Reduced Gray Matter Volume and Increased White Matter Fractional Anisotropy in Women with Hypoactive Sexual Desire Disorder

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ABSTRACT

Introduction. Models of hypoactive sexual desire disorder (HSDD) imply altered central processing of sexual stimuli. Imaging studies have identified areas which show altered processing as compared with controls, but to date, structural neuroanatomical differences have not been described.

Aim. The aim of this study is to investigate differences in brain structure between women with HSDD and women with no history of sexual dysfunction, and to determine sexual behavioral correlates of identified structural deviations.

Methods. Sexual functioning and gray matter (GM) and white matter (WM) were assessed in 29 women with HSDD and 16 healthy control subjects of comparable age and socioeconomic status with no history of sexual dysfunction.

Main Outcome Measures. WM properties were measured using diffusion-weighted imaging and analyzed using fractional anisotropy (FA). GM volume was measured using three-dimensional T1-weighted recordings and analyzed using voxel-based morphometry. Sexual functioning was measured using the Sexual Function Questionnaire.

Results. Women with HSDD, as compared with controls, had reduced GM volume in the right insula, bilateral anterior temporal cortices, left occipitotemporal cortex, anterior cingulate gyrus, and right dorsolateral prefrontal cortex. Also, increased WM FA was observed within, amongst others, the bilateral amygdalae. Sexual interest and arousal correlated mostly with GM volume in these regions, whereas orgasm function correlated mostly with WM FA.

Conclusion. HSDD coincides with anatomical differences in the central nervous system, in both GM and WM. The findings suggest that decreased salience attribution to sexual stimuli, decreased perception of bodily responses and sexual emotional stimulus perception, and concomitant altered attentional mechanisms associated with sexual response induction. **Bloemers J, Scholte HS, van Rooij K, Goldstein I, Gerritsen J, Olivier B, and Tuiten A. Reduced gray matter volume and increased white matter fractional anisotropy in women with hypoactive sexual desire disorder. J Sex Med 2014;11:753–767.**

Key Words. Hypoactive Sexual Desire Disorder; Gray Matter; White Matter; Neuroanatomy; Voxel-Based Morphometry; Female Sexual Interest/Arousal Disorder; Fractional Anisotropy

Introduction

The execution of human sexual behavior depends on a delicate balance within and between biological mechanisms [1], for example, (neuro)endocrinological, (neuro)physiological and vascular, and (socio)psychological mechanisms (e.g., cognitive, affective, sociocultural, and interpersonal) [2]. Imbalance in one or more of these systems can disturb sexual behavior; thus, many medical, psychiatric, and psychological conditions can cause sexual dysfunction as can medication and illicit drug use. There is a large group of women who suffer from sexual problems which are not

accounted for by medical or psychiatric conditions or by drug (ab)use. Before the introduction of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM 5*) [3], these sexual problems were classified into four major categories of women's sexual dysfunction in *DSM 4th Edition—Text Revision* (*DSM 4-TR*) [4]: hypoactive sexual desire disorder (HSDD), female sexual arousal disorder (FSAD), female orgasmic disorder, and sexual pain disorders. In *DSM 5*, HSDD and FSAD have been merged into female sexual interest/arousal disorder (FSIAD). The etiology of sexual disorders, irrespective of the *DSM 4* or *5* classification, is comprised of a large array of biological and psychological factors. Investigations into (common subsets of) biological and/or psychological markers for sexual dysfunctions (as defined by *DSM 4-TR*; research into FSIAD is still lacking) has yielded inconsistent results [5]. Nonetheless, each disorder's core symptoms are the same for each patient suffering from that disorder, suggesting common ground at some level.

To date, no investigations have been made into possible structural neuroanatomical deviations in HSDD. A noninvasive method of investigating possible neuroanatomical differences is the determination of gray matter (GM) volume and white matter (WM) fractional anisotropy (FA). GM contains neural cell bodies, and WM consists mostly of myelinated axon tracts. GM properties can be determined by voxel-based morphometry (VBM) of magnetic resonance images, which is sensitive to GM volume and density. WM properties can be determined by FA of diffusion-weighted images (DWI), which is mainly determined by axonal fiber diameter and density and fiber tract coherence. By investigating differences between women with and women without HSDD in GM and WM, we can infer how these GM and WM deviations impact information-processing within and between different brain areas and how this influences sexual behavior.

Sexual behavior is mediated by specific neurobiological networks. In these networks, incoming sensory information is integrated with the internal state influencing the behavioral state of the individual, which ultimately determines sexual behavior (for review, see [6]). Functional neuroimaging studies investigating women's and men's sexual behavior often show erotic stimulus-dependent (de)activation of the amygdala, insula, anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC), orbitofrontal cortex (OFC), and/or the nucleus accumbens [7–15]. These areas form a network which is involved in evaluation of the emotional significance of stimuli and the production of an affective state elicited by these stimuli [16]. For psychopathologies in general, a deviation in the function or structure in one or more of these areas can be interpreted as a neurobiological correlate of this disorder [17]. Following this same line of reasoning, differences between people with and without HSDD in the structure in one or more of these areas could be indicative of a neuroanatomical correlate for this disorder. To date, there is no direct evidence that one or more of these areas are impaired in women with HSDD, but an fMRI study by Arnow and colleagues [14] provides evidence that for one or more (associated) areas, this may be the case. In their study, women with HSDD had significantly lower activation in bilateral entorhinal cortices and significantly higher activation in the right medial frontal gyrus, the right inferior frontal gyrus, and bilateral putamen, in response to erotic film fragments. The authors concluded that HSDD subjects may differ from non-HSDD subjects in the encoding of erotic stimuli and/or retrieval of past erotic experiences (entorhinal cortex), and that attentional focus to sexual responses may be increased in HSDD (medial and inferior frontal gyri). Investigating neuroanatomical differences between subjects with and without HSDD in GM and WM may substantiate these findings. It may also elaborate on them as certain structural differences may not become manifest in fMRI because of the artificial setting and simplified stimulus-response paradigm.

Sexual desire, arousal, orgasm, and (lack of) pain all contribute to a successful sexual event and are at least partially interdependent in their occurrence and strength. The co-occurrence of these behavioral states is not necessary for a satisfying sexual event (e.g., one can have satisfying sex without reaching orgasm), but dysfunction in one of these domains can affect functioning of another, which often leads to secondary diagnoses. Indeed, a common empirical finding is that sexual desire and arousal highly overlap, as do the dysfunctional states as described by the diagnoses HSDD and FSAD [18]. The overlap between these two is much greater than that between other sexual domains. This overlap was a main reason to merge HSDD and FSAD into the single diagnosis FSIAD (in *DSM 5*). If there are differing degrees of interdependence between sexual desire, arousal, orgasm, and pain, these may be mirrored in differing degrees of interdependence of underlying