

# SSRI-Induced Hypersexuality

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Selective serotonin reuptake inhibitors (SSRIs) are the first-line pharmacotherapy for depressive mood disorders, anxiety disorders, and obsessive-compulsive disorder (OCD) and are widely used in other psychiatric and medical conditions. In the United States, 12.7% of the population over age 12 have taken antidepressant medications (1). Sexual dysfunction is one of the most common side effects of SSRIs. Although symptoms of hyposexuality, such as erectile dysfunction, anorgasmia, and delayed ejaculation, are well recognized, hypersexuality as a potential side effect is less understood but important for providers to identify and manage.

Here we report a case of hypersexuality as an adverse effect of sertraline in an individual seeking treatment for depressive symptoms. We include a brief review of available literature on hypersexuality related to SSRIs. Clinical features of this rare side effect are summarized in hopes of providing directions for management and future study.

## CASE REPORT

Mr. M is a 42-year-old married Caucasian male with a history of papillary thyroid carcinoma, who underwent a total thyroidectomy and left modified radical neck dissection, followed by a full course of radioactive iodine treatment. He presented to the psychiatry clinic for assessment and treatment of inattention and fatigue that began with the cancer treatment and had persisted for 1 year after treatment completion.

During the initial psychiatric interview, Mr. M further characterized his symptoms as fatigue despite good sleep and increased anxiety and irritability. A screening measure indicated a moderate level of depression. The most troublesome symptoms to him were cognitive issues, which included forgetfulness,

inattention, and difficulties with retaining and organizing new information. His symptoms impaired his occupational functioning and family relationships. Neuropsychological testing confirmed that his cognitive symptoms were of new onset and not developmental in nature. He denied any history of depression, anxiety, bipolar disorder, psychotic disorder, OCD, trauma, or substance use disorder. He had no past inpatient psychiatric hospitalizations. Psychiatric review of systems was negative for mania-hypomania, psychosis, OCD, posttraumatic stress disorder (PTSD), eating disorder, suicidality, and homicidality. The patient did not report any family history of severe mental illnesses or intolerance of psychotropic medications. His medications on presentation included levothyroxine 0.224 mg daily and omeprazole 20 mg twice a day. His thyroid-stimulating hormone (TSH) was monitored monthly by endocrinology following the surgery, with a goal of 0.1 mIU/L to 0.5 mIU/L. TSH had been consistently within this range until 1 month prior to his psychiatric presentation, when it was elevated to 12.4 mIU/L. His levothyroxine dose was adjusted by his endocrinologist, and TSH returned to normal range in the subsequent months. According to the patient's report, his psychiatric symptoms predated this aberration in TSH and persisted despite normalization of thyroid function. Other lab tests, including vitamin B12 level, were within normal limits. No brain imaging was performed.

The patient started bupropion XL 150 mg once daily 1 month after the initial psychiatric evaluation to address persistent symptoms despite stabilized thyroid function. However, the medication was discontinued 1 week after initiation because of a significant increase in irritability. Sertraline was then started at 50 mg once daily, and the pa-

tient subsequently reported a dramatic improvement in cognitive symptoms, mood, anxiety, energy, fatigue, and self-esteem, stating that he felt "like myself again." Nonetheless, he also developed adverse effects, including hypersexuality (increased sex drive, constant sexual thoughts, and compulsive masturbating throughout the day, including strong urges to do so at work), as well as hyposexuality (delayed ejaculation). He described both these side effects as debilitating and shameful, and he noted that the hypersexuality in particular was negatively affecting his marriage and career, although not as severely as his presenting symptoms had. There were no signs of mania or hypomania.

Sertraline was switched to duloxetine 30 mg once daily because of these side effects. The sexual side effects were attenuated but persistent, and the patient complained that the duloxetine was not effective in controlling the cognitive and mood symptoms on 2-month follow-up. Escitalopram was trialed for 2 months subsequently, but it elicited no positive treatment effects, even though no further sexual side effects were reported. After consideration of other treatment options, the patient elected to restart on sertraline, because he felt the benefits had outweighed the side effects. Sertraline was started at 50 mg daily. With this trial, he experienced no symptoms of hypersexuality, and delayed ejaculation was subjectively less severe than with the prior trial. The daily dose was subsequently increased to 100 mg; side effects were unchanged. He described a complete resolution in his cognitive, mood, and energy symptoms on 2-month follow-up.

## DISCUSSION

Sexual side effects are highly prevalent but underreported in patients receiving treatment with SSRIs. The rate of pa-

**TABLE 1. Case reports of hypersexuality induced by selective serotonin reuptake inhibitors (SSRIs)**

Study	SSRI and dose	Description	Management
Das et al. (5)	Sertraline (100 mg daily)	Male, age 55. Heightened sexual desire and increased demands to have sexual intercourse (which did not occur when on bupropion monotherapy), resulting in spousal distress. Lengthier and firmer erection but no evidence of priapism.	Discontinued sertraline Continued bupropion
Ellison (8)	Fluoxetine (20 mg daily)	Female, age 50. Increased difficulty achieving orgasm during sexual intercourse but experienced unintended exercise-induced orgasms that occurred with predictable regularity and ease. No genital arousal during exercise-induced orgasms.	Cyproheptadine 4 mg orally prior to sexual intercourse improved anorgasmia but induced sedation. Discontinuation of fluoxetine resolved exercise-induced orgasms.
Elmore and Quattlebaum (9)	Patient 1: fluoxetine (20 mg daily)	Patient 1: female, age 60. Marked sexual arousal after 10 years of no sexual activity or masturbation.	Discontinuation
	Patient 2: paroxetine (20 mg daily)	Patient 2: female, age 41. Pelvic sexual sensations, frequent sexual arousal, and sexual fantasies with masturbation. These experiences were apparently not preceded by a state of desire.	Discontinuation
	Patient 3: fluoxetine (20 mg daily); fluvoxamine, dose not reported	Patient 3: female, age 33. Fluoxetine first for 6 months; then fluvoxamine for 2 months. Increase in sexual desire starting with both initial doses, as well as a sexual pelvic sensation and arousal.	Discontinuation
Garcia-Campayo et al. (10)	Fluoxetine (20 mg daily)	Male, age 69. Bursts of sexual excitement, one to two episodes per day, lasting 30 to 60 seconds, associated with a tingling feeling over genital skin. No penile erection.	Discontinuation
Modell (12)	Fluoxetine (20–40 mg daily)	Female, age 30. Repeated yawning, clitoral engorgement, spontaneous orgasms (“little tingly orgasms for no apparent reason”) in a typical “slow-crescendo, rapid-decrescendo intensity of sensation.”	Discontinuation
Morris (13)	Fluoxetine (20 mg daily)	Male, age 69. Frequent short episodes of sexual excitement described as feeling like an orgasm, two to four times per day, lasting 10 to 30 seconds, associated with tingling feeling over skin and without an erection. Relationship was dose dependent.	Dose decreased to 20 mg every other day
Pae et al. (14)	Patient 1: paroxetine (10 mg daily)	Patient 1: female, age 64. Spontaneous and repeated sexual orgasm with genital arousal, particularly in a bumpy ride, such as the subway. Episodes lasting 30 to 60 seconds, ten to 15 times per day. Increased sexual stimulation during intercourse.	Discontinuation
	Patient 2: paroxetine (15 mg daily)	Patient 2: female, age 48. Frequent and increased sexual desire, with a feeling of clitoral engorgement. Masturbation after sexual intercourse. Sexual urges and excitement during doctor’s appointment.	Discontinuation
	Patient 3: paroxetine (30 mg daily)	Patient 3: female, age 54. Heightened sexual arousal, excitement and desire resulting in more frequent sexual intercourse.	Switched to mirtazapine
Kurtses-Gursoy (16)	Escitalopram (10 mg daily)	Male, age 40. Spontaneous erection, once or twice daily, without sexual arousal and intermittently spontaneous ejaculation without any stimulation or erection.	Switched to citalopram
Viritt and Savas (17)	Citalopram (20 mg daily)	Male, age 25. Spontaneous ejaculation that started 2 weeks after drug initiation. Occurred daily and was not associated with sexual fantasy or arousal, without erection and feeling of orgasm.	Switched to paroxetine

tients self-reporting sexual side effects is around 14%, whereas the likelihood of endorsement of such side effects when asked directly by a physician is reported to be 58% (2). Although limited to case reports, a growing body of evidence has suggested that hypersexuality is part of the side-effect profile of SSRIs and other serotonin-enhancing medications, in-

cluding duloxetine (3) and venlafaxine (4). Das et al. (5) reported a similar case of sertraline-induced hypersexuality, characterized by heightened sexual desire resulting in marital discord, without signs of mania or hypomania in a 55-year-old male with history of PTSD and major depressive disorder. In their report, a confounding factor was that the

patient was taking bupropion when sertraline was added. However, the temporal relationship between the initiation of sertraline and the onset of hypersexuality convinced those authors that sertraline was at least partially involved in the development of this side effect. Drug-drug interaction should also be considered in that case, given that sertraline

can inhibit the metabolism of bupropion (6), potentially by inhibiting CYP2B6 (7).

Our case was different in that bupropion preceded sertraline, with no overlap between the two medications throughout the treatment course. This further supported the conclusion that sertraline caused the hypersexual side effects. A series of cases have been reported on hypersexual side effects from fluoxetine, paroxetine, fluvoxamine, citalopram, and escitalopram (8–17) (Table 1). Some described a similar clinical profile with enhanced sexual desire and excessive masturbation (5, 9, 14), as noted in our case. However, most reported a unique cluster of symptoms (8, 10–14), and except for one case of exercise-induced orgasm (8), these symptoms included brief and automatic episodes of sexual excitement or an orgasm-like feeling, lasting 10 to 60 seconds, with a frequency ranging from one to four or more times per day. The episodes might be associated with tingling feelings in the genital area but not always with penile or clitoral engorgement. These episodes were not necessarily unpleasant, but they could be ego-dystonic and could trigger shame and anxiety, especially when they occurred without sexual stimulation in public scenarios.

Other potential clinical features of SSRI-induced hypersexuality have been noted. Episodes may occur as early as 2 weeks into treatment, and in cases where there is a quick and prominent antidepressant response that could occur sooner than 4 weeks after initiation of SSRI medication (8, 14). There

are no other signs of mania or hypomania could explain the hypersexuality (4, 5, 14). In some cases, the propensity for such episodes occurred in those with preexisting neurologic conditions, including stroke, or in those that had undergone radiation therapy (3, 10, 13). In other cases, the hypersexuality episodes were accompanied by yawning (9, 11, 12). Intriguingly, citalopram and escitalopram have not been independently associated with heightened sexual desire or arousal or with automatic orgasm, but only with clitoral priapism (15) and spontaneous erection (16) and ejaculation (16, 17). Yanik (4) reported a case of spontaneous orgasms initiated by venlafaxine, which persisted after the venlafaxine was switched to citalopram. It is worth noting that in Yanik's report, the patient eventually ceased drug treatment because of the side effects and started electroconvulsive therapy, after which she recovered from both hypersexuality and depression.

The mechanism of SSRI-induced hypersexuality is unclear. Up-regulation (which can be induced by brain injuries or neurologic conditions) of serotonin receptors (5-HT<sub>2</sub>) has been suggested as having the main role in enhanced sexual stimulation (13). This may explain only a portion of the cases with preexisting brain organicity, e.g., stroke (3, 13). The co-occurrence of yawning and spontaneous orgasms, which can occur in opioid withdrawal, raised the hypothesis that endogenous opiates may decrease with fluoxetine, explaining the sexual side effects (12, 18). Overall, it has

been suggested that abnormal increases in central serotonergic neuronal activity may underlie the hypersexual side effects caused by SSRIs (10). Further studies are required to understand the pathophysiology.

It appears that SSRI-induced hypersexuality may be a distinct entity, with characteristic clinical features. It is important for clinicians to identify this unique side effect, be aware of the range of the SSRI sexual side-effect spectrum, and differentiate it from an antidepressant-induced mood switch. Management of hypersexuality induced by SSRIs should involve psychoeducation, to reassure and destigmatize this phenomenon by informing patients of the existence of this side effect in order to alleviate possible anxiety and guilt. Second, in most cases, the hypersexuality diminished when the SSRI doses were decreased or the medication was discontinued; some of the patients also benefited from switching medication (14, 16, 17) or substituting other treatment modalities, e.g., ECT (4). For patients whose hypersexuality continues despite a switch to other antidepressants, it may be worthwhile to rechallenge with the original SSRI that elicited significant treatment response (as reported in our case), because the sexual side effects may not recur.

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The authors confirm that details of the case have been disguised to protect patient privacy.

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## KEY POINTS/CLINICAL PEARLS

- Although less common than hyposexuality, hypersexuality is a potential sexual side effect of selective serotonin reuptake inhibitors (SSRIs) that warrants monitoring and management.
- Hypersexuality associated with use of SSRIs should be differentiated from iatrogenic mood switch and from mania-hypomania symptoms resulting from underlying bipolar disorder.
- SSRI-induced or SSRI-associated hypersexuality could be clinically characterized by increased sexual desire or ego-dystonic sexual hyperarousal and automatic orgasms.
- Consider decreasing the dose of, discontinuing, or switching the SSRI associated with hypersexuality or consider neuromodulation as an alternative management.

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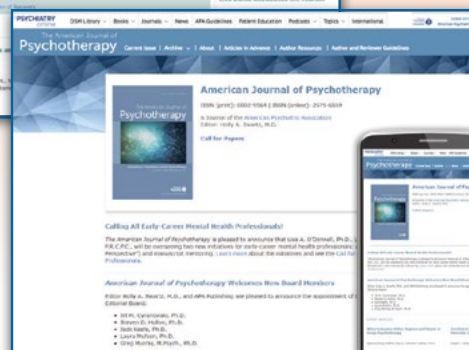
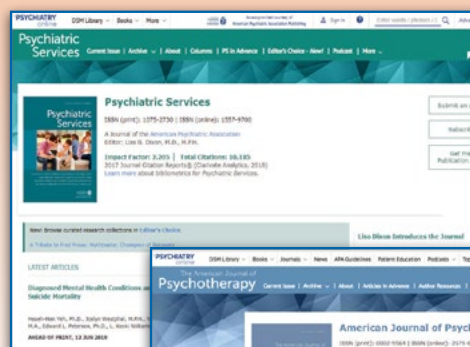
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