SEXUAL MEDICINE REVIEWS

Neuroimaging of Female Sexual Desire and Hypoactive Sexual Desire Disorder

Stephanie Cacioppo, PhD

ABSTRACT

Introduction: Recent advances in neuroimaging offer an unprecedented window into the female sexual brain. The small samples and poor statistical power of individual functional magnetic resonance imaging studies have limited what can be gleaned about the systematic brain network that is involved in female sexual desire and female sexual dysfunction (eg, hypoactive sexual desire disorder [HSDD]).

Aim: To quantitatively determine the brain network involved in HSDD.

Methods: Systematic retrospective review and statistical meta-analysis of pertinent neuroimaging literature.

Main Outcome Measures: Review of published literature on functional magnetic resonance imaging studies illustrating brain regions associated with female sexual desire and female HSDD.

Results: HSDD is associated with a specific fronto-limbic-parietal dysfunction characterized by (i) lower blood oxygen level-dependent responses in the sexual desire brain network and (ii) higher blood oxygen level-dependent responses in the self-referential brain network.

Conclusion: The meta-analytic results are in line with a top-down neurofunctional model of HSDD in which inspecting, monitoring, and evaluating oneself (rather than sensory experience) before or during sexual activities interfere with sexual desire. These results raise new questions regarding the necessity and sufficiency of dysfunctional activation in the sexual desire and self-referential brain networks, whose answers bear on the development and evaluation of personalized treatments for HSDD. **Cacioppo S. Neuroimaging of Female Sexual Desire and Hypoactive Sexual Desire Disorder. Sex Med Rev 2017;X:XXX–XXX.**

Key Words: Neuroimaging; Functional Magnetic Resonance Imaging; Woman's Health; Female Sexual Desire; Hypoactive Sexual Desire Disorder; HSDD; Social Cognition

INTRODUCTION

Hypoactive sexual desire disorder (HSDD) is one of the most prevalent female sexual health problems.[1,2] Because of HSDD's negative impact on health-related quality of life,[2] happiness and relationship satisfaction, life satisfaction, and well-being, there is a crucial need to better understand the foundation of this sexual disorder.[1–5]

HSDD Definition

Throughout the past 30 years, HSDD has been defined in various ways. For instance, the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) edited by the American Psychiatric Association defined HSDD as a "persistent or recurrent deficiency (or absence) sexual fantasies and desire for sexual activity" that causes "marked distress or interpersonal difficulty not otherwise accounted for by a general medical or psychiatric condition." In 2004, the International Society for the Study of Women' s Sexual Health (ISSWSH) expert panel built on this DSM-IV definition and specified the following: "During HSDD, there are absent or diminished feelings of sexual interest or desire, absent sexual thoughts or fantasies and a lack of responsive desire. Motivations (here defined as reasons/incentives) for attempting to have sexual arousal are scarce or absent. The lack of interest is considered to be beyond the normative lessening with life cycle and relationship duration."[1,2,6,7]

Although this ISSWSH definition was the consensus for years, the fifth edition of the DSM (DSM-5) eliminated HSDD as a distinct entity and replaced it with an amalgamation of the DSM-IV HSDD and female sexual arousal disorder diagnoses, termed *female sexual interest/arousal disorder*.[1,2] This revised classification is controversial among experts in sexual medicine

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Biological Sciences Division, Department of Psychiatry and Behavioral Neuroscience, Center for Cognitive and Social Neuroscience, The University of Chicago Pritzker School of Medicine, Chicago, IL, USA

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for several reasons.[8–11] First, very little empirical or clinical data support or validate the new DSM-5 diagnostic classification. Second, the distinction between female sexual desire and female sexual arousal as distinct dysfunctions is supported by several lines of evidence, including genetic evidence from twin studies,[12] studies of specific single-nucleotide polymorphisms,[13] studies of the use of serotonergic antidepressant medications,[14] and neuroimaging studies (for review, see[15,16]). To address the controversial classification of female sexual dysfunctions in the DSM-5, the ISSWSH expert consensus panel met again in January 2016 and included 13 researchers and clinicians who are experts in female sexual dysfunction.[1] The ISSWSH report reads as follows: "Concern over what some consider to be the inappropriate elimination of the diagnostic category of HSDD in DSM-5 has resulted in the development of an autonomous nosology for female sexual dysfunctions by two international panels of experts in sexual medicine (the ISSWSH Nomenclature Committee and the International Consultation in Sexual Medicine). Importantly, the ISSWSH nosology retains HSDD as a distinct diagnostic entity, consistent with what many believe to be empirically based clinical experience."[1]

In the present review, the author adopts this ISSWSH view and considers HSDD as a distinct entity, as it had been in the DSM system before the DSM-5. Importantly, the ISSWSH nomenclature is in line with that of the well-accepted *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (code F52.0).[1,2]

HSDD Prevalence

Epidemiologic reviews have reported that HSDD is present in 8.9% of women 18 to 44 years of age, 12.3% of those 45 to 64 years of age, and 7.4% of those older than 65 years.[2] In addition, epidemiologic studies have suggested that 30% of premenopausal and 50% of naturally menopausal women have low sexual desire[2–4,17–19] and that 10% of woman have HSDD.[1–4,17–19] A recent cross-sectional, nationally representative, community-based sample of 2,020 Australian women 40 to 65 years old found that these numbers are increasing worldwide in midlife women.[17] In their sample, Worsley et al[17] showed that the prevalence of low desire was 69.3% (95% CI = 67.3–71.3), that of sexually related personal distress was 40.5% (95% CI = 38.4–42.6), and that of HSDD was 32.2% (95% CI = 30.1–34.2). Despite these alarming statistics, HSDD is often overlooked or misdiagnosed. Many physicians rarely broach this topic with their patients. Contributing to this landscape is the fact that sexual desire has long been regarded as little more than an archaic emotion (or a drive) with no redeeming function. For instance, sexual desire has long been believed to be driven by sex hormones and archaic subcortical brain regions[20] involved in addiction and primitive behaviors that needed to be suppressed. However, the increasing number of scientific publications on sexual desire (Figure 1) is shedding new light on the nature of sexual desire, its neural bases, and its beneficial effects on mental and physical health.[1,5–8,21–29]

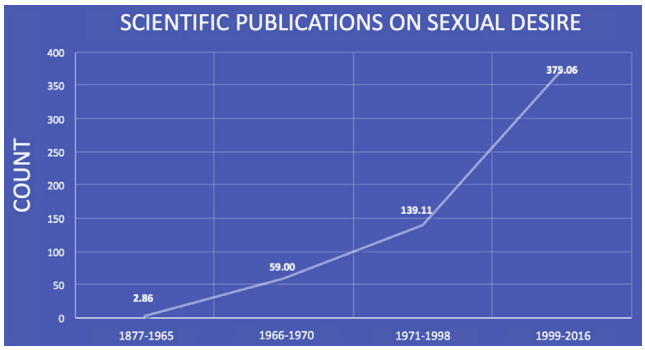

Figure 1. Schematic representation of the number of scientific publications on sexual desire from 1877 to 2016.

A wealth of data from neuroimaging studies have shown that the female sexual desire brain network (SDBN) involves subcortical and cortical brain areas extending well beyond the reptilian brain.[1,2,16] Based on these data and based on clinical evidence, sexual desire is currently seen as a complex psychological state that involves interacting cognitive and emotional components with implications for sexual, mental, and physical health and well-being.[2] For instance, clinical studies have shown associations between sexual interest and a woman's self-worth, body image, negative emotional states, depression, and subjective feelings of isolation.[2,30–34]

Female SDBN

The *Journal of Sexual Medicine* is the world's leading journal for empirical studies of the basis of sexual function and dysfunction. Although functional brain imaging accounted for fewer than 2% of the studies reported in the journal, it was clear early on that functional brain imaging held tremendous promise for expanding the understanding of relevant constructs, representations, and processes, including sexual dysfunction. Neuroimaging studies using functional magnetic resonance imaging (fMRI) or positron emission tomography have shown that the SDBN involves an interaction of excitatory and inhibitory neural pathways and their associated neurotransmitters (dopamine, norepinephrine, and serotonin) and hormone receptors (oxytocin, prolactin, estrogen, androgens, and melanocortins).[1,2,16,35–39] For instance, sexual excitation involves sexual cues activating limbic and hypothalamic norepinephrine and oxytocin (which in turn stimulate sexual arousal) and dopamine and melanocortins (which stimulate attention and sexual desire). However, sexual inhibition involves the recruitment of serotonin and brain opioids that occur in several brain regions, such as the prefrontal cortex (PFC).[1,2,16,35–39]

Reviews of the literature of neuroimaging studies investigating brain activity of subjects while they view erotic stimuli[1,16] have suggested that the SDBN involves specific subcortical and cortical areas, such as the PFC, medial preoptic area, locus coeruleus, paraventricular nucleus, ventral tegmental area, and