If you ever felt low D (Desire), you are not alone. Prevalence of HSDD or Female Sexual Interest/Arousal Disorder (FSIAD) is rising worldwide.
Yet, HSDD/FSIAD is often misunderstood.
If we are serious about treating HSDD/FSIAD we need to understand it correctly.
• Complex Disorder
• Multi-disciplinary approach recommended
Neuroimaging and Female Sexual Dysfunction

**Take-Home Points**

- Sexual desire is regulated not only by the sex hormones testosterone and estrogen, but also by the neurotransmitters dopamine and norepinephrine, which enhance sexual interest and desire, and serotonin, which inhibits sexual interest and desire.

- Brain circuits that connect the prefrontal cortex (PFC) with limbic pleasure centers theoretically mediate motivation, interest, and desire. These circuits are hypothesized to be the sites of inefficient information processing associated with sexual disorders that are characterized by reduced interest and desire.

**TODAY:**

- Specific brain areas, rather than gross hemispheric differences.

- Sexual desire & Love: Not mutually exclusive nor antagonist.

- How the underlined neurobiology can be synergetic between love and sexual desire.

- Finally, fMRI has good spatial resolution but poor temporal resolution.

- How timing matters in the neurobiology of sexual desire.
This sexual desire-related network includes the insula, hypothalamus, ventral striatum (nucleus accumbens), ventral tegmental area (VTA), amygdala, thalamus, hippocampus, plus limbic and cortical areas (such as the anterior cingulate, specific regions of occipital and temporal cortex, medial prefrontal cortex, middle frontal gyrus, superior temporal and precentral gyrus, temporo-parietal junction [TPJ], somatosensory cortex, and inferior parietal lobule [IPL]).

Statistical results:

$P < 0.001$ corrected

*N = 309 participants*

Stephanie Cacioppo et al., *Journal of Sexual Medicine*, 2012
The co-activation of subcortical emotion-related areas and higher-order cortical areas that mediate more complex cognitive functions (e.g., body image, mental associations, and self-representation) reinforces the top-down neurofunctional model of interpersonal relationships and the potential role of past experiences on emotional feelings.
Reminder: Limbic system: a complex system of nerves and networks in the brain, involving several areas near the edge of the cortex concerned with instinct and mood. It controls the basic emotions (fear, pleasure, anger) and drives (hunger, sex, dominance, care of offspring). It includes several areas, including orbitofrontal cortex (decision making), limbic lobe, hippocampus, amygdala, ventral striatum (or nucleus accumbens), hypothalamus.
Activation of the Reward System
OXYTOCIN

STIMULUS

AROUSAL

BASIC EMOTION

MOTIVATION

DRIVE

5 Brain oxytocin (OT) system. Cells arise in two hypothalamic regions: the paraventricular nucleus (PVN) and the supraoptic nucleus (SON). Large (magnocellular) neurons in these regions project to the posterior pituitary gland, where OT is released directly into the bloodstream. Smaller (parvocellular) neurons project to other regions of the hypothalamus and the limbic system. This system is involved in the stimulation of genital blood flow during sexual arousal and in linking sexual rewards to bonding. AC = anterior cingulate gyrus; mPOA = medial preoptic area; NAcc = nucleus accumbens; mPFC = medial prefrontal cortex; VTA = ventral tegmental area; MeA = medial amygdala; PIR = piriform cortex. J. Pfaus, 2009.
With concomitant autonomic outflow that controls sympathetic activation in some tissues (such as the heart) and parasympathetic activation of genital blood flow, respectively

Stephanie Cacioppo et al., *Journal of Sexual Medicine*, 2012
Brain norepinephrine system. This system arises in the locus coeruleus (LC) and projects caudally to the cerebellum and brain stem and rostrally to the hypothalamic, limbic, motor, and cortical systems in the forebrain. This system controls a variety of arousal mechanisms through response selection and autonomic activation. 

mPOA = medial preoptic area; NAcc = nucleus accumbens; mPFC = medial prefrontal cortex. J. Pfaus, 2009
Heightened Cognitive Functions

This sexual desire-related network includes the insula, hypothalamus, ventral striatum (nucleus accumbens), ventral tegmental area (VTA), amygdala, thalamus, hippocampus, plus limbic and cortical areas (such as the anterior cingulate, specific regions of occipital and temporal cortex, medial prefrontal cortex, middle frontal gyrus, superior temporal and precentral gyrus, temporo-parietal junction [TPJ], somatosensory cortex, and inferior parietal lobule [IPL]).

CORTICAL BRAIN AREAS

Non-HSDD Brain
N = 309 participants
Statistical results:
P < 0.001 corrected

Stephanie Cacioppo et al., Journal of Sexual Medicine, 2012
Left angular gyrus activation

[-58 -52 28, xyz, mm MNI coordinates]

R = 0.608

P < 0.001

Sexual desire scores

Ortigue, Bianchi-Demicheli; 2008
Beyond Somatosensory Response

E.g., medial prefrontal cortex, hippocampus, hypothalamus, angular gyrus
The Common Neural Bases Between Sexual Desire and Love: A Multilevel Kernel Density fMRI Analysis

Stephanie Cacioppo, PhD,*† Francesco Bianchi-Demicheli, MD,‡ Chris Frum, MS,§ James G. Pfaus, PhD,¶ and James W. Lewis, PhD§

Stephanie Cacioppo et al., Journal of Sexual Medicine, 2012
Stephanie Cacioppo et al., *Journal of Sexual Medicine*, 2012
From these results, one may consider sexual desire and love on a spectrum that evolves from integrative representations of affective visceral sensations to an ultimate mental representation of feelings incorporating mechanisms of reward expectancy and habit learning.

S. Cacioppo et al., 2012
TIMING MATTERS

If you have chemistry, you only need one other thing. Timing.
When does sexual desire arise in the human brain?
The Brain dynamics of Sexual Desire
A total of 13 women with HSDD and 15 healthy heterosexual, sexually active women (mean aged 31.1±7.02 years), who were dating engaged or married, participated in the present study.
Less subjective sexual arousal and Less visual attention
Greater activation of brain areas that are involved in spectatoring, emotion suppression, and body image.
• Barlow’s (1986) model of sexual dysfunction and “spectatoring” i.e., HSDD patients are “mentalizing” erotic images but not enjoying them.

• This model implicates cognitive interference in the cause and maintenance of sexual difficulties and suggests that inspecting, monitoring, and evaluating oneself before or during sexual activities interrupts sexual desire, with cognitions directed towards one’s own self rather than on sensory aspects of the sexual experience.
• HSDD is due to both:
  • HYPOfunctional sexual arousal +
  • HYPERfunctional sexual inhibition
Flibanserin: A Multifunctional Serotonin Agonist and Antagonist (MSAA)

Flibanserin is an agonist at presynaptic 5-HT1a autoreceptors (which shuts down serotonin release) and an antagonist at 5-HT2a receptors, which blocks residual action of serotonin at that receptor.

- Widely expressed
- Present in area known to be dysfunctional in HSDD patients e.g., prefrontal cortex, parietal cortex, and somatosensory cortex

About 5-HT$_{1A}$

- Most widespread of all the 5-HT receptors.
- Present in key brain areas involved in sexual desire e.g., ventral striatum.

About 5-HT$_{2A}$

- Widely expressed
- Present in area known to be dysfunctional in HSDD patients e.g., prefrontal cortex, parietal cortex, and somatosensory cortex
• **ACTION ON HYPO**functional sexual arousal + **HYPER**functional sexual inhibition

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**Flibanserin**

The multifunctional serotonergic agent flibanserin is both a serotonin 1A agonist and a serotonin 2A antagonist. Flibanserin theoretically improves sexual functioning by enhancing downstream release of dopamine and norepinephrine while reducing serotonin release in the brain circuits that mediate symptoms of reduced sexual interest and desire.
Effects of Flibanserin on the Pre- and Post-menopausal Female Brain

This study is currently recruiting participants. (see Contacts and Locations)

Verified October 2016 by University of Chicago

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University of Chicago

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History of Changes
Beyond Somatosensory Response

Cognitive construct

Past personal experiences

Emotion

Body Image

Motivation

Self esteem

Sexual Desire

Love
Thank you for your attention