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# A Genome-Wide Association Study of Female Sexual Dysfunction

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## Abstract

***Background:*** Female sexual dysfunction (FSD) is an important but controversial problem with serious negative impact on women's quality of life. Data from twin studies have shown a genetic contribution to the development and maintenance of FSD.

***Methodology/Principal Findings:*** We performed a genome-wide association study (GWAS) on 2.5 million single-nucleotide polymorphisms (SNPs) in 1,104 female twins (25–81 years of age) in a population-based register and phenotypic data on lifelong sexual functioning. Although none reached conventional genome-wide level of significance (10×-8), we found strongly suggestive associations with the phenotypic dimension of arousal (rs13202860, $P = 1.2\times10^{-7}$; rs1876525, $P = 1.2\times10^{-7}$; and rs13209281 $P = 8.3\times10^{-7}$) on chromosome 6, around 500kb upstream of the locus *HTR1E* (5-hydroxytryptamine receptor 1E) locus, related to the serotonin brain pathways. We could not replicate previously reported candidate SNPs associated with FSD in the *DRD4*, *5HT2A* and *IL-1B* loci.

***Conclusions/Significance:*** We report the first GWAS of FSD symptoms in humans. This has pointed to several "risk alleles" and the implication of the serotonin and GABA pathways. Ultimately, understanding key mechanisms via this research may lead to new FSD treatments and inform clinical practice and developments in psychiatric nosology.

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## Introduction

People vary in their enjoyment of sexual activity and relationships – a source of significant mental wellbeing or problems. Female sexual dysfunction (FSD) describes a cluster of sexual symptoms including desire, arousal, orgasm and pain. It appears relatively common in the general community and population-level samples and is associated with a severe decrease in quality of life in women [1–3]. The etiology of FSD is largely unknown although several biological and psychological correlates have been reported [3–5]. Nevertheless, no clear disease mechanisms have emerged and this lack of knowledge has hampered progress in both, psychiatric nosology and treatment strategies for this growing burden on women's psychiatric health. Both, the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* and *International Classification of Diseases, Tenth Revision* [6] have arranged FSD into categories based largely on clinical similarities, while in 1998 a consensus based definition and classification system was designed by a panel of experts during the International Consensus Development [7].

Biological research into FSD is woefully inadequate. Recent twin studies suggest FSD is familial, with genetic factors accounting for up to 51% of the phenotypic variance [8–10]. Twin studies also show evidence of genetic and environmental contributions to psychological factors previously linked to FSD (such as depression, anxiety, personality traits) [11–13]. Thus, it is possible that some of the covariation between FSD and these psychological correlates is explained by shared genetic and non-genetic factors. However, there have been no large-scale studies to identify single genes or gene variants robustly associated with FSD-phenotypes (and no genome-wide association study - GWAS - has ever been performed). To date, only a handful of candidate gene studies of sexual desire and function exist. One candidate gene study has linked serotonin polymorphisms (*5HT2A*) to reduced sexual desire as a side-effect of SSRI-medication in 89 adult men and women [14]. A further study reported an association between the dopamine D4 receptor gene (*DRD4*) with self-reports of sexual desire and arousal in 52 men and 92 women [15]. Interleukin-1beta gene (*IL-1B*) has been correlated with variation in vulvar vestibulitis syndrome scores, a broader phenotype for sexual pain symptoms [16]. All these studies have methodological shortcomings that limit their interpretation, primarily the candidate gene design, small samples in mostly clinical populations (thus lacking power to detect phenotype – DNA variant associations), and the

use of non-standardized instruments that lack coverage of the phenotypic heterogeneity in sexual function. Moreover, none of these studies examine women and FSD directly, making them unsuitable for clarifying the etiological mechanisms under FSD at the population-level.

We present here the results of the first GWAS of FSD in a female population-sample published to date. By scanning a dense set of genetic variants throughout the whole genome, we can test replication of previously located genes from candidate gene investigations and also identify novel genes that may lead to the discovery of unknown biological pathways involved in the development of FSD.

## Materials and Methods

### Participants

The TwinsUK adult twin registry based at St. Thomas' Hospital in London is a volunteer cohort of over 10,000 twins from the general population [17]. This twin population has been involved in a wide range of studies on common traits and diseases and has been shown to be representative of the general population for a wide variety of medical, behavioral, and sexual traits [3,18,19]. The twins were not selected on the basis of the phenotypes being studied and were unaware of any hypothesis being tested. All twins provided written informed consent and the study was approved by St. Thomas' Hospital Research Ethics Committee.

All participants were dizygotic (DZ) pairs and monozygotic (MZ) singleton twins of white European ancestry. A total of 1,489 subjects were included, all sexually active, heterosexual with no history of any major psychological or medical condition (depression, bipolar disorder, anxiety disorder, diabetes, multiple sclerosis, endometriosis) and with all items on the Female Sexual Function Index-Lifelong (FSFI-LL) available.

### Sexual Dysfunction Phenotype

We used the recently developed 19-item Female FSFI-LL questionnaire to measure long-term variation in female sexuality, including periods of dysfunction and healthy function [20,21]. For genetic analysis, the FSFI-LL is preferable to the "snapshot" measures used in some previous research and it better captures the variation in *enduring* female sexual functioning required for resolving the underlying genetic and non-genetic mechanisms of FSD symptoms. The FSFI-LL assesses 6 dimensions of women's average sexual functioning "since they have been sexually active" including desire (2 items), arousal (4 items), lubrication (4 items), orgasm (3 items), satisfaction (3 items), and pain (3 items). Desire items are rated on a Likert-type scale ranging from 1 to 5. The remaining items are rated from 0 to 5 with the supplementary option "no sexual activity". Dimension scores are derived by summing the item scores within each dimension and multiplying the sum by the dimension factor weight [20]. The dimension factor weighting converts the dimension scores to a consistent range from 0 to 6, except for the desire, which has a dimension score range from 1.2 to 6. Total scores are calculated via a simple computer algorithm and low scores on the FSFI-LL indicate more sexual problems and high scores indicate fewer problems. The FSFI-LL has excellent psychometric properties for both, total- and dimensions-specific scores, including test-retest reliability, internal consistency, external/discriminant validity [20,21]. Exploratory and confirmatory factor analyses have successfully reproduced the original factor. According to response operator curve (ROC)-derived cut-off scores, all dimensions and the total FSD score displayed a good sensitivity to 1-specificity profile (as measured by the area under the curve = AUC), with arousal (AUC = 0.92) displaying the best trade-off and desire the lowest (AUC = 67.55%). Overall, the FSFI-LL demonstrates excellent comparability to the standard FSFI in terms of factor structure and psychometric properties [21].

Detailed information on prevalences, potential environmental risk factors and heritability estimates for FSD-symptoms in this panel are reported elsewhere (3).

### Genotyping, Quality Control, and Imputation

Genotyping was carried out using two genotyping platforms from Illumina: the HumanHap 300k Duo for a part of the

**Table 1.** Top SNPs associated with sexual function related measures in a cohort of females of European ancestry.

| *Phenotype* | *SNP* | *CHR* | *Position* | *Locus* | *Allele* | *Effect** | *s.e.m* | *P* |
|---|---|---|---|---|---|---|---|---|
| Arousal | rs13202860 | 6 | 87211973 | | A | −0.421 | 0.08 | 1.213E−07 |
| Arousal | rs1876525 | 6 | 87208811 | | C | −0.421 | 0.08 | 1.213E−07 |
| Arousal | rs13209281 | 6 | 87201368 | | A | −0.443 | 0.09 | 8.329E−07 |
| Overall FSD | rs4820255 | 22 | 35533796 | PVALB | C | −0.366 | 0.076 | 1.687E−06 |
| Overall FSD | rs4821535 | 22 | 35533452 | PVALB | G | −0.366 | 0.076 | 1.687E−06 |
| Overall FSD | rs2284024 | 22 | 35528729 | PVALB | T | −0.366 | 0.077 | 1.838E−06 |
| Overall FSD | rs5750311 | 22 | 35533286 | PVALB | G | −0.367 | 0.077 | 2.104E−06 |
| Overall FSD | rs739031 | 22 | 35532649 | PVALB | T | −0.364 | 0.077 | 2.144E−06 |
| Overall FSD | rs4821536 | 22 | 35533947 | PVALB | T | −0.355 | 0.076 | 3.196E−06 |
| Lubrication | rs2370759 | 22 | 32674978 | EPC1 | G | 0.237 | 0.05 | 1.7E−06 |
| Lubrication | rs11594963 | 10 | 32665742 | EPC1 | G | 0.236 | 0.05 | 1.95E−06 |
| Lubrication | rs11599044 | 10 | 32655451 | EPC1 | A | 0.236 | 0.05 | 1.95E−06 |
| Lubrication | rs10508773 | 10 | 32615450 | EPC1 | C | 0.234 | 0.05 | 1.952E−06 |
| Lubrication | rs16933243 | 10 | 32655141 | EPC1 | T | 0.233 | 0.05 | 2.565E−06 |
| Lubrication | rs11008865 | 10 | 32614848 | EPC1 | C | 0.232 | 0.05 | 2.704E−06 |

*Effect, β coefficient of linear regression. The effect sizes denote changes in phenotype unit per each additional copy of the reference allele.
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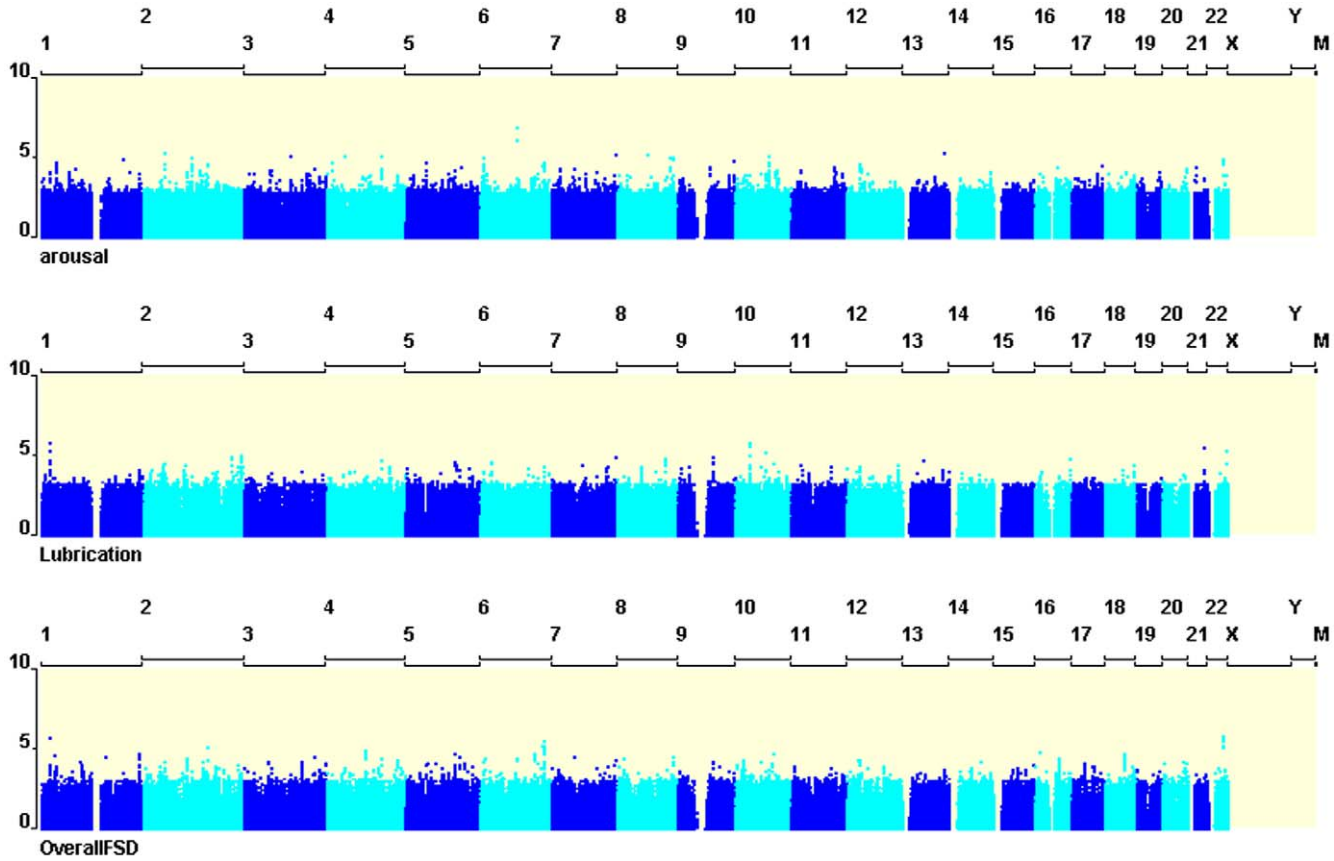


**Figure 1. Manhattan plots describing the association of 2.5 M SNPs with sexual arousal, lubrication and overall sexual functioning.** SNPs with $P \leq 10–6$ are highlighted with a red circle (n = 1104 females).
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TwinsUK Cohort (n = 505) and the HumanHap610-Quad array for the remainder of the TwinsUK Cohort (n = 599). Genotyping with the HumanHap 300k Duo was conducted at the Centre National de Génotypage, Duke University, NC, USA; Helsinki University, Finland; and the Wellcome Trust Sanger Institute, Cambridge, UK. Genotyping with the Infinium 610k assay (Illumina, Inc., San Diego, USA) for the remaining individuals was conducted at the Centre for Inherited Diseases Research (USA) and the Wellcome Trust Sanger Institute.

We applied stringent quality control (QC) criteria to the genotype data. Genotypes were cleaned before analysis by removing single-nucleotide polymorphisms (SNPs) or individuals not fulfilling the QC criteria. The following QC filters were applied for samples: call rate at least 95%; autosomal heterozygosity between 33 and 37%. At the SNP level, Hardy Weinberg Equilibrium (HWE) with P-value $>10^{-4}$, Minor Allele Frequency (MAF) at least 1%, and call rate at least 95% for SNPs with MAF 0.05 and above or at least 99% for SNPs with MAF less than 0.05. We further visually inspected all intensity cluster plots of SNPs that showed either an association for over-dispersion of the clusters, biased no calling, or erroneous genotype assignment and discarded all SNPs with any of these characteristics.

Genotypes from the TwinsUK were imputed using the genotypes from the 3,855,687 autosomal markers available from the HapMap Phase 2 CEPH population [22]. After imputation using IMPUTE2 a total of 2,558,978 non-monomorphic autosomal markers became available. After removing very rare markers (MAF<0.1) and markers in Hardy-Weinberg Disequilibrium (p<e−6) and individual with poor imputation scores (<0.5), we obtained results from 2,287,762 loci across the chromosome.

## Statistical Analysis

Of the 1,489 women with recorded phenotype, genotype data was available for 1,104 subjects after QC check. Data handling and preliminary analyses were conducted using STATA software (StataCorp., College Station, TX) and Merlin (PMID 11731797) [23]. Association analyses were performed using MERLIN. Ancestry was determined through principal component analysis of individual genotypes (compared with subjects participating in the HapMap Phase II standard populations).

All traits were included in multiple regression models, with age and menopausal state included as covariates. Traits were inverse-normalized to avert undue effects of non-normality of their distributions. Regression slopes (β) are given as numbers of standard deviation units per each additional copy of the effect allele from this point onwards in the text. Given the experimental size with hundreds of thousands of SNPs being analysed individually, the commonly used "genome wide significance" (GWS) threshold was used which is the standard approximation routinely set at $5\times10^{-8}$ [24]. However, given the cost of a strict Bonferroni adjustment in results from relatively small datasets, we considered all the associations with $P \leq 5\times10^{-5}$, as others have done in other studies of similar sizes (UK IBD Genetics Consortium, 2009; Amundadottir et al., 2009) [25,26].

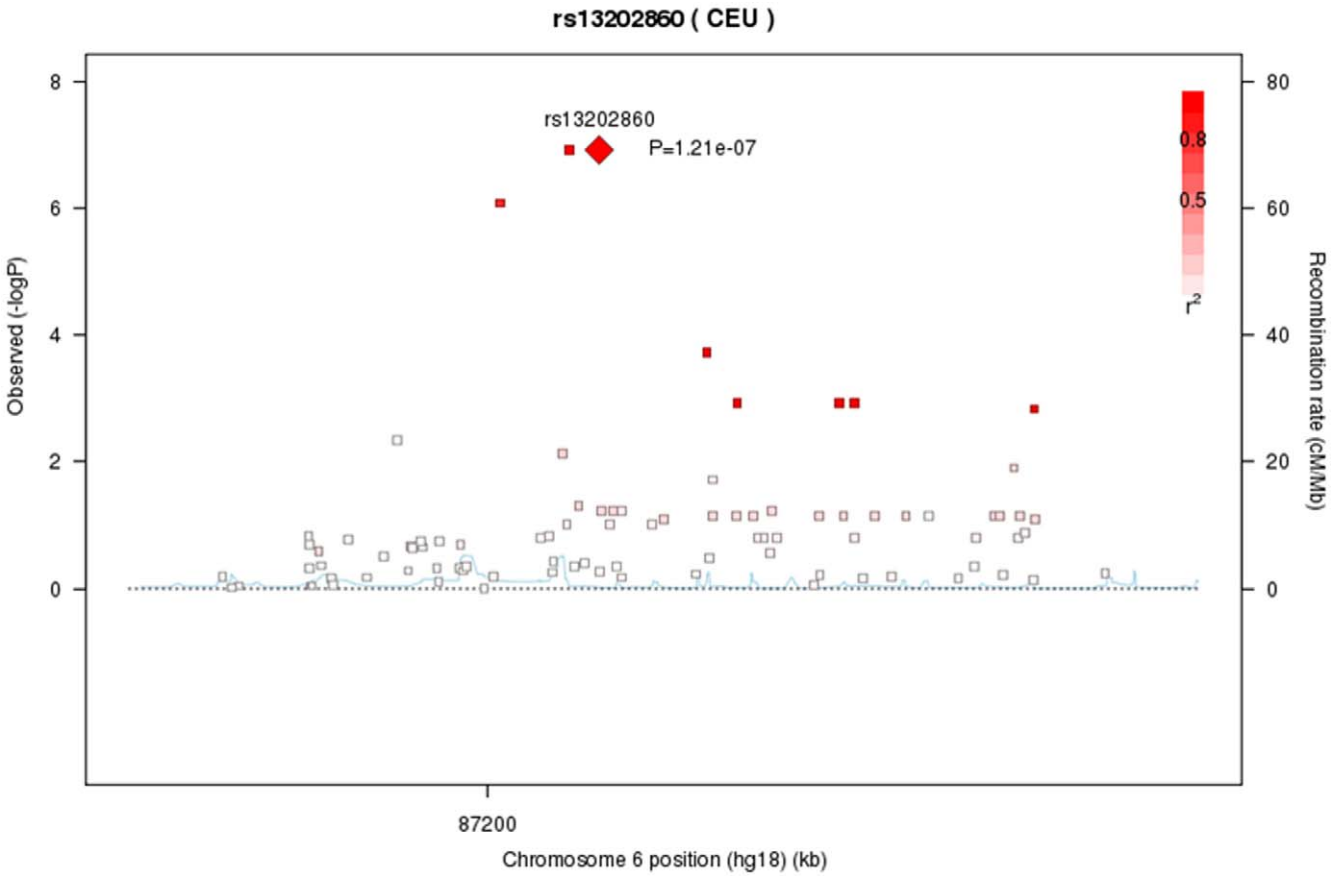


**Figure 2. Association scatter plot for SNPs in the gene desert approximately 1Mbp upstream of the *HTR1E* gene.** TwinsUK discovery cohort. Negative logarithms of the P values for the association of each SNP with spherical equivalence are plotted. The lead SNP is plotted in diamond shape, with the GWAS-analysis P value for that SNP indicated. Genotyped SNPs are plotted as squares, with the colour indicating the degree of pairwise LD between the lead and neighbouring SNPs. Red indicates strong pairwise LD, with r2≥0.8; orange indicates moderate LD, with 0.5<r2<0.8 yellow indicates weak LD, with 0.2<r2<0.5; and white indicates no LD, with r2<0.2. The recombination rates are shown as light blue line.
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## Results

Racial and ethnicity stratification was checked through eigenvector analysis and the above mentioned samples only contained individuals of certified and pure European ancestry. The genotyped samples were tested for population stratification, by comparison to the three HapMap phase 2 reference populations (CEU, YRI, CHB+JPT; www.hapmap.org) using principal component analysis.

The mean age of participants in the study was 57 years (range 25–81 years). The GWAS analysis was performed using both observed and imputed genotypes. The genomic inflation factor ($\lambda$) ranged from 0.98 to 0.99 for the different phenotypes, showing no evidence for population stratification or inflated results due to imputation. We identified 34SNPs with P-values $\leq 10^{-5}$ of association with FSD-related measures. These results are summarized in Table 1. The most significant association was found between rs13202860 on chromosome 6 and sexual arousal, with $P = 1.2\times10^{-7}$. Two additional nearby SNPs showed P-values less than $4\times10^{-7}$, (rs1876525, rs13209281; $P = 1.2\times10^{-7}$ and $8.3\times10^{-7}$, respectively; Table 1 and Figure 1). All three SNPs were associated with arousal levels and spanned a region of 11 kb, around 500 kbp upstream from the *HTR1E* (5-hydroxytryptamine receptor 1E) locus (Figure 2 and Figure 3).

We also identified a locus on chromosome 22 with multiple adjacent SNPs showing similar, albeit modest levels of associations with overall sexual function (Table 1; Figure 1). Association was maximal for rs4820255 and rs4821535 (both $P = 1.2\times10^{-6}$), two SNP located 344 bp apart within intron 3 of the parvalbumin (*PVALB*) gene. Similarly, six SNPs associated with lubrication levels could be detected ($P<3\times10^{-6}$ for all) on chromosome 10 near the *EPC1* gene (Table 1; Figure 1).

Previous association studies have suggested several potential candidates to be associated with FSD. More specifically, earlier studies identified several variants on the dopamine D4 receptor (*DRD4*) and the serotonin 2A receptor gene (*5HT2A*) to be linked with levels of sexual desire and arousal (14,15). In this GWAS, observed and/or imputed genotype information was available for 2 SNPs in the *DRD4*, 5 SNPS in the *5HT2A* and 3 SNPS in the *IL-1B* gene, and were hence evaluated for the replication of previously reported associations. However, none of the markers showed significant associations with the previously suggested phenotypes (or with any of the outcome variables), as displayed in Table 2.

## Discussion

Here we reported the results of the first ever GWAS of female sexual function levels in an unselected population-based cohort of

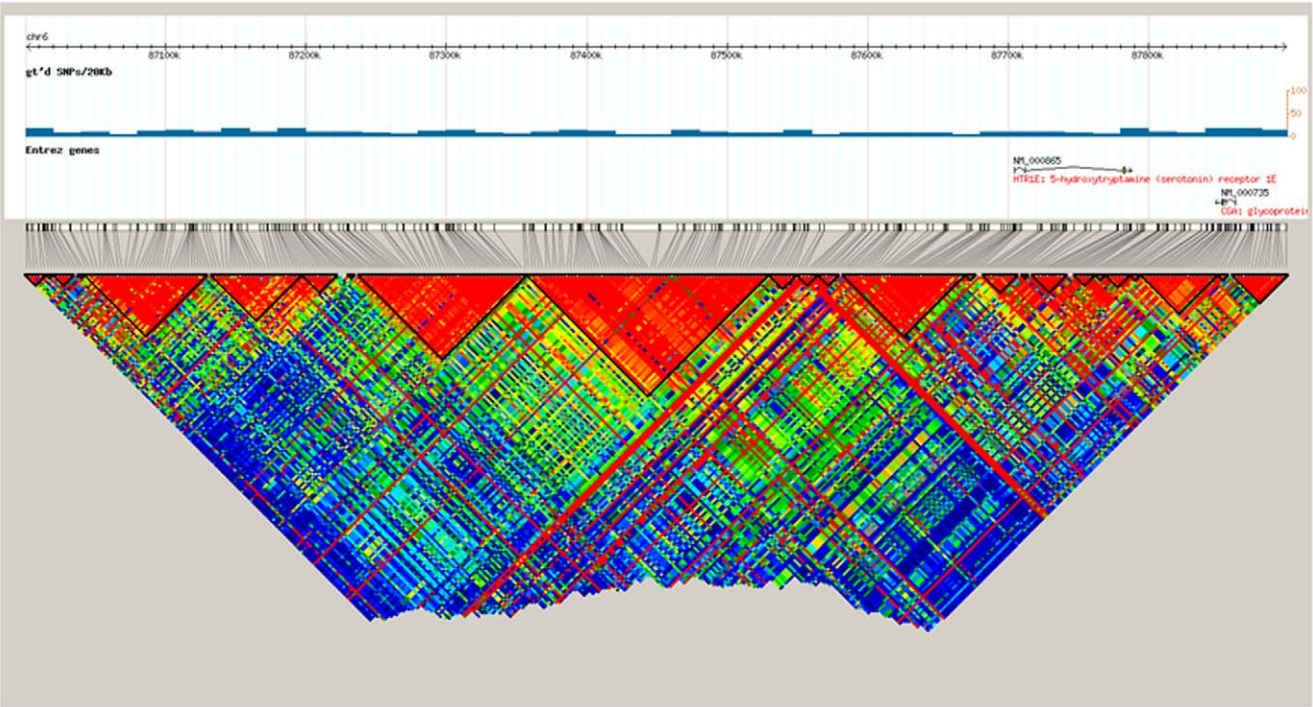


**Figure 3. Haploview LD plot. The plot uses the hapmapPhase3 data on the CEU and the TSI Caucasian populations and encompasses an 800 kbp segment containing the associated SNP on chromosome 6 and *HTR1E*.** The LD blocks were defined by confidence intervals according to Gabriel and colleagues [45]. The x-axis corresponds to the genomic position in kb and the red triangles defined by black lines represent LD blocks. The yellow arrow and the red box indicate the location of three GWAS associated SNP and the position of *HTR1E*, respectively.
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British women. There were no associations at conventional genome-wide level of significance ($P<5\times10^{-8}$), but we found strongly suggestive associations. Several studies of similar size have considered any association with P-values $\leq1\times10^{-5}$ as being suggestive [25,26]. Moreover, numerous suggestive associations below the genome-wide cut-off have been replicated in independent studies, strongly suggesting that these are indeed real associations rather than spurious results. For example, the Genetic Analysis of Psoriasis Consortium & the Wellcome Trust Case Control Consortium 2 in a GWAS study for psoriasis, replicated many of the suggestive associations found by Nair and colleagues including SNP nearby *IL-23A* and *TNFIP3* with $P\leq2\times10^{-5}$ and $P\leq1\times10^{-5}$, respectively [27,28]. Here, we identified several strong suggestive associations with much stronger levels of significance. Our strongest association ($P$ $1.2\text{x}10^{-7}$), was on the phenotypic dimension of arousal with a serotonin receptor gene (*HTR1E)* which represents a strong biological candidate previously shown to be involved in female sexuality. This potential susceptibility locus resides within a ~1 Mbp segment of the genome devoid of annotated genes, located about 500 kbp downstream of the *HTR1E* gene. To assess the relationship between rs13202860 and *HTR1E* we plotted the LD pattern of the region. HapMap 3 data from two Caucasian populations (CEU and TSI) shows that rs13202860, rs1876525 and rs13209281, which show association with arousal in our study, are located in different LD blocks than *HTR1E* (Figure 3). Although *HTR1E* is an interesting candidate gene because of its known physiology, the large distance between both loci, together with the evidence that the significant SNP lie in other LD blocks than *HTR1E* clearly suggest that these three SNPs are tagging independent associations and that the causal polymorphism is more likely to regulate gene expression rather than the protein structure of *HTR1E*. Enhancers are elements of the genome that regulate gene expression of nearby or distant genes and which can be located within gene deserts [29]. Recent research suggests that polymorphisms in gene

**Table 2.** P-values of available markers in our GWAS, reported to be associated with specific sexual problems in previous candidate gene studies.

| Genes | SNP | Associated phenotypes | |
|---|---|---|---|
| | | *P** | *P** |
| **DRD4** | | **Desire** | **Arousal** |
| | rs3758653 | 0.7495 | 0.4242 |
| | rs11246226 | 0.2303 | 0.7294 |
| **HTR2A** | | **Desire** | **Arousal** |
| | rs2760345 | 0.6594 | 0.1266 |
| | rs7326071 | 0.795 | 0.3783 |
| | rs2770293 | 0.03697 | 0.9446 |
| | rs2760347 | 0.9225 | 0.1493 |
| | rs4941570 | 0.04381 | 0.4987 |
| **II-B** | | **Pain** | |
| | rs1143643 | 0.6775 | |
| | rs1143634 | 0.7558 | |
| | rs1143633 | 0.6775 | |

*Bonferroni corrected p-value.
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deserts could impact on disease by altering an enhancer element [29–31]. Thus, it is possible that our causal variant is altering an enhancer element located in the gene desert influencing *HTR1E*.

*HTR1E* encodes one of the families of highly conserved serotonin receptor genes and is strongly expressed in neurons, primarily in limbic brain regions (including caudate putamen, claustrum, hippocampus, and amygdala) [32–33]. This high degree of evolutionary conservation of genetic sequence suggests an important physiological role of the *HTR1E* receptor in humans. However, the actual function of the *HTR1E* receptor remains unknown. Nevertheless, *HTR1E* is a gene with considerable biological relevance to our phenotype of sexual functioning as it shares amino acid sequence homologies and some pharmacological characteristics with other 5-HT receptors (serotonin) and is therefore closely related. Comparative research has documented the critical role of serotonin receptors in modulating human and non-human mammalian sexual behavior and functioning acting on both central and peripheral (genital) sites [34–35]. SSRI (selective serotonin reuptake inhibitors)-associated sexual side effects, which include peripheral dysfunctions (e.g., erectile) as well as central problems in desire and arousal are well documented at high prevalence among users (up to 60%) [36]. These post-SSRI sexual dysfunctions (PSSD) point strongly to the involvement of serotonin receptors in human sexual behavior. Central serotonergic activity affects female sexual functioning via limbic projections of serotonin neurotransmitter are co-localized with norepinephrine receptors – and both transmitters seem to work in conjunction in the regulation of arousal and lubrication [35,37]. However, the involvement of serotonin receptors in several reward-related behavioral functions (e.g. satiety, sexual behavior, nociception, escape, and stress) suggests that these receptors may function in the "higher-order" integration of rewarding behavior.

Our finding of a putative association between *PVALB* and overall sexual functioning scores on the FSFI-LL is entirely new. *PVALB* is a calcium-binding albumin protein present in GABAergic interneurons, expressed predominantly in the prefrontal cortex. Similar to serotonin, GABA is a major inhibitory neurotransmitter. Several lines of research demonstrate that GABA levels are associated with sexual function. Animal studies show that GABA(A) and GABA(B) receptors are involved in the inhibition of lordosis (a response shown by female animals indicating sexual receptivity) as well as mediating the effects of sex steroids such as estrogen in appetitive sexual behavior (e.g., sexual exploration) [37,38]. Elevated levels of stress have also been shown to dampen sexual response in animal models as well as being a significant psychological correlate of FSD in women [39,40]. The number of hippocampal PV-containing GABAergic interneurons is highly responsive to chronic external stressors, offering the potential of stress-induced neuro-structural alterations.

The EPC1 gene encodes the enhancer of polycomb homolog 1 and is a component of the NuA4 histone acetyltransferase complex. Previous research has suggested that this complex may be required for the activation of transcriptional programs associated with oncogene and proto-oncogene mediated growth induction, tumor suppressor mediated growth arrest and replicative senescence, and apoptosis. It has also shown to be involved in skeletal muscle differentiation [41,42]. At this stage it is unclear through which mechanisms EPC1 could have an effect on vaginal lubrication and would need to be further investigated.

The present study had some methodological limitations and the findings should be interpreted with caution. Our study sample consisted mostly of peri- or postmenopausal women (70%). For this reason, representativeness of our study might be limited to the older female population, especially when considering that sexual dysfunction is more common in peri- and postmenopausal than in the non-climacteric period. However, prevalence rates of FSD in our sample are comparable to estimates found in other, younger populations [3]. Ideally, although similar populations are hard to come by, it would be important to replicate our GWAS findings in larger and independent samples before pursuing research into the underlying biological disease pathways. Our sample size may be one reason why our analysis did not reach conventional levels of GWA significance. Unfortunately, as is common in this field, there are no additional genotyped cohorts available with matching phenotypic data that could have been used to replicate our findings. Common diseases are typically influenced by multiple environmental as well as genetic factors. Our case and control participants may differ systematically for several of these environmental characteristics (e.g. education, anxiety levels, personality) which in turn could theoretically be related to genetic variation and to the disorder itself. Future studies in much larger sample sizes may be able to partition effects of known psychological predictors of FSD (such as sexual distress and anxiety levels) and if family-based differentiate genetic architecture of these co-morbid traits. Current approaches to perform GWAS are most successful if the common disease/common variant (CDCV) assumption holds [43]. Currently, exome sequencing has proven to be a powerful tool to identify rare coding variants and has the potential to overcome certain GWAS limitations by focusing on the identification of functional genomic structural variants rather than markers. Gene-environment interaction is also likely to have an influence on the development and maintenance of FSD [44]. In this regard, high throughput sequencing approaches would be again very useful as it can be used to interrogate functional aspects of the genome to identify epigenetic modifications such as DNA methylation, DNA-protein interaction, chromatin accessibility, etc.

In summary, we report the first GWAS of female sexual dysfunction symptoms in humans. This has pointed to several "risk alleles" and the implication of the serotonin and GABA pathways which we hope encourages further replication in large and independent population-based cohorts and then biological investigation to elucidate possible mechanisms. Ultimately, understanding key mechanisms via this research may lead to new FSD treatments and inform clinical practice and developments in psychiatric nosology.

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## Author Contributions

Conceived and designed the experiments: AB PH TS AC. Performed the experiments: AB PH. Analyzed the data: AB PH. Wrote the paper: AB QR.

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# The acute effects of intranasal oxytocin administration on endocrine and sexual function in males

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**Summary**
The role of the neuropeptide oxytocin (OT) ranges from the modulation of neuroendocrine physiological effects to the establishment of complex social and bonding behaviours. Experimental studies in animals, as well as case reports in humans, suggest that OT affects different aspects of sexual behaviour and has predominantly facilitating properties for sexual appetence and performance.
Using a previously established experimental paradigm of sexual arousal and masturbation-induced orgasm, this study investigated the acute effects of intranasal OT application (24 I.U.) on endocrine parameters and measures of sexual appetence and function in healthy men ($n = 10$). In a double-blind, placebo-controlled, balanced cross-over design, sexual arousal, and orgasm were induced by an erotic film and masturbation. In addition to the continuous recording of endocrine (OT, cortisol, prolactin, epinephrine, norepinephrine) and cardiovascular data (heart rate), parameters of appetetive, consummatory, and refractory sexual behaviour were assessed using the acute sexual experience scale (ASES). OT plasma levels were significantly elevated after intranasal OT throughout the whole experiment (>60 min). In addition, OT treatment induced significantly higher increases in epinephrine plasma levels during sexual activity without affecting cortisol levels, prolactin levels or heart rate. OT treatment did not alter appetitive, consummatory, and refractory sexual behaviour according to the ASES. However, when subjects were asked about their subjective perception of whether OT or placebo had been applied, eight out of 10 subjects

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in the OT group answered correctly, thus pointing to an altered perception of arousal. In conclusion, intranasally administered OT leads to a marked increase in OT plasma levels together with increased secretion of catecholamines when subjects are engaged in sexual activity in a laboratory setting. As the effects of OT on sexual behaviour were equivocal, future studies should examine possible facilitating effects further by including males, females, and couples in a field setting, taking into account that OT exerts the most prominent behavioural effects in pair bond formations.


## 1. Introduction

The neuropeptide oxytocin (OT) is well characterized for its role in parturition (Blanks and Thornton, 2003) and lactation (Heinrichs et al., 2002). More recently, it has been demonstrated that OT receptors are distributed over various brain areas (Landgraf and Neumann, 2004) associated with social behaviour, including sexual and parenting behaviours, affiliation and attachment, social memory, and reactivity to social stress in non-human mammals (Carter, 1998; Ferguson et al., 2000; Young and Wang, 2004; Lim and Young, 2006). Neuropeptides have been shown to cross the blood-brain barrier after intranasal administration (Born et al., 2002), with several studies reporting direct effects on human social behaviour (Heinrichs et al., 2003, 2004; Kosfeld et al., 2005; for review, see Heinrichs and Domes, 2008). In particular, OT appears to reduce responses to social stress and to increase trust and the ability to infer another individual's mental state (Heinrichs et al., 2003; Kosfeld et al., 2005; Domes et al., 2007). Data from animal studies suggest that OT facilitates sexual behaviour (Argiolas and Gessa, 1991; Carter, 1992, 1998; Cushing and Carter, 1999; Argiolas and Melis, 2004).

At the level of endocrine sexual physiology, OT has been identified as a marker of orgasm in humans, with circulating levels of OT significantly increasing in males and females around the time of orgasm, though less consistently so than those of prolactin (Carmichael et al., 1987; Murphy et al., 1987, 1990; Krueger et al., 1998, 2003a; Blaicher et al., 1999). It has been postulated that OT may play a facilitating role in sperm and egg transport by increasing smooth muscle contractility in the reproductive tracts (Wildt et al., 1998). Moreover, in multiorgasmic women, OT levels were positively correlated with subjective reports of orgasm intensity (Carmichael et al., 1994), indicating an involvement in sexual experience.

Regarding behavioural aspects of sexual physiology, numerous animal studies document that OT facilitates consummatory sexual behaviour by inducing penile erection via descending projections from the paraventricular nucleus to the lumbosacral spinal cord (Argiolas and Melis, 1995; Giuliano et al., 2001) as well as by decreasing ejaculation latency (Fjellstrom et al., 1968) in male rats, while in females it establishes lordosis behaviour (Benelli et al., 1994). Moreover, OT increases sociosexual interactions and OT receptor antagonists prevent non-contact erections (Melis et al., 2000), which are considered as an index of sexual arousal, confirming the facilitatory role of OT for appetitive aspects of sexual behaviour.

In contrast to these experimental data in animals, little is known about the role of OT in human sexual behaviour (Lidberg and Sternthal, 1977; Herbert, 1994; Anderson-Hunt and Dennerstein, 1995). In particular, whether and to what extent OT administration affects appetitive, consummatory, and refractory aspects of sexual behaviour in humans has not yet been systematically investigated. Thus, in the present study the effects of acute intranasal OT administration on measures of sexual behaviour and endocrine parameters in healthy young males were examined using a previously established experimental paradigm (Krueger et al., 1998, 2002, 2003a; Exton et al., 1999, 2000, 2001). In a double-blind, placebo-controlled, balanced cross-over design, sexual arousal, and orgasm were induced by an erotic film and masturbation. Cardiovascular and neuroendocrine parameters were continuously recorded, and variables of sexual experience were evaluated using a questionnaire especially developed for the assessment of acute sexual experiences in a laboratory setting (Krueger et al., 2003b).

## 2. Methods

### 2.1. Subjects

Ten healthy male volunteers (mean age 27.4±6.7, range 22–45 years) participated in this study after providing written informed consent. Subjects were recruited via advertisement by the University of Zurich, Switzerland. The study was approved by the institutional review board of the University of Zurich.

Participants were screened by the completion of general medical/health questionnaires, which enabled us to exclude individuals taking medication, involved in drug/alcohol abuse or exhibiting endocrinological or psychological disorders. Additionally, a German version of the brief questionnaire for the evaluation of sexual problems and dysfunctions in males was employed (Brief Sexual Function Questionnaire, Reynolds et al., 1988). All participants were sexually active and had been in a relationship for at least 12 months (mean 31.3, range 12–120 months) in order to avoid any confounding endocrine effects of romantic love (Marazziti and Canale, 2004). According to the sexual medical history, none of the participants suffered from sexual dysfunction or maladjustment. All subjects showed heterosexual interests and experiences, were sexually active (∅ 3–4 times a week) and reported having a relaxed relationship towards masturbation and erotic movies.

## 2.2. Design and procedure

The investigation was performed using a double-blind, placebo-controlled, counterbalanced cross-over design. A repeated-measure design was used, with each subject participating in two experimental and two control conditions, i.e., experimental session with placebo, experimental session with OT, control session with placebo, and control session with OT. In total, each subject participated in four sessions. They were blinded to the order of the different sessions. With regard to the circadian rhythms of specific hormones, such as cortisol, all sessions took place at 16:00 h. A 7-day interval separated each session, representing a wash-out period in the case of OT administration. Subjects were asked to abstain from drinking alcohol, from going in for sport and from sexual activities during the 24 h preceding the experiment and to avoid a high consumption of coffee and cigarettes.

In the two experimental sessions, a documentary film was observed for 20 min, followed by 20 min of a pornographic film, and a further 20 min of a documentary (Figure 1). After the first 10 min of the erotic film, subjects were asked to masturbate until orgasm. Participants indicated the time point of orgasm by putting a marker on a wristwatch. Subjects also participated in two control sessions, where a documentary film was shown for 60 min. Different documentary and erotic sequences were employed throughout the sessions so as to avoid habituation effects. The documentary was neutral in content, without violent or stirring scenes, and therefore consisted of travel stories or natural science films, whereas the erotic sequences showed heterosexual couples stimulating each other and having intercourse. All visual stimulations were established in previous studies (Krueger et al., 1998, 2003a, 2006; Exton et al., 1999–2001). Subjects completed questionnaires before, in the middle/after orgasm (in retrospect) and immediately after the sessions.

Experiments were conducted in a separate, soundproofed room equipped with a reclining armchair, a colour television and a DVD player. All leads including the blood line passed through the wall into the adjacent room where the cardiovascular data and blood samples were collected, allowing subjects to be completely isolated throughout the entire experiment. At the beginning of the experiments subjects positioned themselves in the armchair in front of the screen. The investigator administered 24 I.U. OT (Syntocin® spray, Novartis) or an identical placebo spray without OT, both in the form of a clear nose spray (three puffs in each nostril). In order to ensure optimal substance concentration in the central nervous system, OT was administered 50 min before masturbation (Figure 1). The methodology of the administration used has been described in detail by Heinrichs (2000). Intranasal OT is widely prescribed in lactating women and is well tolerated. Several studies have been conducted in humans using doses between 16 and 60 I.U. and no adverse side effects have been reported (for review, see Heinrichs and Domes, 2008).

The cardiovascular monitor was started 20 min prior to the film and a steady baseline reading was obtained. Immediately thereafter, an i.v. cannula was inserted into a forearm vein for continuous blood sampling. A resting period of about 20 min before the beginning of the experiment served to avoid potential stress artefacts induced by cannula insertion in the endocrine and cardiovascular parameters. Stylets (Vasofix-Mandrin, Braun, Germany) were used for the closure of the indwelling cannula in order to inhibit blood coagulation. Continuous blood sampling was initiated immediately before the beginning of the film, with six samples being taken at 10-min intervals. Specifically, samples 1 and 2 represented basal values during the neutral stimulus, sample 3 represented the response to film-induced sexual arousal, sample 4 depicted the response to orgasm, and the last two samples (5 and 6) displayed the recovery phase. Endocrine parameters were analysed in all samples with the exception of OT, which merely served as a control variable and was detected only at the beginning (sample 2), during (sample 4) and at the end (sample 6) of the experiments.

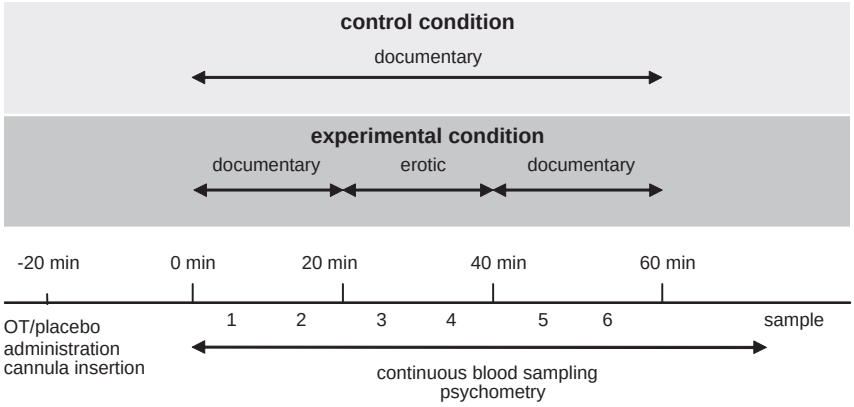


**Figure 1** Experimental paradigm. The experimental paradigm consisted of two experimental and two control sessions, each lasting 60 min and divided into six 10-min intervals. Each subject completed four sessions in a balanced cross-over design, with continuous assessment of endocrine, psychometric, and cardiovascular parameters throughout each session. Samples 1 and 2 represented basal value during the neutral stimulus, sample 3 represented the response to film-induced sexual arousal, sample 4 demonstrated the response to orgasm, and samples 5 and 6 displayed the recovery phase.

## 2.3. Measures

### 2.3.1. Endocrine measures

For continuous blood sampling we used a commercial heparinized catheter system, which consisted of catheter tubing with an internal diameter of 0.8 mm and a length of 100 cm (ConFlo 100, Carmeda, Stockholm, Sweden), and an i.v. cannula (20 G, Insyte-W, Carmeda, Stockholm, Sweden). The dead volume of this system was 1.2 ml. The i.v. cannula was inserted into a forearm vein of the non-dominant arm and connected to the catheter tubing. Blood flow was adjusted to approximately 1.8 ml/min, collected into 9 ml EDTA tubes (Sarstedt, Nümbrecht, Germany), containing aprotinin for protease inhibition (Trasylol, 500 K I.U./ml blood), and divided into 10-min intervals to allow a time kinetic. In sum, approximately 120 ml of blood per session were taken and stored in a polystyrene box filled with ice until the end of the experiment. After the experiment, the blood samples were immediately centrifugated for 10 min at 7 °C with 3500 rpm to separate plasma from blood cells. Plasma samples were then stored at −80 °C until further analysis of endocrine parameters.

Catecholamine plasma levels were measured by high-performance liquid chromatography (HPLC) (Ehrenreich et al., 1997; Smedes et al., 1982). The intra- and interassay variability for plasma measures of norepinephrine were 3.8% and 7.5%, respectively, and for epinephrine 3.9% and 7.1%, respectively. Prolactin and cortisol were detected by the Automated Chemiluminescence-Immunoassay-System 180 (ACS: Centaur; Chiron Diagnostics, Leverkusen, Germany). The intra- and interassay coefficients of variance were 2.5% and 3.6%, respectively, for prolactin, and 4.5% and 6.4%, respectively, for cortisol. OT concentrations were evaluated by immunoradiometric assay with a detection limit of 0.3 pg/sample, the cross-reactivity of the antiserum with related peptides, including vasopressin and OT, was $<0.7\%$ (for details see Landgraf, 1985). The intraassay coefficient of variation at relevant concentrations of the standard curve was between 7% and 10%. To eliminate interassay variation, all samples to be compared were measured in the same assay.

### 2.3.2. Cardiovascular measures

Heart rate was monitored continuously with a Polar heart rate measuring device. The Polar S810i (Polar Electro Oy, Finland) is composed of a belt, which is worn around the chest, and a wristwatch, that is used as a receiver and storage device for the data sent by wireless transmission from the belt. Heart rate was measured beat to beat. The heart rate was then averaged over the 10-min intervals and analysed in parallel with the 10-min interval blood samples (Krueger et al., 1998).

### 2.3.3. Psychometric measures

For the evaluation of acute sexual experience in this experimental situation we used the acute sexual experience scale (ASES). This scale was developed to measure different qualities of appetitive, consummatory, and refractory sexual behaviour in men, and contains six subscales with 52 items (Krueger et al., 2003b). For the current study the ASES was adapted, resulting in four subscales with a total of 42 items. One part of the questionnaire consists of control items evaluating parameters such as the occurrence of orgasm and ejaculation latency. Apart from control items, the questionnaire comprises self-reporting sexual-functioning ratings using visual analogue rating scales (0–100 mm, from ''not at all'' to ''extremely''). The scales examine sexual functioning, both in absolute values and compared with normally experienced sexuality in a real-life situation, such as masturbation and sexual intercourse. In detail, the first subscale, ''appetitive phase'', assesses features of sexual arousability, lust, and desire during the first 10 min of erotic video presentation, when subjects remained passive (e.g. 'please estimate the intensity of sexual arousal while watching the pornographic video'). The second subscale, ''consummatory phase'', evaluates the quality, intensity, and duration of orgasm and sexual release associated with orgasm during the second part of the erotic sequence when subjects were asked to masturbate (e.g. 'please estimate the intensity of your orgasm'). The third subscale, ''refractory phase'', evaluates both negative aspects of refractoriness like tiredness, recovery, and soberness (negative scale, e.g. 'please estimate the grade of tiredness you perceived after orgasm') and positive aspects like sexual release and relaxation (positive scale, e.g. 'please estimate the feeling of being far away after orgasm').

In addition to the ASES, participants filled in a continuous visual analogue scale (VAS, 0–100 mm, from 'not at all' to 'extremely'), assessing subjective general arousal/excitement at the beginning, in the middle and at the end of the experiment. The monopolar VAS was developed for the examination of stress impact in field studies and has proved its validity (Schedlowski and Schmidt, 1996). Furthermore, a short debriefing tool was employed at the end of each session to ascertain the participants' subjective perception of whether OT or a placebo was administered and the possible reasons—such as altered sexual arousability—leading to this assumption. Objective measurements of penile function such as Rigiscan were not used in the current study due to the incompatibility with masturbation.

## 2.4. Statistical analysis

Deviations from normal distributions were tested with the Kolmogorov–Smirnov test ($p>0.1$ for all variables). Levene's test was used to verify the assumption that the samples had equal variances. Following statistical confirmation of normal distribution and variance homogeneity, cardiovascular, and endocrine data from all subjects were analysed by a two-way analysis of variance (ANOVA, condition $\times$ time) for repeated measures. Moreover planned, paired sample $t$-tests of the different conditions were conducted for each scale of the ASES. An $\alpha$ of 0.05 was considered statistically significant for all analyses. Data are expressed as means $\pm$ S.E.

# 3. Results

## 3.1. Endocrine measures

Intranasally administered OT led to significantly increased OT plasma concentrations throughout both the experimental

(group effect: $F = 16.66$, $p < 0.01$) and the control sessions compared to the placebo condition (group effect: $F = 6.03$, $p < 0.05$) (Figure 2).

Regarding the activity of the sympathetic nervous system, participants in the placebo condition revealed a transient increase in epinephrine plasma levels during orgasm (sample 4) and an immediate postorgasmic decline thereafter (samples 5 and 6). After OT administration, plasma levels of epinephrine significantly increased during sexual arousal and orgasm and were generally higher at samples 2 and 3 than in the placebo condition (interaction effect: $F = 2.98$, $p < 0.05$). No significant alterations in epinephrine plasma levels were observed in the control sessions of either group (Figure 3A).

Plasma concentrations of norepinephrine showed a marked increase during the period of orgasm and in the refractory interval in the placebo group (time effect: $F = 3.30$, $p < 0.05$). However, this effect was masked after OT administration which induced a general elevation of norepinephrine levels that was, however, not statistically significant (group effect: $F = 2.89$, $p = 0.124$). There were no significant alterations in norepinephrine levels in the control session (Figure 3B).

A continuous decline in cortisol plasma levels throughout both the experimental (time effect: $F = 31.02$, $p < 0.001$) and control sessions (time effect: $F = 13.57$, $p < 0.001$) was observed, with no significant differences in response to sexual activity (Figure 4A).

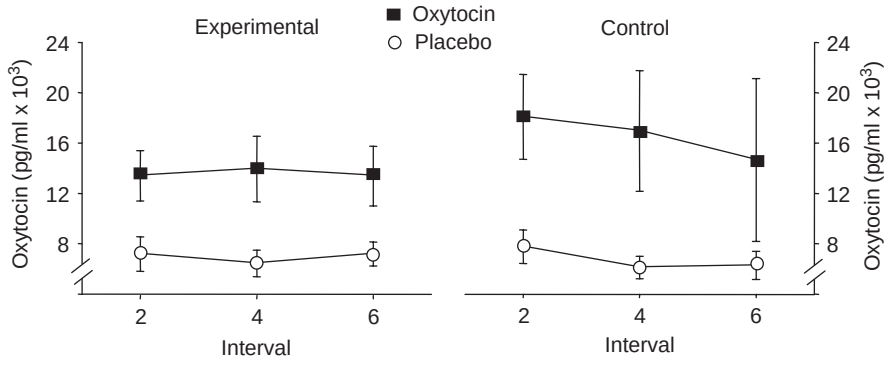


**Figure 2** Plasma concentrations of oxytocin analysed at 10-min intervals during the experimental and control conditions. OT primarily served as a control variable and was analysed only at the beginning (sample 2), in the middle (sample 4), and at the end (sample 6) of the experiments. Values are expressed as means ± S.E.

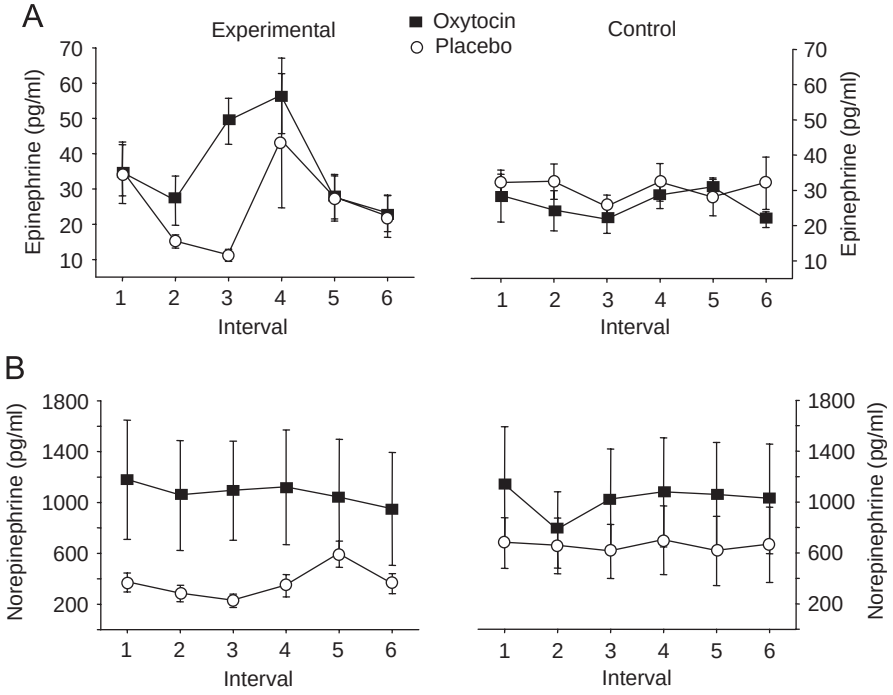


**Figure 3** Plasma concentrations of epinephrine (A) and norepinephrine (B) analysed at 10-min intervals during the experimental and control conditions. Samples 1 and 2 represented basal value during the neutral stimulus, sample 3 represented the response to film-induced sexual arousal, sample 4 demonstrated the response to orgasm, and samples 5 and 6 displayed the recovery phase. Values are expressed as means ± S.E.

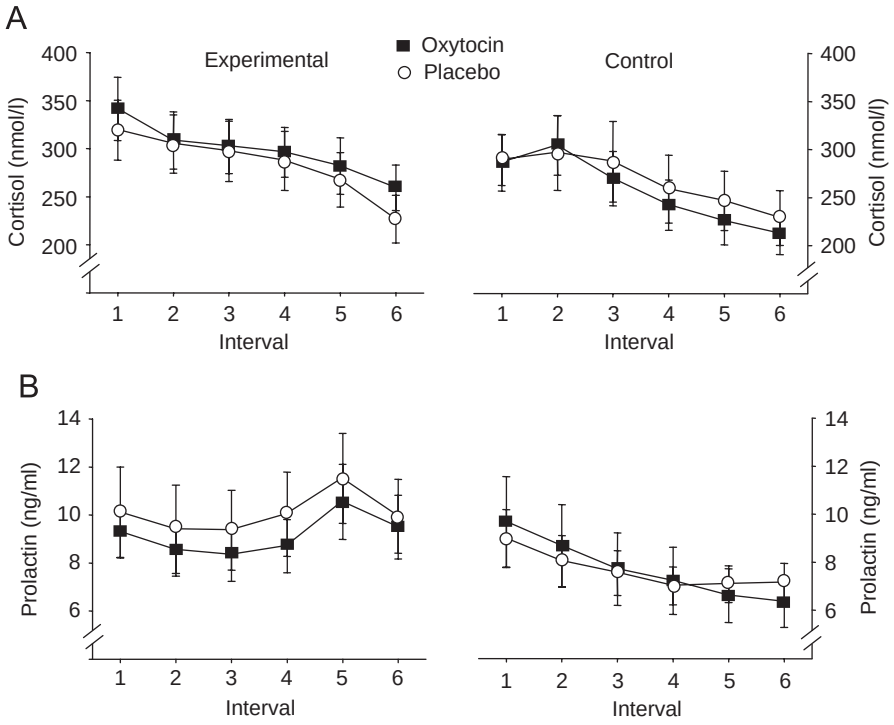


**Figure 4** Plasma concentrations of cortisol (A) and prolactin (B) analysed at 10-min intervals during the experimental and control conditions. Samples 1 and 2 represented basal value during the neutral stimulus, sample 3 represented the response to film-induced sexual arousal, sample 4 demonstrated the response to orgasm, and samples 5 and 6 displayed the recovery phase. Values are expressed as means $\pm$ S.E.

**Table 1** Time course of heart rate (means with standard error) in the different experimental and control conditions.

| | Sample no. | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Experiment with OT | 81.9(8.5) | 81.3(8.9) | 85.6(7.0) | 94.1(11.2) | 80.8(10.9) | 76.8(7.3) |
| Experiment with placebo | 78.1(8.9) | 74.2(12.8) | 79.1(15.2) | 90.8(16.4) | 76.9(10.1) | 73.3(7.9) |
| Control with OT | 71.4(10) | 68.5(9.1) | 67.7(4.1) | 66.9(5.2) | 69.7(8.1) | 71.9(10.2) |
| Control with placebo | 70.2(8.8) | 68.5(8.1) | 69.0(6.6) | 67.0(5.9) | 67.9(7.3) | 68.9(7.0) |

Samples 1–6 represent the different phases of sexual activity as explained in Figure 1.

As previously observed, participants revealed a significant increase in prolactin plasma levels during orgasm, reaching maximal concentrations during the refractory period (time effect: $F = 5.16$, $p < 0.01$), and these remained elevated for the remainder of the experimental sessions. In the two control sessions, prolactin plasma concentrations showed a constant decrease during the course of the sessions (time effect: $F = 13.47$, $p < 0.001$) (Figure 4B).

## 3.2. Cardiovascular measures

Participants showed a transient increase in heart rate during sexual arousal and orgasm (samples 3 and 4) in the OT and placebo group with an immediate decline below baseline levels after orgasm (time effect: $F = 21.98$, $p < 0.001$). Heart rate levels tended to be higher after OT administration in the experimental session without showing statistical significance. There were no significant alterations in heart rate after OT or placebo administration in the control conditions (Table 1).

## 3.3. Analysis of psychometric measures

At the beginning of each session there was small-to-moderate general emotional activation on the VAS, with a significant decrease over time during the experimental (time effect: $F = 6.27$, $p < 0.05$) and the control sessions (time effect: $F = 9.23$, $p < 0.01$). However, no significant modulation by OT was observed.

All subjects reported having achieved an orgasm in the 10-min sequence of sexual activity in the experimental sessions with shorter ejaculation time after placebo

**Table 2** Analysis of the ASES subscales.

| | Appetitive phase | Consummatory phase | Positive aspects of refractory period | Negative aspects of refractory period |
|---|---|---|---|---|
| After oxytocin | 42.9(16.8) | 41.8(14.7) | 39.6(16.1) | 35.4(18.2) |
| After placebo | 44.8(20.1) | 37.6(16.6) | 39.0(15.5) | 36.7(17.5) |

Effects of OT and placebo on appetitive parameters, consummatory sexual experience as well as negative and positive aspects of the refractory period during the sequence of sexual activity in the experimental sessions, as measured by the ASES using control items (occurrence of orgasm, ejaculation latency) and visual analogue rating scales (all other parameters). Questionnaire values represent a percentage of maximum sexual experience. Values are expressed as means ± S.E.

(5.3 ± 0.6 min) than after OT (6.3 ± 0.6 min; $t = -2.78$, $p = 0.021$). No participant reported having difficulty in achieving an orgasm or having been particularly intimidated or distracted by the setting during this sequence of sexual activity. Further analysis of the participants' subjective assessment of acute sexual experience according to the ASES revealed no significant differences between the OT and the placebo conditions. Specifically, OT did not significantly enhance any of the parameters of sexual drive and function, including appetitive ($t = 0.47$, n.s.) and consummatory ($t = -0.83$, n.s.) sexual behaviour, during the sequence of sexual activity. Moreover, the scales for positive and negative aspects of the refractory period did not display any significant OT-induced alterations (positive scale: $t = 0.18$, n.s.; negative scale: $t = -0.12$, n.s.) (Table 2).

Interestingly, however, when subjects were asked about the subjective perception of whether OT or placebo had been applied in the experimental session, eight out of 10 participants who received OT named the correct group due to increased sexual arousability. Similarly, all subjects who received a placebo reported this correctly in the experimental session and perceived this condition to be less arousing.

## 4. Discussion

Experimental research has delineated a wide spectrum of central and peripheral effects of OT ranging from the modulation of physiological functions to the establishment of complex social and bonding behaviours (Carter et al., 1995; Carter, 1998; Young et al., 1998). Although there is evidence of the facilitating role that OT plays with regard to various parameters of animal sexual behaviour (Carter, 1992; Cantor et al., 1999; Cushing and Carter, 1999; Argiolas and Melis, 2004) as well as a case report on one woman (Anderson-Hunt and Dennerstein, 1994), it has not yet been investigated whether and to what extent OT administration affects anticipatory and consummatory aspects of human sexual behaviour. Using a previously established, double-blind, balanced, cross-over design (Krueger et al., 2003b), the current study demonstrates that a single intranasal administration of 24 I.U. OT induces a prolonged increase in OT plasma levels for at least 80 min in males. Furthermore, OT increased the sympathetic outflow in that there were increased levels of catecholamines during sexual arousal and masturbation, together with a subjective perception of increased arousability, which was, however, not reflected in the measures of sexual physiology according to the ASES.

Confirming preliminary results in a sample of three subjects (Landgraf, 1985), the current paradigm of intranasal administration of OT was able to significantly increase OT plasma levels within less than 20 min. The lacking OT decrease during the following sessions is noteworthy given the short plasma half-life of 5–12 min. Kinetic parameters of intranasal OT administration have never been systematically investigated before. Thus, the current data may indicate that OT is retained in the nasal mucosa and slowly released to nearby blood vessels (sustained release). In addition to intranasal resorption and sustained delivery into the bloodstream, OT—like many other neuropeptides—has also been shown to enter the cerebrospinal fluid (CSF) and reach brain tissues, resulting in specific effects on neurobehavioural functions (Illum, 2000; Born et al., 2002; Heinrichs et al., 2003, 2004; Kosfeld et al., 2005; Domes et al., 2007; Heinrichs and Domes, 2008).

Regarding the cardiovascular system, OT is known to exert vasoactive effects on peripheral and cerebral vessels with primarily vasodilative effects (Thibonnier et al., 1999; Gimpl and Fahrenholz, 2001). In humans, rapid intravenous OT injections can lead to a short-term relaxation of smooth vessel with a consecutive decrease in blood pressure, erythema, and reflex tachycardia. Furthermore, intravenous injections of 0.5 I.U. OT within 2.5 min lead to a reduction in blood flow velocity in the middle cerebral artery indicating that OT may induce both a vasodilative effect on large cerebral arteries and/or a vasoconstrictive effect in small cerebral resistance vessels (Stolz-Born et al., 1996). The vasodilative effects of OT have been demonstrated in animal studies by a decrease in mean arterial pressure, e.g. in rats, though one study also described a short-term increase in blood pressure in response to the OT-potentiating effect of female steroid hormones in rats (Petersson et al., 1999; Gimpl and Fahrenholz, 2001). In the current study, heart rate measures tended to be higher after OT administration in the experimental condition and showed the typical increase during sexual arousal and orgasm together with a rapid decline during the refractory period as previously shown (Krueger et al., 1998, 2003a; Exton et al., 1999, 2000). Thus, there was only a marginal, insignificant alteration in heart rate which was limited to the experimental session.

In contrast to cardiovascular function, the release of catecholamines after OT administration was significantly high, although it was again limited to the experimental session. This may lead to the assumption that OT has a

stimulatory effect on the sympathetic nervous system, possibly dependent on psychophysiological activation, which is provided here by sexual activity and/or its anticipation. This role of OT in fact is supported by animal studies, where OT induced a sympathetically mediated pupillary dilatation response (Sansone and Komisaruk, 2001). In the sense that it acts as an endogenous stimulator of autonomic sympathetic preganglionic neurons in the thoracic spinal cord, OT may also be responsible for the increased secretion of catecholamines by the adrenal medulla, as observed here. However, the lack of such effects in the control condition, where subjects merely watched a documentary, may point to the above-mentioned combinatory effects of psychophysiological activation and OT, which need further investigation.

The moderately increased sympathetic tone in the experimental session was not related to the elevation of self-perceived general arousal as measured by the visual analogue rating scales, even though subjects indicated elevated sexual arousability after OT administration. Thus, it was possible to demonstrate that OT has a direct effect on the sympathetic nervous system, but the relationship between unspecific arousal and subjective perception of sexual arousal still has to be analysed further. This is of specific importance since the facilitating effect of moderate sympathetic activation on sexual drive and arousal has been described in animal as well as human studies (Vincent and Etgen, 1993; Meston, 2000).

As OT is able to modulate hypothalamic–pituitary–adrenal (HPA) axis responsiveness to stress (Heinrichs et al., 2003), cortisol plasma concentrations were analysed throughout the whole experiment. In contrast to the attenuating effects of OT on cortisol responses to psychosocial stress, no significant alterations in cortisol were observed following OT administration in the present study. Nevertheless, previous observations have reported on the combined impact of OT administration and social support on the buffering of cortisol levels (Heinrichs et al., 2003). We therefore assume that the effects of OT on HPA-axis activity depend on the additional influence of psychosocial interaction, which was not provided in the current paradigm where sexual activity took place alone in a laboratory setting without a sexual partner. Future studies will extend the paradigm by incorporating sexual interaction with a partner in the laboratory (Exton et al., 2001) as well in a naturalistic setting.

Apart from cortisol, prolactin plasma concentrations were also monitored due to their involvement in sexual and stress responses (Schedlowski and Schmidt, 1996; Krueger et al., 1998, 2003a). In addition, the stimulatory influence of OT on lactotrophs in the adenohypophysis has been discussed, however, this may be restricted to specific reproductive stages such as the end of gestation (Gimpl and Fahrenholz, 2001). In our study we observed a significant increase in prolactin plasma levels with the onset of orgasm, as previously described (Krueger et al., 1998, 2003a), although the modulatory influence of OT was not significant. This supports the assumption that OT has restricted influence on prolactin secretion depending on the factors mentioned above. The most prominent regulatory factor of prolactin secretion is the inhibition by dopaminergic neurons.

One important issue in our study was the assessment of sexual drive, arousal, and function according to the ASES. Since a questionnaire for the assessment of acute sexual experience in an experimental setting is lacking, we recently developed such a scale for a study on the sexual-physiological effects of pharmacological prolactin manipulation in males (Krueger et al., 2003b). In that study the ASES proved to be a valid and reliable instrument consistently confirming the correlation between altered prolactin levels and appetetive, consummatory, and refractory sexual behaviour. In the current study, the ASES did not confirm significant alterations in perceived sexual arousal and function after OT administration, although the majority of subjects correctly indicated having received OT, due to increased sexual arousability. The ejaculation time after OT was slightly longer than after placebo administration, which may point towards both diminished and enhanced sexual experience. These discrepancies may be due to several factors. As outlined above, the current paradigm incorporates the sexual activity of subjects who are alone in a laboratory setting. This paradigm, though highly controlled experimentally, does not account for the importance of social interaction in the behavioural effects following OT administration, as recently demonstrated in studies on intranasal OT in male volunteers (Heinrichs et al., 2003; Kosfeld et al., 2005). In future studies, we will therefore alter the paradigm to include partner contact in the laboratory setting as described before (Exton et al., 2001) and add a naturalistic setting, that is, sexual intercourse in a private setting, with retrospective assessment of sexual parameters. Previous anecdotal studies in women (Anderson-Hunt and Dennerstein, 1994, 1995) as well as comprehensive animal data (e.g. Insel et al., 1997; Caldwell and Moe, 1999; Giuliano et al., 2001; Insel and Young, 2001; Pedersen and Boccia, 2002; Komisaruk and Sansone, 2003) have demonstrated the facilitating role that OT plays in various parameters of sexual behaviour. Remarkably, several of these studies have emphasized the importance of the steroid-priming effect on the plasticity and function of the central OT system in females. However, in this first study only males were examined and such pretreatment was not appropriate. To further elucidate the priming role of sex steroids, future studies regarding the effects of OT on sexual behaviour will have to incorporate females using hormonal contraception to investigate progestogenic and oestrogenic processes. As another point, the ASES still remains to be standardized and normalized. Therefore the lack of reported enhancement in subjective sexual arousal and orgasm quality may also reflect the need for re-evaluation of this questionnaire, and this is now the subject of a current investigation. Nevertheless, our previous study showed a high level of strength and consistency in the relationship between altered hormone levels and scores in the ASES (Krueger et al., 2003b). Moreover, ceiling effects may have been introduced by including only young and healthy males, making it difficult to demonstrate the potentially facilitating effects of OT. This may point to the need for future studies to include older males and/or men with disorders affecting sexual appetence and erectile function. Finally, the subjective reports as to whether OT or placebo had been administered that were based on the degree of sexual arousability need further attention in future studies.

In conclusion, this initial study on the impact of intranasal OT on endocrine and sexual function was able to

demonstrate that the activation of the sympathetic nervous system correlates with sexual activity. However, the parameters of sexual drive and function were not significantly altered by OT administration as measured by the ASES. As the facilitating properties of OT are well documented in the animal literature, future studies should extend the experimental paradigm to incorporate males, females, and couples, using both a laboratory and a naturalistic setting, and also to assess the biological significance of sex steroids in sensitizing brain systems to the facilitating effects of OT in women.

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## Conflict of interest

All authors declare that they have no conflicts of interest.

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## ORIGINAL RESEARCH—EPIDEMIOLOGY

# Recent and Lifelong Sexual Dysfunction in a Female UK Population Sample: Prevalence and Risk Factors

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**ABSTRACT**

***Introduction.*** To date, no studies have tried to explore the prevalence and risk factors of recent and lifelong female sexual dysfunction (FSD) in the United Kingdom using validated questionnaires for the assessment of symptom severity and levels of associated sexual distress.

***Aim.*** To estimate the prevalence and comorbidity of recent and lifelong FSD and to further identify potential psychosocial and behavioral risk factors in a nationally representative sample of UK women.

***Methods.*** One thousand four hundred eighty-nine unselected female twin individuals aged 18–85 years. Validated questionnaires, such as the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale, were used for the assessment of symptom severity and degree of sexual distress.

***Main Outcome Measures.*** Prevalence and comorbidity of recent and lifelong FSD according to the FSFI cutoff points and the existence of sexual distress. Lifelong FSD refers to an individual's average sexual function ever since they have been sexually active. We further calculated odds ratios (ORs) with 95% confidence interval for FSD.

***Results.*** We found that 5.8% of women reported any recent sexual dysfunction and 15.5% reported any lifelong sexual dysfunction. Hyposexual desire was the most prevalent recent and lifelong sexual complaint (21.4% and 17.3%, respectively). High intercorrelations were found for both recent and lifelong FSD ($r = 0.3–0.7$). The most common independent, clinical predictor of recent and lifelong FSD diagnosis was relationship dissatisfaction (OR 1.2–4.5). Experience of abuse (OR 1.6–2.1), increased anxiety, and obsessive compulsive behavior were the most common predictors for lifelong FSD.

***Conclusions.*** The study provides the first UK population-based assessment of recent and lifelong FSD using validated outcome measures and accounting for sexual distress. Our results indicate that FSD is common in the general population and is influenced by psychosocial factors with different pathoetiologies underlying recent and lifelong FSD. **Burri A and Spector T. Recent and lifelong sexual dysfunction in a female UK population sample: Prevalence and risk factors. J Sex Med 2011;8:2420–2430.**

***Key Words.*** Epidemiology; Prevalence; Recent and Lifelong Female Sexual Dysfunction; UK; Risk Factors

### Introduction

Female sexual dysfunction (FSD)—an umbrella term used to capture disorders related to sexual desire, arousal, orgasm, and pain—is still controversial regarding its existence and definition [1]. The absence of dependable population-based data, combined with a lack of standard uniformly applied definitions of FSD—especially regarding the degree of dysfunction and distress—and use of nonvalidated outcome measures, has made it difficult to measure or compare the prevalence and etiology of FSD [2].

In 2000, a consensus-based definition and classification system for FSD was proposed by the International Consensus Development Conference [3,4]. Accordingly, a woman should show evidence of significant personal distress in relation to

her sexual problem in order to qualify for the diagnosis of FSD. Numerous epidemiological studies, however, have been criticized for producing estimates of FSD that are widely agreed to be inflated by not assessing FSD-related personal distress [5]. In an extensively cited U.S. study, for example, Laumann and colleagues found a prevalence rate of 43% for any sexual dysfunction, which seriously calls into question whether this can indeed be regarded a pathology or be representative of the norm [6]. Similarly, many studies have failed to use stringent definitions of FSD by, for example, not accounting for the duration or the degree of severity. A precise phenotype definition in epidemiologic research, however, is crucial to avoid misclassification and to facilitate comparisons among studies.

Today, FSD is believed to be a multifactorial phenomenon, rarely caused by a single factor, although one may predominate. Knowledge about the pathoetiology of FSD involves anatomical, physiological, biological, medical, and psychological factors which, in turn, are affected by environmental variables. It has become increasingly evident that despite the numerous biophysiological factors known to be associated with FSD, mood and psychological entities seem to correlate even more strongly with FSD. The psychosocial risk factors affecting women's sexual functioning are broad and comprise emotional difficulties, such as untreated anxiety, depression, stress, and a history of sexual and physical abuse [7–9].

More recently, emphasis has been placed on interpersonal relationships and personality [10,11]. Relationship imbalances, marital conflicts, extramarital affairs of the partner, and lack of trust and intimacy have all been reported to affect women's sexuality, as have poor communication, the partner's sexual performance, a woman's inability to express her desires, and a lack of knowledge about anatomical and physiological processes involved in sexual arousal and stimulation. In a large case control study by Harris et al., specific personality traits—namely introversion, emotional instability, and not being open to new experiences—have been shown to be significant risk factors for orgasmic infrequency [11]. These findings have been supported by the results of a recent study that found a positive association between emotional intelligence and orgasm frequency, albeit on same population sample [12].

To date, only a few studies have tried to explore the prevalence and risk factors of FSD in the United Kingdom, all of which relied on self-constructed questionnaires or semistructured interviews and did not account for concurrent distress [13–17]. The aim of the present study was to complement the epidemiologic knowledge on FSD in a nationally representative sample of female adults in the United Kingdom by estimating the prevalence and comorbidity of recent and lifelong FSD (including sexual distress as a diagnostic criterion) and to explore its association with commonly reported sociodemographic, behavioral, and psychological risk factors using validated outcome measures.

## Materials and Methods

### *Sample Definition*

This study was part of a larger project aiming at the disentanglement of genetic and environmental influences underlying FSD. Therefore, the study sample for this postal questionnaire consisted of monozygotic (N = 757) and dizygotic (N = 732) female twins enlisted in the Adult TwinsUK registry [18]. The UK Adult Twin Registry is a cohort of unselected volunteer Caucasian twins that started in 1993. All volunteers in the registry have been recruited through successive national media campaigns in the United Kingdom and Ireland and from other twin registers, including the Aberdeen Twin registry and the Institute of Psychiatry Adult Registry. The TwinsUK population has been compared for a number of diseases, traits, and environmental factors with an age-matched UK population and a singleton population cohort from North-East London and was found to be no different in terms of disease prevalence and lifestyle characteristics [19]. The cohort has further shown to be representative of the general population for a wide range of lifestyle and sexual behavioral factors [12,20]. The study targeted a subsample of 3,154 (29.7% of twins from the entire TwinsUK registry; aged 25–85, mean age 56.2) female twin individuals who had previously filled in sexuality-related questionnaires and stated their willingness to participate in studies of this and similar nature. The study was approved by the St. Thomas' Hospital Research Ethics Committee and all twins provided informed consent. The twins were unaware of any specific hypotheses.

### *Measures*

#### Demographic, Psychological, and Interpersonal "Risk Factor" Measures

Sociodemographic information on all twins including age, current marital status, social class, and

years of education was obtained from the TwinsUK database. The Index of Multiple Deprivation was calculated based on UK postcodes and used as a marker to estimate the twins' socioeconomic status [21]. Information on women's body mass index (BMI) and smoking habits, as well as the number of pregnancies (including miscarriage) and having children (yes/no), was obtained from an independent questionnaire on general health that had been sent to the twins a few months ahead of this survey. BMI was calculated according to the commonly used formula: BMI = kg/meters$^2$. As an approximation, women <50 years of age were classified as premenopausal and women >50 years as postmenopausal according to average age of menopause (51 years) [22]. Events of physical, emotional, and sexual abuse were responded to on a yes/no dichotomous scale. Current and lifelong relationship dissatisfaction was assessed with a single question with response options ranging from "very satisfied" (1) to "not satisfied at all" (6). Data on obsessive-compulsive behavior were available from the 42-item measure "obsessive compulsive inventory" (OCI) [23]. The measure is primarily used in clinics to aid the diagnosis and determine the severity of obsessive-compulsive disorder (OCD). The OCI has shown excellent internal consistency ($r = 0.93$) and high test–retest reliability in an OCD sample ($r = 0.84$–$0.87$) and in nonpatient controls ($r = 0.90$–$0.89$). Data on anxiety were obtained from the 16-item self-report "anxiety sensitivity index" (ASI) [24]. The psychometric properties and predictive validity of the widely used instrument have been well established and a number of studies have provided replicated evidence that the ASI has adequate internal consistency ($\alpha = 0.81$–$0.94$), a good degree of test/retest reliability ($r = 0.71$–$0.75$), and a high degree of interitem relatedness. The Big Five personality dimensions and the related construct of emotional intelligence were assessed using the "Ten-Item Personality Index" (TIPI) and the "trait emotional intelligence questionnaire" (TEIQue-SF) [25,26]. The TIPI has adequate levels in terms of convergence with widely used multi-item Big-Five measures (e.g., Big Five Inventory [BFI]) in self, observer, and peer reports (mean of $r = 0.77$) and good test–retest reliability ($r = 0.62$–$0.77$). Similarly, the TEIQue-SF has also shown to have high levels of internal consistency (Cronbach's $\alpha > 0.80$) and good construct validity.

### FSD and Sexual Distress Measures

The well-established Female Sexual Function Index (FSFI) was used for multidimensional assessment (desire, arousal, lubrication, orgasm, satisfaction, and pain) of female sexual function over the past 4 weeks [27]. Details on response options, domain score computation, and domain factor weights can be found in Rosen et al. [27]. The questionnaire has received extensive psychometric evaluation in clinical and nonclinical samples [27,28]. The specifically developed 12-item Female Sexual Distress Scale (FSDS) was used for the assessment of subjective distress associated with FSD [29]. Response options are on a five-point scale, ranging from "Never" (0) to "Always" (4), with a higher score indicating increased sexual distress. Information on psychometric properties of the instrument can be found elsewhere [29,30].

Two modified questionnaire versions—the Female Sexual Function Index-lifelong (FSFI-LL) and the Female Sexual Distress Scale-lifelong—were used to assess individual's average sexual function and distress "ever since they have been sexually active." Lifelong FSD therefore represents an individual's average level of sexual functioning which can include periods of malfunction as well as periods of good function. Scoring was computed using the same algorithm as in the original questionnaire versions. Evidence of psychometric properties of the FSFI-LL can be found in Burri et al. [31].

#### *Statistical Analyses*

Data handling and all statistical analyses were carried out using STATA software (StataCorp. 2007. Stata Statistical Software: Release 10. College Station, TX, USA: StataCorp LP). For all analyses, a $P$ value less than 0.05 or odds ratios (ORs) with a 95% confidence interval (CI) not including "1" were considered statistically significant, unless stated otherwise. All tests were two-tailed.

Prevalence rates of FSD reported in this study are based on the discrimination between functional and dysfunctional women according to the FSFI cutoff score of 26.55—with inclusion of reported sexual distress (cutoff of 15). For all analyses, the six domains of FSD were handled as dichotomous traits coded "functional" (0) and "dysfunctional" (1). The cutoff scores to determine the presence of difficulties on the six domains of the FSFI were obtained from published sources [28]. Accordingly, scores less than 4.28 on the desire domain, less than 5.08 on the arousal domain, less than 5.45 on the lubrication domain, less than 5.05 on the orgasm domain, less than 5.04 on the satisfaction domain, and less than 5.51

on the pain domain were used to classify participants as having difficulties in that domain. Phi correlations were used to explore patterns of association between the various subdomains of sexual function. Simple logistic regression analyses were conducted to investigate the effects of potential confounders on sexual function. Significant variables were entered in the multiple regression models as independent variables. A stepwise backward method was used. In all regression analyses, nonindependence of twin pairs was accounted for by using the cluster function for familial relatedness, which is a form of conditional regression. Bonferroni correction as implemented in STATA software was applied to account for multiple testing.

## Results

### *Cohort Characteristics*

Out of 3,154 targeted women, 1,589 (50%) returned the questionnaire. Of these, nine who reported never having been sexually active were excluded from further analyses. The few existing epidemiological studies on FSD and associated risk factors in homosexual women tentatively indicate different prevalence rates and predictors of FSD in homosexual women [32]. Furthermore, the proportion of exclusively gay women in our sample was too small to conduct any meaningful, comparative analysis in terms of prevalence of FSD in homosexual vs. heterosexual women. Hence, for reason of standardization, 19 (1.3%) women reporting being homosexual were also omitted. Seventy-two (4.8%) women with more than five of the 19 items in the FSFI and FSFI-LL and/or more than two items of the FSDS missing were further dropped from the sample [33]. To maximize the number of individuals for analyses—in cases where subjects had answered less than five of the 19 items in the FSFI and FSFI-LL and/or less than two items of the FSDS—missing values were imputed with item-specific means of the nonmissing values, separately calculated for four different age groups: 18–30, 31–45, 46–55, and 56–85 years (72 individuals, 4.8%).

After applying exclusion criteria and imputation, a total of 1,489 women were eligible for analyses of lifelong sexual function. The authors of the FSFI imply that to derive an unambiguous full-scale score, the FSFI should only be used for subjects who have engaged in sexual activities during the measurement period; therefore, women reporting no sexual activity during the past 4 weeks were excluded from analyses of recent sexual function (N = 559), resulting in a sample of 930 women [27]. Characteristics of the overall sample (N = 1,489) are shown in Table 1. The mean age of participants in the study was 56.3 years (standard deviation 11.6; range 18–85) (Table 1).

**Table 1** Lifestyle and behavioral risk factors and demographic characteristics of the overall sample (N = 1,489)

| | Mean (SD) | Range |
|---|---|---|
| Age | 56.3 (11.6) | 18–85 |
| Education in years | 10.5 (2.9) | 6–32 |
| BMI | 24.9 (4.2) | 17–45 |
| No. of pregnancies | 2.7 (1.2) | 1–11 |
| No. of cigarettes | 7.9 (8.5) | 1–54 |
| | **N (%)** | |
| Marital status | | |
| Single | 87 (5.9) | |
| Married | 756 (57.1) | |
| In a relationship | 468 (31.4) | |
| Divorced | 121 (8.2) | |
| Widowed | 57 (3.9) | |
| Socioeconomic status | | |
| 1 | 95 (6.4) | |
| 2 | 179 (12.0) | |
| 3 | 295 (19.8) | |
| 4 | 420 (28.2) | |
| 5 | 519 (34.9) | |
| Occupation | | |
| Employed | 741 (49.8) | |
| Unemployed | 748 (50.2) | |
| Smoker | 582 (39.1) | |
| Children | 1,366 (91.7) | |
| Menopause | 1,067 (72.0) | |
| Sexual abuse | 157 (10.5) | |
| Physical abuse | 171 (11.5) | |
| Emotional abuse | 323 (21.7) | |

SD = standard deviation.

Differences in sociodemographic variables were found between women who reported sexual activity during the past 4 weeks compared with women who did not (results not shown). Recently, sexually inactive women were significantly older (61 vs. 52 years; $P < 0.001$) and more often single (8.4% vs. 4.3%; $P < 0.005$), divorced (15.02% vs. 3.9%; $P < 0.001$), or widowed (7.16% vs. 1.8%; $P < 0.001$) than sexually active ones. In terms of potential lifestyle and behavioral risk factors for FSD, no differences were found between the two groups.

### *Prevalence and Comorbidity of FSD*

Analyses of our data resulted in a point prevalence of 5.8% and a lifetime prevalence of 15.5% for total FSD (Figure 1). Recent difficulties related to desire were the most common sexual complaint, being present in 21.4% of women. Approximately

**Table 2** Cross-trait correlations with 95% CIs for the six domains of sexual function—desire, arousal, lubrication, orgasm, satisfaction, pain—as measured by the FSFI and the FSFI-LL. All correlations were significant ($P < 0.05$)

| | Desire | Arousal | Lubrication | Orgasm | Satisfaction | Pain |
|---|---|---|---|---|---|---|
| Recent sexual problems (N = 930) | | | | | | |
| Arousal | 0.4 | | | | | |
| Lubrication | 0.3 | 0.7 | | | | |
| Orgasm | 0.2 | 0.7 | 0.5 | | | |
| Satisfaction | 0.3 | 0.5 | 0.4 | 0.5 | | |
| Pain | 0.2 | 0.3 | 0.4 | 0.3 | 0.2 | |
| Lifelong sexual problems (N = 1,489) | | | | | | |
| Arousal | 0.5 | | | | | |
| Lubrication | 0.4 | 0.6 | | | | |
| Orgasm | 0.4 | 0.6 | 0.6 | | | |
| Satisfaction | 0.3 | 0.5 | 0.4 | 0.6 | | |
| Pain | 0.2 | 0.3 | 0.4 | 0.3 | 0.2 | |

every 10th woman reported recent arousal (11.4%), lubrication (8.7%), orgasm (8.8%), and satisfaction (10.4%) problems, whereas sexual pain was reported by only 6.0% of women. Frequencies of lifelong FSD were consistently higher compared with recent sexual dysfunctions across all domains except desire (21.4% vs. 17.3%) (Figure 1).

Results of our intercorrelation analysis to investigate the relationship between the different domains within FSD indicated clear significant associations between all domains, ranging from $r = 0.2$ to $r = 0.7$, with the highest correlation between both recent and lifelong arousal and orgasm and the lowest between desire and pain (Table 2). Since sexual problems rarely present themselves exclusively in one domain, we further analyzed the pattern of comorbidity among the various dimensions. In addition, 82.7% (N = 769) and 78.6% (N = 1,170), respectively, of women of our total sample reported no sexual dysfunctions at all (Table 3). Fifty-four subjects (5.8%) reported only one recent sexual dysfunction, and 40 individuals (2.7%) reported only one lifelong sexual dysfunction. A considerable proportion of women (11.6% and 18.7%, respectively) presented a recent or lifetime sexual dysfunction in at least one additional domain, and a small proportion of women (1.6% and 3.6%, respectively) even suffered from sexual dysfunctions in all domains. In women reporting only one sexual dysfunction, the most common complaint was hypoactive sexual desire (32.3% and 29.5%, respectively) (Tables 2 and 3).

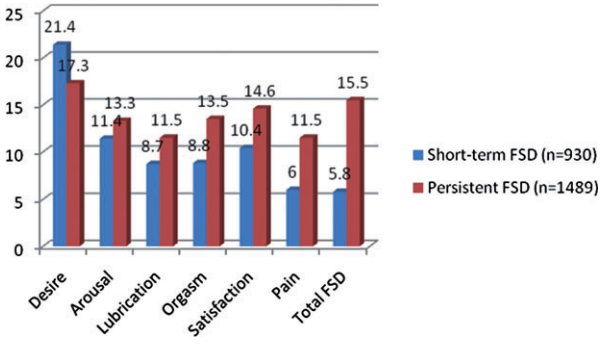


**Figure 1** Comparison of point and lifetime prevalence rates of females sexual dysfunction (FSD) in the overall sample.

**Table 3** Proportion of women reporting none, one, or more sexual dysfunctions in our population sample. Proportions are displayed as percentages of the total sample.

| | Number of sexual dysfunctions | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 |
| Recent FSD (N = 930) | 82.7 | 5.8 | 3.1 | 2.5 | 2.0 | 2.3 | 1.6 |
| Lifelong FSD (N = 1,489) | 78.6 | 2.7 | 3.2 | 3.2 | 4.2 | 4.4 | 3.6 |

### *Sexual Distress*

26.6% of women in our study reported recent sexual distress and 25.9% reported lifelong sexual distress. To meet the criteria of FSD, individuals must feel significant distress over their sexual problems. However, not every individual categorized as "dysfunctional" felt distressed about her low sexual function. Only, on average, a quarter of women with recent sexual problems directly reported distress. From women suffering from recent hypoactive desire problems, for example, only 33.6% felt distressed, whereas, still, 19.9% classified as having "normal" libido levels felt sexual distress. The proportion of women feeling distressed about their lifelong sexual problems was generally higher, ranging from 25.5% for hypoactive sexual desire to 42.9% for dissatisfaction,

compared with 20.1% for recent arousal and 33.6% for recent hypoactive sexual desire problems (results not shown).

### Risk Factors of FSD

All variables significantly correlated with sexual problems in the univariate regression were entered in the multiple regression models. The results are expressed as ORs, *P* values, and $r^2$, separately for each domain in Table 4. Age, relationship dissatisfaction, and emotional intelligence were found to be the most common risk factors for recent FSD, being independently and significantly correlated with the prevalence in most of the subdomains (Table 4). Women dissatisfied with their relationship showed a substantially higher risk of reporting any kind of sexual dysfunction except for arousal (ORs ranging from 1.20 to 4.49). The strongest association was found between relationship dissatisfaction and sexual dissatisfaction (OR 4.49, 95% CI 3.44–5.80, $P < 0.001$). Emotionally less intelligent women were also at a higher risk of reporting desire, arousal, and satisfaction problems, even though the effect sizes were small, yet still significant (ORs ranging from 0.80 to 0.95). We further found a small but significant association between anxiety sensitivity and sexual pain, with more anxious women being slightly more likely to report sexual pain (OR 1.04, 95% CI 1.01–1.04, $P < 0.001$). Previously reported confounders of FSD, including BMI, history of emotional, sexual, and physical abuse, number of pregnancies and children, and smoking, did not emerge as significantly contributory to the development of recent sexual problems.

As to be expected, the effects of age on the more enduring phenotype of lifelong sexual problems were minimal, emerging in a weak but significant association with arousal disorder only (OR 1.02, 95% CI 1.01–1.04, $P < 0.01$). Fewer years of education were significantly associated with the variability in lifelong arousal and lubrication (OR 0.92, 95% CI 0.87–0.95, $P < 0.05$ and OR 0.87, 95% CI 0.82–0.93, $P < 0.001$, respectively). In contrast to recent FSD, significant associations between experience of sexual, physical, and emotional abuse and the various subdomains were found. While experienced emotional abuse doubled the risk of women reporting sexual dissatisfaction (OR 2.1, 95% CI 1.50–3.22, $P < 0.05$) and physical abuse increased the risk of reporting sexual pain (OR 1.9, 95% CI 1.2–1.3, $P < 0.05$), women reporting sexual abuse showed a higher risk of reporting arousal (OR 1.6, 95% CI 1.1–2.3, $P < 0.05$), lubrication (OR 1.4, 95% CI 0.9–1.9, $P < 0.05$), and orgasm (OR 1.7, 95% CI 0.9–2.1, $P < 0.05$) problems. We further found relationships between women's levels of anxiety sensitivity and obsessive-compulsive behavior and lubrication, orgasm, satisfaction, and pain

**Table 4** Results from multivariate logistic regression analysis of potential risk factors for recent and lifelong FSD

| | OR (95% CI) | *P* | $r^2$ |
|---|---|---|---|
| Recent FSD | | | |
| Desire | | | 0.15 |
| Emotional intelligence | 0.80 (0.78–0.83) | <0.001 | |
| Relationship dissatisfaction | 1.56 (1.43–1.71) | | |
| Arousal | | | 0.08 |
| Age | 1.05 (1.03–1.07) | <0.001 | |
| Emotional intelligence | 0.95 (0.94–0.97) | 0.02 | |
| Lubrication | | | 0.12 |
| Age | 2.88 (2.64–2.98) | 0.05 | |
| Relationship dissatisfaction | 1.51 (1.37–1.80) | <0.001 | |
| Orgasm | | | 0.09 |
| Age | 1.03 (1.01–1.05) | 0.04 | |
| Relationship dissatisfaction | 1.53 (1.32–1.85) | <0.001 | |
| Satisfaction | | | 0.74 |
| Emotional intelligence | 0.82 (0.79–0.85) | 0.04 | |
| Relationship dissatisfaction | 4.49 (3.44–5.80) | <0.001 | |
| Pain | | | 0.04 |
| Relationship dissatisfaction | 1.20 (1.08–1.43) | 0.02 | |
| Anxiety | 1.04 (1.01–1.04) | <0.001 | |
| Lifelong FSD | | | |
| Desire | | | 0.04 |
| Openness | 0.81 (0.71–0.85) | 0.01 | |
| Relationship dissatisfaction | 1.86 (1.80–1.91) | <0.001 | |
| Arousal | | | |
| Age | 1.02 (1.01–1.04) | 0.01 | 0.07 |
| Education | 0.92 (0.87–0.95) | 0.02 | |
| Sexual abuse | 1.61 (1.13–2.26) | 0.04 | |
| Emotional intelligence | 0.93 (0.91–0.59) | <0.001 | |
| Relationship dissatisfaction | 1.21 (1.14–1.28) | <0.001 | |
| Lubrication | | | 0.09 |
| Education | 0.87 (0.82–0.93) | 0.01 | |
| Sexual abuse | 1.40 (0.89–1.94) | 0.05 | |
| Emotional intelligence | 0.92 (0.88–0.95) | 0.01 | |
| Relationship dissatisfaction | 1.21 (1.13–1.29) | <0.001 | |
| Anxiety | 1.21 (1.11–1.33) | 0.04 | |
| Orgasm | | | 0.04 |
| Sexual abuse | 1.68 (0.96–2.10) | 0.03 | |
| Openness | 1.14 (1.04–1.29) | 0.05 | |
| Relationship dissatisfaction | 1.15 (1.12–1.26) | <0.001 | |
| Anxiety | 1.30 (1.19–1.43) | 0.04 | |
| Satisfaction | | | 0.08 |
| Emotional abuse | 2.06 (1.50–3.22) | 0.01 | |
| Relationship dissatisfaction | 1.28 (1.21–1.37) | <0.001 | |
| Obsessive compulsive | 1.22 (1.11–1.29) | 0.04 | |
| Pain | | | 0.04 |
| Physical abuse | 1.89 (1.23–2.34) | 0.02 | |
| Emotional intelligence | 0.89 (0.87–0.94) | 0.03 | |
| Obsessive compulsive | 1.11 (1.03–1.19) | 0.04 | |

CI = confidence interval.
Significant variables in the univariate model (results not shown) were entered into the multivariate model.
Only significant results of the multivariate regression are displayed in this table.
$r^2$ = overall phenotypic variance explained by the factors included in the model. Familial relatedness of the twins was accounted for by using conditional regression.
All *P* values were Bonferroni corrected to account for multiple testing.

problems. Similar to recent FSD, relationship dissatisfaction was significantly associated with elevated risk of reporting sexual problems on all domains, except pain (ORs ranging from 1.2 to 1.9) (Table 4).

## Discussion

To our knowledge, this is the first study using personal distress in the definition of FSD to investigate prevalence and comorbidity of recent and lifelong sexual dysfunctions in a large unselected UK population and to explore a wide range of social and psychological risk factors. Only a few surveys have looked at female sexual problems in a UK population, all of which relied on self-constructed questionnaire or semistructured interviews [13–17]. Contrary to these local community studies, we chose the internationally applied and extensively validated FSFI to assess the frequency of sexual problems in women and considered the presence of sex-related distress as a primary diagnostic criterion in order for women to be classified as dysfunctional [4,5]. In addition, we assessed prevalence and potential predictors separately for recent and lifelong FSD. A woman's lifelong sexual function represents her level of average sexual functioning ever since she has been sexually active and may include periods of malfunction as well as periods of good function. Especially for studies (such as, for example, genetic studies) investigating the etiology and pathoetiology underlying FSD, the assessment of an individual's average levels of sexual function, hence the assessment of more enduring differences in, e.g., desire levels, could be a more efficient approach to identify potential causes of FSD.

Before a detailed discussion, several potential limitations to our study design need to be addressed more thoroughly. First, it would be wrong to infer a direct causal relationship between sexual problems and some of the variables found in this study to be cross-sectionally associated with FSD. Ideally, longitudinal studies should be conducted to address this problem. Because we studied a considerable set of potential risk factors simultaneously, errors in inference further are more likely to occur. To compensate for the number of inferences being made, we used a conservative Bonferroni correction, which requires a stronger level of evidence in order for a result to be accepted as statistically significant. This may be over conservative as many of our tests were co-correlated. However, the significant associations remained consistent throughout the different analyses, increasing the probability that they are true findings.

We cannot exclude the possibility that our data are affected by reporting biases given the sensitive nature of the questions leading to some underestimation of sexual distress and FSD symptoms [34]. However, while our response rates might appear low (50%), they are in fact respectable relative to other epidemiological-level sex surveys [32,35,36]. Dunne and colleagues reported that surveys of sexual behavior may overestimate sexual liberalism, activity, and dysfunction (in reporting) but that this bias does not seriously compromise population estimates as judged by the pattern of effect sizes [35]. Furthermore, a low response rate does not automatically mean that the results are systematically biased. Our post-hoc comparison of available sociodemographic information on responders and nonresponders revealed only few significant differences between the two responder groups and did not support a potential bias. Besides having slightly fewer years of education (10.2 years vs. 10.6 years), nonresponders were significantly less often in a relationship (27% vs. 31%) or married (43% vs. 49%) compared with responders, suggesting that women who were not in a relationship at the time when the survey was conducted felt less capable to answer the questions due to a lack of or due to lower levels of sexual activities.

The generalizability of our results may be limited, as a convenience sample of volunteers, instead of a complete random sample of the general population, was used. This is unlikely, as our twin cohort has already shown to be representative of the general population and to be similar to singletons for a wide range of common health and lifestyle factors [19]. Besides that, prevalence rates of FSD are comparable to estimates found in other populations and the sample has not initially been selected for sexual traits [36]. Also important to mention is that our study sample consisted mostly of perimenopausal or postmenopausal women (70%). For this reason, representativeness of our study might be limited to the older female population, especially when considering that sexual dysfunction is more common in perimenopausal and postmenopausal than in the nonclimacteric period [37]. However, we believe that with these caveats, these results are useful indicators of the likely prevalence and comorbidity of the condition and offer an important insight into the associated risk factors.

### Prevalence of FSD

The prevalence figures found in this study are comparable to those from other studies where distress was included in the diagnosis. Overall, only a quarter of women from the total sample (26.6%) reported sexually related personal distress, resulting in prevalence for sexual dysfunctions ranging from 5.8% to 21.4%, which is similar to the 7–23% described by Witting et al. for a Finnish adult population sample (N = 5,463) using the same diagnostic criteria [38]. In line with previous findings, hyposexual desire was the most prevalent recent and lifelong sexual complaint in our study (21.4% and 17.3%, respectively), closely followed by arousal (11.4% and 13.3%, respectively) and orgasm problems (8.8% and 13.5%, respectively) [39]. Our estimates, however, are significantly lower compared to other population-based studies on FSD, not taking into account sexual distress. Cayan et al., for example, found an overall 46.9% prevalence of FSD in Turkish women using solely the FSFI scores to classify women into healthy vs. dysfunctional [40]. Similarly, in the Natsal 2000 study—a probability sample of 11,161 British men and women aged 16–44 years—Mercer and colleagues found prevalence estimates ranging from 9.2% (problems with lubrication) to 40.6% (lack of interest in sex) [13]. Another population study set in four general practices in England (N = 979 with a mean age of 49) also found substantially higher prevalences for sexual problems compared with our estimates, ranging from 17% for arousal problems to 28% for vaginal dryness [17].

This underlines that it is clinically important to include sexual distress in the diagnosis of FSD, as prevalence estimates might be crucially inflated when not doing so. The inclusion of sexual distress as a primary diagnostic criterion for FSD is still subject to debate and is currently being reevaluated by the Diagnostic and Statistical Manual of Mental Disorders (DSM) V Working Group. The discrepancy in prevalence figures when not accounting for sexually related personal distress illustrates the need for more stringent definitions of FSD in order to delineate the dysfunction from a normal variant of functioning. Prevalence of up to 50% for FSD, as found by previous population studies, calls into question whether this can indeed be regarded a real pathology.

### Pattern of Comorbidity

All FSFI domain intercorrelations reached statistical significance, inferring that the diverse components of sexual functioning are strongly associated. The pattern of comorbidity was almost identical for recent and lifelong FSD. In the present study, the strongest correlation was observed between orgasm and arousal for recent and lifelong sexual functioning ($r = 0.7$ and $r = 0.6$, respectively). Pain was the dysfunction displaying the lowest comorbidity with other dysfunctions correlating, for example, with desire only by $r = 0.2$. It has been previously suggested that pain should not be classified as a sexual dysfunction and our present results endorse the assumption that pain might indeed be phenomenologically different from other dysfunctions [33,41].

The high rates of comorbidity, and the fact that out of the women reporting one sexual problem, more than half also reported difficulties in at least one other domain, emphasize the degree of overlap among female sexual difficulties. Moreover, some underlying common etiological factor (endophenotype) might exist, especially for the highly intercorrelated domains of desire, arousal, lubrication, and orgasm. On the other hand, the correlations were not very strong, which supports earlier literature and the current classification proposing that the phenotypes are not identical and may still be discrete entities [3,4].

### Risk Factors for FSD

Several strong associations between sexual problems and various psychological and contextual determinants (e.g., emotional intelligence [EI], anxiety, and relationship satisfaction) have been reported here. One of the most surprising findings was the different associations observed for recent and lifelong FSD, with a previous experience of abuse, relationship satisfaction, and anxiety being the most consistent associations with lifelong FSD, and age and relationship satisfaction with recent FSD.

#### Relationship Satisfaction

In our study, relationship dissatisfaction came out as the main predictor for recent and lifelong FSD, for example, increasing the odds for reporting orgasmic disorder by 1.5-fold. Our findings are in line with recent research on FSD, emphasizing the impact of interpersonal factors, such as relationship imbalances, the partner's sexual performance, poor communication, etc., on the development and the maintenance of sexual problems [10,38].

#### Emotional Intelligence

Low emotional intelligence was the second factor significantly associated with the report of recent and lifelong sexual dysfunctions in almost every domain. Research on emotional intelligence sug-

gests that people differ in how they experience emotions, how able they are to differentiate between them, and how much emotional information they can utilize and process—intrapersonally and also interpersonally [42]. Only one study has so far investigated the extent to which sexual problems are associated with normal variations in emotional intelligence [12]. The study based on a subset of the same cohort (N = 2,035) found a significant association between female orgasmic infrequency and normal variations in emotional intelligence, with less emotionally intelligent women reporting a 2.5-fold increased risk of reporting infrequent orgasm. Emotional intelligence seems to have a direct impact on women's sexual functioning and on her ability to communicate her expectations and desires to her partner and might lead to emotional stress and sexual anxiety.

### History of Abuse and Anxiety as Predictors of Lifelong FSD

Overall, the associations observed between FSD and abuse in this study are in line with a wealth of data reporting comparable findings [43,44]. In our study, however, history of sexual, emotional, and/or physical abuse turned out to be an important contributor to most types of lifelong but not recent FSD. Our results further suggest that the specific form of abuse is irrelevant, pointing toward a common effect of sexual, physical, as well as emotional abuse on women's self-esteem and emotional regulation, which might eventually contribute to disrupted interpersonal and intimate bonding behavior.

Women with higher anxiety levels reported significantly more lifelong lubrication and orgasmic problems. This observation is in accordance with the findings from a large community epidemiological survey, where women with moderate to high scores of self-reported anxiety were at a significantly higher risk for a variety of sexual problems [45]. However, the exact role of anxiety in the pathogenesis of FSD is not firmly established. Feelings of anxiety are also a big part of OCD, which was found to be associated with sexual dissatisfaction and pain in our study. Only a handful of studies have reported on sexual function in obsessive patient populations, all of which suggest similar findings to ours [46,47].

In conclusion, this study provides the first UK population-based assessment of FSD using validated outcome measures and DSM-IV-derived diagnosis. Our results indicate that sexual dysfunctions are associated with both self-reported interpersonal and psychosocial factors. We further conclude that different etiologies underlie recent and lifelong FSD. While interpersonal factors such as relationship satisfaction seemed to be equally important in the pathogenesis of recent FSD compared with lifelong FSD, contextual (abusive experience) and psychological factors (emotional intelligence and anxiety) clustered with lifelong FSD only.

Our data implicate that the most important targets for intervention and prevention in the field of sexual health are experiences such as relationship quality and satisfaction, the partner's sexual performance, history of emotional or sexual abuse, etc. Furthermore, the partition of FSD into subcategories for research purposes, where, for example, duration and situation are taken into account, has been neglected. In the future, this might eventually yield greater insights into the determinants of FSD and help the development of better diagnostic and therapeutic strategies.

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#### Statement of Authorship

*Category 1*

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# Female Partner's Perception of Premature Ejaculation and Its Impact on Relationship Breakups, Relationship Quality, and Sexual Satisfaction

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**ABSTRACT**

***Introduction.*** Women's perceptions of the men's ejaculatory behavior, as well as the impact premature ejaculation (PE) has on the couple's functioning, are important factors that need to be considered.

***Aim.*** This survey investigated women's perception and importance of ejaculatory function, as well as the specific aspects of PE that cause distress. In addition, the survey further identified the factors with a greater impact on intimacy, relationship, and sexual behavior.

***Methods.*** The 1,463 females belonging to a web panel from three different countries (Mexico, Italy, and South Korea), aged 20–50 years, participated in the survey. A combination of validated and self-constructed questionnaires to assess women's perception of PE, relationship satisfaction and quality, and sexual functioning and satisfaction were used.

***Main Outcome Measures.*** Descriptive statistics in form of proportions and percentages, correlation, and regression analyses.

***Results.*** A significant correlation between the importance of ejaculatory control and felt distress could be observed (rho = 0.55, $P < 0.001$). Women reporting less sexual problems considered ejaculatory control more important and reported more PE-related distress (rho = 0.23 and 0.11, respectively; $P < 0.001$ for both). The male's lack of attention and focus on performance was the most frequently reported reasons for sexual distress (47.6%) followed by "the short time between penetration and ejaculation" (39.9%), and "the lack of ejaculatory control" (24.1%). Almost a quarter of women reported that the man's ejaculatory problem had previously led to relationship breakups (22.8%). Women considering duration to be important were more likely to report breakups.

***Conclusions.*** The study highlights the detrimental effects of PE on relationship and sexual satisfaction in the female partner and how it can lead to the termination of the relationship. Most notably, this is the first study to report that an important source of female distress are not only parameters related to performance such as control or duration but rather inappropriate attention focus and the negligence of other forms of sexual activities. **Burri A, Giuliano F, McMahon C, and Porst H. Female partner's perception of premature ejaculation and its impact on relationship breakups, relationship quality, and sexual satisfaction. J Sex Med **;**:**–**.**

***Key Words.*** Premature Ejaculation; Women's Perception; Relationship Quality; Separation; Sexual Satisfaction; Intimacy; Relationship and Sexual Behavior

## Introduction

Several definitions of premature ejaculation (PE) exist, and how to accurately capture the phenomenon still remains a major debate. The most commonly quoted definitions are the Diagnostic Statistical Manual of Mental Disorder (DSM IV-R and DSM V) and similar authority-based definitions that heavily rely on experts' opinion without any evidence-based support from, e.g., clinical trials. Such definitions also tend to be conceptual and vague in terms of operational specificity and have no or little support from controlled clinical trials and epidemiologic studies [1]. To address the issue of ambiguous and nonuniform definitions, in 2008, the International Society for Sexual Medicine appointed a panel of PE experts to formulate the very first evidence-based definition of PE [2]. After critically evaluating the published data, the Committee agreed on three key points that characterize this condition including timing, the feeling of loss of control over ejaculation, and couple distress. The latter aspect and partner perception of the problem is supported by clinical evidence showing that relationship factors often influence sexual function [3–5]. In this respect, PE has to be considered largely a partner-oriented male sexual symptom.

Most studies exploring attitudes and behaviors about PE have generally focused on the impact of PE on the man [6]. The majority of these studies report strong associations between PE and adverse psychosocial and quality of life consequences, including detrimental effects on the partner relationship. More specifically, a significantly greater proportion of men—and partners of men with PE—report interpersonal difficulties and relationship dissatisfaction compared with non-PE groups [3–5]. Only recently attempts have been made to assess the impact of PE on the women's sexual and relationship satisfaction, and hence their quality of life [7–11]. These reports about the impact of PE on female partners are affected by some discrepancies and present themselves ambiguous. Though, most studies report significantly higher levels of sexual distress and more sexual dissatisfactions in female partners of PE men, other research findings point toward a negative effect of PE on sexual satisfaction but not on overall relationship and personal functioning [7–11]. Furthermore, only moderate correlations between the ratings for interpersonal difficulty given by the men and their female partners ($r = 0.41$) have been reported [3]. Likewise, men's and women's reports on the man's ejaculatory behavior (including the aspects of ejaculatory latency, ejaculatory control, concern over ejaculating to soon, and satisfaction with the ability to select the moment of ejaculation) show only moderate to nonsignificant correlations, highlighting the subjective dimension of the disorder [10].

Although current literature provides strong evidence for an association between PE and sexual dissatisfaction and—to a lower degree between PE and interpersonal difficulties—in both partners, a number of aspects remain clouded. First, the actual reason for distress remains unknown. Is it the lack of ejaculatory control or the brief ejaculatory latency time per se that causes distress or is it the indirect, consequential factors, such as the PE-man himself being distressed and therefore not focusing enough on the woman's sexual needs. Furthermore, to the best of our knowledge, no study has investigated how much a woman's perception of PE and its consequences are mediated by her own sexual functioning, such as her orgasm ability, the overall importance of sex and the relative importance sex has for her relationship satisfaction. These are important questions that need to be clarified in order to get a more holistic understanding of the condition and to develop more effective and extensive managing strategies that not only target the PE-individual but also the interpersonal and intrapsychic issues that might precipitate the dysfunction and lead to relationship problems.

## Aims

To fill these gaps, a survey was conducted, aiming at investigating the following questions: (i) What is the woman's perception of PE?; (ii) how important is ejaculatory performance for the woman?; (iii) which aspects of PE are most distressing to the woman?; (iv) how much does PE impact on intimacy, relationship quality, and satisfaction?; (v) what impact does PE have on the woman's sexual satisfaction and functioning?; and (vi) how much does a woman's own sexual functioning influence her perception of PE?

## Material and Methods

### *Sample and Procedure*

Recruitment was conducted by GfK market research company between April and June 2013. The screening and principal questionnaires were

sent to women aged between 20 and 50 years and belonging to an online consumer panel that is generally used by the GfK group. This platform enables the project manager to run a live count of available members of the panel matching the desired target profile. A random sample was then pulled out of the overall panel. For this survey, women from three different countries—Mexico, South Korea, and Italy—were included to capture maximum cultural differences. Women further had to meet the following inclusion criteria: being sexually active, having engaged in sexual intercourse with a man, considering themselves as hetero- or bisexual, having had sexual experiences predominantly with men or with both men and women equally, and being with a PE man. PE status of the man was assessed via subjective self-report of the female partner (see Material and Methods). No objective data (e.g., intravaginal ejaculation latency time [IELT] measurement) were available for the diagnosis of PE. In the end, a total of n = 1,643 women filled in the entire questionnaire. After checking for inclusion criteria, the final sample consisted of n = 1,463 women with a homogenous distribution across the three nations/cultures (n = 502 for Italy, n = 508 for South Korea, n = 453 for Mexico). A summary of sociodemographic characteristics of the sample can be found in Table 2. Informed consent was provided by each individual when registering to the panel. No ethical approval was needed to conduct this online study.

### *Material*

For this survey, a mix of study-specific questions and questions taken from validated and standardized instruments were used.

#### Sociodemographic Information

Sociodemographic information and information regarding inclusion criteria were assessed using self-constructed questions. To assess the PE status of the male partner (the main criteria to be included in the survey), women were asked the following questions. "Are you currently with a man who ejaculates earlier than you would like him to?"; "Are you currently with a man (i.e., relationship) who has been given the clinical diagnosis of Premature Ejaculation (ejaculation that occurs too early)?"; "Are you currently with a man whose IELT (i.e., time from penetration until ejaculation) is on average less than 2 minutes most of the times?"; and "Has your current partner ever reported the wish to have more control over his ejaculation?" To be included in the study, one of the four questions had to be positively answered.

#### PE and Women's Perception of PE

Study-specific questions relating to women's perception of PE are listed in Table 2. Response options for quantitative questions were on Likert-type scales ranging from 1 (not at all) to 5 (extremely).

#### Women's Sexual Functioning and Distress

Women's sexual functioning and problems were explored using the Female Sexual Function Index (FSFI) short version and a set of self-constructed questions (asking e.g., "do you suffer from low desire") [12]. The FSFI is a widely used 19-item self-report questionnaire that captures six dimensions of sexual functioning including desire, arousal, orgasm, lubrication, satisfaction, and sexual pain. Recently, a six-item version as a rapid screening tool for female sexual dysfunction (FSD) has been developed [13]. Response options are on a Likert-type scale with low scores indicating more problems with sexual function ever since with the PE partner (in this study termed FSFI-PE). To assess women's overall sexual function ever since they have been sexually active, a short version of the Female Sexual Function Index—Lifelong (FSFI-LL) was used (in this study termed FSFI-Ever). The original FSFI as well as the FSFI-LL have received extensive psychometric evaluation in clinical and nonclinical samples, and the amended short version has also proven good psychometric properties [12–14].

Women's orgasmic ability was defined primarily using three questions on frequency of orgasm across three different settings, including "during vaginal penetration," "with your current PE partner," and "with any kind of stimulation." Responses were on a seven-point scale labeled as follows: always, in more than 75% of times, between 75% and 50% of times, between 25% and 50% of times, less than 25% of times, never.

Women's sexual distress was assessed with an amended version of the Female Sexual Distress Scale specifically developed for the purpose of assessing distress in women with PE partners [9,15]. Response options are on a five-point scale, ranging from 0 = never to 4 = always, with a higher score indicating increased sexual distress.

Other self-constructed questions assessing women's sexual attitudes and functioning included

in the questionnaire can be found in Table 2. For these questions, response options for quantitative questions were on Likert-type scales ranging from 1 to 5.

### Relationship Satisfaction and Quality

Relationship satisfaction was assessed with self-constructed questions and the Relationship Assessment Scale (RAS) [16]. The RAS is a seven-item generic measure, useful as a brief measure for partnered love relationships. Respondents answer each item using a five-point scale ranging from 1 (low satisfaction) to 5 (high satisfaction). Other self-constructed questions to assess relationship satisfaction can be found in Table 2.

### *Statistical Analyses*

For sample characteristics and descriptive statistics, dichotomous and categorical data were expressed as percentages and continuous data as means. To investigate the relationship between the variables, a set of correlation and regression analyses were used including point-biserial correlation coefficient ($r_{pb}$) and logistic regression to examine relationships between binary and continuous variables, Spearman correlation (rho) multinomial logistic regression between categorical and continuous variables, Pearson correlation ($r$), and linear regression for continuous variables.

To be included in the survey, women had to answer "yes" to any of the four questions specified in the Material and Methods section and were subsequently assigned to the following four groups: (i) women whose partners ejaculate earlier than she wants him to (PEW group); (ii) women whose partners had been given the clinical diagnosis of PE (CD group); (iii) women whose partner had an estimated IELT of <2 minutes (IELT group); and (iv) women whose partners repetitively express the wish to have more control over his ejaculation (PEM group). If not explicitly stated otherwise, analyses were conducted on the whole sample. For some of the more specific analyses and group comparisons, the four groups were considered separately.

Because normality and multivariate normality of the data could not be assumed, univariate Kruskal–Wallis analyses (nonparametric test, equivalent to analysis of variance) were calculated for group comparisons of continuous data. Where indicated, multiple sample contrasts were performed post hoc to these analyses. To control for the influence of potential covariates (such as age) on the outcome variables, Kruskal–Wallis tests were performed on covariate-adjusted residuals. Covariate-adjusted residuals were obtained from the overall regression line fit to the entire data set. Comparison of dichotomous and categorical data was conducted using $\chi^2$ test.

All tests were two-tailed. For all analyses, a $P$ value less than 0.05% was considered statistically significant, unless stated otherwise. All analyses were corrected for multiple testing with Bonferroni. For all analyses, Likert-type scaled variables were treated as continuous. Data handling and all statistical analyses were carried out using STATA software (StataCorp, College Station, TX, USA).

## Results

### *Sample Description*

The mean age of women participating in the survey was 34.3, and the average relationship duration was 85.9 months (SD 81.1, range 0–360; Table 1). The three countries included in this survey differed significantly from each other in most sociodemographic and otherwise assessed variables. However, despite the differences reaching statistical significance, the trends were comparable and no extreme deviation from the overall distributional/proportional pattern could be detected for the sociodemographic characteristics. For a detailed comparison of the three different countries that is beyond the scope of the present article, see Burri & Graziottin, in preparation.

The majority of women (63.1%) belonged to the PEM group, followed by the PEW group (53.7%). Only 9.1% of women reported being with a partner with a clinical diagnosis of PE (CD group), and around a quarter of women (24.5%) subjectively felt that the IELT was <2 minutes.

### *Women's Perception and Importance of PE*

As reported in Table 2, around 40% of women considered ejaculatory control to be extremely or very important ("How important is your partner's ejaculatory control to you?"). A significant correlation between the importance of ejaculatory control and felt distress could be observed (rho = 0.55, $P < 0.001$), with almost a fifth of women feeling distressed by his lack of control (Table 2). Significant differences in how important women considered ejaculatory control and reported distress could be observed across the four PE definition groups (Table 3). Ejaculatory

**Table 1** Sociodemographic characteristics of the overall sample (n = 1,463)

| | Mean | SD | Range |
|---|---|---|---|
| Sociodemographic variables | | | |
| Age (in years) | 34.26 | 7.86 | 20–50 |
| Relationship duration (in months) | 85.88 | 81.09 | 0–360 |
| Age current partner (in years) | 37.52 | 8.82 | 15–65 |
| | n | | % |
| Education | | | |
| Primary | 878 | | 60.01 |
| Secondary | 532 | | 36.36 |
| Higher education | 53 | | 3.62 |
| Occupation | | | |
| Manager | 60 | | 4.10 |
| Business owner | 163 | | 11.14 |
| Tradesman | 75 | | 5.13 |
| White collar | 559 | | 38.21 |
| Blue collar | 85 | | 5.81 |
| Housewife | 272 | | 18.59 |
| Student | 126 | | 8.61 |
| Pensioner | 2 | | 0.14 |
| Unemployed | 121 | | 8.27 |
| Marital status | | | |
| In relationship, living together | 1,204 | | 82.29 |
| In a relationship, living separately | 259 | | 17.71 |
| Ejaculatory function | n | | % |
| Woman's subjective perception (PEW) | | | |
| Yes | 696 | | 53.70 |
| No | 600 | | 46.30 |
| PE clinical diagnosis (CD) | | | |
| Yes | 119 | | 9.1 |
| No | 941 | | 72.61 |
| Not that I am aware of | 236 | | 18.21 |
| IELT <2 minutes (IELT) | | | |
| Yes | 318 | | 24.54 |
| No | 884 | | 68.21 |
| Not that I am aware of | 94 | | 7.25 |
| Man's subjective perception (PEM) | | | |
| Yes | 818 | | 63.12 |
| No | 407 | | 31.40 |
| Not that I am aware of | 71 | | 5.48 |
| Number of male partners with PE | | | |
| 0 | 1,172 | | 80.11 |
| 1 | 174 | | 11.89 |
| 2 | 81 | | 5.54 |
| ≥3 | 36 | | 2.46 |

control was considered most important for women in the IELT group and least important for women in the PEW group who subjectively felt that the partner suffered from PE ($\chi^2 = 39.33$, $P < 0.001$). Corresponding to these findings, distress was greatest for women in the IELT group and smallest to women in the PEW group ($\chi^2 = 38.28$, $P < 0.001$; Table 3).

Asking about the reasons for the distress related to the lack of ejaculatory control, the majority of women indicated "lack of attention to her other sexual needs such as caressing, kissing, etc." (47.6%) followed by "the short time between penetration and ejaculation" (39.9%), and "the lack of ejaculatory control" (24.1%) (Figure 1). Only 20.3% indicated "the partner's distress." Following up on this finding, women were asked whether they felt distressed about the partner being focused on his ejaculatory control and ignoring her other sexual needs, rather than about the lack of ejaculatory control itself, with 24.9% responding "extremely" or "very much" (Table 2). Similarly, almost a quarter of women (22.62% = "extremely" and "very much") indicated that the PE partner was much more focused on his performance and on delaying ejaculation compared with other male lovers that they had been with who did not suffer from PE (Table 2).

### *Women's Sexual Functioning and Views on Sexuality*

A percentage of 77.9 of women reported at least one sexual problem, with low libido being the most prevalent problem (49.8%) closely followed by sexual dissatisfaction (41.3%). Out of women with a self-reported sexual problem, 78.6% stated that they experienced these problems while being in a relationship with the PE-man, with 64.2% of these women reporting that the problems started when entering the relationship with the PE-man and only 35.8% saying that they were present prior to the relationship (data not shown). The prevalences of self-reported sexual problems were compared with the FSFI scores (FSFI-Ever and FSFI-PE). Correlations between self-reported sexual problems and FSFI-PE scores were significant for all domains (ranging from $r = -0.09$–$0.28$, $P < 0.05$ for all), except for desire ($r = 0.03$, $P > 0.01$; data not shown). FSFI-PE and FSFI-Ever scores also correlated significantly on all domains, indicating that women's levels of sexual functioning while being with a PE-man corresponded only mildly with their overall levels of sexual functioning.

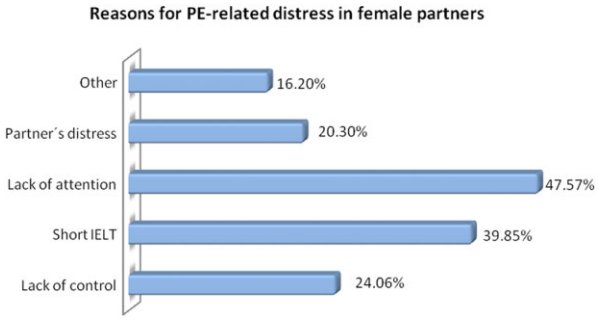


**Figure 1** Specific reasons for PE-related distress in female partners

**Table 2** Questions and response patterns as assessed in the present survey (n = 1,463 but sample sizes vary depending on the variables/questions due to missing)

| Question | % | n | | | |
|---|---|---|---|---|---|
| Does your current partner's lack of control over his ejaculation cause distress in him or you? | | | | | |
| In both of us | 36.91 | 375 | | | |
| In me only | 19.88 | 202 | | | |
| In him only | 20.28 | 206 | | | |
| In none of us | 22.93 | 233 | | | |
| | Mean | SD | Range | | |
| What would be your ideal intercourse duration (in minutes)? | 23.17* | 19.01 | 1 to 200 | | |
| | Extremely % (n) | Very % (n) | Moderately % (n) | Slightly % (n) | Not at all % (n) |
| How important is ejaculatory control to you? | 13.12 (192) | 24.81 (363) | 37.73 (552) | 20.51 (300) | 3.83 (56) |
| How distressed are you because of his lack of ejaculatory control? | 6.90 (101) | 13.67 (200) | 28.91 (423) | 35.2 (515) | 15.31 (224) |
| Do you feel distressed about him being focused on his ejaculatory control and ignoring your other sexual needs, rather than about the lack of ejaculatory control itself? | 6.49 (86) | 18.39 (228) | 32.66 (405) | 35.24 (437) | 6.77 (84) |
| Is your partner so focused on delaying his ejaculation that he ignores your "other" sexual needs (e.g., caressing, kissing, etc.)? | 6.15 (90) | 14.42 (211) | 28.71 (420) | 35.06 (513) | 15.65 (229) |
| In your view, is he more focused on performance (delaying ejaculation) compared with other male lovers you were with who did not have that condition? | 6.49 (95) | 16.13 (236) | 29.60 (433) | 32.54 (476) | 15.24 (223) |
| Have you been significantly more satisfied in your previous relationships (i.e., with a man having "normal" ejaculatory pattern) compared to your relationship with a man with PE or probable PE? | 14.56 (213) | 22.56 (374) | 30.01 (439) | 22.21 (325) | 7.66 (112) |
| Do you consider the PE condition to be a major problem for your relationship? | 6.08 (89) | 14.22 (208) | 23.79 (348) | 34.24 (501) | 21.67 (317) |
| Did your relationship satisfaction change during the course of the relationship compared with the initial level? | 9.09 (133) | 20.57 (301) | 33.9 (496) | 29.87 (437) | 6.56 (96) |
| How much is it due to your sexual frustration due to his ejaculatory pattern? | 4.85 (71) | 13.88 (203) | 26.04 (381) | 33.42 (489) | 21,8 (319) |
| How much is/was it due to frustration relating to your partner being taken up by his condition (i.e., showing behavioral changes such as inattention, aggression, frustration, being less caring, etc.) rather than the actual ejaculatory pattern itself? | 6.29 (92) | 16.54 (242) | 28.78 (421) | 29.8 (436) | 18.59 (272) |
| Does his ejaculatory pattern affect your levels of intimacy? | 9.77 (143) | 17.22 (252) | 28.91 (423) | 27.89 (408) | 16.2 (237) |

*without inclusion of outliers still a mean of 22.9 minutes

Asking women about "what constitutes good sex for you," the majority (69.2%) indicated versatility (defined as being creative in bed and not just focused on penetration) to be most important. Almost half of women said that duration of sexual activity was important too (45.9%) and only 18.8% indicated "other" (not specified). When asked about the ideal penetrative intercourse duration (without foreplay), a mean of 23.2 minutes was reported (SD 19.01, range 1 to 200; Table 2), with younger women preferring a slightly longer duration ($r = -0.09$, $P < 0.01$; Table 4). Significant positive correlations were also observed between ideal intercourse duration and importance of ejaculatory control and felt distress (rho = 0.16, $P < 0.001$ and rho = 0.11, $P < 0.01$). Asking women about the reasons for the indicated duration, 60.9% said that the duration was ideal because it allowed them to reach orgasm and 60.4% because it created intimacy. Only 3.1% mentioned "other reasons" (not specified). Around a quarter of women (23.8%) considered both intimacy and orgasm to be important. The four groups of women differed significantly in what they considered ideal intercourse duration, with the highest mean being reported by the CD and the lowest by the IELT (31 minutes vs. 17.9 minutes; $\chi^2 = 13.98$, $P < 0.001$; Table 3).

**Table 3** Response patterns across the four PE definition groups. Kruskal–Wallis test were conducted for continuous variables and $\chi^2$ tests for binary and categorical variables (note that items 1, 2, and 3 are inversely scored, ranging from "extremely" 1 to "not at all" 5)

| | PEW (n = 696) Mean | SD | CD (n = 119) Mean | SD | IELT (n = 318) Mean | SD | PEM (n = 818) Mean | SD | $\chi^2$ | Contrasts |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 How important is his ejaculatory control to you? | 3.23 | 0.94 | 2.8 | 0.83 | 2.61 | 0.95 | 2.72 | 1.03 | 39.33*** | 1 > 2 and 3 |
| 2 How distressed are you because of his lack of ejaculatory control? | 3.75 | 0.91 | 3 | 1.22 | 2.8 | 1.21 | 3.24 | 1.01 | 38.28*** | 1 > 2 and 3, 3 < 4 |
| 3 Ideal intercourse duration | 22.55 | 14.3 | 31.0 | 12.9 | 17.94 | 16.3 | 22.7 | 18.8 | 13.98** | 1 < 2, 2 > 3 and 4, 3 < 1, 2 and 4 |
| 4 Relationship satisfaction (RAS total score) | 19.52 | 1.78 | 18.80 | 1.09 | 19.03 | 2.52 | 19.22 | 2.01 | 2.76 | — |
| 5 Number of relationship breakups due to PE | % 11.76 | | % 26.67 | | % 22.49 | | % 34.57 | | Chi² 38.71*** | Contrasts 1 < 4, 2 < 4, 3 < 4 |

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

Regression analyses revealed that women who consider versatility more important are significantly more likely to report sexual problems (Table 5). This association, however, could only be found for overall sexual functioning (ever since she has been sexually active) and not while with a PE man. Women who feel that their PE partner is so focused on his performance that he ignores her other sexual needs were also more likely to report sexual problems compared with women who did not feel this inappropriate focus (Coef = –0.23, 95% CI: –0.38–0.09, $P < 0.01$).

In terms of orgasm ability, 2.9% of women reported never being able to experience orgasm under no circumstances, 7.3% were unable to orgasm during intercourse, and 4.4% while engaging in sexual activities with their current partner (Figure 2). A weak correlation with age for vaginal orgasm and overall ability to orgasm could be observed, with younger women reporting lower frequency of orgasms (rho = 0.05, $P < 0.05$ for both). Additionally, significant correlations between orgasm ability (in any of the three circumstances) and ideal intercourse duration (rho = 0.11 to rho = 0.13; $P < 0.001$ for all), and importance of ejaculatory control and distress could be detected (see Table 4). Women having more difficulties in achieving vaginal orgasm considered versatility to be more important compared with the rest of women ($\chi^2 = 19.95$, $P < 0.05$; results not shown). In accordance with these findings, we also observed a positive correlation between women's overall sexual functioning and importance of ejaculatory control and related distress (rho = 0.23 and 0.11, respectively; $P < 0.001$ for both).




**Figure 2** Percentage of women reporting that the partner's PE condition has previously led to relationship breakups.

**Table 4** Correlations between the variables

| | Age | Duration | Importance | Distress | Vaginal orgasm | Ever orgasm | Partner orgasm | FSFI-Ever | FSFI-PE | Breakups |
|---|---|---|---|---|---|---|---|---|---|---|
| Age | — | –0.09** | 0.00 | –0.07 | 0.05* | 0.05* | –0.02 | 0.09* | 0.06* | 0.02 |
| Duration | –0.09** | — | 0.16*** | 0.11** | 0.13*** | 0.13*** | 0.10*** | 0.15*** | 0.06* | 0.09** |
| Importance PE | 0.00 | 0.16*** | — | 0.55 | 0.08** | 0.09*** | 0.04 | 0.23*** | 0.01 | 0.22*** |
| Distress | –0.07 | 0.11** | 0.55 | — | 0.10*** | 0.13*** | 0.20*** | 0.11*** | 0.02 | 0.31*** |
| Vaginal orgasm | 0.05* | 0.13*** | 0.08** | 0.10*** | — | 0.69*** | 0.69*** | 0.27*** | 0.24*** | 0.04 |
| Ever orgasm | 0.05* | 0.13*** | 0.09*** | 0.13*** | 0.69*** | — | 0.79*** | 0.36*** | 0.25*** | 0.01 |
| Partner orgasm | –0.02 | 0.10*** | 0.04 | 0.20*** | 0.69*** | 0.79*** | — | 0.32*** | 0.24*** | –0.04 |
| FSFI-Ever | 0.09* | 0.15*** | 0.23*** | 0.11*** | 0.27*** | 0.36*** | 0.32*** | — | 0.56*** | 0.09* |
| FSFI-PE | 0.06* | 0.06* | 0.01 | 0.02 | 0.24*** | 0.25*** | 0.24*** | 0.56*** | — | 0.06* |
| Breakups | 0.02 | 0.09** | 0.22*** | 0.31*** | 0.04 | 0.01 | –0.04 | 0.09* | 0.06* | — |

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

### *Impact of PE on Relationship Breakups, Relationship Satisfaction, and Sexual Satisfaction*

Almost a quarter of women reported that the man's ejaculatory problem had previously led to relationship breakups (22.8%; Figure 2). In 4.4% of cases, women indicated that this happened more than once. The proportion of women reporting a breakup differed significantly across the four PE-definition groups (Table 3). Women whose partner ejaculated earlier than she subjectively wished (PEW group) showed the lowest breakup rates (11.7%) and women whose partners repeatedly expressed the wish to have more ejaculatory control the highest rates (34.6%; $\chi^2 = 38.71$, $P < 0.001$).

Women considering ejaculatory control to be important and feeling more distressed also reported more relationship breakups compared with women who did not feel distressed (rho = 0.22 and rho = 0.31, $P < 0.001$ for both; Table 4). Furthermore, women with sexual problems (self-reported and according to FSFI-PE and FSFI-Ever) were also more likely to report breakups ($r = 0.13$, $P < 0.001$, $r = 0.09$ and $r = 0.06$, $P < 0.05$ for both). No significant association between women's orgasm ability and relationship breakups could be detected. However, women who considered duration to be important (as opposed to versatility) also reported more relationship breakups (Table 5).

In terms of relationship satisfaction, 40.1% reported having been "extremely" more or "much" more satisfied in previous relationships with men without PE compared with the current relationship with a PE-man (Table 2). Around 20% of women considered PE to be a major problem for the relationship, whereas the same percentage considered it not a problem at all. Relationship satisfaction (as measured by the RAS) did not differ significantly across the four PE definition groups (Table 3). When asking women about whether their relationship satisfaction deteriorated over the course of the relationship with a PE-man compared with the initial levels, 29.7% responded extremely or very much, with 18.7% saying that this was mostly due to their own sexual frustration because of his ejaculatory pattern (rho = 0.36, $P < 0.001$). Similarly, a quarter of women (22.7% answering extremely or very much; Table 2) reported that their sexual frustration was mostly due to him being taken up by his condition and therefore having an inappropriate attention focus (rho = 0.38, $P < 0.001$). Finally, 26.9% reported that his lack of ejaculatory control also affected their levels of intimacy (Table 2).

## Discussion

This large cross-cultural survey reports a link between untreated PE and relationship separation. It is the first study indicating that the most common reason causing distress in women with partners with PE is the lack of attention he pays to her other sexual needs due to him being caught up by his condition, rather than the lack of control or the short IELT.

**Table 5** Predictors of sexual problems and relationship breakups

| | Coef | SD | 95% CI | *P* value |
|---|---|---|---|---|
| IV | DV: FSFI-Ever | | | |
| Versatility | 0.11 | 0.27 | –0.06–0.41 | 0.000 |
| Ignoring needs | –0.24 | 0.07 | –0.39–0.09 | 0.001 |
| | DV: Breakups | | | |
| Duration | –0.57 | 1.50 | –0.86–0.27 | 0.000 |
| Versatility | 0.12 | 0.21 | –0.29–0.53 | 0.56 |

IV = independent variable; DV = dependent variable

### Relationship Dissatisfaction and Separation

Studies have repeatedly shown the detrimental effects that sexual problems—or more specifically PE—can have on relationship satisfaction and how it can lead to interpersonal distress [4,5,17]. According to our data, men's lack of ejaculatory control has been reported to be an important reason for separation in almost every fourth previous relationship. A percentage of 5 of women even reported having separated from previous partners with PE more than once due to relationship difficulties resulting from his condition. Interestingly, women whose partner ejaculated earlier than they wished were least likely to report a previous breakup, whereas women whose partners repeatedly expressed the wish to have more ejaculatory control were most likely to report a previous separation due to PE. It seems that although some women feel the wish for a longer intercourse duration, it is not considered a necessity for a satisfying relationship and hence, a short duration is something that can be tolerated and does not unavoidably lead to relationship dissatisfaction. However, men who subjectively feel that they are lacking control might feel underachieving and unable to satisfy the woman. This in turn might bother him to the extent that it disrupts the healthy dynamics of a relationship, by becoming the main point of attention.

Although the impact of sexual problems such as PE does not need to be as detrimental and end in separation in every case, our additional findings of reduced relationship satisfaction reported by female partners of PE men illustrate the disruptive capacity of such problems in terms of dyadic satisfaction and interpersonal and personal well-being and functioning. These findings are in accordance with previous evidence reporting significant decrease in sexual satisfaction and overall quality of life, and increase in distress and interpersonal difficulties in female partners of men with PE [4,5,17]. A study by Limoncin, for example, found female partners of men with PE to experience significantly higher levels of sexual distress compared with controls—with no detectable differences across age groups and no influence of relationship duration [9]. Another study on 152 men and their female partners by Byers and Grenier (2003) found that low levels of sexual satisfaction, deriving from one or more characteristics of PE, are detectable both in men and female partners [10]. Similar to these reports, PE was also associated with sexual and relationship distress in the female in the present study, with a substantial proportion of women reporting having been more satisfied in previous relationships with non-PE men compared with being with a PE man. Although other reasons could have led to this dissatisfaction, women indicated that the main reasons were indeed sexual frustration and lack of intimacy due to him being taken up by his condition and therefore not being able to address her sexual needs and her longing for intimacy.

The extent to which PE impacts on relationship satisfaction, however, seems not only to depend on the man's behavior and coping with his condition, but also on factors relating to the female partner. According to our data, women suffering from any sexual problem themselves were slightly more likely to report a previous relationship separation due to PE. In line with these findings, women considering ejaculatory control and longer intercourse duration to be important (as opposed to versatility) also reported more relationship breakups. In other words, the impact PE has on relationship satisfaction in both partners cannot be assessed by merely focusing on the man's sexual functioning and his handling of the problem, but clearly the female partner's sexual functioning and views on sexuality have to be taken into account as well. Sexual problems clearly are a couple's problem and disruptions of dyadic processes and well-being not only affects both parties but can also be precipitated and aggravated by both of them.

### Importance of Ejaculatory Control and Reasons for Distress

Previous studies have shown that both men with PE and their partners consider the feeling of control over ejaculation to be a central issue in PE [4]. Consistently, the majority of women in our study considered the partner's ejaculatory control to be very important, with the levels of reported distress being positively associated with the relative importance assigned to his ejaculatory pattern. Interestingly, ejaculatory control was considered most important in women who subjectively felt that the time between penetration and ejaculation was below 2 minutes, whereas women stating that the partner ejaculated earlier than she wished considered it least important and also reported the lowest level of PE-related distress. It is possible that women reporting a "subjectively felt" IELT of less than 2 minutes are the ones who really are frustrated by his lack of control and even if the

IELT might be longer in reality, it feels shorter to them, explaining the high levels of distress encountered in this group. Likewise, it is possible that women stating the wish for more control, again, do not consider it a necessity but mainly a convenient "add-on." This is supported by the fact that this group also reports the lowest rates of relationship breakups due to PE.

More interesting than the finding of PE-related distress in female partners was the actual reason that according to the majority of women led to personal suffering. Almost half of women said that it was the lack of attention that the partner paid to her other sexual needs such as kissing and caressing, the lack of other forms of stimulation (including oral stimulation), as well as his exaggerated focus on performance and endurance. Because the attempts to form operational definitions of PE have mainly focused on "objective and physiologic" measures such as latency and voluntary control over ejaculation to capture the phenomena, it seems especially noteworthy that these condition-specific cardinal symptoms are not perceived as the weightiest issues by the female partner. The findings further suggest the possibility that cognitive behavioral approaches focusing on teaching men control, either alone or in combination with PE pharmacotherapy, might result in too much sufferer focus on controlling ejaculation to the detriment on the partner. An accurate focus on interpersonal and partner-related consequences therefore is necessary and highlights the necessity for psychosexual education and sexological approaches where PE sufferers equally learn about the partner's specific needs and wishes and how to appropriately address them.

Although normative data are lacking, the consensus according to the DSM V is to regard men with an IELT below 1 minute as suffering from PE [1]. However, other criteria for the definition of PE have been suggested, such as, e.g., the control and voluntary ability to defer ejaculation [17,18]. Attempts to find a significant correlation between both measures, however, were not always successful, leading to the conclusion that the dimensions of ejaculatory control and latency might be distinct concepts [19,20]. In a sample of n = 57 males, Grenier & Byers for example found that some men with a brief ejaculatory latency time reported adequate ejaculatory control and vice versa [20]. Contrary to this, other authors have reported a moderate correlation between IELT and the feeling of ejaculatory control [21,22]. Although clearly the two concepts are related, ejaculatory control is considered more important by clinicians, as it allows deliberate variation of intercourse duration, whereas a long latency does not necessarily mean that situation and specific individual variation and playfulness are granted. Contrary to this, however, women in the present study considered the short IELT to be more distressing compared with lack of control. Although these results might represent a true finding, it is also possible that they are subject misunderstanding and the inability to grasp the differences between the two concepts.

### *Women's Sexuality and Impact of PE on Their Sexual Satisfaction*

Overall, it seems that duration of lovemaking is not as important to women as it is for men and as it is for experts trying to formulate objective diagnostic criteria. Indeed, previous reports have shown that according to the partner, the major concern with PE is the abrupt break in intimacy and/or sexual pleasure caused by the man ejaculating too soon, rather than the short duration of lovemaking [23]. This is supported by the present study. Women preferring a longer duration also considered ejaculatory control to be more important and were likewise more distressed by the lack of it. This was mainly due to either not being able to experience an orgasm with such a short duration or because it did not allow the nascence of intimacy. It is well known that women's orgasm ability shows immense variation, with a great proportion of women being anorgasmic or not being able to experience orgasm through penetration alone [24,25]. This pattern also emerged in our findings and, as expected, women who preferred a longer intercourse duration and who were more distressed by the lack of control also reported a higher orgasm frequency and a better orgasm ability. For women showing low orgasm ability, versatility—defined as being creative in bed and not just focused on penetration—was considered more important as opposed to duration. It seems that there are "subgroups" of women and that the amount of PE-related distress depends not only on how important they consider ejaculatory control to be but also on their own sexual functioning and her individual importance of sexuality and what they consider good and fulfilling sexuality.

At this point, addressing the finding of an ideal intercourse duration of on average 23 minutes seems necessary. This finding does not correspond to previous reports and should therefore be inter-

preted with caution. In a study conducted on 152 couples by Miller & Byers, for example, ideal mean intercourse duration for women was 14.34 minutes and 18.45 minutes for men [26]. Importantly, however, lay public perceptions about how long intercourse should last are discrepant not only from objective data on ejaculatory latencies but also from expert opinions. A study conducted on members of the Society for Sex Therapy and Research in the United States and Canada found that therapists' beliefs about ejaculatory latencies were consistent with objective data on ejaculatory latency considering 3–13 minutes to be of no clinical concern. One possible reason of why the figure presents itself so high in our study might be the fact that women's ideal duration might be less representing her own sexual preferences but rather reflects perceptions of their partner's ideal duration and hence of his sexual stereotype.

Data from previous studies show significantly worse sexual functioning in female partners of men with PE compared with women with partners who do not suffer from PE [7,8]. Although the majority of these studies used a case–control design that allowed direct comparison of FSD prevalence in both groups, the cross-sectional nature of the studies still does not allow any final conclusion on whether the sexual problems encountered by women were the result of the men's PE or whether they were already present at the beginning of the relationship. Although the present study also relied on a cross-sectional design, we tried to overcome this problem by comparing women's levels of sexual functioning ever since they have been sexually active and while being with a PE partner. The high correlations found between the two measures indicated that although the levels largely corresponded, there was still room for variation (*r*'s around 0.5). In addition, two third of women with sexual problems stated that the problems started while being in the relationship with the PE man and were not encountered before. Most noteworthy, women who considered versatility to be important were also more likely to report sexual problems, as were women who felt that their PE partner was so focused on his performance that he ignored her other sexual needs. In summary, the results support previous findings of the impairing effects of PE on the female partner's sexual functioning and satisfaction and further highlight how these effects tend to be more drastic in women who are not focused on intercourse alone but tend to for a more varied sex life.

### *Limitations*

The present findings should be considered in light of several methodological limitations. First, it should be noted that we relied on subjective and restricted measures to assess men's PE status. Nevertheless, using these items led to results that were consistent with previous findings. Moreover, the main focus of the study was to specifically assess women's perception of the male's ejaculatory function therefore warranting such subjective assessment methods. We further had four different groups of women stating that their partner suffers from PE that were based on four different criteria. Although not a study limitation per se, it is important that these four groups looked at individually, which has been adequately done throughout the analyses and the reporting of the results. Nevertheless, it should be noted that recent data suggest that most men (60%) who either self-report PE or seek treatment have either variable or subjective PE [27]. In other words, men overreport PE, and this might be the case for women as well. Second, we were not able to directly determine the direction of causality between our variables, in particular between the effect of PE on female sexual functioning and relationship satisfaction. Further prospective research is needed to investigate these links. Third, we cannot exclude the possibility that our data were affected by biases, such as reporting biases given the sensitive nature of the questions, leading to, for example, some underestimation of FSD symptoms. However, Dunne et al. reported that surveys of sexual behavior may overestimate sexual liberalism, activity, and dysfunction (in reporting) but that this bias does not seriously compromise population estimates, as judged by the pattern of effect sizes [28]. Fourth, the low percentage of anorgasmic women (10.2%) is not in accordance with previous study reports, hence, raises the question as to the representativeness of our sample [24,25]. However, the prevalences of self-reported sexual complaints are in line with previously reported estimates which, however, was beyond the scope of this study [29]. Finally, women self-identifying as bisexual but who were currently in a relationship with a man suffering from PE were also included. Although differences in sexual responses and attitudes between heterosexual and bisexual women might exist, it is unlikely that the low proportion (2.32%) of bisexual women included in this study could have biased our results in any way. Ideally, we would have conducted comparative analyses to explore,

whether bisexual women differ from heterosexual women—however, given the small proportion of bisexual women such analyses were not feasible.

## Conclusion

Women's perceptions of the men's ejaculatory behavior and his affective responses as well as the impact PE has on the overall couple's functioning are important factors that need to be included when assessing the condition and when trying to formulate adequate and representative definitions of the disorder. The present findings are in accordance with results from previous studies reporting a strong link between PE and relationship dissatisfaction in the female partner. Our results further suggest that it must be considered an important motivational factor for women when terminating the relationship with a PE man. Women's perception of PE and related distress, however, shows strong variation and depends not only on her own sexual functioning but also on her view of what good and fulfilling sexuality constitutes. In this regard, an important source of distress are not only parameters related to performance such as control or duration, but rather inappropriate attention focus possibly due to lack of control and the negligence of sexual needs and preferences other than penetration. Clearly, ejaculatory function cannot be evaluated outside the dyadic framework and without taking into account both the men's and women's cognition of the condition and how their subjective perception impacts on the evaluation of the relationship and sexual quality. It therefore seems that female sexual distress and women's attitude toward sex should be assessed more thoroughly when the men present at clinics looking for a therapy and that the psychological and behavioral interventions that parallel pharmacological treatment should target interpersonal and intrapsychic issues that might precipitate or maintain the dysfunction, by emphasizing pleasure, versatility, and creativity. Furthermore, sexual health education, not only in clinical settings but also in educational ones (such as schools), should also draw attention to this largely ignored impact of PE.

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*Conflict of Interest:* AB: investigator, speaker and Advisory Board Member for Menarini; FG: lecturer for Pfizer, Menarini, Lilly; Consultant for Allergan, Menarini, Sanofi; Investigator and consultant for Bayer-Schering, Lilly, Johnson & Johnson, GSK. AB: investigator for Menarini; CMcM consultant for Johnson & Johnson; Principal investigator, Advisory Board Member, and speaker for Menarini, Bayer Schering and Plethora Solutions; Advisory Board Member and speaker for Ixchelsis-Consultant; HP investigator, speaker and consultant for Eli Lilly, Menarini/Berlin Chemie and Auxilium.

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