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Marie Gombert, Pura Ballester, Ana Segura & Ana M Peiró

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REVIEW



Introducing sexual dysfunction in mental care

Marie Gombert^a, Pura Ballester^{b,c}, Ana Segura^{d,e} and Ana M Peiró^{b,e}

^aDepartment of Paediatrics, Obstetrics and Gynecology, University of Valencia, Valencia, Spain; ^bDepartment of Pharmacology, Paediatrics and Organic Chemistry, Alicante, Spain; ^cNeuropharmacology on Pain (NED) Group, Alicante Institute for Health and Biomedical Research (ISABIAL), Alicante, Spain; ^dAndrology Unit, Department of Health of Alicante - General Hospital, Alicante, Spain; ^eClinical Pharmacology Unit, Department of Health of Alicante - General Hospital, Alicante, Spain

ABSTRACT

Introduction: People with any psychiatric disorder tend to have difficulties in responding sexually. However, sexual dysfunction (SD) is usually under-recognized, even the tightly hormonal and neuronal common connexions through the brain-sex axis. Multiple sources of resistance to SD assessment and intervention persist.

Areas covered: The present review aims to underline the feasibility to introduce SD evaluation in patients with any psychiatric disorders, evaluating the potential mutual benefits of their management.

Expert opinion: Women and men living with mental disorders frequently display sexual difficulties; however, some of them consider sexuality as a relevant parameter of their quality of life. In fact, SD as a side effect is a frequent reason for stopping the intake of medication. What is more, a holistic approach integrating sexual function could foster a better understanding of mental pathologies due to a common origin of pathogenesis. This could improve care quality, in keeping with the global tendency toward the development of personalized medicine. Consistently, the integration of SD assessment is highly recommended in mental health, all the more so when a psychotropic drug is prescribed. An expected consequence would be a reconstruction of the healthcare professional's consideration for the sexuality of people experiencing mental disorders.

ARTICLE HISTORY

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KEYWORDS

Sexual dysfunction; mental disorders; brain-sex axis; adverse events

1. INTRODUCTION

Sexuality constitutes an integral part of human life through psychological states, such as affection, intimacy, support, and life satisfaction. But equally importantly, it involves numerous physiological processes, throughout the organism, due to tight hormonal and neuronal connexions through the brain-sex axis [1–4]. This is why it is common to find a relation between emotional disorders (i.e. subjective feelings, depression, anxiety) and sexual dysfunction (i.e. low libido, lack of pleasure, presence of sexual pain, genital and non-genital response) that can reduce the ability to feel sexual stimuli, intercourse, erection, or orgasm. Here, outcomes can influence future motivations. In fact, people with mental illnesses often display complex sexual health needs that are not being routinely addressed and thus remain under the radar [4,5]. This is relevant because most therapy should begin by explaining, to the patient and her/his partner, the human biological and cognitive-emotive sexual response cycle, to guide treatment [6,7].

The expression of SD involves any difficulty experienced during one or more stages of a regular sexual activity (such as desire, physical pleasure, arousal, or orgasm), associating an extreme distress and interpersonal strain [8]. In line with this definition, on many occasions, sexual problems are considered to be pure psychological factors [9], or they are even assumed

to be part of the nature of mental diseases. Thus, they are scarcely being reported and evaluated, with higher inter-country variability reports that could be highly influenced by culture and beliefs [10]. What is striking is that it remains untreated since it can be a sentinel symptom of other problems, sharing many of the mental pathophysiological mechanisms. This drifts away from the classic approach in medicine that defines a disease by its etiology, trying to improve it according to its cause.

Sexual dysfunction in mental patients should not be considered as irrelevant or inevitable. In fact, many patients who discontinue antipsychotic medication report the onset of SD (loss of desire, erectile, and orgasm problems) as reasons for stopping them. There is thus a need to start addressing the concerns regarding sexual health in clinical practice to improve individualized care, tailored to the needs of patient-centeredness medicine. A greater effort needs to be made to compare pre-SD with drug-sexual side effects, trying to assign a causal attribution to psychotropic medications. With this in mind, a search was performed in PubMed/MEDLINE and Web of Science databases. The keywords used were as follows: sexual side-effects, sexual dysfunction, and mental disorders. The online search was based on studies (clinical trial (CT), systematic review) published in English, over the last ten years, from May 2010 to May 2020. A total of 358 studies (270 CTs, 88 from reviews) were included.

The present review, to the best of our knowledge, is the first that aims to put into perspective the signs of a strong sex-brain axis, a connection between sexual and cerebral functions in a physiological context; then, this link is replaced in the context of psychiatric illness. We then go on to underline the relevance of the benefits and the feasibility of an approach for a better management of sexual health in mentally ill individuals, with special attention to women's SD, that use to receive less attention.

2. MAIN BODY OF THE ARTICLE

Sexual and mental health is a dynamic balance of interconnected regulatory processes, fitting into a model of a bidirectional neuroendocrine communicating axis. The parameters of mental function, which modulate sexual desire, arousal, and orgasm, are also shaped by sexual activity, forming a loop. It appears logical that when one is affected, it can have an impact on the other. This process of integration into the model of a brain-sex bidirectional communication axis is a key element in a physiological and in pathological context as presented in Figure 1.

2.1. Sex-brain axis: a promising connection between mental health and sexual dysfunction

Sexual intercourse activates sensorial receptors of the skin and the sexual organs, and even, can control the sexual microbiota [11]. These inputs are directly mediated through a modulation of neuronal activity and endocrine expression in the direction of the central nervous system. Said mechanisms influence sexual behavior and activity through hormonal and neuronal control of primary and secondary sexual characteristics. The physiological modulations induced including vasodilatation, erection of cavernous bodies in males and females, lubrication, muscular contractions, and skin sensitivity, ultimately leading to the orgasmic phase [12].

In the brain, the secretion of hormones and neuropeptides is modulated consecutively to those direct and indirect signals. The hippocampus seems to control the signals coming from the external environment, while the amygdala and the hypothalamus control the response to social stimuli [13]. Stimulation of amygdala increases sexual performance and in parallel, triggers violent emotional responses. In addition, the dopaminergic system is known to be associated with sexual function as a pro-sexual neurotransmitter [14] due to the reward circuit. Sex stimulates dopamine, activating this process and inducing the pleasant sensation associated with sexual activity. During orgasm, oxytocin is secreted, regulating dopaminergic neurons exerting a mutual regulatory

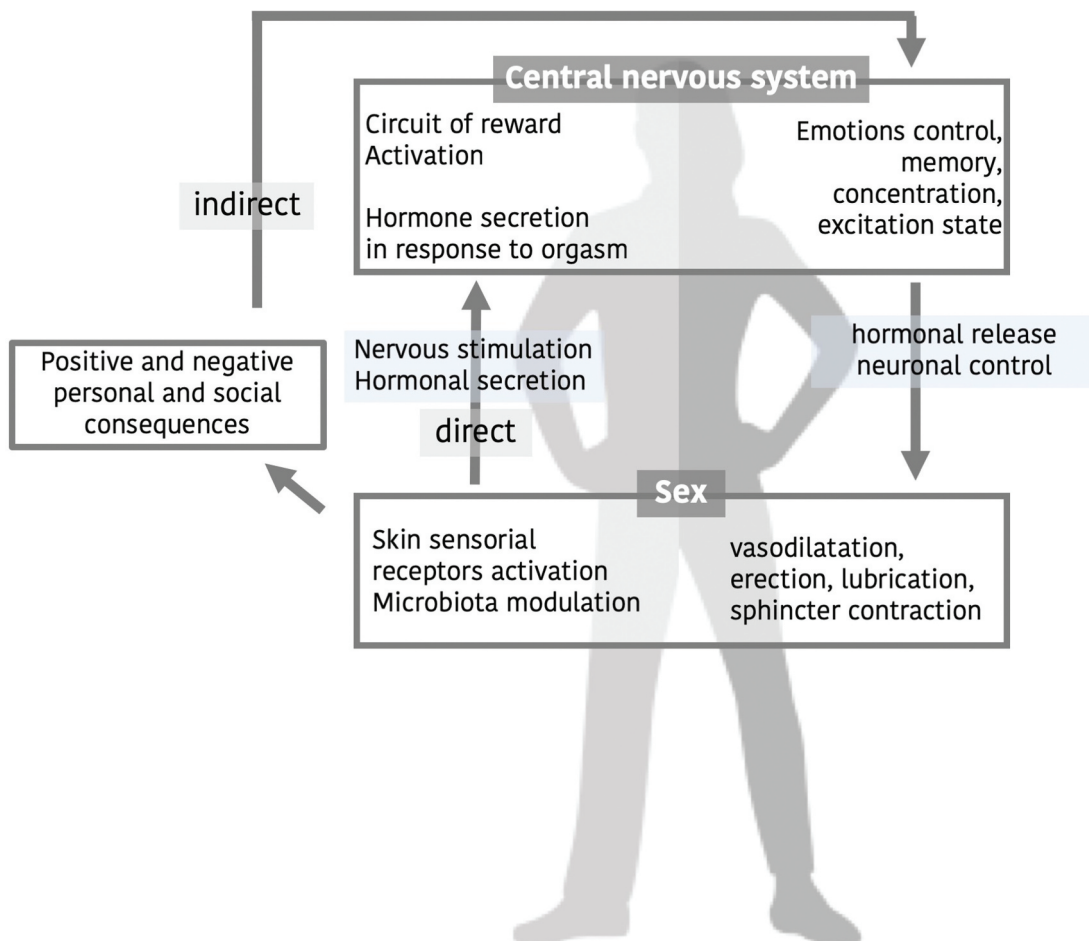


Figure 1. Sex-brain axis: Physiological communication between sexual and cerebral function.

role [7,15]. However, chronic increased prolactin levels are associated with a delay in ejaculation and therefore an altered sexual function. In contrast with dopamine, serotonin exerts an inhibitory control on sexual function. This phenomenon appears to be mediated by an inhibition of the dopaminergic action through a regulation of dopaminergic neurons in the midbrain by serotonin, triggering the effect of dopamine in structures such as the nucleus accumbens [16]. Also, kisspeptin, a neuropeptide whose receptors are expressed in the limbic structures, participates in the control of the gonadotropic axis showing therapeutic action on sexual and reproductive disorders [17].

The strictly controlled regulation of this axis is critical to maintain mental and physical health, since it is the neurotransmitters themselves that regulate both [9].

However, there are several other parameters implicated such as the control of emotions, memory, cultural environment, and concentration or control of an excitation status. In fact, flibenserin, a full agonist of the 5-HT1A and partial agonist of the D4 to treat low female sexual desire was not effective. At that moment, Katz [18] wondered if things that were labeled as sexual desire problems in women could be fixed with a drug.

Multiple bio-psycho-social processes involve bidirectional connections between genital and higher central regulation. All in a biological (such as age and hormone levels), psychological (such as sexual self-concept feeling sexually excited, impact of body image), and social (such as culture) delicate balance. This psychological aspect is at the interface between the social and the biological processes shaping sexual activity [19]. Figure 2 aims to illustrate this integrative perspective and its impacting SD. Here, the quality of personal relationships, the roles of parents and partners, and the social media can also exert a great impact on the patient's self-esteem [20]. Furthermore, sex differences due to hormonal influence could condition some variance which is not yet fully understood [21]. Sexual hormones have receptors all over the brain

and are therefore susceptible to affect numerous behavioral functions such as sex, mood, cognitive function, motor coordination, pain, between others. Furthermore, stress hormone, via gene expression regulation, can also interact with sex hormone receptors molecular machinery and signaling [22]. Consistently, the contribution of chronic stress to the mental illness development is likely to be additionally different between the sexes [23]. These differences emerge, in many brain regions, throughout the life course via both genetics and the interaction with experiences (referred to as the epigenetic mechanisms) because of this widespread distribution of sex hormone receptors [24].

In other chronic illness with a high degree of psychological comorbidities, such as pain, results indicate a stronger primary sensorimotor structural and functional disorders due to sex. Higher insula reactivity in males, differences in the degree of anterior cingulate structural alterations, and differences in emotional-arousal reactivity were cited [25]. What is more, Basson [26] defined a different female sexual response model, trying to understand the differences in female desire and motivational (willingness, expectation of intimacy) forces. For example, women's subjective arousal may be minimally influenced by genital congestion. Thus, absence of subjective arousal disorder was proposed to be separate from all types of sexual stimulation, or when the only stimulus is genital. Furthermore, fundamental changes to the existing women's SD definitions (such as dyspareunia or vaginismus) were recommended [27,28] due to the influence of context and psychosexual development that exceed the woman's own sexual response system [29]. The interest was to propose new subtyping definitions of female sexual dysfunction (FSD) for a better understanding assessment and pharmacological therapies based on physiological, psychological pathophysiology, and a personal distress criterion [30]. However, the mixed-sex studies carried out are liable to produce biased

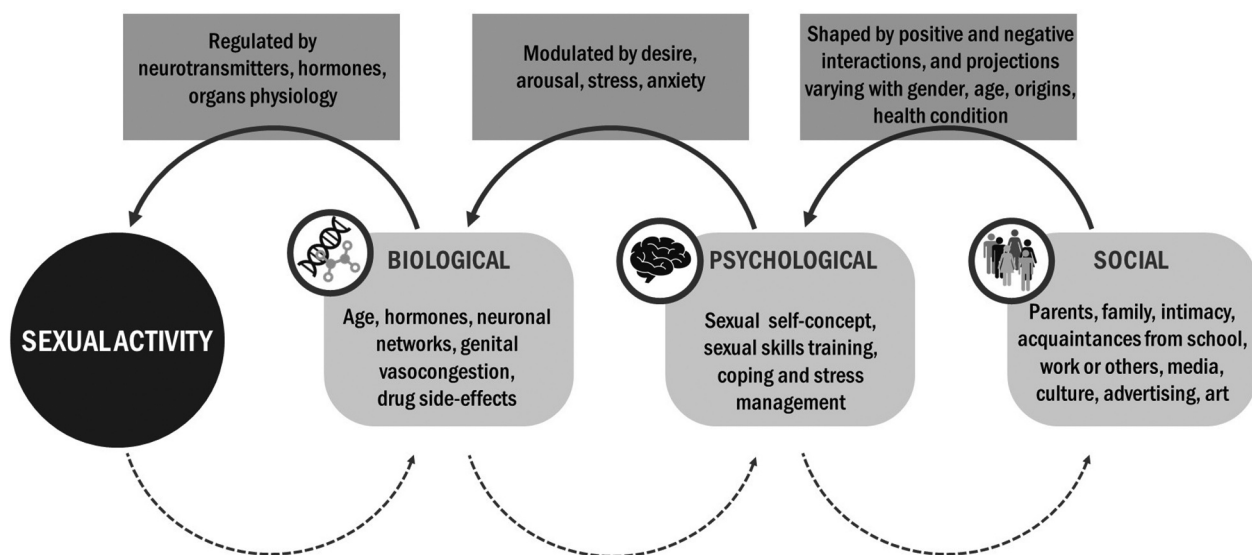


Figure 2. Multiple bio-psycho-social processes balance in sexual dysfunction.

data or to miss important information. Therefore, they have limited generalizability. Databases of large-scale neuroimaging are good candidates to complete the current knowledge about sex differences in cerebral physiology and its underlying chronic diseases.

2.2. Relationship between sexual and psychiatric illness

Several mental imbalances have been shown to induce SD as shown in Figure 3.

In fact, up to 90% of chronically psychotic population display SD of complex etiology because of the number of potential sources, such as the complexity in engaging in relationships and maintain them, and also by high frequency of drug sexual-side effects [31]. Here, most of the psychotropic prescription (i.e. antipsychotics, benzodiazepines, antidepressants) can be independently associated with higher SD [32]. In the meantime, whereas bipolar disorder individuals show troubles in desire, arousal (genital and subjective), and achieving orgasm, they showed high risky sexual behaviors and frequently, a greater increase in sexual partner change [5]. Briefly, all of them are very likely to present some dysfunction at all sexual response cycle phases, with the prevalence of sexual pain being 10 times more common [5]. This induces a negative feedback in terms of self-esteem, interaction skills that can affect relationships favoring social isolation [33]. However, the presence of psychological symptoms should not be incompatible with healthy sexual relationships. This point is

relevant, what is more, inpatients who previously had satisfactory sexual relationships and do not want to lose it after the start of any pharmacological treatment. In fact, many patients who discontinue antipsychotic medication report the onset of SD (loss of desire, erectile, and orgasm problems) as reasons for stopping them [34].

3. Sexual dysfunction assessment in the care of mental patients

The relationship between DS and mental health cannot be ignored, since may be bidirectional. It is clear that mental health causes SD as part of the disease, including psychopharmacological therapy-side effects, and SD that cause mental health problems (such as vaginismus and genitopelvic pain disorder). Thus, SD should be screened in all men and women, in mental care, given its high correlation with prescription drugs, lifestyle issues, and other chronic medical conditions [35,36].

Another aspect of interest in mental care is to differentiate between minor or major disorders. Feelings of anxiety, depression, or somatic problems including insomnia, fatigue, irritability, or difficulty concentrating [37] suggest that the population needs attention. However, major mental disorders can be directly associated with poor sexual skills such as schizophrenia in causing blunted affect and apathy; depressive disorder causing lack of sexual pleasure; or panic disorder with less

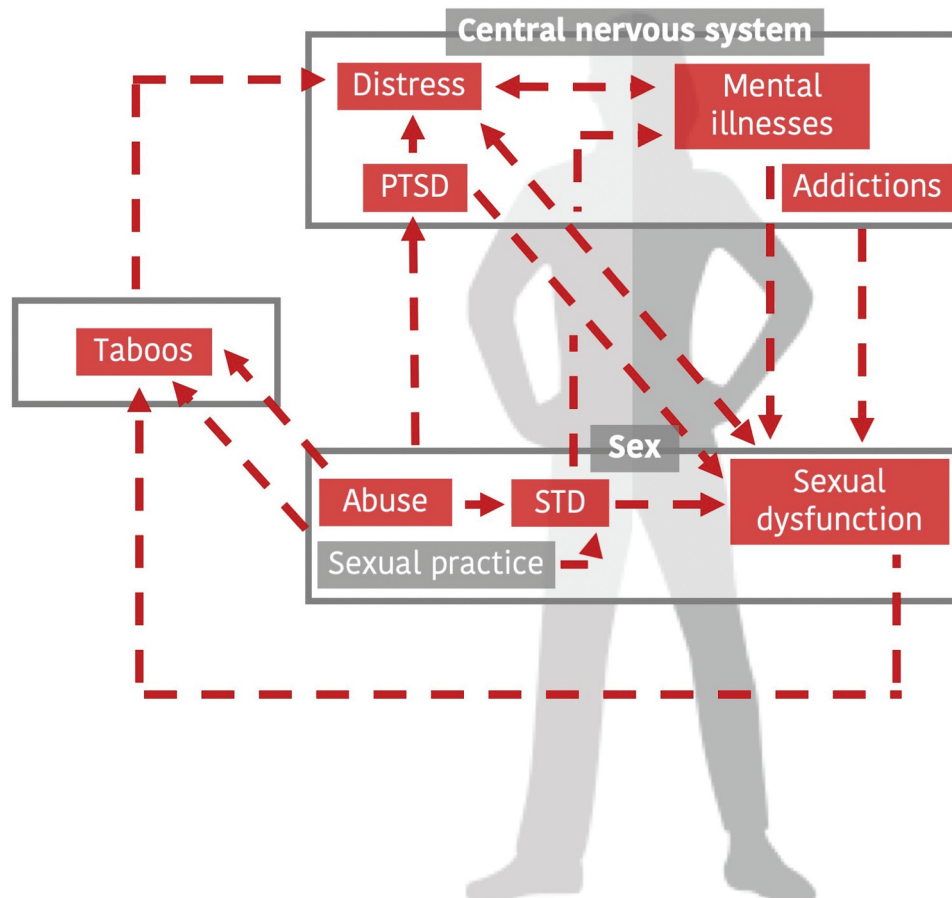


Figure 3. Pathological communication between sex and central nervous system. [PTSD = Post-traumatic stress disorder, STD = Sexually transmittable diseases].

sexual contact. This relationship between SD and mental health cannot be overlooked at any medical interview [38].

In consequence, SD should be managed as a systematic approach with multidisciplinary inputs, following integrated bio-psycho-social interventions. Firstly, a proper assessment of modifiable risk factors (i.e. clinical interview, psychosocial assessment through validated questionnaires, and laboratory determinations) has to be done. Here, it is important to obtain an accurate medication history [39], any illicit drug abuse (such as opiates or amphetamine) [40] or use of herbal or any diet supplements that could be linked to SD. Secondly, it is a priority to design the proper individualized intervention (i.e. pharmacology – drug dose reductions or deprescription-, referral to other specialists). Thirdly, a reevaluation of all clinical management has to be done properly and through validated scales that can evaluate SD (International Index of Erectile Function (IIEF) and Female Sexual Function Index (FSFI)) and the impact on patients sexual life quality (Sexual Life Quality Questionnaire, mSLQQ-QOL) [41] as can be seen at Table 1.

3.1. Diagnostic tools

3.1.1. Regarding medical history

Inquiry about sexual function should be made previously and periodically, to any mental disorder pharmacological treatment. Validated scales measure the impact in patient's sexual life quality, any sexual dysfunction or experience, or exploring the impact of any psychotropic drug, body dissatisfaction, or experience of care/abuse (Table 1). What is more, clinical evaluation should also include, sexual, medical, and psychosocial histories, as well as thorough laboratory tests to identify comorbid conditions such as diabetes mellitus, high cholesterol, cardiovascular disease (such as atherosclerosis or hypertension), chronic diseases such as kidney failure, depression, alcoholism, or any other substance abuse. All of them may favor SD development, and, even more, contraindicate certain drug prescription. Even more in mental illness that used to present increased risk of some comorbidities as metabolic syndrome (characterized by abdominal obesity, hypertension, dyslipidemia, and hyperglycemia) [42], sleep disorders, neurological or brain disorders like epilepsy or any intellectual disability [43]. In addition, the gender perspective must be taken into account in SD because women manifest other range of symptoms related to fatigue, muscular weakness or depression [44]. Moreover, a physical examination, and a history of the partner's sexual function should be obtained.

Additional testing such as hormone level measurements is required in selected patients as SD increases, among others, nitric oxide, α -1 blockade, anticholinergic effects, dopamine, serotonin, and increased prolactin [45]. More specifically in men, *American and European Urological Associations* Guidelines recommend the evaluation of additional risk factors as endocrinopathy, neurologic disease, pelvic radiation, any trauma or surgery, Peyronie's disease, as well as smoking, obesity, or dyslipidemia [46]. Some validated scales with the potential to be useful in this population are gathered in Table 1.

Table 1. Questionnaires for sexual dysfunction assessment in males and females.

Questionnaire	Items-scores	Areas under evaluation
Sexual Life Quality Questionnaire (mSLQQ-QOL) (10–90 points) [101]	10 assessment items Compare experiences prior SD and after, since treatment beginning (50 scores, no change)	Frequency of sex and duration; achieving orgasm; initiating sex pleasure; carefree feelings during sex; pleasure of orgasm, overall, and partner
International Index of Erectile Function (IIEF) (5–25 points) [102]	15 items Assess male sexual functioning as erectile dysfunction (ED): no (score 22–25), mild [17–21], mild to moderate [12–16], moderate [8–11], and severe [5–7].	Erectile function, orgasmic function, sexual desire, and satisfaction with sexual intercourse and overall satisfaction.
Female Sexual Function Index (FSFI) (2–36 cores) [103]	19 questions into 6 domains Assess female sexual function in women. Lower scores mean higher SD "not sexually active and no desire"	Desire, arousal, lubrication, orgasm, satisfaction and pain.
Arizona Sexual Experience Scale (ASEX) (5–30 scores) [104]	5 major aspects of SD Higher scores indicating higher SD	vaginal lubrication or penile erection, drive, arousal, capability/pleasure from orgasm
Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ-SALSEX) (0–15 scores) [105]	Different aspects of sexual dysfunction after the onset of any psychotropic treatment and the tolerability after these sexual changes for patients as well.	Loss of libido, Delayed orgasm or ejaculation, Lack of orgasm or ejaculation, Arousal Dysfunction: erectile dysfunction in men or vaginal lubrication dysfunction in women, Patient's acceptability of the SD
Body Uneasiness Test (BUT) [106]	71 items to explore body uneasiness and dissatisfaction. Higher scores indicating higher disorder	Weight phobia, body image concerns, avoidance, compulsive self-monitoring, detachment and estrangement feelings toward one's own body (depersonalization); and specific worries about particular body parts or functions.
Changes in Sexual Function Questionnaire (CSFQ) [107]	14 items Measure illness and drug-related changes in sexual function with questions and scale adapted to the patient's sex	Sexual dysfunction diagnosis

3.1.2. Regarding pharmacology history

According to legal requirements, all healthcare professionals need to have a consistent set of routine data available for potential adverse drug reactions (ADRs) [47,48]. Psychotropic-Related Sexual Dysfunction Questionnaire can be very useful. What is more, when most ADRs are predictable from the known pharmacology of a drug as antipsychotics [49–51], mood stabilizers [52] or antidepressants [53]. The factors linking drug use and SD should also be investigated more deeply,

Table 2. Drugs associated with sexual dysfunction.

Drug	↓ Desire	↓ Arousal	↓ Orgasm
Antidepressants	amitriptyline	amitriptyline	-
	clomipramine	clomipramine	clomipramine
	fluoxetine	fluoxetine	fluoxetine*
	imipramine	imipramine	imipramine
	paroxetine	paroxetine	paroxetine*
	sertraline	sertraline	sertraline*
	phenelzine	phenelzine	-
		tranylcypromine	tranylcypromine
		citalopram	citalopram
		nortriptyline	nortriptyline
	doxepin	escitalopram	
		-	venlafaxine
Psychotropic	risperidone	risperidone	risperidone
	chlorpromazine	chlorpromazine	-
	fluphenazine	fluphenazine	-
	lithium	lithium	-
	haloperidol	-	haloperidol
	alprazolam	-	alprazolam
Cardiovascular	clonidine	clonidine	-
	digoxin	digoxin	-
	hydrochlorothiazide	hydrochlorothiazide	-
	methyl dopa	methyl dopa	-
	spironolactone	spironolactone	-
		beta blockers	-
Other drugs	cimetidine	cimetidine	-
	-	antihistamines	naproxen
	-	cyproterone	-
	-	disulfiram	-
	-	gonadotrophin-releasing hormone agonists	-
	-	pseudoephedrine	-

*Associated with orgasm issues. [Adapted from: Conaglen, H. & Conaglen, J., 2013].

particularly the mechanisms regulating prolactin levels, and also binding to dopaminergic, histaminergic, cholinergic, serotonergic, and α -adrenergic receptors [54]. Investigating drug-induced sexual side-effects, and their consecutive impact on adherence to treatment, will make it possible for the clinicians to personalize the best treatment for each patient. Currently, known drugs associated with sexual dysfunction are listed in Table 2 [55].

Drugs involving a low risk of SD should be preferred. To decrease SD as a side effect of a drug, choose olanzapine, ziprasidone, quetiapine, and aripiprazole, rather than paliperidone, risperidone, and amisulpride. Avoid serotonergic antidepressants and choose agomelatine or bupropion. Interestingly, adding or switching to another medication may also be associated with ADRs, and with the risk of favoring a prescribing cascade. The adjunct strategies for treatment should be personalized [56]: (a) Giving time for a spontaneous ADR reduction; (b) Total or partial suspected drug deprescription as 'drug holiday' that can be a suspension of drug for 2 days in the week following half-life pharmacokinetic data; (c) Switch to a drug with fewer SD; (d) Diagnose, monitor, and treat the specific ADR.

3.2. Therapeutic tools

A reason that may favor SD diagnostic or interpretation can be due to the disparities in sexual function assessment methods. Since sexual problems can have a wide variety of medical and psychological causes [57] and many effects on other aspects of the patient life, therapy has to be designed in order to review all the individual factors that can induce an SD [58]. Thus, basic scales as IIEF and FSFI are important to be used as clinical routine.

Another poor consequence of this, is the scarce number of studies on sexual health-related to mental care specifically, although it is well recognized that epidemiology, etiology, and approach to assessment and treatment are distinct from those of the general population [59,60]. What is more, the four phases of sexual response cycle (desire, arousal, orgasm, and resolution) can be experienced differently in terms of order, intensity, or time spent in each one, from men to women. Understanding these differences may help partners better understand one another's responses, and enhance the sexual experience. In this way, sexual partners can have an important role and should be involved throughout all therapeutic procedures, all the more so in situational SD where couple friction due to problems in handling mental health issues may cause conflict and anger and lead to low sexual desire [61,62].

Here we have focused on both male SD (MSD), female SD (FSD), and their interrelationship.

3.2.1. MSD

Among the phenomena of aging in man, there is a decrease in erectile function and testosterone levels. We can add to these an increased risk for cardiovascular diseases, muscle wasting, decrease in bone density and libido, with all of these factors having an interplay with testosterone metabolism [63]. Androgen deprivation has been shown to result in impairment of nitric oxide synthase release, altered phosphodiesterase-5 (PDE5) expression and activity, impaired cavernous nerve function, and contribution to vein-occlusive disease in the penis. The role of testosterone replacement therapy as a potential to improve erectile function in the man with erectile dysfunction (ED) remains an issue for patient and physicians [64]. In addition, investigators have demonstrated that recommending testosterone replacement therapy (TRT) in hypogonadal men can improve erectile function even without the benefit of PDE5 inhibitors [65].

The iPDE5s are recommended as first-line therapy for ED, unless the patient has any contraindications due to the increasing penis blood flow to facilitate erection when the patient is sexually stimulated. What is more, patients with decreased libido and/or ED might present low serum testosterone levels; thus, prescription of testosterone use to be performed. Risk-factor modification, including lifestyle interventions (i.e. exercise, weight loss), is usually recommended. What is more, there are some promising pharmacogenetic research lines related to andrological drug response [66]. The most likely candidate gene is related to NOS expression levels [67], considered an independent risk factor for ED pathogenesis.

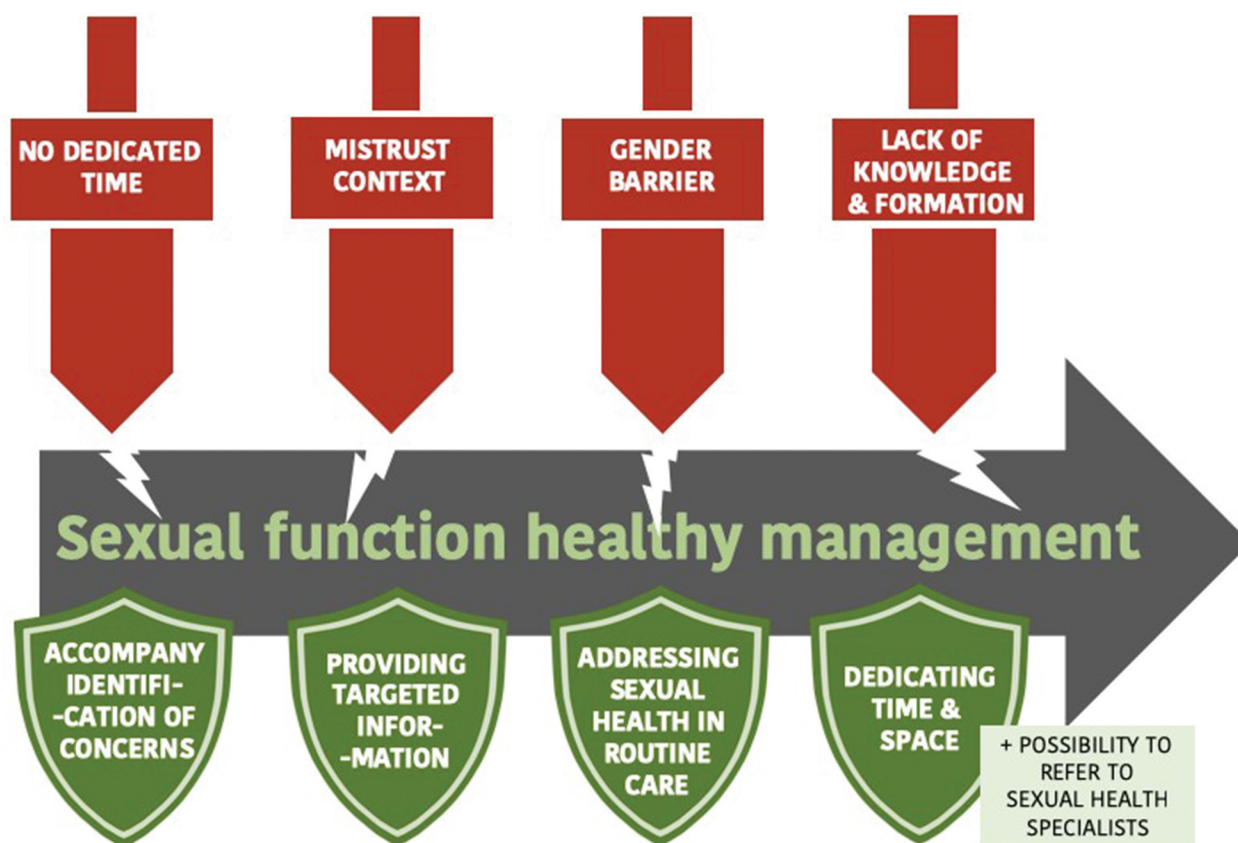


Figure 4. Barriers to addressing sexuality [Adapted from: Traumer, L., Jacobsen, M.H. & Laursen, B.S., 2018].

3.2.2. FSD

Here, we initially focus on hypoactive sexual desire disorder (HSDD) as a driving force in any other FSDs which are the trigger of female sexual response cycle activation [68]. It has been suggested that women with HSDD should be combined into two subgroups due to: (a) insensitive brain systems for sexual cues; or (b) enhance sexual inhibitory mechanisms [69]. This repartition in etiologic state suggested the intake of testosterone, in combination with an iPDE5 in second case, in order to enhance sexual responsiveness. Testosterone plus estrogen has been associated with improvements in sexual functioning in menopausal period (i.e. dyspareunia associated with genitourinary syndrome), but there is a need for studies on long-term risks and benefits [70]. On the other hand, for women with an overly active sexual inhibition mechanism, buspirone, a 5-HT_{1A} receptor partial agonist in combination with testosterone, was proposed to increase sexual motivation. This combination can be used when SD could be related to a selective serotonin reuptake intake; however, evidence is limited to include it into clinical routine [71,72]. The majority of these issues can be addressed by clinicians, in complement to women's sexual health education and validation of concerns [73]. However, the lack of well-defined endpoints for studies has impeded the approval of new treatments, promoting off-label use of other drugs not tested for FSD. In addition, recent studies point to a possible involvement of gene coding for the specific regions on genes related to serotonin 5HT_{2A} receptors [74] and dopamine receptor D4

(DRD4) [75] that exhibits an unusual amount of expressed polymorphism, and to interleukin-1 receptor antagonist, a down-regulator of pro-inflammatory immune responses [76], more common in vulvar vestibulitis syndrome [77], which are being researched.

3.2.3. MSD and FSD interrelationship

Life-span physiological changes can influence sexual health. For women, menopause syndrome can be accompanied by dyspareunia and relationship distress, and for men, testosterone deficiency of ED with impact in quality of life. There can be a dynamic linked between SD, i.e. sexual desire disorder, sexual arousal disorder (genital and subjective), orgasmic dysfunction, and sexual pain disorder. For example, HSDD will lead to issues with sexual arousal; and repeated orgasmic dysfunction may lead to poor sexual desire (i.e. ED repeatedly may cause partner to be disinterested in sex). Thus, both members may experience negative sexual consequences and concurrently need an integrated approach [78].

What is more, epidemiology, diagnostic, related medications in usual polypharmacy patterns or medical comorbidity differences (alcohol/tobacco consumption, cardiovascular diseases, depression, vaginal/pelvic disorders, psychological stress, or any other event with high emotional content (such as a couple under infertility treatment) [79]), should orientate different strategies for SD treatments according to gender and couple [80,81]. Antidepressants with a predominantly serotonergic activity, antipsychotics likely to induce hyperprolactinemia, and mood

stabilizers with hormonal effects are often linked to moderate or severe SD including delayed orgasm and anorgasmia in both genders. In addition, it has been recorded that antipsychotics generate premature ejaculation and erectile problems and decrease satisfaction with sex and less pleasure at orgasm [30].

Assuming that sexual function can be a surrogate marker of systemic health, we need to understand the distress and consequences experienced, at MSD and FSD interrelationship, during partnered sex. Increasing communication about sexual needs, addressing relationship satisfaction, and expanding behavioral repertoire of activities may increase sexual satisfaction [82] decreasing perceived partner distress [83] (anxiety or depressive symptom incidence [83]). Thus, a collaborative SD management may benefit couples' sexual and relational well-being [84]

3.3. Care advice

Individuals who are forced to grow up without autonomy or to lose it due to any mental disease lack the opportunity to freely develop their sexuality and have a healthy sexual life [47]. Instead, sexual expression is usually perceived as a marker of illness worsening their capacity to build satisfactory relationships. Hiding this aspect of life induces a feeling of vulnerability and shame when discussions about sexuality are compromised [9].

Urry and Chur-Hansen showed that sexuality was perceived as relevant and dangerous in the mental health setting [85]. These false dichotomies of sexual autonomy versus danger deny people a full range of feelings and experiences, and in doing so, it could reproduce social inequalities [86]. These factors contribute to the so-called 'two-way taboo' and to the complexity of the recovery acting as a vicious circle. A taboo entails many different facets: from cultural prohibition to feelings of shame, embarrassment, and stigmatization. Here, as neither healthcare professionals nor patients initiate conversations about patient sexuality, rendering such conversations deficient or non-existent [9]. An accumulation of those factors is liable to worsen patients' preexisting SD, resulting in significantly reduced quality of life and affected mental well-being [87] increasing depression, loneliness, and self-esteem issues as reasons for engaging in high-risk sexual behaviors [88]. Figure 4 shows a number of barriers for mental health clinicians to skip sexual function assessments [89] due to lack of knowledge, embarrassment or discomfort with the topic, prioritization of other issues [90]. An encouraging discussion with the patient about sexuality is essential to develop skills in the area of healthy sexuality [91,92] and to provide safety strategies to manage potential problem [93], more than for promoting their sexual activity [94]. Data revealed that individuals experiencing psychological illness appear to display the poorest degree of sexual health, as well as a higher prevalence of sexually transmitted diseases [95], unplanned pregnancy, and even sexual assault [96]. These individuals could be more prone to engaging in risky sexual behavior such as infrequent condom use [51]. Also, they may be more vulnerable to sexual exploitation and may have coexisting drug and alcohol problems often associated with sexual risk taking [97]. What is

more, SD represents a complex conceptual framework due to its heterogeneity and there is not always a sexual problem linked to a mental disease. For example, patient with vaginismus or genitopelvic sexual pain may not have any mental health issue, unless the chronicity of the problems will lead to depression/anxiety as a new comorbidity. In any case, sexual health should be evaluated as routine.

It is important to note that there is a special need to study sexual health in females [98]. Female sexuality, desires and pleasure, in mental disability settings, have not received much attention. Meanwhile, women's reproductive health has been regularly discussed [99]. Therefore, there is a paradox of highlighting the reproductive aspect, making the sexual area invisible. Throughout, it highlights the issue of providing sexuality education, emphasizing gender, seeing themselves as equal members who are able to protect their health [100]. What is more sexual health is related to perception, attitude, awareness, and personality issues in sexuality. There are other complex issues such as transgender, sexual transmission disease, culture, or philosophy that are not covered in present review. Perhaps by expanding the knowledge of the sexual physiological basis, healthcare professionals can address sexual problems in mental care with more precision [99].

4. CONCLUSION

Sexuality is an intrinsic part of human beings, but evidence suggests that this area of life is often overlooked in mental care and not integrated into regular healthcare assessment. This review has tried to clarify brain-sex axes that are intimately connected, involving mutual regulation mediated by a neurological and endocrinal dialogue. Numerous hormones and neuronal systems are known to participate in the process of sexual function (desire, arousal, pleasure, orgasm) highly impacted in populations suffering from mental illness.

Furthermore, physicians should also routinely ask about the patients' sexual background, in psychopathologically distressed patients, before prescribing any psychotropic drug. What is more, they should be aware about the safety profile of the prescribed drugs, monitoring any change in sexual function, and reporting any potential SD adverse event, especially if it is serious. These aspects are essential, given the scarce scientific evidence of drug sexual side effects on socially disadvantaged patients, in the context of mental illness.

Identification and management on the needs and barriers facing an optimal SD diagnosis should be integrated into mental practice routine. In fact, the increased emphasis on individual's rights should force healthcare systems to reconsider their views around the sexual health mental care.

5. Expert opinion

Sexual health is an important, yet overlooked, aspect of quality of life in mental illness patients as well. Although psychiatric patients are frequently confronted by sexual health concerns, with a high impact on several aspects of personal life and in

their relationships, there are limited efforts to address these problems which fall under the radar in health care

Sexual dysfunction in females and males with mental diseases is multifactorial, due to chronic disease aspects, disease activity, and drugs. Through brain-sex axis, both biological and psychosocial mechanisms are involved in sexual difficulties in mental health patients. The neurotransmitter systems and sex hormones act on multiple sites. In fact, expression of estrogen and progesterone receptors is very high in many brain regions such as the amygdala or the hippocampus. Thus, a comprehensive understanding of their relationship needs to be prioritized in order to improve mental care medicine.

This includes routinely the screening of patient's perceptions regarding the way in which the disease affects their sexual health, and the need for further intervention taking into account the common physiopathological mechanisms. This is why there is a need to develop more suitable tools in order to explore sexual health status in people with any psychological disorder. A baseline screening with a regular monitoring of sexual function, using validated scales, is strongly recommended prior to starting any medication regimen in mental care. Increasing the knowledge from both perspectives may help to diagnose and therefore implement a better pharmacological approach if needed. A multidisciplinary approach is essential to offer preventive measures adapted to these patients.

Managing treatment-emergent side effects adequately is also crucial to facilitate compliance and achieve the best possible outcomes. Sexual side effects should be important when initially selecting long-term psychotropic drugs. Different strategies are advised when dealing with sexual dysfunction in patients treated with psychotropic drugs: waiting for a spontaneous resolution, reduction in drug dosages, drug holidays, adjunctive pharmacotherapy, or switching the drug. For example, PDE inhibitors may benefit induced male ED due to antidepressant or antipsychotic drugs or antidepressant-induced female orgasmic disorder. Furthermore, clinicians should be aware that, during long-term psychotropic use, side effects are common and persistent because in many cases, patients suffer in silence or try to resolve them by themselves. It is thus paramount to improve the information provided and research about sexual health in people with mental illness. Improved physician-patient communication, due to effective sexual healthcare strategies, can help mental patients cope with SD.

Multiple sources of resistance to comprehensive assessment and intervention are present in the mental healthcare environment. The diversity of needs and values presented by this population may encourage healthcare professionals to improve their education in this regard so they can deliver a patient-centeredness assistance. Sexual health risk reduction interventions may also improve beliefs, reducing risky sexual behaviors. Robust research is required to identify effective courses of action in real-world mental illness settings.

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