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FEMALE SEXUAL FUNCTION

Stability of Genetic and Environmental Influences on Female Sexual Functioning

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ABSTRACT

Background: Genetic factors have been implicated in the etiology of female sexual dysfunction. Yet, how much the dynamic nature of sexual functioning is influenced by changes in genetic and/or environmental factors remains unknown.

Aim: To explore temporal stability of genetic and environmental influences on female sexual functioning over a 4-year period.

Methods: Data on desire, arousal, lubrication, orgasm, satisfaction, and pain were collected in 2009 and 2013 using the Female Sexual Function Index and were available for 1,209 British twin women.

Outcomes: To track the stability of genetic influences the Female Sexual Function Index sub-domain and total scores were subject to multivariate twin analyses for repeated measures.

Results: Desire showed a lower heritability at follow-up (37% vs 14%) whereas for arousal and sexual pain the heritability at follow-up was higher compared to baseline (28% vs 34% and 30% vs 45%, respectively). The heritability of lubrication remained stable at 27%. According to the best-fitting additive environmental (AE) Cholesky model for all domains except for sexual pain there were no new genetic factors expressing themselves over the 4-year period, but an addition of new, unique environmental determinants could be observed. For sexual pain an additional genetic factor could be observed at follow-up, explaining 39% of the phenotypic variance.

Clinical Translation: The biological pre-disposition to sexual problems seems to remain relatively stable over time.

Conclusions: This is the first study to investigate the genetic stability of female sexual functioning in a large population sample of women. White ethnicity and the relatively high mean age of women asks for caution in extrapolating the findings to other ethnic and age groups. The findings highlight the value of more in-depth exploration of the non-shared environmental influences that could provide clues to the mechanisms behind remittance and/or persistence of sexual problems. Integration of these findings may provide a useful conceptual framework for the treatment and prevention of certain types of sexual problems. **Burri A, Ogata S. Stability of Genetic and Environmental Influences on Female Sexual Functioning. J Sex Med 2018;XX:XXX–XXX.**

Key Words: Female Sexual Functioning; Female Sexual Dysfunction; Genetics; Twins; Longitudinal

INTRODUCTION

Sex is an integral part of most people's life and well-being. It is therefore not surprising that impaired sexual functioning can negatively impact the quality of life and lead to a range of psychological comorbidities (eg, affective disorders).[1–3] Such sexual problems are not only prevalent in clinical populations but also in the general population of men and women.[4,5] In women, the umbrella term "female sexual dysfunction" (FSD) has been coined, nowadays comprising a range of problems, including hypoactive sexual desire, diminished subjective and/or genital arousal (eg, reduced lubrication or vaginal blood flow), pain or discomfort during vaginal intercourse, and the inability to achieve orgasm.[6]

The disease mechanisms underlying FSD remain largely unknown, although evidence from the vast number of epidemiologic and clinical studies highlight the multifactoriality in its pathogenesis, with genetic factors also influencing the

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vulnerability to FSD.[5,7] In the 2 very first twin studies trying to quantify the genetic contribution to women's sexual problems, the authors found evidence for a moderate genetic influence explaining 51% of the inter-individual variation in women's orgasmic frequency.[8,9] Subsequent twin studies conducted in the United Kingdom and Finland focused on all domains of sexual functioning (ie, desire, arousal, lubrication, orgasm, pain, and sexual satisfaction) and also found evidence of a genetic influence although heritabilities were considerably lower, with findings ranging from 22−39% in the study of Burri et al[10] and from 3−11% in the study of Witting et al.[11] These substantial differences in the study findings could be explained by the use of different measures and differing samples in terms of the sociodemographic characteristics (age in particular).

While informative on the etiologic mechanisms that may explain inter-individual differences in sexual functioning at a specific time point, the fact that these studies relied exclusively on cross-sectional designs does not allow exploration of the extent to which the genetic influences remain stable over a certain period of time. Commonly, epidemiologic and genetic epidemiologic studies focus on understanding inter-individual differences in the etiology of complex conditions such as FSD by assuming the phenotype to be temporally stable. More realistically, however, sexual functioning and related problems are dynamic. This is somewhat supported by a recent epidemiologic study where the authors found different etiologic mechanisms underlying short-term and long-term sexual functioning.[5] Furthermore, a dynamic nature of genetic and environmental influences has been demonstrated for a range of quantitative phenotypes, such as cognitive abilities,[12] intelligence,[13] or fears and phobias.[14]

Given the likely dynamic nature of sexual functioning, studies should focus on the disentanglement of the processes that underlie the development of sexual problems and the factors that might contribute to their maintenance and/or remittance. Yet, to the best of our knowledge, no study to date has examined the dynamic nature of sexual functioning in a longitudinal and genetically informative manner to elucidate the patterns of temporal stability or changes in genetic influences. One might expect the genetic effects on sexual functioning to decrease with age, as we become more and more exposed and affected by an increasing number and different types of more or less random environmental factors such as education, prior sexual experiences, different partners, life traumata, and so on. However, the more of those random factors there are, the more they tend to cancel each other out, making the underlying (in this case presumably genetic) factor more prominent. In other words, the common assumption would be that all these environmental factors are cumulative and display a certain degree of path dependency. An increasing heritability over time, however, would provide evidence for the fact that these effects can well be temporary and can fade out over life course rather than building on themselves and enhancing their effects. Eventually, the "true" genetic disposition could manifest itself again. Overall, consideration of such fluctuations of genetic and environmental influences on sexual functioning can have important implications for the treatment and prevention of FSD, where this specific knowledge may lead to the formulation of novel treatment designs.

Aim

Given the lack of knowledge regarding the (in)stability of genetic influences on female sexual functioning, the aim of the present study was to investigate patterns of temporal stability or changes in genetic and environmental influences on sexual functioning over a 4-year period in a sample of British twin women.

MATERIAL AND METHODS

Participants and Study Design

The study sample for this longitudinal study consisting of 2 assessment points (4 years apart) that included women from the population-representative TwinsUK registry. More detailed information on the twin recruitment and the registry can be found elsewhere.[15,16] The representativeness and comparability of the cohort of twin women in terms of behavior, lifestyle factors, diseases, and sexual functioning have been repeatedly demonstrated.[5,17] The present study was a sub-study within a larger project aiming at elucidating the role of genetic factors in sexual health and the vulnerability to sexual problems in particular. The first data collection was conducted in 2009, where a sub-set of twins was contacted who had previously stated their willingness to participate in studies relating to sexual health. Of the 3,154 targeted women, 1,589 returned the postal questionnaire (50% response rate). Data collection on follow-up was conducted in 2013 via an online questionnaire. The same 1,589 women who had returned the questionnaire at baseline were contacted. The following exclusion criteria were applied at baseline (T1) and follow-up (T2): never having been sexually active (N = 9 at T1), women indicating their sexual orientation to be on the Kinsey scale 5−7 (predominantly or exclusively homosexual; N = 19 at T1 with no information at T2), not being in a sexual and/or romantic relationship at T1 (relationship status was not re-assessed at T2, see "Limitations" section), and >5 missing Female Sexual Function Index (FSFI) items (N = 72 women at T1 and none at T2 because of the online format that did not allow participants to skip or leave items unanswered).[5,18] For all twins, zygosity had been previously assigned using a standard questionnaire and had been confirmed with multiplex DNA genotyping and, more recently, by means of genetic association markers on DNA obtained from venous blood samples. Twin individuals with non-white ethnicity (to ensure ethnic homogeneity) and with uncertain zygosity were also removed from the data set. At baseline, no follow-up was planned that might explain the relatively low follow-up rate. In the end, data from N = 1,209 twin individuals were available, including 633 monozygotic (MZ) twins (195 complete MZ pairs) and 576 dizygotic (DZ) twins (143 complete DZ pairs). All descriptive and