



## Review Article

### Sexual Dysfunction: Overview of Neurological Diseases and Depression

Nasrin Abolhasanpour <sup>a</sup>, Amirreza Naseri <sup>b,c</sup>, Sakineh Hajebrahimi <sup>a,d</sup>, Leila Vahedi <sup>e</sup>, Fatemeh Rahmati <sup>a</sup>, Hanieh Salehi-pourmehr <sup>a\*</sup>

<sup>a</sup>Research Center for Evidence-based medicine, Iranian EBM Centre: A Joanna Briggs Institute (JBI) Center of Excellence, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>b</sup>Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>c</sup>Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>d</sup>Urology Department, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

<sup>e</sup>Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

#### Abstract

Sexual expression is dependent on physiological and psychological systems, and it is one of the most complex aspects of human life. Neurological disorders can alter the processing of sexual stimuli. Previous studies investigated that up to 85% of women with multiple sclerosis (MS), 43% of Parkinson's Disease (PD) or other neurological diseases have a degree of sexual dysfunction (SD). The release of neurotransmitters such as glycine, gamma-aminobutyric acid (GABA), glutamate, serotonin, and norepinephrine levels may have altered in various neurological diseases. Furthermore, many physical complications of neurological disorders and several psychological disorders such as depression are common in these patients. The current evidence showed that 40% of spinal cord injury (SCI) patients experience depression after the injury. Depression is a serious and debilitating disorder and has various negative consequences for physical health and sexual function.

Moreover, the involvement of neurotransmitters in several different body's functions has an impact on sexual behaviour in both sexes. Serotonin has a critical role in sexual activity. Also, depression is a direct risk factor for worsening SD. This review discusses the SD in patients with neurological disorders like SCI, PD, Cognitive impairments, and MS, with an especial focus on depression-induced SD.

**Keywords:** Sexual dysfunction, Neurological diseases, Depression.

#### Correspondence

Hanieh Salehi-pourmehr  
Research Center for Evidence-based  
medicine, Iranian EBM Centre: A Joanna  
Briggs Institute (JBI) Center of Excellence,  
Tabriz University of Medical Sciences,  
Tabriz, Iran.  
Tel/Fax: +984133342219  
Email: [poormehr@yahoo.com](mailto:poormehr@yahoo.com)

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#### Introduction

Sexual expression is dependent on physiological and psychological systems, and it is one of the most complex aspects of human life [1]. Sexual dysfunction (SD) describes in many ways in which a person is unable to engage in sexual intercourse as he or she wishes. It affects approximately 43% of women and 31% of men and occurs in any phase of the sexual response cycle, such as excitement, plateau, orgasm, and resolution [2]. Four categories of SD, including desire, arousal, orgasm, and pain disorders demonstrated in patients with sexual disorders [3]. Both physical/medical and psychological conditions can trigger problems in sexual function. Emotional/behavioural problems, marital status, lifestyle, spouse satisfaction, aging, low economic level, depression, anxiety and stress, education level, diabetes, hyperlipidemia, cardiovascular disease, and high blood pressure are among the common cause of SD [4].

Furthermore, neurological disorders can exert remarkable effects on the alteration of the processing of sexual stimuli [5]. Neurological diseases like spinal cord injury (SCI), Parkinson's disease (PD), traumatic brain injury, and multiple sclerosis (MS) have a critical impact on sexual function. Previous studies investigated that up to 85% of women with MS, 43% of PD or other neurological diseases experience some degree of SD with the following complications: decrease or loss of libido, decreased lubrication, orgasmic difficulties, dyspareunia, and sexual satisfaction [6].

The quality of personal relationships, especially sexual relationships, has a significant impact on the self-esteem of patients and consequently on the quality of life [7]. Given the importance of SD in patients affected with neurological diseases, this issue has often ignored by health care providers. Therefore, these individuals should give more attention to any

physical, psychological, and emotional changes after different neurological diseases [8]. The releasing critical neurotransmitters (NTs), including glycine, gamma-aminobutyric acid (GABA), glutamate, serotonin, norepinephrine (NE), may be altered in various neurological diseases [9]. Any alteration in production, release, reuptake, breakdown, or reception of different NTs and also affinity of their receptors leads to neurologic or psychiatric complications like depression [10]. Besides many physical difficulties induced by neurological diseases and even several psychological disorders such as depression, are common in these patients. The current evidence showed that 40% of SCI patients experience depression after the injury [11]. Depression is one of the most common and complex mental disorders of our decade that affects people's lives in different nations, ages, social and cultural groups [12]. According to the WHO statement it is estimated that over 300 million people (about 4.4% of the world's population) suffer from depression [13]. In depression, hypoactivity of several monoamines, especially norepinephrine (NE), dopamine (DA), and serotonin (5-HT), has been demonstrated in the midbrain [14]. In PD patients, 45.5% of men and 54.9% of women had depressive symptoms, and 11% of men and 15.7% of women reported the major depression disorder [15]. Depression is a debilitating disorder and has various negative consequences for physical health, and most importantly, on sexual function [16].

Regarding the involvement of NTs on the whole of the body functions, their effects on sexual function are undeniable. Serotonin is one of the critical NTs in depression and has a role in sexual activity. Also, depression is a direct risk factor for worsening SD [17].

Although there is an association between depression and SD, it is not clear, which is the precedent condition. Besides, despite the association between neurological disorders, depression, and SD, it is not clear, which is cause or effect. This review discusses the SD in patients with neurological dysfunctions include SCI, PD, cognitive disorders, and MS, with an especial focus on depression-induced SD.

### **SD in Spinal Cord Injury**

SCI is a life-threatening condition that can significantly disrupt a person's relationship with his or her spouse, siblings, and even children. After gaining the skills of self-care and control of urination and defecation and skincare, the most crucial issue for a person with SCI is adapting to the problems caused by sexual issues. In this regard, the patient experiences periods of sadness, dissatisfaction, and loss of self-confidence. SCI can have negative effects on sexual function by affecting physiological factors (disorders of the vascular-nervous system-endocrine glands) and psychology (decreased self-confidence and changes in self-image). Furthermore, SCI leads to neurogenic bladder dysfunction (NBD) [18, 19], which has a consequent effect on depression [20]. The location, extent, and severity of the lesion affect the rate of SD. Three spinal segments have the most effect on sexual function: the T11-L2 sympathetic, the S2-S4 parasympathetic, and the somatic centers [21, 22]. Injury to the medial region of the second and fourth sacral vertebrae causes a reactionary erectile dysfunction (ED) that is involuntary.

Erection in these people is more in the form of mental erection. Injury to the 10th thoracic vertebrae and the second lumbar vertebrae causes mental ED, and these individuals are more likely to be stimulated by reactive erections [23].

According to recent studies, sixty percent of men with SCI need the use of erection enhancement [24]. The most common type of SD in men with SCI is ED. The inability to achieve and maintain a proper erection to receive completely satisfying sexual intercourse is the sexual needs of both sexes. The second most frequently observed disorder in men with SCI is ejaculation disorders. The capacity to achieve ejaculation depends on the location and extent of the nerve damage. Reversible ejaculation to the bladder instead of the urethra and the excretion of semen are other types of ejaculation disorders seen in these patients. Eighty percent of men with SCI are at reproductive age, and 18% of them encounter infertility problems; However, a systematic review of the literature found phosphodiesterase-5 (PDE5) inhibitors as an effective and safe treatment for EDs secondary to SCI [25].

Women are less likely than men to experience SCI, and also the effect of SCI on sexual function in women is less. Although women may have a normal sexual function after SCI [26], it is estimated that 59% of women reported at least one SD after SCI [27]. Sexual satisfaction in women with SCI decreases with age. The most common disorders that patients complain of include disorder in the lubrication of the genital tract [28]. Contraction and the presence of sensitive areas can make it torturous to maintain a proper posture during sexual activity. In this regard, it recommends that individuals take a position that feels most comfortable. The use of urinary catheters during intercourse reduces defecation problems during sexual intercourse. Also, despite the lack of a menstrual cycle, ovulation may occur, which can lead to pregnancy. Therefore, it is recommended that contraceptive methods be followed and implemented with special care in these women [29].

Sixty percent of people with SCI suffer from depression, and 20 to 25% of them show severe depression. Fatigue, depression, pain, and stress have a negative impact on sexual desire. It should be noted that even conversely, SD can be a sign of depression. In people with SCI since childhood, abnormal muscle contractions, urinary tract infections, and pressure sores can harm sexual function [30, 31]. Table 1 represents the characteristic of SD in SCI patients.

### **SD in Parkinson's Disease (PD)**

SD in Parkinson's disease (PD) is a progressive neurological disease, the mean age at the beginning is 55, and its incidence elevates with age, from 20/100,000 to 120/100,000 (from 55 to 70 age) [37]. PD is the second most common neurological disorder, also the first most common motor disorder [38]. These patients are characterized by a gradual onset of tremors in the limbs and head at rest, muscle stiffness, decreased mobility, and loss of balance, all of which progressively worsen and can interfere with speech and gait. So that the person will lose the ability to do simple daily tasks [39]. Although PD considers as a movement disorder, other non-motor disorders, and autonomic dysfunction

n like anxiety, constipation, sleep disorders, depression, and sexual dysfunction (SD) have also been observed [40] It demonstrated that psychiatric disorders, such as anxiety and depression likely precede several years before motor manifestations of PD [41].

PD is related to some chemicals in the brain that is related to depression that depleted (chemicals such as serotonin, norepinephrine, and dopamine) [42]. That’s why a lot of medical research shows that PD is more likely to cause depression than other chronic diseases [43, 44].

**Table 1.** Characteristic of sexual dysfunction in SCI patients.

Characteristic	Explains
<b>Erection</b>	is associated with two spinal segment
<b>Parasympathetic</b>	in sacral segments, S2–S4 is responsible for reflexogenic erection
<b>Sympathetic nervous systems</b>	situated in T11–L2 segments of the spinal cord, which is responsible for psychogenic erection, activated by various stimuli from sense organs like eye, ear, nose, and tongue.
<b>Ejaculation</b>	is under the control of the sympathetic, parasympathetic, and somatic nervous system
<b>Orgasm and lubrication</b>	Orgasm is achieved in 50% of women with SCI at the level of T12–L1 injuries, and <17% can achieve it with level S2–S5 injuries.
<b>Psychogenic</b>	The area of the spinal cord responsible for psychogenic erections has located at T11–L2. When a spinal cord injury is above this level, the message from the brain cannot get through the damaged part of the spinal cord. Stimulation of the sympathetic nervous system can lead to a partial erection but not more effective for penetration.
<b>Reflexogenic</b>	The ability to get a reflex erection controlled by nerves found in the lowest part of the spinal cord (S2-3-4). Reflex erections from touch are possible in most men with an injury at T10 or above.
<b>Spontaneous/Nocturnal</b>	Some men after SCI may still get spontaneous erections during the night or in the morning.
	The genital reflexes are completely stopped or decreased below the level of the lesion.
	<b>lesion is below L2</b> The sympathetic nervous system is intact, and stimulation can lead to penile swelling and lengthening without rigidity
	<b>lesion above T11</b> Rigidity can be obtained for penetration.
<b>Spinal shock phase</b>	<b>lesion between L2-S2</b> Mixed erection occurs
	<b>Upper motor neuron lesion</b> Spontaneous erection occurs
	<b>lesion above or at T6 level</b> Autonomic dysreflexia (sudden severe headache, flushing, sweating, and cardiac arrhythmias during sexual arousal) [26, 32-36].

However, about 45 percent of patients with PD have mild to moderate symptoms of depression [45]. Mild depression causes a person to feel sad, frustrated, and indifferent, which may be temporary and a natural reaction to frustrating situations in daily life [46]. At the other end of the spectrum, depression can cause a severe state of frustration, low self-esteem, or a desire to hurt oneself, and accompanied by behavioural changes such as insomnia, anorexia, lack of interest in daily activities, and social isolation [47]. Both anxiety and depression are most common in patients with PD [48]; consequently, this condition may affect libido and sexual performance in the patients or partners. Lipe et al. in the study on investigating the sexual function of patients with arthritis and male PD patients found an increase in sexual problems related to the disease severity and depression in both groups [49].

SD is one of the most common disorders in patients with PD in both men and women [50]. The prevalence of SD in adult patients with PD is higher than in the general population. Gender differences in sexual problems demonstrated in PD. ED, premature ejaculation (PE), hypersexuality, and difficulty in reaching orgasm are predominant SD in men. In contrast, low sexual desire, urination during sex, loss of lubrication, and difficulty in arousal and reaching orgasm are the most predominant SD disorders in women. [51, 52]. Both genders encountered with loss of desire and dissatisfaction in their sexual life [52].

PD complications such as motor disorders, body pain, and especially depression may affect sexual function in PD patients [53, 54], while in the case of autonomic dysfunction related to SD, little evidence was reported [50]. Impaired sexual function in PD could appear due to aging, psychogenic factors, or organic factor, which categorized as drug-induced, diseases related, neurogenic, vascular, and hormonal [55]. Several previous studies have shown that the key area in the brain responsible to penile erection and also sexual drive, regarding dopaminergic neurons, are located in the hypothalamic area particularly the paraventricular nucleus and medial preoptic area (MPOA) [56, 57]. Furthermore, it was reported that depression in PD patients might occur due to the damage to the coeruleus/subcoeruleus complex and most importantly disruption of serotonergic afferent pathways [58, 59]. The ED often initially can be observed in men with multiple system atrophy [60]; this issue amplifies the possibility of the existence of a central mechanism in men with PD involved in SD. However, several studies have been demonstrated the critical role of the central dopaminergic system in the total etiology of ED [49, 61, 62]. In the central nervous system (CNS), the mesolimbic dopaminergic system considers as the major reward pathway. The last pathway accompanied by a mesolimbic dopaminergic system, with projection from the ventral segmental area to the nucleus accumbens and also to other limbic areas [63]. The mesolimbic dopaminergic pathway by producing the pleasure sensation responds to both natural and artificial rewards. This response creates by encoding the memory of pleasurable cues, and via promoting various motor or behavioural responses that prepare the situation for conducting the individual towards the pleasure source [64]. For instance, activation of this pathway was observed during sexual activity,

breastfeeding in neonates, or in performing pleasant tasks in individuals [62]. In addition to motor disorders in these patients, depression, and cognitive impairment strangely affect the quality of life [65]. With 3.5% percent of prevalence [66], hypersexuality (which is a rare complication of treated PD) is the other side of this coin. Recent studies found that dopamine agonists are more commonly lead to hypersexuality compared with levodopa [67].

### SD in Cognitive Impairments

Deteriorations in memory, thinking, behaviour, and the ability to perform everyday activities, which is defined as dementia, can also cause SD. With about 50 million people affected, dementia is considered pandemic in aging societies [68]. With the progression of the disease, changes in sexual behaviour may occur. Several complications, like cognitive deterioration, worsening judgment, and personality changes, may have a relation with changes in sexual attitude and behaviour in demented patients. Alzheimer's disease (AD) is the most cause of dementia, but cognitive declines are a common problem in MS and PD, too [69]. AD in 50% of cases is associated with depression [70]. A study on American society in older adults with lower cognitive scores found the rate of sexual activity was 50% and 20% in men and women, respectively [71], but the level of sexual problems was high [72]. These patients still have their sex drive, but cognitive issues due to AD may lead to some new acts, which is different from what they do before. Hypersexuality can be one of these changes [73]. It observed that there is a correlation among reduction of testosterone levels in men and lower sexual desire and higher rates of SD [74] but a consistent correlation not reported in women [75].

### SD in Multiple Sclerosis

MS, as the most prevalent demyelinating disease, affected around 2 million people all around the world [76]. Unlike PD and AD, a wide range of MS patients are young adults, and its prevalence is about three times higher in women comparing to men [77]. SD is a common problem among MS patients. A study of 271 MS patients found that about 63% of women with MS suffer from SD [78]. Reduced libido, difficulty in achieving orgasm, reduction in the tactile sensations originating from the thigh and genital regions, and vaginal dryness with consequent dyspareunia are the most common described SD in women, and ED is the most prevalent complaint of SD in men. Female dyspareunia also can be one of these problems. SD in patients with MS is categorized into three distinct parts. Primary SD is defined as the direct effect of MS on the CNS, which leads to sensory, motor, or autonomic dysfunction that arises problems in achieving and maintaining an erection, vaginal lubrication, and orgasm. Secondary SD, like spasticity and contractures, fatigue, also bladder and cognitive dysfunction, affected sexual response indirectly. The tertiary SD occurs by physiological, social, and cultural issues. Depression-induced SD is one of these problems [79]. The rate of depression among MS patients is near 30.5% [80], which affects every aspects of patients' quality of life, including the sexual function.

### conclusion

It seems that due to the importance of sexual relations in daily life and its impact on mental health and personal life, the need to expand studies in this field and thus improve the complications of these disorders continuously felt. The concern of SD following neurological disorders should be known by clinicians, so this part of patients' lives should not be neglected by them. A wide range of treatments from oral medications to psychological consultants is available for these problems, so they are only effective interventions when the problem is diagnosed and given importance by the healthcare providers. In most cases, patients didn't discuss these problems, and the neurologist should ask about their sexual lives to reach a compressive treatment plan and boost patients' quality of life the best as possible.

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### Conflicts of Interest

The authors declare no conflict of interest.

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