A Multivariate Twin Study of Female Sexual Dysfunction

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ABSTRACT

Introduction. There is little work on the etiology of female sexual dysfunction (FSD), a highly contentious and heterogeneous disorder from classification and clinical perspectives. Clarifying causative mechanisms may enhance current psychiatric nosology.

Aim. To elucidate the structure of genetic and environmental risk factors underlying the major subtypes of FSD.

Methods. Self-report questionnaires and multivariate twin model fitting on a population-based adult twin register (TwinsUK, London) including 1,489 female twins aged 18 to 85, comprising 244 MZ pairs, 189 DZ pairs, and 623 women whose co-twins did not participate.

Main Outcome Measures. Scores on the Female Sexual Function Index–Lifelong and its six dimensions (desire, arousal, lubrication, orgasm, satisfaction, and pain) were subject to univariate and multivariate variance component analysis.

Results. The best-fitting multivariate model was an ACE Cholesky model, in which both additive genetic effects and non-shared environmental effects loaded on four FSD dimensions. There was significant genetic sharing between desire, arousal, lubrication and orgasm, but there was also significant genetic sharing between arousal, lubrication and orgasm independent of desire. These genetic loadings were small to modest effects (7% to 33%). Bivariate heritabilities suggested that a third of the covariance between these dimensions was genetic. Desire shared the least amount of genetic association with lubrication and orgasm. Non-shared environmental effects (which were stronger than genetic effects) were somewhat more dimension-specific.

Conclusions. FSD is not etiologically homogeneous. There are at least two genetic factors to FSD symptomatology, and a tendency for more dimension-specific non-shared environmental factors as a more important indicative of unique factors involved in specific types of sexual problems reported by women. These results emphasize genetic factors as possible organizing principles for an etiologically based classification approach of FSD. **Burri A, Greven C, Leupin M, Spector T, and Rahman Q. A multivariate twin study of female sexual dysfunction. J Sex Med 2012;9:2671–2681.**

Key Words. FSFI; Female Sexual Dysfunction; Genetic; Heritability; Multivariate

Introduction

Female sexual dysfunction (FSD) is a broad term encompassing disorders of sexual desire, arousal, orgasm, and sexual-activity-related pain. It appears relatively common in general community settings (up to 40% of adult women report at least one dysfunction) and severely impacts women's quality of life [1–3]. However, the diversity of FSD-related disorders suggests positing a single diagnostic entity is over-simplistic and has drawn heavy criticism from scholars across disciplines. Moreover, the etiology of FSD-related constructs is largely unknown although researchers have proposed biological and psychological factors [4]. This lack of knowledge has hampered

progress in both psychiatric nosology and treatment strategies for this critical aspect of women's mental health. Both *DSM-IV* and *International Classification of Diseases, Tenth Revision* have arranged FSD into categories based largely on clinical similarities, while in 1998 a consensus-based definition and classification system was designed by the International Consensus Development Conference [1,5].

Preliminary basic research findings as well as observations from clinical practice have challenged several features of the current classification system (*DSM-IV-TR*), especially in view of the deliberations regarding *DSM-V* gender identity and sexual disorders categories [6–11]. For example, the current requirement of sexual distress as the primary diagnostic criterion is not supported by epidemiological studies. These show that sexual problems, independent of degree of severity, do not always cause distress. Shifren et al. reported that the prevalence of low sexual arousal decreased from 25.3% to approximately 6% when including distress [12], whereas Dennerstein & Hayes observed that 16% of women aged 20–49 years had low sexual desire compared with only 7% when personal distress was included as a diagnostic criterion [13]. For a comparison of classification problems for ICD-10 diagnosis of FSD, see King et al. [14]. Moreover, there is burgeoning evidence for a separation of sexual desire and arousal and the division of arousal into subjective and genital arousal [6,15]. Several pieces of psychophysiological evidence suggest that women's self-reported, subjective arousal does not necessarily correlate with the levels of their genital response [16–18]. A meta-analysis by Chivers et al. quantified the degree of agreement between self-reported and genital measures of sexual arousal and reported low agreement between the two measures ($r = 0.26$) [16]. The authors proposed that moderating variables such as stimulus variability and timing of the assessment of self-reported sexual arousal may explain the poor correlation. Moreover, neuroimaging studies report that the magnitude of hypothalamic activation (an area of the brain known to play a crucial role in physiological sexual arousal, sexual preferences and behavior) is less correlated with self-reported levels of sexual arousal in women than it was in men [18]. A large body of quantitative psychophysiological evidence using vaginal photoplethysmographic amplitude (VPA) also shows that a VPA response occurs to sexual stimuli, but subjective sexual arousal remains low or non-existent [17].

These studies suggest that part of the confusion surrounding FSD arises from symptom heterogeneity. This heterogeneity may be due to overlapping or partially overlapping etiological mechanisms. For example, if one set of etiologies explains most FSD-type reported problems, then conceptualizing FSD as possessing a relatively unitary underlying structure may benefit diagnosticians, researchers, and mental health professionals. Alternatively, FSD might be associated with common and unique etiologies (some causative factors may be common to all FSD symptoms and others unique to specific symptoms), which may support the burgeoning multidimensional approach to definition, classification, and treatment. The structure of these putative etiological pathways has yet to be tested.

Several factors unique to specific FSD symptoms have indeed been identified in cross-sectional and epidemiological-level studies (including anxiety, depression, and personality risk factors) and many of these factors have a strong heritable basis as tested by twin models [19–21]. Only one twin study has quantified the genetic contribution to FSD symptoms suggesting that both genetic and environmental factors may contribute [22]. However, genetic effects in this study were small, 0% to 15%, and the remaining proportion of the variance was entirely due to individual-specific environmental factors, so called non-shared environments, and measurement error. Two other studies, not directly testing FSD, found modest genetic influences (20% to 45%) on orgasm frequency, depending on whether orgasm was measured during sexual intercourse or other sexual activity [23,24]. The difference in the size of the genetic contributions to orgasm between these studies requires further testing. These studies are also somewhat limited by their use of measures that do not capture lifetime reporting of FSD symptoms. A lifetime-reporting measure of Female Sexual Function Index (FSFI) may offer better characterization of the FSD phenotype because lifetime sexual function is more enduring compared to the oft-used 4-week reporting measure (which, while capturing short-term variation in sexual responses, may be overly sensitive to idiosyncratic contextual and environmental effects). These shortcomings limit the interpretation of the data in these studies about the putative underlying structure of variations in sexual problems reported by women [25]. Variation between twin studies in genetic estimates may in part be due to poor phenotypic