thus, it is clear that there must be strong mutual interactions between primordial brain areas and more recently evolved areas of the brain like the cerebral cortex.

For food-related behaviors, we readily accept this: in most societies, eating is strongly regulated, and people learn to ignore, or control, homeostatic signals, at least to a certain extent. Even when we consume food, we are expected to behave according to societal rules and

mores, which include what we eat and how we eat it, and even saying we like food when we do not. Strangely, we would be less inclined to admit that most of the above properties also apply to sexual behavior, including the actual physical consummation of sex. Yet, the way we do this, be it alone or with another person, is strongly shaped by cultural forces and learning from experience. This learning can take extreme forms, like tantric sex where people learn to postpone or even avoid orgasm to enhance interconnectedness, or sadomasochistic practices where sexual pleasure is derived from noxious stimulation. If sexual encounters indeed help to shape future sexual behavior, the nature of sexual experiences should be very important. However, influential sexual experiences need not be positive, which may explain at least to some extent how sexual difficulties or even dysfunctions may develop (Both et al., 2008; Hoffmann, Peterson, & Garner, 2012; Woodson, 2002).

In the present concise review, I focus on the structure that may be considered the crown of human evolution, the cerebral cortex, to show that it plays a decisive role in something as primal as sexual activity. More specifically, I will make an attempt to identify cortical areas and brain mechanisms that should be most relevant or susceptible to sexual learning.

### Disclaimer

A few remarks are in order before I continue this review. First, I will primarily review results from positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies. For those interested in detailed information on the workings of these functional neuroimaging methods and the interpretation of the data they produce, some great reviews are available (e.g. Poldrack et al., 2008; Raichle & Mintun, 2006). Second, whenever I speak of sexual activity, I refer to the physical consummation of sexual arousal, either partnered or via self-stimulation. In the human neuroimaging laboratory, this entails stimulation of aroused genitalia (penis, clitoris, and vagina) and orgasm induced by such stimulations. Unfortunately, it excludes intimate love-making or coital intercourse (Georgiadis, in press). In this review, the focus will be on genital stimulation and high sexual arousal. Third, most parts of the cerebral cortex are unique to human beings or at least primates. This frustrates comparisons with rodent models of sexual behaviour, which largely ignore cortical functionality and focus on subcortical control mechanisms (this statement by no means implies that subcortical involvement is unimportant in sexual neuroimaging paradigms). Finally, human neurobiological research on sexual activity is sparse, which is mainly due to methodological difficulties and cultural constraints (Georgiadis, in press). One of the consequences is that there is very little empirical evidence – if any – that learning shapes human

brain function with respect to components of sexual activity. The appetitive phase has received more attention in this respect and will be considered by other authors in this issue.

### Sexual reward

Sexual activity is very rewarding in both women and men. This reward is necessary for the conditioning of sexual preferences and heightened anticipation for sex in the long term, even when intense reward after ejaculation or orgasm causes sexual quiescence short term (Pfaus, 2009). In other words, the pleasure felt during sex, particularly during orgasm, serves to reinforce future sexual behavior. The opposite, a state of sexual non-reward (i.e. *bad sex*), may be induced by naloxone, a mu-opioid antagonist, when given *during* sexual activity (Holloway, 2012; Murphy, Checkley, Seckl, & Lightman, 1990). At least in rats, this leads to decreased sexual interest and motivation (Kippin & Pfaus, 2001). These observations demonstrate that the quality of sexual activity contributes to sexual learning, i.e. shapes subsequent sexual behavior.

What we call sexual reward in male rats usually relates to ejaculation and may therefore be the equivalent of the effect of ejaculation and orgasm in men. Recent studies demonstrate that sexual activity (clitoris stimulation) is also rewarding for female rats (Parada, Chamas, Censi, Coria-Avila, & Pfaus, 2010). However, human orgasm and the high sexual arousal leading up to it are more than reward or simple pleasure. They may encompass – next to a strong sympathetic tone and impressive changes in peripheral physiology – a wide array of cognitive and mental transitions, including loss of behavioral control and feelings of release, changes in self-awareness, and altered appreciation of space and time, all of which are most prominent during orgasm (Levin, 2004; Mah & Binik, 2001; Masters & Johnson, 1966). Though it is impossible to verify, such experiences may be unique to the human situation, and one could therefore argue that they are associated with cerebral cortical functionality. This is also supported by the fact that orgasms (including the full range of peripheral physiological responses) may be induced by sheer mental force (e.g. imagery), independent of any sexual bodily stimulation (Whipple, Ogden, & Komisaruk, 1992). In turn, these particular mental phenomena might significantly add to subjective sexual pleasure and, thereby, also to the sexual learning mechanisms I briefly touched upon earlier.

### Input to the central sexual system: genital somatosensory inflow

Genital afferent inflow may signal multiple sensory qualities and travel *via* multiple pathways to reach brainstem, midbrain, and foremost, the somatosensory

and visceral thalamus (Everaert et al., 2010; Hubscher & Johnson, 2003; Hubscher, Reed, Kaddumi, Armstrong, & Johnson, 2010; Komisaruk et al., 1996). From these relay centers, genital afferent information should be capable of reaching many parts of the brain, particularly cortical areas specialized in processing somatosensory information, i.e. somatosensory cortices and insula. Though there is no direct proof, pleasurable genital stimuli (warm temperature, friction, etc.) are likely to be already encoded at the peripheral level. Slowly conducting unmyelinated C fibers, which are perhaps best known for their role in conveying noxious information to the brain, may, under certain conditions, also convey pleasant touch (Vallbo, Olausson, Wessberg, & Norrsell, 1993). Interestingly, such fibers are particularly abundant in the glans (distal end) of the penis (Halata & Munger, 1986) and, therefore, most likely also in the glans clitoridis.

Human neuroimaging studies have revealed that external genitalia (or the somatosensory nerves supplying them), when stimulated, undergo very similar central processing as other areas of the body. Most of the evidence supports a distinct dorsolateral location on the postcentral gyrus (primary somatosensory cortex, SI) for both penis and clitoris, regardless of whether the stimulation happened in an intentionally erotic context (Georgiadis et al., 2006, 2010) or not (Kell, von Kriegstein, Rosler, Kleinschmidt, & Laufs, 2005; Michels, Mehnert, Boy, Schurch, & Kollias, 2010). The secondary somatosensory cortex (SII), located in the parietal operculum, is also readily activated by stimulation of (nerves of) the external genitalia (Georgiadis et al., 2006, 2010; Georgiadis & Holstege, 2005; Kell et al., 2005; Komisaruk et al., 2011; Mäkelä et al., 2003; Michels et al., 2010; Pukall et al., 2005), and this activation gains strength when stimulation becomes more salient (e.g. painful, see, e.g. Pukall et al., 2005). Like on SI, the penis seems to occupy a distinct location on SII (Kell et al., 2005). The third area implicated in processing of genital sensitivity is the insula, in particular its middle and posterior divisions. This involvement was found upon dorsal penile (Mäkelä et al., 2003) and clitoral (Michels et al., 2010) nerve stimulation, during tactile genital stimulation in a sexual context (Georgiadis et al., 2006, 2010; Georgiadis & Holstege, 2005) and during stimulation of the vestibulum (area around vaginal opening) that was unintended to be erotic (Pukall et al., 2005). However, middle and posterior insula responses were much stronger in subjects who perceived the vestibular stimulation as painful, whereas during intentionally non-erotic genital stimulation insular activation was absent or at least not reported (Kell et al., 2005; Komisaruk et al., 2011). These findings support a growing body of evidence that the posterior insula is an important area for surprisingly detailed encoding

of 'salient' C fiber stimulation, like that related to noxious stimulation (Henderson, Rubin, & Macefield, 2011) or pleasant touch (Björnsdotter, Löken, Olausson, Vallbo, & Wessberg, 2009), and/or the fundamental behavioral responses that are tightly coupled to such input (Berthier, Starkstein, & Leiguarda, 1988; Craig, 2002). One might conceive genitalia, especially when aroused, to also be distinctively encoded in posterior insula, but this remains to be determined.

Penile tumescence often occurs without any form of somatosensory stimulation, e.g. as a result of visual input or imagery. These so-called psychogenic erections are insufficient to produce activity in SI, but readily correlate with activity in middle and especially posterior insula (Arnou et al., 2002; Moulrier et al., 2006; Mouras et al., 2008; Redouté et al., 2000). In addition, in a direct group comparison, sexual tactile penis stimulation elicited greater activity in posterior insula than similar stimulation on the clitoris (Georgiadis, Reinders, Paans, Renken, & Kortekaas, 2009). These observations suggest that posterior insula activation in sexual paradigms relates to genital engorgement more than to the stimulation *per se*. Of note, seeing and feeling a caress activate a very similar area of posterior insula (Morrison, Björnsdotter, & Olausson, 2011), and this vicarious property of the posterior insula could explain why it activates to visual erotica. Other relevant information is that C fiber stimulation causes sympathetic responses (Olausson et al., 2008) and that psychogenic erections are believed to stand under sympathetic control (Giuliano & Rampin, 2000). Together, this suggests that, regardless of the modality of the sexually salient sensory input, the posterior insula mediates a behavioral response that involves sufficient sympathetic tone for engorgement of the erectile bodies. At least in macaque, the posterior insula is connected to supracallosal cingulate cortex (Mesulam & Mufson, 1982), a region (midcingulate cortex) that in humans plays a pivotal role in coordinating behavioral responses with arousal levels and cognitive constructs (Paus, 2001). Not only midcingulate cortex but also premotor and supplementary motor areas showed the same association with penile erection and sexual penis stimulation as the posterior insula (Georgiadis et al., 2010), indicating a possible gateway for higher cortical and motor systems to connect to genital inflow and/or responses.

### Prefrontal influences

When we assume that different elements of genital sensory information, at least at the outset, can be processed with a fair degree of specificity in human cortex, the question is how this kind of information is integrated with other elements of the situation to become a unified sexual experience. To date, no study in humans has been able to answer this key question.

Yet, it is intriguing to realize that, depending on context, sexually salient stimulation does or does not cause genitalia to become engorged and that either response may or may not lead to subjective sexual arousal. This suggests that other brain areas are in a position to modify sexually salient input to allow or disallow sexual and genital arousal. Such modification is likely to be driven by homeostatic needs, learned associations, and prefrontal sociomoral templates of adequate behavior (Forbes & Grafman, 2010). One of the first studies trying to expose sexual regulation in the brain showed that attempted voluntary inhibition of visually evoked sexual desire involved enhanced medial prefrontal (PFC) and cingulate cortex activity and downregulation of subcortical activity (Beauregard, Levesque, & Bourgouin, 2001). Another example comes from clinical practice: certain classes of serotonin-reuptake inhibitors (SSRI's) are effective in delaying ejaculation in men suffering from premature ejaculation (McMahon et al., 2008), which probably owes to serotonergic modulation of PFC function (Pfaus, 2009). Recent developments in neuroimaging analysis are expected to open up exciting new avenues to more precisely outline neuronal networks and functional connections relevant to higher-order regulation of sexual function, which could encompass the role of learned associations.

One of the cerebral hallmarks of high sexual arousal during genital stimulation is a steady decrease of activity in ventromedial PFC and medial temporal cortices (Georgiadis et al., 2006, 2010; Georgiadis & Holstege, 2005). Conversely, ventromedial PFC and adjacent subgenual anterior cingulate cortex were most *active* during the phase of steepest penile *detumescence* after sexual stimulation had ceased (Georgiadis et al., 2010). It is well-documented that these areas play a critical role in moral affiliations, self-other relations, self-awareness, and related behaviors (Forbes & Grafman, 2010; Lou, Gross, Biermann-Ruben, Kjaer, & Schnitzler, 2010). One way to conceptualize deactivation of these areas in relation to high sexual arousal is that it helps to dissolve normal body boundaries, thereby facilitating sexual interactions. In turn, this might contribute significantly to the experience of sexual arousal. If, conversely, enhanced activity of these areas is inhibitory to sexual arousal, these areas would provide an interesting gateway to sexual regulation. For one, it would predict their activation to counteract sexual arousal. Moreover, it would imply that exaggerated moral or self-referential thinking, which can in fact be taken from cultural learning or learning from experience, counteracts sexual arousal. These predictions are in line with clinical findings of ventromedial PFC and subgenual anterior cingulate cortex hyperactivity in depressed people (Hamani et al., 2011; Mayberg, 1997). During orgasm, activity in these areas seems to approach minimum

levels and, moreover, spreads to orbitofrontal and dorsal parts of the PFC, which might at that point reflect one of the main features of orgasm, the experience of 'loss of control' (Georgiadis, in press; Georgiadis et al., 2006, 2009; Georgiadis, Reinders, van der Graaf, Paans, & Kortekaas, 2007).

### Role of other areas outside the somatosensory matrix

Returning to the general activation pattern during sexual genital stimulation, it is clear that areas outside the classic somatosensory matrix are also involved. A particularly intriguing observation in male subjects is that visual cortices, especially extrastriate visual areas in the inferior temporal gyrus (ventral occipitotemporal cortex, vOT), show clear involvement in sexual genital stimulation, even when subjects had their eyes closed (Georgiadis et al., 2010; Georgiadis & Holstege, 2005). Further, this vOT effect was stronger in men than in women when their genitalia were stimulated (Georgiadis et al., 2009). How can this effect, which was robust across subjects, be understood? First, it supports findings of vOT responding to both somatosensory and visual stimuli (Beauchamp, 2005), underscoring the multimodal nature of this area. Second, there is strong evidence that it not only reflects enhanced arousal and emotional intensity in visual emotion paradigms (Mourao-Miranda et al., 2003) but also can be activated during mental imagery in the absence of visual input (Kosslyn, Ganis, & Thompson, 2001). Third, the vOT area houses neurons that preferentially respond to body parts and bodily shapes (Downing, Jiang, Shuman, Kanwisher, 2001; Orlov, Makin, Zohary, 2010). Combining these different vOT properties, one could reconstruct a situation whereby male subjects, especially when highly sexually aroused, were having strong bodily fantasies. The common-life experience that sexual fantasy is amplified by arousal would then correspond with the fact that vOT activity tracked both penile circumference and subjective sexual arousal levels (Georgiadis et al., 2010). Finally, vOT seems to share functionality with posterior insula, because both areas were more strongly activated in men than in women during sexual genital stimulation, and both areas are functionally coupled with the middle cingulate cortex (Borg, De Jong, Renken, & Georgiadis, in press; Mesulam and Mufson, 1982).

Whereas men showed stronger vOT activity, possibly related to bodily fantasies, women showed stronger activity in left dorsal frontoparietal regions, including premotor areas and posterior parietal areas (Georgiadis et al., 2009). The involvement of these higher-order cortical areas is difficult to interpret: A possible explanation is that women were building a different mental representation of the stimulation paradigm, but like in the case of the vOT involvement in men, this interpretation

is speculative. Research better tailored to such specific hypothesis should deliver more satisfactory answers. These results nonetheless demonstrate clear involvement of high-end cerebral cortical areas, possibly hinting at high-level ‘human functions’, like perspective taking, in sexual activity. They also suggest potential gender differences in high-level processes associated with sexual activity.

## Conclusions

The study of how the brain comes to produce sexual activity – and, for that matter, sexual experience – is still in its infancy. Nevertheless, it is clear that the cerebral cortex has something to say about sexual activity. Future studies should provide us with more detailed insights into its exact contribution, which is best achieved through contemporary network and connectivity approaches.

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## References

- Arnow, B.A., Desmond, J.E., Banner, L.L., Glover, G.H., Solomon, A., Polan, M.L., et al. (2002). Brain activation and sexual arousal in healthy, heterosexual males. *Brain*, *125*, 1014–1023.
- Beauchamp, M.S. (2005). See me, hear me, touch me: Multisensory integration in lateral occipital-temporal cortex. *Current Opinion in Neurobiology*, *15*, 145–153.
- Beauregard, M., Levesque, J., & Bourgouin, P. (2001). Neural correlates of conscious self-regulation of emotion. *Journal of Neuroscience*, *21*, RC165.
- Berthier, M., Starkstein, S., & Leiguarda, R. (1988). Asymbolia for pain: A sensory-limbic disconnection syndrome. *Annals of Neurology*, *24*, 41–49.
- Björnsdotter, M., Löken, L., Olausson, H., Vallbo, A., & Wessberg, J. (2009). Somatotopic organization of gentle touch processing in the posterior insular cortex. *Journal of Neuroscience*, *29*, 9314–9320.
- Borg, C., De Jong, P.J., Renken, R.J., & Georgiadis, J.R. (2012). Disgust trait modulates frontal-posterior coupling as a function of disgust domain. *Social Cognitive and Affective Neuroscience*. doi: 10.1093/scan/nss006
- Both, S., Laan, E., Spiering, M., Nilsson, T., Oomens, S., & Everaerd, W. (2008). Appetitive and aversive classical conditioning of female sexual response. *Journal of Sexual Medicine*, *5*, 1386–1401.
- Coolen, L.M., Allard, J., Truitt, W.A., & McKenna, K.E. (2004). Central regulation of ejaculation. *Physiology & Behavior*, *83*, 203–215.
- Craig, A.D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature Reviews Neuroscience*, *3*, 655–666.
- Downing, P.E., Jiang, Y., Shuman, M., & Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. *Science*, *293*, 2470–2473.
- Everaert, K., de Waard, W.I., Van Hoof, T., Kiekens, C., Mulliez, T., & D’Herde, C. (2010). Neuroanatomy and neurophysiology related to sexual dysfunction in male neurogenic patients with lesions to the spinal cord or peripheral nerves. *Spinal Cord*, *48*, 182–191.
- Forbes, C.E., & Grafman, J. (2010). The role of the human prefrontal cortex in social cognition and moral judgment. *Annual Review of Neuroscience*, *33*, 299–324.
- Gall, F.J. (1822). *Sur les fonctions du cerveau et sur celles de chacune de ses parties, avec des observations sur la possibilité de reconnoître les instincts, les penchans, les talents, ou les dispositions morales et intellectuelles des hommes et des animaux, par la configuration de leur cerveau et de leur tête*. Paris: J.B. Balliere.
- Georgiadis, J.R. (2012). Exposing orgasm in the brain: A critical eye. *Sexual and Relationship Therapy*. doi: 10.1080/14681994.2011.647904
- Georgiadis, J.R., & Holstege, G. (2005). Human brain activation during sexual stimulation of the penis. *Journal of Comparative Neurology*, *493*, 33–38.
- Georgiadis, J.R., Reinders, A.A., Paans, A.M., Renken, R., & Kortekaas, R. (2009). Men versus women on sexual brain function: Prominent differences during tactile genital stimulation, but not during orgasm. *Human Brain Mapping*, *30*, 3089–3101.
- Georgiadis, J.R., Reinders, A.A., van der Graaf, F.H., Paans, A.M., & Kortekaas, R. (2007). Brain activation during human male ejaculation revisited. *Neuroreport*, *18*, 553–557.
- Georgiadis, J.R., Kortekaas, R., Kuipers, R., Nieuwenburg, A., Pruim, J., Reinders, A.A.T.S., et al. (2006). Regional cerebral blood flow changes associated with clitorally induced orgasm in healthy women. *European Journal of Neuroscience*, *24*, 3305–3316.
- Georgiadis, J.R., Farrell, M., Boessen, R., Denton, D., Gavrilescu, M., Kortekaas, R., et al. (2010). Dynamic subcortical blood flow during male sexual activity with ecological validity: A perfusion fMRI study. *Neuroimage*, *50*, 208–216.
- Giuliano, F., & Rampin, O. (2000). Central neural regulation of penile erection. *Neuroscience & Biobehavioral Reviews*, *24*, 517–533.
- Halata, Z., & Munger, B.L. (1986). The neuroanatomical basis for the protopathic sensibility of the human glans penis. *Brain Research*, *371*, 205–230.
- Hamani, C., Mayberg, H., Stone, S., Laxton, A., Haber, S., & Lozano, A.M. (2011). The subcallosal cingulate gyrus in the context of major depression. *Biological Psychiatry*, *69*, 301–308.
- Henderson, L.A., Rubin, T.K., & Macefield, V.G. (2011). Within-limb somatotopic representation of acute muscle pain in the human contralateral dorsal posterior insula. *Human Brain Mapping*, *32*, 1592–1601.
- Hoffmann, H., Peterson, K., & Garner, H. (2012). Field conditioning of sexual arousal in humans. *Socioaffective Neuroscience & Psychology*, *2*, 17336 - doi: 10.3402/snp.v2i0.17336.
- Holloway, K.S. (2012). Opioid mediation of learned sexual behavior. *Socioaffective Neuroscience & Psychology*. *2*, 14874 - doi: 10.3402/snp.v2i0.14874
- Hubscher, C.H., & Johnson, R.D. (2003). Responses of thalamic neurons to input from the male genitalia. *Journal of Neurophysiology*, *89*, 2–11.
- Hubscher, C.H., Reed, W.R., Kaddumi, E.G., Armstrong, J.E., & Johnson, R.D. (2010). Select spinal lesions reveal multiple ascending pathways in the rat conveying input from the male genitalia. *Journal of Physiology*, *588*, 1073–1083.
- Kell, C.A., von Kriegstein, K., Rosler, A., Kleinschmidt, A., & Laufs, H. (2005). The sensory cortical representation of the human penis: Revisiting somatotopy in the male homunculus. *Journal of Neuroscience*, *25*, 5984–5987.

- Kippin, T.E., & Pfaus, J.G. (2001). The nature of the conditioned response mediating olfactory conditioned ejaculatory preference in the male rat. *Behavioral Brain Research*, *122*, 11–24.
- 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. *Journal of Sexual Medicine*, *8*, 2822–2830.
- Komisaruk, B.R., Bianca, R., Sansone, G., Gomez, L.E., Cueva-Rolon, R., Beyer, C., et al. (1996). Brain-mediated responses to vaginocervical stimulation in spinal cord-transected rats: Role of the vagus nerves. *Brain Research*, *708*, 128–134.
- Kosslyn, S.M., Ganis, G., & Thompson, W.L. (2001). Neural foundations of imagery. *Nature Reviews. Neuroscience*, *2*, 635–642.
- Levin, R.J. (2004). An orgasm is . . . who defines what an orgasm is? *Sexual and Relationship Therapy*, *19*, 101–107.
- Lou, H.C., Gross, J., Biermann-Ruben, K., Kjaer, T.W., & Schnitzler, A. (2010). Coherence in consciousness: Paralimbic gamma synchrony of self-reference links conscious experiences. *Human Brain Mapping*, *31*, 185–192.
- Mah, K., & Binik, Y.M. (2001). The nature of human orgasm: A critical review of major trends. *Clinical Psychology Review*, *21*, 823–856.
- Mäkelä, J.P., Illman, M., Jousmaki, V., Numminen, J., Lehecka, M., Salenius, S., et al. (2003). Dorsal penile nerve stimulation elicits left-hemisphere dominant activation in the second somatosensory cortex. *Human Brain Mapping*, *18*, 90–99.
- Masters, W.H., & Johnson, V.E. (1966). *Human sexual response*. Boston: Little, Brown and Company.
- Mayberg, H.S. (1997). Limbic-cortical dysregulation: A proposed model of depression. *The Journal of Neuropsychiatry & Clinical Neurosciences*, *9*, 471–481.
- McKenna, K.E. (2002). The neurophysiology of female sexual function. *World Journal of Urology*, *20*, 93–100.
- McMahon, C.G., Althof, S., Waldinger, M.D., Porst, H., Dean, J., Sharlip, I., et al. (2008). An evidence-based definition of lifelong premature ejaculation: Report of the international society for sexual medicine (ISSM). ad hoc committee for the definition of premature ejaculation. *Journal of Sexual Medicine*, *5*, 1590–1606.
- Mesulam, M.M., & Mufson, E.J. (1982). Insula of the old world monkey. III: Efferent cortical output and comments on function. *Journal of Comparative Neurology*, *212*, 38–52.
- Michels, L., Mehnert, U., Boy, S., Schurch, B., & Kollias, S. (2010). The somatosensory representation of the human clitoris: An fMRI study. *Neuroimage*, *49*, 177–184.
- Morrison, I., Björnsdotter, M., & Olausson, H. (2011). Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *Journal of Neuroscience*, *31*, 9554–9562.
- Moulier, V., Mouras, H., Pelegrini-Issac, M., Glutron, D., Rouxel, R., Grandjean, B., et al. (2006). Neuroanatomical correlates of penile erection evoked by photographic stimuli in human males. *Neuroimage*, *33*, 689–699.
- Mourao-Miranda, J., Volchan, E., Moll, J., de Oliveira-Souza, R., Oliveira, L., et al. (2003). Contributions of stimulus valence and arousal to visual activation during emotional perception. *Neuroimage*, *20*, 1955–1963.
- Mouras, H., Stoleru, S., Moulier, V., Pelegrini-Issac, M., Rouxel, R., Grandjean, B., et al. (2008). Activation of mirror-neuron system by erotic video clips predicts degree of induced erection: An fMRI study. *Neuroimage*, *42*, 1142–1150.
- Murphy, M.R., Checkley, S.A., Seckl, J.R., & Lightman, S.L. (1990). Naloxone inhibits oxytocin release at orgasm in man. *Journal of Clinical and Endocrinology Metabolism*, *71*, 1056–1058.
- Olausson, H., Cole, J., Rylander, K., McGlone, F., Lamarre, Y., Wallin, B.G., et al. (2008). Functional role of unmyelinated tactile afferents in human hairy skin: Sympathetic response and perceptual localization. *Experimental Brain Research*, *184*, 135–140.
- Orlov, T., Makin, T.R., & Zohary, E. (2010). Topographic representation of the human body in the occipitotemporal cortex. *Neuron*, *68*, 586–600.
- Parada, M., Chamas, L., Censi, S., Coria-Avila, G., & Pfaus, J.G. (2010). Clitoral stimulation induces conditioned place preference and fos activation in the rat. *Hormones & Behavior*, *57*, 112–118.
- Paus, T. (2001). Primate anterior cingulate cortex: Where motor control, drive and cognition interface. *Nature Reviews. Neuroscience*, *2*, 417–424.
- Pfaus, J.G. (2009). Pathways of sexual desire. *Journal of Sexual Medicine*, *6*, 1506–1533.
- Poldrack, R.A., Fletcher, P.C., Henson, R.N., Worsley, K.J., Brett, M., & Nichols, T.E. (2008). Guidelines for reporting an fMRI study. *Neuroimage*, *40*, 409–414.
- Pukall, C.F., Strigo, I.A., Binik, Y.M., Amsel, R., Khalife, S., & Bushnell, M.C. (2005). Neural correlates of painful genital touch in women with vulvar vestibulitis syndrome. *Pain*, *115*, 118–127.
- Raichle, M.E., & Mintun, M.A. (2006). Brain work and brain imaging. *Annual Review of Neuroscience*, *29*, 449–476.
- Redouté, J., Stoleru, S., Gregoire, M.C., Costes, N., Cinotti, L., Lavenne, F., et al. (2000). Brain processing of visual sexual stimuli in human males. *Human Brain Mapping*, *11*, 162–177.
- Vallbo, A., Olausson, H., Wessberg, J., & Norrsell, U. (1993). A system of unmyelinated afferents for innocuous mechanoreception in the human skin. *Brain Research*, *628*, 301–304.
- Whipple, B., Ogden, G., & Komisaruk, B.R. (1992). Physiological correlates of imagery-induced orgasm in women. *Archives of Sexual Behavior*, *21*, 121–133.
- Woodson, J.C. (2002). Including 'learned sexuality' in the organization of sexual behavior. *Neuroscience & Biobehavioral Reviews*, *26*, 69–80.

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