Parkinson's disease and sexuality

Sexual dysfunction rarely threatens physical health but can take a heavy psychological toll. Sexual dysfunction is common in Parkinson's disease, occurring as a non-motor manifestation of the illness but often compounded by secondary problems relating to physical disability, psychological factors and medication effects.

Parkinson's disease, typically characterized by tremor at rest, akinisia, rigidity and postural abnormalities, is the most common neurodegenerative disease after Alzheimer's disease. The prevalence in the UK for Parkinson's disease is approximately 100–200/100 000 of the population increasing above the age of 50 years to 500/100 000 (1 in 200), giving estimates of around 100 000 patients with Parkinson's disease in the UK.

Introduction

Research and care in Parkinson's disease has tended to focus on the more obvious motor aspects of the illness. The diagnostic hallmark in terms of pathology remains the presence of Lewy bodies and Lewy neuritis in the substantia nigra and pars compacta accompanied by selective neuronal degeneration of melanised dopaminergic neurones projecting to the striatum.

However, nigral damage is accompanied by widespread extranigral pathology and involvement of other neurotransmitter systems. Indeed, Lewy body pathology first appears within lower brainstem regions involved in olfaction, sleep homeostasis and autonomic function (Braak et al, 2003). Subsequent upward spread reaches midbrain, basal forebrain and eventually the cortex, with particular involvement of the motor, limbic and autonomic systems.

Parkinson's disease patients experience a broad range of non-motor symptoms reflecting the underlying pathology (Chaudhuri et al, 2006b). The mixture of motor, autonomic, cognitive and psychological problems would predict difficulties with sexual function, yet this aspect is commonly ignored by clinicians and has had scant research attention (Lambert and Waters, 1998; Castelli et al, 2004). While this may stem in part from hesitancy to intrude on an intimate subject it may also reflect an assumption that these patients, being generally middle-aged or elderly, are less interested in sex. However, Mulligan et al (1988) highlighted the possibly unchanged role of sexual wellbeing in the elderly. Parkinson's disease can also begin in early or mid-adult life, when an active sex life is the norm.

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Prevalence and nature of sexual dysfunction in Parkinson's disease

Studies differ in the frequencies and type of problems reported, depending on the Parkinson's disease patient population studied (Wermunth and Stranger, 1995). Although impaired function is the commonest reported problem, sexual function can increase following neurosurgery (Mendez et al, 2004), and in response to medication especially dopamine agonists. While this can be positive, hypersexuality out of proportion to premorbid sexual profile can rarely occur with potentially devastating consequences. Hypersexuality is particularly likely in the context of high dose dopamine agonist therapy and prescribing clinicians need to ensure adequate monitoring and make sure patients are aware of this potential as well as other possible side effects (Uitti et al, 1989; Heaton, 2002).

In general, female patients with Parkinson's disease are less likely to report problems with sexual function (36–41%) than men (65–81%) (Longstreth and Linde, 1984; Brown et al, 1990). Females have a lower response rate to questions relating to sexuality, suggesting possible gender differences in how comfortable people are in discussing such matters. However, female patients are more likely to be living alone (36% *vs* 6%) (Macht et al, 2005) and may consider the topic less relevant.

Sexual dysfunction increases with age in the general population (Avis, 2000). In a comparative study, 60% of men with Parkinson's disease had sexual dysfunction as compared with 37% of healthy age-matched control subjects (Koller et al, 1990), supporting the presence of disease-specific factors in Parkinson's disease.

Neuroanatomy of sexual function and dysfunction in Parkinson's disease

Sexual function involves a complex interplay of behavioural, psychological and physiological processes. Dopaminergic and noradrenergic neurotransmission in the pontine and mesencephalic ascending reticular activating systems are thought to be important for activating libido via the limbic and paralimbic structures and cortex. The thalamus, basal ganglia, hippocampus, amygdala and hypothalamus are similarly believed to be involved in both libido and arousal. The paralimbic cortex, frontal lobes and non-dominant temporal lobe may also be involved (Arnow et al, 2002; Temel et al, 2006).

Within the CNS, the brain sends both activatory and inhibitory projections to the spinal centres driving the sexual organs (McKenna, 1999).

Impaired desire and arousal would be expected in the context of dopamine depletion in Parkinson's disease while denervation hypersensitivity offers a possible theoretical explanation for dopaminergic drugs increasing libido to premorbid levels or beyond.

Historically, the prosexual effect of dopamine agonists in human was first suggested by the observation of increased sexual activity in some patients with Parkinson's disease treated with dopamine agonists (Uitti et al, 1989; Courty et al, 1997), and several reports confirmed the ability of levodopa (the precursor of dopamine) to induce erections (Bowers et al, 1971; Goodwin, 1971; O'Brien et al, 1971). Dopaminergic drugs stimulate the D2 receptors, which in turn induce the release of oxytocin from the paraventricular nucleus from the hypothalamus; this stimulates erection, the final vascular response being mediated primarily via the sacral parasympathetic nerves (Melis et al, 1994; Drolet et al, 1996).

Causes

The issues surrounding sexuality in Parkinson's disease are complex, involving an interplay between the effects of the illness on the physiology of the sexual response and medication effects, as well as indirect, secondary problems. Problems are classified by gender in *Table 1* and issues of particular relevance to Parkinson's disease listed in *Table 2*.

There are commonly several interacting problems and management requires careful analysis with specific questioning to elicit where the difficulties lie.

Libido and arousal

Is sexual interest maintained? Questions should enquire about fatigue, self esteem and mood. The sexual partner may also be experiencing disturbed sleep, low mood and fatigue as part of their altered role as care giver – and may simply feel they have neither the energy nor interest left over to maintain a sexual relationship. Are there any issues relating to a mismatch of interest between partners?

Table 1. Types of sexual dysfunction in Parkinson's disease

Men	Erectile dysfunction
	Difficulty reaching orgasm
	Ejaculatory failure
Women	Vaginismus
	Altered pattern of sexual arousal
	Altered pattern of orgasm
	Decrease vaginal lubrication
Common to both sexes	Loss of sexual desire or satisfaction
	Decreased sexual arousal
	Medication side effects
	Hypersexuality (rare)

Table 2. Factors affecting sexual functioning in Parkinson's disease

Autonomic dysfunction
Motor fluctuations
Disease progression
Disease severity
Depression
Medications
Dissatisfaction with physical appearance (mainly women)
Involuntary loss of urine
Sleep disorders

Physical or motor problems

Are there problems relating to immobility and/or difficulty with fine finger movements needed to caress a partner. During sexual arousal, tremor is frequently enhanced which makes sexual activity more difficult. Muscle rigidity and akinesia contribute to difficulties in performance. After orgasm, muscle rigidity may increase for some 30–60 minutes, whereas tremor and abnormal movements quickly return to baseline. Given the increased tone of striated muscle associated with idiopathic parkinsonism, increased tone in the perivaginal muscles could produce a clinical picture of vaginismus (Brown et al, 1990). Sleep disorders experienced by Parkinson's disease patients may result in reduced opportunities for spontaneous sexual activity as partners sleep in separate beds. Fear of incontinence or concern about perineal hygiene can also be a problem.

Autonomic factors

Autonomic dysfunction, resulting in erectile disorder, is a common cause of sexual dysfunction in male Parkinson's disease patients. In addition, drooling, excessive sweating or excessive facial oiliness may interfere with self esteem and the perceived attractiveness of the partner with Parkinson's disease (Brown et al, 1990). Erectile and ejaculatory failure occurs in 20–60% of patients with Parkinson's disease (Singer et al, 1992) with absent nocturnal and morning erections. Many affected men are unable to ejaculate and women have difficulty achieving orgasm. The pathophysiology for this is unclear but is presumably cerebral as the peripheral nerves involved in orgasm are somatic rather than autonomic.

Effects of medication and co-morbidity

Concurrent co-morbidity, for example diabetes mellitus, and the medications for these conditions may impair sexual function (*Tables 3* and *4*). Excess smoking and alcohol may also be relevant. Antidepressants are a particular problem as depression is part of the symptomatology of Parkinson's disease and often needs treatment.

Table 3. Co-morbidities which may affect sexual function

Diabetes mellitus
Depression
Heart failure
Chronic renal failure
Hypothyroidism
Stroke
Rheumatoid arthritis or osteoarthritis
Benign prostatic hyperplasia

Table 4. Medication which may affect sexual function

Antihypertensives	Beta-blocker
	Alpha-blockers
	Calcium channel blockers
	Angiotensin-converting enzyme inhibitors
	Thiazide diuretics
Antidepressants	Tricyclic antidepressants
Antiandrogens	
Others	Spironolactone
	Cimetidine
	Digoxin

Management

The multifactorial basis of sexual problems in Parkinson's disease requires a broad approach which takes account of the physiological effects of the illness as well as medication related and other secondary problems.

General treatment principles

Many Parkinson's disease patients are reluctant to raise these issues with their doctor, and may not connect the symptoms to the disease at all. Health-care providers should include questions regarding intimacy and sexuality when evaluating the symptoms and quality of life. Sensitivity is required to recognize when this is not appropriate and patients' reluctance should be respected. A non-motor symptom questionnaire can allow the topic to be raised in a non-intrusive manner (Chaudhuri et al, 2006a). There are useful treatments, both medical and non-medical, for many of these problems.

The Parkinson's disease nurse specialist may be able to provide counselling and advice to patients and partners. This may be best done in the patient's home rather than in the clinic. Referral to an urologist, gynaecologist or sex therapist can help identify issues affecting sexuality and help rule out non-Parkinson's disease related problems.

Treatment options

Non-drug measures should be explored first and are complementary to any medications which may then be added. Reduced sexual arousal may benefit from a psychological approach and couples may need help to explore different ways of providing sexual satisfaction in the form of foreplay and touch. Vibrators may provide a faster stimulus promoting orgasm, sometimes producing sufficient penile firmness to preclude the need for phosphodiesterase inhibitors. Vacuum erection devices can be helpful for erectile enhancement.

Medication

These include medications that can be taken orally, administered through penile (intracavernosal) injection, transurethral administration or topically (*Tables 5* and *6*).

The phosphodiesterase inhibitors block cyclic guanosine monophosphate (cGMP) degradation via phosphodiesterase inhibition and by this mechanism enhance the effect of nitric oxide in inducing smooth muscle relaxation and erection (Boolell et al, 1996) but are contraindicated in patients already receiving nitrates, and in patients with ischaemic heart disease, who have recently had a stroke and who have a previous history of non-arteritic anterior ischaemic optic neuropathy.

Sildenafil citrate is safe, efficacious and significantly improves sexual function in men with Parkinson's disease and erectile dysfunction (Zesiewer et al, 2000; Hussain et al, 2001). Sexual satisfaction was improved as well as satisfaction with sexual desire, ability to achieve and maintain erection and ability to reach orgasm, but no observed effect was seen on premature ejaculation and intensity of sexual desire. The main problem is postural hypotension hence the need for monitoring postural blood pressure.

Apormorphine, a potent dopaminergic agonist useful in the treatment of motor fluctuations, is able to induce erections (Hughes et al, 1990; Steiger et al, 1992). In view of additional benefits to Parkinsonian motor symptoms, subcutaneous apomorphine has been suggested as an alternative to sildenafil in treating patients with Parkinson's disease and erectile dysfunction (O'Sullivan, 2002). Sublingual preparations of apomorphine have been developed for this indication (Dula et al, 2001).

Erections have been reported as a side effect of treatment with the dopaminergic agent ropinirole (Fine and Lang, 1999).

Antiandrogens have been considered in the management of hypersexuality presenting with high sexual desire, as reducing the dopaminergic medication might not be an option in all cases. Spironolactone acts mainly by suppressing conversion of testosterone to dihydrotesteterone, competing with the testosterone receptor and reducing luteinizing hormone and thus testosterone production (Cole and Cole, 1981). Medroxyprogesterone has been used as a useful antiandrogenic agent.

Other behaviour-altering agents that are not dopamine antagonists might be considered, including clozapine and remoxipride.

Potential side effects must be discussed and patient consent obtained.

Conclusions

Issues of sexuality are overlooked or avoided in patients with Parkinson's disease. Sexual problems in Parkinson's disease encompass impaired sexual function in the majority of patients or hypersexuality in a minority. Although sexual dysfunction rarely threatens physical health, it can significantly impact on relationships and quality of life. BJHM

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Table 5. Drugs for erectile dysfunction in men

Class of drugs		Mechanism of action
Phosphodiesterase type 5 inhibitors	Sildenafil (Viagra) Vardenafi (Levitra) Tadalafil (Cialis)	Enhances inflow of blood in the corpus cavernosum
Dopaminergic agents	Apomorphine Ropinirole	Centrally release of oxytocin from the hypothalamus which stimulates erection
Postaglandins	Alprostadil	Works by enhancing blood flow
Androgens	Depo-Testosterone Delatest Andro-gel Testoderm Testim	Facilitates the action of phosphodiesterase type 5 inhibitor
Alpha-adrenergic blockers	Phentolamine	Blocks action of adrenalin in the penis (the major inhibitor of erection) leading to erection

Table 6. Drugs for sexual dysfunction in women

Class of drugs	Mechanism of action
Oestrogen	Improves low interest and/or arousal disorders
Progesterone	To oppose oestrogen's adverse effects
Androgens (controversial)	Improves sexual desires
Phosphodiesterase inhibitors	

KEY POINTS

- Sexual function in patients with Parkinson's disease has received little attention.
- While sexual dysfunction rarely threatens physical health, it can affect quality of life.
- Sexual problems are either sexual dysfunction in the majority of patients or hypersexuality out of proportion to the premorbid state in a minority of patients.
- Sexual dysfunction in Parkinson's disease is a multifactorial disorder.