
The Impact of Mental Illness on Sexual Dysfunction

Zvi Zemishlany · Abraham Weizman

Geha Mental Health Center, Petah-Tikva, and Sackler Faculty of Medicine,
Tel-Aviv University, Tel Aviv, Israel

Abstract

Sexual dysfunction is prevalent among psychiatric patients and may be related to both the psychopathology and the pharmacotherapy. The negative symptoms of schizophrenia limit the capability for interpersonal and sexual relationships. The first-generation antipsychotics cause further deterioration in erectile and orgasmic function. Due to their weak antagonistic activity at D2 receptors, second-generation antipsychotics are associated with fewer sexual side effects, and thus may provide an option for schizophrenia patients with sexual dysfunction. Depression and anxiety are a cause for sexual dysfunction that may be aggravated by antidepressants, especially selective serotonin reuptake inhibitors (SSRIs). SSRI-induced sexual dysfunction may be overcome by lowering doses, switching to an antidepressant with low propensity to cause sexual dysfunction (bupropion, mirtazapine, nefazodone, reboxetine), addition of 5HT₂ antagonists (mirtazapine, mianserin) or coadministration of 5-phosphodiesterase inhibitors. Eating disorders and personality disorders, mainly borderline personality disorder, are also associated with sexual dysfunction. Sexual dysfunction in these cases stems from impaired interpersonal relationships and may respond to adequate psychosexual therapy. It is mandatory to identify the specific sexual dysfunction and to treat the patients according to his/her individual psychopathology, current pharmacotherapy and interpersonal relationships.

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Proper sexual functioning is one of the most important components of quality of life and of maintaining a satisfying intimate relationship. Sexual dysfunction is a common phenomenon in the general population, affecting an estimated 43% of women and 31% of men in the US [1]. The most common dysfunction amongst women is decrease in sexual desire reported by approximately a third of the women. The most common dysfunctions amongst men are erectile dysfunction (ED; mainly in older age) and premature ejaculation. Despite the importance and high prevalence of sexual dysfunction, most sufferers do not seek help either due to feeling of embarrassment or because they do not view it as a medical problem [1, 2].

Table 1. Assessment of sexual dysfunction

Premorbid sexual function
Primary psychiatric disorder
Comorbid psychiatric disorders
Comorbid physical illnesses
Psychotropic medications
Concomitant medications

The prevalence of sexual dysfunctions is higher in persons with mental disorders, particularly those treated with psychotropic medications. For instance, sexual dysfunction has been reported in as many as 30–60% of patients with schizophrenia treated with antipsychotic medications [2], up to 78% of individuals with depression treated with antidepressants [3–5], and up to 80% in patients suffering from anxiety disorders [6, 7].

An evaluation of a sexual dysfunction in psychiatric patients should take into consideration primary sexual functioning, the psychiatric disorders, physical diseases and the various medications (table 1). Sexual dysfunction may be comorbid with, and often a first sign of many physical illnesses and contributes significantly to reduction in quality of life. Awareness of the prevalence and of the hypothesized mechanisms of sexual dysfunctions in psychiatric patients would improve the attitude of the treating physicians towards sexual difficulties in those patients and result in increased compliance with treatment on the patients' part.

Neurotransmitters and Sexual Functioning

Sexual functioning is mediated and influenced, in a complex manner, by endocrine factors, neurotransmitters and neuropeptides.

The endocrine factors include androgens, estrogens, progesterone, prolactin, oxytocin, cortisol and pheromones. Neurotransmitters that are implicated in sexual functioning, mainly dopamine, serotonin and epinephrine, are also implicated in the pathophysiology of the major psychiatric disorders and in their pharmacological treatment.

Dopamine

Studies in humans and animals have suggested that the central dopaminergic system is involved in all components of male sexual behavior: desire, erection, orgasm and satisfaction [8, 9]. Dopaminergic agonists such as L-dopa, apomorphine, amantadine, bupropion and amphetamines have been reported to arouse sexual behavior while central dopaminergic blockers, like antipsychotics, suppress sexual functioning in both animals and humans.

Serotonin

Findings from animal studies suggest that 5-HT may facilitate, inhibit, or have no effect on sexual behavior, depending on which serotonin receptor subtype is involved. Studies on the effect of antidepressants on human sexual functioning suggest that activation of the 5-HT₂ receptor impairs all stages of sexual response in males and females [8, 9]. Paroxetine, an SSRI, has been shown to be also a nitric oxide synthase inhibitor, and may diminish nitric oxide levels and function [10].

Epinephrine

Epinephrine inhibits erectile response in men, while blocking α_1 -receptors stimulates erection. By contrast, in women epinephrine facilitates vasocongestion while suppression of adrenergic activity impairs sexual arousal and orgasm [9].

Norepinephrine

Norepinephrine levels increase during sexual arousal in both men and women. The few studies that were done so far on this subject suggest that increasing the level of norepinephrine may facilitate erectile response in men [for review, see 9].

Acetylcholine

Acetylcholine facilitates penile erection via the relaxation of smooth muscles of the corpus cavernosum. The role of acetylcholine in female vasocongestion is unclear [9].

Sexual Dysfunctions in Schizophrenia Patients

Patients suffering from schizophrenia (about 1% of the population) are prone to experience sexual dysfunction as a part of the nature of the disease. The premorbid personality of these patients is often schizoid or schizotypal with few interpersonal relationships and lack of sexual experience. Negative symptoms of the disorder, such as anhedonia, avolition and blunted affect related to hypodopaminergic activity in the frontal cortex, severely harm the ability to enjoy sexual life. In addition, these patients face difficulties in establishing relationships due to recurrent psychotic episodes, obesity and low self esteem. Schizophrenia patients are regularly treated with antipsychotics whose common mechanism (at least for the typical antipsychotics) is blockade of postsynaptic D₂ dopaminergic receptors.

Few studies have investigated the prevalence of sexual dysfunction amongst schizophrenia patients. The available data focus mainly on dysfunction in males. In one of the first studies, Kotin et al. [11] have shown that 60% of schizophrenia patients treated with thioridazine exhibit sexual dysfunction (35% ED) compared with 25% of patients treated with other typical antipsychotics. Other studies have also found that the prevalence of sexual dysfunction in schizophrenia patients, maintained on first-generation antipsychotics, is 37–54% [12, 13]. Aizenberg et al. [14] examined two groups of

treated and untreated male schizophrenia patients and found that both groups reported high prevalence of sexual dysfunction compared to a healthy control group. Untreated patients reported diminished sexual desire and poor sexual performance. Antipsychotic treatment was associated with further deterioration in erection, orgasm and satisfaction with sexual functioning. The antipsychotic-induced ED interferes with the adherence to the medication regime and results in recurrences of psychotic episodes and rehospitalizations.

A recent study assessed sexual dysfunction in men and women with schizophrenia, using a self-completed, gender-specific questionnaire, and compared the results to the general population [15]. At least one sexual dysfunction was reported by 82% of men and 96% of women with schizophrenia. Male patients reported less desire for sex (52 vs. 12%), ED (52 vs. 9%) and more frequently had no sexual intercourse or masturbation (27 vs. 0%). Female patients reported less enjoyment than the control group (46 vs. 5%). Sexual dysfunction in female patients was associated with negative schizophrenia symptoms and general psychopathology. In both men and women there was no association between sexual dysfunction and type of antipsychotic medication. The results of this study, although interesting, are limited due to a small sample size and usage of a self-reporting questionnaire not previously validated. Moreover, few of the patients but most controls had a partner. It was not possible to separate the effects of the illness from those of the medication on sexual dysfunction.

Attempts to treat sexual dysfunction in patients maintained on typical antipsychotics by coadministration of dopaminergic agonists did not bring about the desirable results. Furthermore, the addition of L-dopa may exacerbate psychotic states in schizophrenia patients [16]. Apomorphine causes severe nausea and has, therefore, minimal utility as a therapeutic agent [17]. Coadministration of 100 mg/day of amantadine, a dopamine reuptake inhibitor, for 6 weeks in an open-label study showed some statistically significant improvement in sexual function scores, but insufficient clinically [18]. However, the degree to which placebo effects contributed to the improved sexual function in this open-label study cannot be disregarded. In a double-blind placebo-controlled crossover preliminary study in 10 antipsychotic-treated male schizophrenia outpatients, selegiline (L-deprenyl) 15 mg/day was coadministered with the regular antipsychotic treatment. Selegiline is a selective monoamine oxidase B inhibitor. In low doses (up to 15 mg/day), it selectively inhibits the oxidation of dopamine and phenylethylamine [19]. Selegiline was not found to be effective in improving any domain of sexual functioning in spite of a significant decrease in prolactin levels [20].

The introduction of the new atypical antipsychotics carried expectations for fewer sexual side effects. Atypical antipsychotics as a group have a number of potential advantages over typical antipsychotics in minimizing sexual dysfunction. They display stronger 5-HT_{2a} receptor affinity, relative to D₂ receptor affinity and comprise a lower risk for plasma prolactin elevation as well as for extrapyramidal symptoms,

which may interfere with sexual function. Atypical antipsychotics have less effect on peripheral cholinergic and α_1 -adrenergic receptors involved in sexual function [21].

Hummer et al. [22] conducted a prospective investigation of 100 schizophrenia patients treated with clozapine and 53 patients treated with haloperidol. They found no statistically significant difference between haloperidol and clozapine with regard to their propensity to induce sexual side effects. However, in a similar comparison in male outpatients with chronic schizophrenia, Aizenberg et al. [23] found that, compared to first-generation antipsychotics, maintenance therapy with clozapine may be associated with a better orgasmic function, enjoyment of sex and sexual satisfaction. It seems that the beneficial properties of clozapine (fewer extrapyramidal symptoms, no prolactin elevation) were offset by its relatively greater antiadrenergic and anticholinergic activity, thereby explaining the absence of significant differences in sexual function as regards desire and erectile function [21].

Among atypical antipsychotics, risperidone has been associated with the most substantial changes in serum prolactin concentration and has been found to produce dose-dependent increases in serum prolactin that are comparable to those produced by first-generation antipsychotics [24]. An international trial showed that 4–8 mg of risperidone resulted in sexual side effects comparable to those of haloperidol [25].

In recent years, there has been cumulative clinical evidence that the atypical antipsychotics olanzapine, quetiapine and ziprasidone, which do not bring about a massive blockade of dopamine transmission, cause less disturbances in sexual functioning and may have an advantage over other antipsychotics.

Bitter et al. [26] examined sexual functioning among schizophrenia patients treated for the first time. Five hundred and seventy patients were examined at baseline and again, after 3 and after 6 months of antipsychotic medication. Sexual dysfunction and loss of libido were not rated using a specific rating scale. The sample was divided into three groups: olanzapine, risperidone and first-generation antipsychotics. At baseline, prior to taking any medication, 37% of the patients reported some sexual dysfunctions. After being treated, patients receiving olanzapine showed the lowest rate of loss of libido and of sexual dysfunction. These findings are in line with an older, double-blind study that compared olanzapine to risperidone in the treatment of schizophrenia patients [27]. Sexual dysfunction was significantly lower in olanzapine-treated patients than in those treated with risperidone.

A large sample of 3,828 schizophrenia outpatients was examined by Dossenbach et al. [28]. The outpatients were treated with either olanzapine ($n = 2,638$), risperidone ($n = 860$), quetiapine ($n = 142$) or haloperidol ($n = 188$). Sexual dysfunction was evaluated through patients' and investigators' perception using the UKU Side Effect Rating Scale. Patients in the olanzapine-treated and quetiapine-treated groups experienced significantly less sexual dysfunction (55.7 and 60.2%, respectively) than patients who received risperidone (67.8%) or haloperidol (71.1%). Quetiapine and ziprasidone have not been associated with elevated prolactin levels [21, 29]. The lower propensity of quetiapine to cause sexual dysfunction has also been demonstrated in

several recent studies [30]. Controlled studies for sexual dysfunction induced by ziprasidone are still needed.

In recent years, reports about the efficacy of treatment with sildenafil (Viagra) in sexual disorders in schizophrenia patients have been accumulating. Case reports and an open-label study, as well as clinical experience of psychiatrists revealed that sildenafil may be an efficient treatment in less deteriorated patients who are capable of having a proper relationship with their spouse [31, 32].

This has also been demonstrated in a double-blind placebo-controlled study [33]. Thirty-two patients with ED suffering from schizophrenia or delusional disorder randomly received either sildenafil (25 mg, 1–2 times per day) or placebo, and were crossed over to the other arm after 2 weeks. Duration and frequency of erections, as well as satisfaction with intercourse, were superior in sildenafil-treated patients. The drug was well tolerated; therefore, the authors suggest that sildenafil can be a useful approach in treating ED in schizophrenia patients.

In summary, the therapeutic approach to sexual dysfunction in schizophrenia patients should be according to the following stages: (1) adjusting medication to minimal effective dose; (2) switching to atypical antipsychotics: quetiapine, olanzapine, ziprasidone or clozapine; (3) psychotherapy: couple/family intervention to restore relationship; (4) in males, addition of a PDE-5 inhibitor (sildenafil, vardenafil, tadalafil).

Sexual Dysfunction in Patients Suffering from Depression

About 10% of the population suffers from depressive episodes with a severe impairment in the quality of life and functioning. Decreased libido commonly accompanies an episode of major depression. Casper et al. [34], in the classic study on a sample of moderate to severe hospitalized drug-free patients with major affective disorder, found that the majority of these patients (72% of unipolar depressed, 77% of bipolar depressed) experienced loss of sexual interest. Increasing severity of depression and anxiety were associated with loss of libido. Age and cognitive impairment also showed a strong correlation with the reduction in sexual interest. Depressed patients with increased appetite were more sensitive in personal relationships, more hostile and reported a greater decrease in libido than the matched depressed group without increased appetite. Depressed persons may also experience diminished ability to maintain sexual arousal or achieve orgasm. In males with severe depression, the rate of ED might reach 90% [35]. Assessment of nocturnal penile tumescence has been used as a measure of erectile capacity. Thase et al. [36] studied a sample of 34 male outpatients with major depression and an age-matched group of 28 healthy controls. Diminution of penile rigidity was found in approximately 40% of the depressed outpatients in addition to a reduction in the duration (in minutes) of sleep-related tumescence (nocturnal penile tumescence time) when compared to the healthy controls [37]. These findings were replicated in a second sample of 51 depressed male