

## Sexual Disorders in Females with Bipolar Disorder

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### Abstract

Two or more attacks of hypomania, mania, depression, or mixed episodes, interspersed with euthymic intervals, constitute bipolar disorder (BD). Among the leading causes of disability globally, BD is a major concern. Among all mental health illnesses, sexual dysfunction is underestimated and more common in the general population compared to those with mental health issues. The purpose of this article is to provide a comprehensive overview of the sexual abnormalities and behaviors that are often seen in bipolar female patients. Final thoughts: Sexual dysfunctions and abnormal behaviors were more common in women with BD. Manic episodes are associated with increased hazardous sexual conduct in people with BD. Additionally, it was mentioned that couples' sexual pleasure is negatively impacted by hypersexuality during manic episodes and hyposexuality during depressed episodes, and this effect typically continues into the times between episodes. On the other hand, sex may be linked to negative emotions rather than diminished desire during depressed periods. Individuals with mental health illnesses have a greater chance of sexual difficulties damaging personal interactions and quality of life.

**Key words:** Bipolar disorder, Sexual disorders, Females.

### 1. Introduction

Two or more attacks of hypomania, mania, depression, or mixed episodes, interspersed with euthymic intervals, constitute bipolar disorder (BD). Among the leading causes of disability globally, BD is a major concern, causing problems with thinking and doing daily tasks, which in turn affects one's social and professional life significantly [28].

While coming into one's own sexual identity is a common occurrence in late adolescence and early adulthood, BD often begins around the same time. When people grow up in a healthy sexual environment, they are better able to make their own decisions about their sexual health and have satisfying sexual relationships, both of which improve people's quality of life [50].

Among all mental health illnesses, sexual dysfunction is underrecognized and more common in the general population compared to those with mental health issues [64].

It seems that sexual health is under-discussed and even taboo in clinical practice, since neither health care practitioners nor patients initiate conversations about it. In order to enhance the sexual health and quality of life of persons with BD, it is important to have a better knowledge of the potential links between sexual health, dysfunction, and the disorder as well as daily living and relationships [50].

This study aims to highlight multiple sexual abnormalities and behaviors linked with bipolar female patients.

### 2. Bipolar disorder

Bipolar disorder is a recurring chronic condition marked by swings in emotional state and energy. It is one of the primary causes of disability in young people, leading to cognitive and functional impairment and elevated mortality, notably death by suicide [36].

Bipolar disorder impact >1% of the worldwide population. Bipolar I disorder has an estimated lifetime frequency of 0.6% and bipolar II disorder of 0.4%. According to the Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5) criteria, some studies have shown higher rates; for instance, bipolar I disorder has a lifetime prevalence of 2.1% and a worldwide 12-month prevalence of 1.5% [23,76]. While both sexes experience about the same frequency of bipolar I condition, women are more likely to suffer from bipolar II. Bipolar disorders occur in childhood, with a mean age of onset of 20 years [36]

A thorough clinical evaluation is used to diagnose bipolar disorder; where available, additional information from third parties, such as family members, is also taken into account. There is currently no biomarker (such as a genetic test) that can be used to diagnose, predict, or evaluate the effectiveness of therapy for bipolar disorder. According to Table 1 [57], the DSM-5 provides an operational description of bipolar disorders.

**Table (1)** Criteria for diagnosing bipolar disorder and associated disorders according to the DSM-5 [57]

	Description
Bipolar I disorder	Diagnosis requires at least 1 true manic episode with or without episodes of depression or hypomania
Bipolar II disorder	Diagnosis requires at least 1 hypomanic episode AND 1 major depressive episode in the absence of any lifetime history of mania
Cyclothymic disorder	2 years (1 in children and adolescents) of hypomanic and depressive symptoms that fall short of meeting DSM criteria for either mood state
Substance/medication-induced bipolar and related disorders	A disturbance in mood that develops during or soon after substance intoxication or withdrawal
Bipolar and related disorders due to another medical condition	The disturbance is a direct pathophysiological consequence of another medical condition
Other specified bipolar and related disorders	Symptoms that fall short of meeting criteria for bipolar I or II disorder (eg, short hypomanic episodes, below-criteria hypomanic symptoms with major depression, hypomania without major depressive episode, cyclothymic symptoms occurring less than 2 years [1 in children and adolescents])
Unspecified bipolar and related disorders	Diagnosis used until a more specific diagnosis can be obtained (ie, limited information, emergency department setting)

### 2.1. Treatment of acute manic episode:

Pharmacological therapy: Although nonpharmacological therapies may be used in individuals with treatment-resistant and severe mania, it is the cornerstone therapy for acute mania. The United States Food and Drug Administration (FDA) first authorized lithium for the treatment of acute manic episodes. Mood stabilizers and antipsychotics used together may be more effective than either drug alone, particularly in cases of severe mental illness [68]. Among the currently available medicines, olanzapine, risperidone, and haloperidol seem to possess the most favorable profile. As a result, anti-psychotic medications are usually the best option for short-term clinical treatment, yet when long-term pharmacological treatment is in the cards, a medicine like lithium would be a superior choice [35].

Acute manic episodes, particularly in individuals with refractory manic episodes, violent behaviors, and/or psychosis, may also be treated with electroconvulsive therapy (ECT), either alone or in combination with pharmaceutical therapies [91].

One meta-analysis [17] found that cognitive-behavioral treatment (CBT) reduced the intensity of manic episodes.

### 2.2. Treatment of acute depressive episode:

Pharmaceutical therapy: Only three antipsychotic medications—olanzapine, quetiapine, and lurasidone—have been authorized for bipolar depression by the FDA, despite the fact that people

with bipolar disorder spend a greater amount of time in depression than in mania or hypomania. Here are three combinations that have been approved: olanzapine fluoxetine, quetiapine lurasidone, and lithium valproate (either quetiapine or lurasidone). Reducing the intensity of depressive symptoms in individuals with bipolar disorders was achieved more effectively with some therapies compared to placebo. These treatments included anticonvulsants (such as divalproex and lamotrigine), olanzapine monotherapy, and combination lithium and lamotrigine therapy [43]. The results showed that quetiapine with lamotrigine was more effective than quetiapine alone. Trials in children and adolescents with bipolar disorder have shown strong outcomes in acute depression with lurasidone, an FDA-approved therapy for bipolar depression in adults [4].

Techniques that do not include the use of pharmaceuticals include electroconvulsive therapy (ECT), deep brain stimulation (DBS), vagus nerve stimulation (VNS), lifestyle changes, and psychotherapies [22].

Both unipolar and bipolar depression, as well as treatment-refractory depression, respond well to electroconvulsive therapy (ECT). In individuals with treatment-resistant bipolar depression, CT had a much higher responder rate compared to algorithm-based pharmaceutical therapies [91].

Psychotherapy, including cognitive behavioral therapy (CBT), interpersonal and social rhythm therapy, mindfulness-based CBT, family-focused therapy, dialectical behavior therapy, and

psychoeducation, may be helpful in controlling bipolar depression, but only as an additional treatment.

**2.3. Maintenance therapy :**

Prompt pharmaceutical treatment, psychological therapy, and lifestyle changes are necessary for long-term management [91].

When combined with psychosocial therapies, pharmacotherapy (often a mood stabilizer on its own or in conjunction with an antipsychotic or antidepressant) may lessen the likelihood of relapse, increase treatment adherence, and shorten hospital stays [84].

**3. Sexual dysfunction in females**

In (DSM-5), sexual dysfunctions, gender dysphoria, and paraphilic disorders are all included as sexual disorders. In all cultures, racial groups, and genders, sexual disorders may manifest [1].

**3.1. Normal female sexual function**

Figure 1 displays the results of clinical and empirical investigations that have elucidated sexual response cycles, with a focus on adult women from North America and Europe who do not report any sexual problems. There is a varied sequence that women describe that combines mental and physical reactions during sexual activity [87]. Three hundred and thirty-five premenopausal North American

women, ranging in age from 42 to 52, were surveyed for baseline data from a longitudinal study<sup>15</sup>. The women were asked whether they had engaged in sexual activity with a partner in the past six months for reasons such as to express love, for pleasure, because their partner wanted to, to relieve tension, or because they were either not interested, too tired, or had physical problems (either with themselves or their partner). Figure 1 shows the sexual response cycle, which demonstrates these results [33].

**3.2. Female Sexual Dysfunction (FSD).**

Desire, arousal, orgasm, or sexual discomfort are all potential symptoms of the diverse range of disorders that make up FSD [63]. FSD affects women of all ages, and the endocrinology of getting older makes it worse. Influence is often nuanced. Symptoms of FSD might show as seemingly unconnected emotions, which can have a negative impact on relationships at home, in social situations, and at work. When a woman has any issue with her sexual response cycle that is outside of her typical range of functioning, we say that she is experiencing female sexual dysfunction. The qualitative character of female sexual function makes it more difficult to provide a universal definition of female sexual dysfunction. One woman's normal could be another's abnormal. Female sexual pathology is a spectrum that includes sexual dysfunction [29].

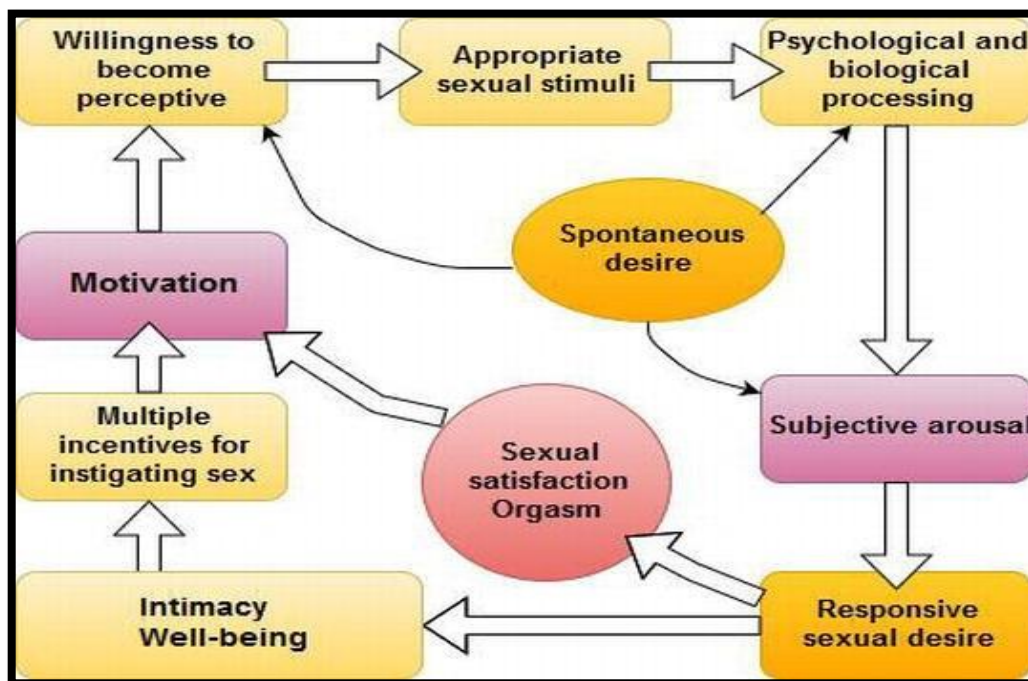


Fig. (1) The female sexual response cycle is shown in Figure 1 as a nonlinear model. [33].

### 3.3 Paraphilias

Paraphilias are sexual desires, impulses, fantasies, or intense behaviors that include unusual items, actions, or settings that persist and occur often. Although paraphilia is not inherently pathological, it may develop into a disorder if it causes suffering, distress, or functional impairment to the lives of those afflicted or others. In the DSM V, eight different types of paraphilia are described, including pedophilia, voyeurism, exhibitionism, sexual sadism, sexual masochism, frotteurism, fetishism, and transvestic fetishism [83].

Any sexual contact between a patient or offender who is at least sixteen years old and a victim who is at least five years younger than themselves is considered pedophilia [30]. Pedophilic disorder has a far lower incidence rate in females, with the DSM-5 stating that it affects 3% to 5% of the male population [9]. The act of watching another person undress or engage in sexual activity while they are unaware is known as voyeurism [5]. The fact that voyeuristic disorder has a lifetime incidence of 12% in men and 4% in females, according to the DSM-5, indicates that it is a prevalent issue. While men are more likely to commit crimes, there are certain girls that fit the profile of a criminal [9].

One definition of exhibitionism is the practice of seeking sexual fulfillment by exposing one's genitalia to an unsuspecting third party [30]. Although offenders sometimes commit several crimes on various occasions, the DSM-5 reports a prevalence of 2% to 4% [21]. Assaulting another person's mental or physical well-being for the sake of sexual gratification is known as sexual sadism [67]. Sexual sadism disorder has a frequency of 2% to 3% according to the DSM-5 [45].

The practice of sexual masochism involves obtaining pleasure via subjecting oneself to psychological or physical torture and/or humiliation [19]. Bondage, punishment, sadomasochism, and submissive behaviors were reported by 2.2% of males and 1.3% of females, according to the study [9]. To touch or rub against someone without their permission is to engage in voyeurism [30]. About 30% of the population has engaged in behaviors that may be classified as frotteuristic, according to prevalence surveys [54].

Among the most popular non-living things used for sexual pleasure in fetishism are shoes and underwear [30]. Those who engage in transvestic fetishism find sexual satisfaction by dressing as members of the other sex [3]. While 3% of men in the DSM-5 report becoming sexual stimulated by wearing clothing associated with the other gender, this is far less prevalent among women [27].

### 3.4. Hypersexuality

The DSM-5 was updated to include hypersexual disorder as a new sexual condition [47].

Hypersexual condition, according to the proposal's detractors, is a medical manifestation of ethical and religious bans on pornography, intercourse outside of committed partnerships, and high-frequency sex [11]. It is believed that 2% to 6% of the population experiences hypersexuality. Some of the potentially harmful outcomes of hypersexuality include STDs and unwanted pregnancies [17].

### 3.5. Gender Identity Disorder (GID)

A person with (GID) has a strong and ongoing sense of belonging to the other sex. They see themselves as "a soul in a wrong body"—victims of a biological accident, if you will. Research on the true incidence of GID is limited and likely underreported. It's also true that more and more people are turning to endocrine treatments for their GID. Statistics show that transsexuality affects 6 out of 100,000 persons globally; it is more frequent in males (1 out of 30,000), while women (1 out of 100,000) have a lower frequency [90].

## 4. Sexual disorders in females with bipolar disorder

Even for those of us without bipolar disorder, sex plays a significant role in our daily lives. However, as complicated as bipolar disorder is, maintaining a good sexual relationship might be much more so. Behaviors might range from very sexually active times to times when desire and function are significantly reduced, depending on the person. A person's capacity to sustain a long-term relationship may be affected by this great degree of variety. [72].

### 4.1. Influence of bipolar disorder on sexuality

*Mania and hypersexuality:* One of the most well-known symptoms linked to manic or hypomanic episodes is hypersexuality. Decreased inhibitions and an increased desire for unlawful sex characterize this condition, which is described as an enhanced demand for sexual fulfillment. A sex addiction may develop when sexual activity becomes an obsession in and of itself [72].

*Risky sexual behavior:* During manic or hypomanic episodes, women with bipolar disorder were more likely to engage in dangerous sexual activities compared to women with other mental diagnoses and males with bipolar disorder [65]. People who misuse parenteral drugs or who suffer from mental illness are more likely to engage in risky sexual conduct, which increases their risk of contracting STIs such as hepatitis B and C, herpes, *Treponema pallidum*, and *Neisseria gonorrhoeae*. Sexually risky behaviors include: having more than one sexual partner, having one-night stands, having sex with someone who is known to be HIV positive, using drugs or prostitutes, having sex with someone who is gay or bisexual, having sex for money or drugs, not using condoms or only using them

sometimes, injecting drugs, sharing needles, and having sexual relations while under the influence of alcohol or psychoactive substances [40].

People with bipolar disorder may sometimes engage in excessive masturbation (Drake, 2021).

*Hypersexual disorder* may be influenced by changes in DNA pathways in the brain and the hormone oxytocin, according to one research [12]. Life stresses may worsen bipolar disorder symptoms, and people with the disorder may also be more likely to resort to unhealthy coping mechanisms when faced with stressful situations. Smoking, masturbation, and theft are examples of pleasurable-seeking activities that are more common among bipolar patients as a way to cope with stress [60].

*Issues with sexual performance and depression:* During a depressive episode, a person may have feelings of sadness, anxiety, or despair. Hyposexuality, defined as a lack of sex desire or near-absence, is another symptom that may develop in a person with bipolar disorder. Symptoms of hyposexuality include a total lack of desire in having sex, feelings of physical unattractiveness or undesirability, and physical tiredness, all of which make having sex difficult [72].

#### 4.2. Effects of sexual dysfunction on bipolar disorder

Therefore, sexual dissatisfaction may impact BD progression and functioning. In addition, stress may cause episodes in borderline personality disorder (BD), and one type of stress that might induce episodes is sexual dysfunction [15].

#### 4.3. Effect of medications on sexuality

Several studies have shown that lithium has a deleterious effect on sexual function [31,25], despite the fact that it is considered the first-line therapy in bipolar disorder. Compared to non-lithium users, patients on lithium report far fewer sexual encounters, fantasies, desires, pleasures, and satisfactions, with 30% attributing these side effects to lithium use [59].

*Anticonvulsants:* The levels of testosterone, androstenedione, and dehydroepiandrosterone sulfate (DHEAS) in the blood may rise if you take valproate [66]. Period problems and polycystic ovarian syndrome are more common in women using this medication because of the rise in testosterone levels [52]. Valproate has been associated with decreased sexual desire and anorgasmia in bipolar women [89]. Hypogonadism, amenorrhea, and diminished sexual function and desire are side effects of carbamazepine that may be linked to lower levels of testosterone, progesterone, and estrogen [62]. Although anorgasmia and

retrograde ejaculation are seldom reported side effects of oxcarbazepine, the drug is often not linked to changes in hormone levels or sexual dysfunction[59].

*Antipsychotic drugs:* When it comes to males, antipsychotics may cause erectile dysfunction, ejaculatory failure, and loss of libido. When it comes to women, it often causes menstruation problems, dry vagina, lack of desire, and orgasmic dysfunction [80]. Haloperidol and thioridazine are examples of first-generation antipsychotics, which are older medicines that are known to produce a variety of sexual dysfunctions. It is often believed that antipsychotic-associated SD is caused by hyperprolactinemia, which occurs when the tuberoinfundibular pathway's D2 receptors are blocked. Risperidone and earlier antipsychotics are known to induce hyperprolactinemia (HPRL) in a significant number of individuals (up to 100% to some extent) [6].

*Antidepressants:* In both sexes, the desire, arousal, and orgasmic stages of sexual activity may be negatively impacted by antidepressant-induced sexual dysfunction. Concerns with sexual desire(72%), sexual arousal(83%), and orgasm (42% of women who use antidepressants report this side effect)[16,32]. Some studies have shown an 80% incidence of erectile dysfunction caused by selective serotonin reuptake inhibitors (SSRIs) [44]. It is believed that antidepressants cause sexual dysfunction in part because they activate post-synaptic serotonin (5-HT)<sub>2A</sub> receptors in the central serotonergic system. The opposite may be true for the effects of dopamine and noradrenaline agonism on arousal and sex desire [46].

#### 4.4. Management

Since mental illness is the leading cause of sexual dysfunction in women, curing the underlying mental illness should be the first priority. To establish remission with pharmacotherapy, it is important to utilize the lowest effective dosage and choose medications that are not sexually neutral [8].

Medications with a reduced frequency of sexual adverse effects (Table 2) or those that may assist cure medication-induced SD are the two most common approaches to treating patients with this side effect. Other pharmacologic approaches include reducing the dosage, waiting for the side effects to go away on their own, or prescribing intermittent drug vacations (two to three days without medication before sexual activity) to patients [20]. Evidence suggests that non-enzyme-inducing anticonvulsants such as oxcarbamazepine and lamotrigine may be more effective than enzyme-inducing ones like valproate. [52].

**Table (2)** A list of medications and their antidotes for SD that have a good profile [20].

More Favorable SD Profile	Antidote
<b>Treatment of antidepressant-induced SD</b>	----
Bupropion	Bupropion
Vortioxetine	PDE-5 inhibitor
Mirtazapine	Mirtazapine
Vilazodone	----
Desvenlafaxine	----
Agomelatine	----
Moclobemide	----
Nefazodone	----
<b>Treatment of antipsychotic-induced SD</b>	----
Aripiprazole	Aripiprazole
Quetiapine	PDE-5 inhibitor (men only)
Ziprasidone	----
Clozapine	----
Olanzapine	----

Medications that have level 1 evidence to support that they either have a more favorable SD profile (known to cause less sexual adverse effects) or are effective at treating the sexual adverse effects caused by other medications when used in an adjunctive role. In making treatment choices, managing the primary psychiatric symptoms should always take priority.

**Abbreviation: PDE-5, phosphodiesterase type 5. • Medications with level 1A (highest level) evidence.**

#### **Adding a Medication to Reverse Sexual Dysfunctions:**

**Aripiprazole:** The reversal of hyperprolactinemia is the probable mechanism by which aripiprazole alleviates the sexual side effects of antipsychotics, as mentioned before [73].

**Vortioxetine plus bupropion:** Reversing SSRI-induced dysfunction may be achieved by adding bupropion [81].

The FDA has authorized the use of flobanserin to treat premenopausal women who have diminished libido. Not only is it an antagonist of 5-HT<sub>2A</sub> receptors, but it also functions as an agonist of serotonin 5-HT<sub>1A</sub>. By doing so, it enhances dopamine's excitatory effects while decreasing serotonin's inhibitory ones [77].

The serotonin-blocking characteristics of Buspirone, particularly its 5HT-2 antagonistic actions, are responsible for the drug's action mechanism [86].

Among the phosphodiesterase-5 (PDE5i) inhibitors is sildenafil. When it comes to treating SD caused by antidepressants, they have the strongest proof. Increased blood flow to the corpus cavernosum of the clitoris, vagina, and labia minor improves FSD, and sildenafil citrate is one of many phosphodiesterase type 5 inhibitors that do this. With a focus on desire, orgasm, and lubrication, sildenafil has the potential to enhance all areas of FSD [63].

**Psychological treatments:** After meds have been fine-tuned, individuals with anxiety and depression may benefit from psychological treatments that help them cope with negative

thoughts, poor self-esteem, and the physical symptoms of elevated sympathetic nerve activity. Cognitive behavioral therapy (CBT) and mindfulness-based cognitive therapy (MBCT) are foundational treatments for arousal and desire dysfunctions in women's sexual dysfunctions, and they have also shown promise in treating anxiety and depressive disorders [7].

**Cognitive Behavioral Therapy (CBT):** By teaching relaxation techniques, addressing avoidance behavior, and restoring or improving sexual functioning, CBT may help women overcome biased attitudes, both during and outside of sexual activity, such as erroneous negative self-critical ideas about their sexuality [39, 34].

Western medicine is increasingly using mindfulness-based treatments, such as MBCT, for a variety of conditions, including but not limited to: depression, anxiety disorders, chronic pain, ADD/ADHD, and cognitive decline. Mindfulness training includes non-judgment, acceptance, and non-reaction to the feelings, thoughts, and bodily sensations experienced in the here and now, as well as enhanced concentration and attention and the capacity to dispel distracting ideas. Consequently, women's awareness and acceptance of their bodily sensations grows, cognitive distractions become less impactful, and negative judgments they hold no more are believed and ruminated over as their mindfulness abilities improve. Recent research has shown that women who have low levels of desire and arousal may benefit from therapy, as compared to both a waitlist control and their sexual function before treatment [14].

In sex therapy, partners take turns engaging in sensate concentration exercises, which are a sequence of planned, gradual, non-demand pleasuring activities in which they engage in sensual and, eventually, sexual touches, caresses, and kisses [71]. Help each other out by pointing out what makes them happy, both vocally and nonverbally [70]. A common component of sex therapy is the development of skills to enhance partner communication and the promotion of erotica exploration [71].

*Physical therapy:* Pelvic muscle physiotherapy can help reduce sexual pain in two ways: first, by reducing the hypertonicity of the pelvic muscles, which can be painful on its own; and second, by helping the patient desensitize to the pain that is associated with the therapy, so that it no longer feels as scary. A mindfulness-based approach to physical treatment has shown to be [78].

## 5. Conclusion

Increased frequency of sexual dysfunctions and behaviors was seen in women with BD. Manic episodes are associated with increased risky sexual behavior in people with BD. Additionally, it was mentioned that couples' sexual pleasure is negatively impacted by hypersexuality during manic episodes and hyposexuality during depressed episodes, and this effect typically continues into the times between episodes. On the other hand, sex may be linked to negative emotions rather than diminished desire during depressed periods. Sexual dysfunction is more common among people with mental health illnesses, which may negatively affect their relationships and overall well-being.

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