Treating Parkinson's disease: Dopamine dysregulation syndrome and impulse control

Parkinson's disease is a progressive degenerative disorder, resulting from the degeneration of the dopaminergic neurons in the substantia nigra and the connections in the basal ganglia. Consequently, the depletion of dopamine results in the core motor features of bradykinesia, muscle rigidity, stooped, flexed posture, and repetitive tremor of the limbs. The progression of the disorder is also associated with cognitive disturbances, including depression, bradyphrenia (slowing of thought processes), visuo-spatial and attention difficulties, and dementia. Other non-motor complications include autonomic dysfunction and sleep disorders. Langston (2006) refers to the term ‘the Parkinson's complex’ to describe a broad range of the clinical features found in Parkinson's disease patients. In the early stages of the disease the first line of treatment is with dopamine replacement therapy (DRT), often used in conjunction with dopamine agonists to prolong the efficacy of levodopa therapy.

In the last 10 years, there has been a growing body of evidence describing a range of abnormal behaviours involving dopamine replacement medication and impulse control. It was first observed by Giovannoni and colleagues (2000) who described a complex of behavioural disorders they termed hedonistic homeostatic dysregulation syndrome. Today this is generally known as dopamine dysregulation syndrome (DDS). In July 2007 the first international meeting devoted to DDS was held in Toronto and brought together over 100 clinicians and researchers to examine a variety of topics and research (Stacy et al, 2008). The representatives came from a range of clinical specialties including neurology, psychiatry, addiction and neuroscience and the success represents the growing interest in this disorder.

DDS is characterized by a compulsive and escalating pattern of dopaminergic medication use, which is disproportionate to the degree of immobility experienced in ‘off’ states in clients with Parkinson’s disease. There is an increasing craving for DRT, even when the results will be an increase in severe and disabling dyskinesia. Evans (2008) suggested that are parallels between the pulsative reward mechanisms seen in addiction disorders, and DDS in respect of medication use.

Following diagnosis, the probable first indications of the developments of the syndrome would be frequent demands for medication increases early in the course of the treatment, coupled with reports of tolerance to the beneficial effects of DRT. The demand for, and escalation of, medication use, will often be made in the presence of quite severe motor fluctuations. Changes in personality may be noticeable with evidence of disorganized thinking and poor judgment. Impaired insight and a lack of self-awareness are prominent features (Lees, 2008).

A key associated feature is the development of impulse control disorders (ICDs) (Table 1), including pathological gambling, hypersexuality, punding (repetitive and excessive, aimless behaviour), excessive shopping and compulsive eating. The consequences of such behaviour can be devastating for people with Parkinson's disease and their carers. The consequences include breakdown of close personal relationships, financial and legal difficulties, inappropriate sexual behaviour, and violence and aggression.

The challenge is for the health professions to develop methods of early detection of DDS so that changes to the

**Abstract**

Dopamine dysregulation syndrome (DDS) has emerged as a recognized complication of dopamine replacement therapy (DRT) in the treatment of Parkinson's disease. This syndrome is characterized by increased addictive patterns of behaviour in relation to DRT use, and results in impulse control disorders (ICDs), including compulsive gambling, compulsive shopping, compulsive eating, hypersexuality and punding (repetitive and excessive, aimless behaviour). Such symptoms can have devastating social, occupational and financial effects on the patient and the carer. The clinical manifestation of DDS is often not straightforward: the patient may not have the insight to recognize symptoms, and the symptoms of the syndrome do not always occur in a recognized pattern of disease progression and may be expressed individually. Clinical staff may find the assessment of DDS in clinical practice very difficult. It is important to gain evidence from carers, but this may not always be easy due to a sense of loyalty or feelings of guilt and shame. This article aims to describe the syndrome and highlight the psychosocial issues related to DDS, and the medical and surgical management options available, as well as developments in psychological therapies.

**Key words**

- Carers
- Parkinson's disease
- Patients
- Compliance

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Table 1

- Patients
- Compliance
treatment regimen and appropriate follow-up monitoring is put in place to minimize the adverse consequences of this syndrome.

**Symptomatology**

Evidence indicates that there is an overlap of patients displaying DDS and ICD (Stamey and Jankovic, 2008; Wolters et al, 2008). Although DDS is often associated with ICD, both presentations can occur independently. Typically, the development of symptoms of DDS is associated with younger patients with early onset Parkinson’s disease, as well as those who present with disabling dyskinesia and are prescribed dopamine-agonist medication (Lim et al, 2008).

Lees (2008: 1332) also suggested that premorbid personality traits may be indicative of the increased risk of developing DDS, particularly in young male sensation seekers with a premorbid history of smoking and illicit drug and alcohol use. Clinicians should be mindful of these predisposing factors when initiating treatment to warn patients and carers of the potential development and risks associated with DDS. The most frequent ICDs related to DDS are discussed below.

**Pathological gambling**

Gallagher et al (2007) conducted a comprehensive study of the relationship between pathological gambling and Parkinson’s disease. They suggested that pathological gambling can affect up to 8% of patients with Parkinson’s disease who were treated with dopamine agonists. They also suggested that there may be premorbid gambling and impulsive sensation-seeking personality traits, which may play a part in the predisposition of this symptom. There are many modes of gambling available to this patient group, such as casinos, betting shops, fruit machines and the purchase of lottery scratch cards. All of these options, however, historically required the patient to make trips to these premises. The Internet and access to online gambling sites may make access easier and increase the risk of adverse consequences. Carers and professionals should be aware that the manifestation of this behaviour may not always be evident through the normal pathways of gambling, i.e. poker websites, but increasingly through responses to email spam and websites offering unrealistic financial gain.

**Hypersexuality**

There have been many reports of hypersexuality in patients presenting with DDS, and it is more common in males (Evans, 2008). The condition can occur in patients prescribed levodopa and dopamine agonists, and may also be prevalent in those taking subcutaneous apomorphine. The initial manifestation usually consists of an increase in libido, and progresses to inappropriate behaviour such as exhibitionism, solicitation of prostitution and excessive use of premium-rate sex phone lines. Excessive and compulsive masturbation may be a prominent feature. The patient may exhibit increased sexual demands on his or her partner, some of which may be inappropriate and excessive. The episodes of this behaviour are likely to occur when a patient is feeling euphoric after taking large doses of DRT. However, paradoxically during such periods, the patient may develop irrational feelings of morbid jealousy, despair and suicidal ideation (Evans and Lees, 2004). Hypersexuality can, in a few cases, take the form of paraphilia (the repeated, intense sexual arousal to unconventional and socially deviant stimuli) (Fenu et al, 2009: 367) or fetishism. Although rare, this type of behaviour could lead to sexual assault and legal repercussions for the patient.

This behaviour may also lead to problems in a marriage, particularly at a time when the spouse’s role may be changing from that of a partner and lover to that of a carer. This is perhaps an aspect of the syndrome that requires more in-depth investigation than the current literature contains.

**Excessive shopping**

Many patients have reported excessive shopping and compulsive buying. Merims and Gilardi (2008: 276) defined this as ‘the presence of repetitive, impulsive and excessive buying, leading to personal or family distress’. The manifestation of excessive shopping and compulsive buying involves the patient making purchases of goods or services that may be extreme and unnecessary. This behaviour can lead to large amounts of debt as well as large stockpiles of unused purchases in the home. This, of course, may have consequences for the patient’s financial status and on the family environment.

**Punding**

Another impulse-control symptom associated with DDS is punding, which was first described by Rylander in 1972 in relation to amphetamine and cocaine addiction. Presentations of this behaviour include excessive hobbyism, aimless walking or driving, and repetitive purposeless activities that are difficult to disengage from. Examples of the latter often include the dismantling of electrical or mechanical equipment, excessive computer use and compulsive sorting of common objects. When this behaviour is interrupted the patient can experience dysphoria and rage. Bonvin et al (2007) reported two case studies of compulsive singing, which they proposed was another distinct feature of DDS-related punding. As with other

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**Table 1. Impulse control symptoms in dopamine dysregulation syndrome**

- Pathological gambling
- Hypersexuality
- Excessive shopping
- Punding
- Drug hoarding
forms of punding, the behaviour in both cases was reported to bring the patient a sensation of relief and could be controlled for brief periods. However, the resulting frustration led to irritation and aggressive behaviour toward carers. O’Sullivan et al (2007) stated that, although the prevalence of debilitating punding behaviour in Parkinson’s disease may be less than 5%, it is often under-reported and can have serious psychosocial consequences. Additionally, it may be associated with pathological gambling and hypersexuality (Gallagher et al, 2007).

Drug hoarding
Another common behaviour in the syndrome is drug hoarding, whereby the patient seeks to ensure a consistent and increasing supply of dopaminergic medication as a result of craving. Patients develop idiosyncratic and increasingly complex patterns of self-medication. This may lead to dishonest and devious strategies to enable access to increasing amounts of medication, and sometimes to risk-oriented behaviour and aggression. Behaviour may become manipulative, resulting in increased stress on the relationship with carers (Lees, 2008).

Psychosocial implications
There are major implications for quality of life in patients with Parkinson’s disease, particularly in occupational and social functions. Most people with Parkinson’s disease are cared for in their own homes, and the burden of care usually falls on informal carers such as spouses and family members. As with other degenerative diseases such as dementia, it can often be the psychological rather than the physiological changes in the patient that results in increased carer stress (Aarsland et al, 1999).

Schrag et al (2000), in a study designed to assess the quality of life in Parkinson’s disease patients, found that the level of disability and the effects on quality-of-life issues were most prominent in young-onset Parkinson’s. This is exactly the group of patients for whom the risk of DDS is highest. One can therefore conclude that the quality-of-life issues are magnified for this patient group.

Much of the literature has concentrated on the neurobiological theories of the development of DDS. There are, however, case reports and descriptions of the debilitating nature of the syndrome in relation to lifestyle, relationships and finances.

Voon et al (2006) reported a case in which one client lost more than US$100 000 as a result of pathological gambling. In a series of case reports Kurlan (2004) reported higher amounts lost as a result of gambling and additionally these cases resulted in bankruptcy, theft and divorce.

In patients who have developed hypersexuality, many notice financial implications from the use of high-tariff sex phone lines, and monies spent on prostitution and in sex shops. However, possibly the most devastating effect of hypersexuality will be the effect on social and marital relationships. Merims and Gilardi (2008) suggested that the combination of low self-esteem due to motor and autonomous disturbances, combined with limited social activity and paranoid thoughts, may drive the patient to more aggressive and sexually challenging behaviours.

Carers of this patient group must adapt their role of spouse or relative to that of a carer at the initial onset of the disease, which in itself can cause a significant strain to a relationship. With the additional burden of DDS, the carer is likely to find the prospect daunting. Spouses and relatives must struggle to understand such abnormal behaviours, if only because the personality of the patient with DDS shows no relation to the personality of the person they knew before the onset of the illness.

Management issues
Medication management
When clinicians initially identify DDS, the common course of action is to review the medication regimen and employ medication strategies. Clinicians will be mindful of the evidence of the association of dopamine agonists with DDS (Voon and Fox, 2007). Any decrease in dopamine agonists may be counterbalanced by an increase in levodopa, as the patient’s level of mobility will be reduced. However, it is likely that the patient will experience an increase in motor complications.

Concordance may become an issue and medication reduction strategies are fraught with difficulty. Patients with DDS frequently invest a great deal of time and energy constructing complex and frequent treatment regimens for themselves and any attempt to reduce dosage may be met with strong resistance (O’Sullivan et al, 2009). Specialist nurses, physicians and carers should be aware of subtle changes in the personality of the patient. A great deal of emphasis needs to be placed on reports from carers. Particular attention should be paid to indications of increased secrecy and preoccupation regarding dosages, and increasing requests for prescriptions before a scheduled appointment. Additionally, any reports from carers indicating concerns about devious or manipulative behaviour, particularly in relation to obtaining medication, needs to be taken seriously by professionals.

Deep brain stimulation
Deep brain stimulation (DBS) is accepted as an effective treatment for DDS, particularly in the late stages of Parkinson’s disease. The procedure involves the implantation of electrodes into the brain, most commonly to the subthalamic nucleus. The amount of stimulation is governed by a pacemaker controlled by the patient. DBS can reduce the “off” motor symptoms, enabling a postoperative reduction in dopamine therapy. Knobel et al (2008) reported on two cases of DDS when there were beneficial outcomes following DBS, which allowed a reduction in dopaminergic medication. However, DBS procedures are not without risks, including impaired cognitive function, severe psychiatric complications and the risk of suicide following surgery (Lim et al, 2008). Of particular concern are reports of the development of ICDs including pathological gambling following DBS surgery (Smeding et al, 2007).
In a survey of a specialist movement disorder clinic for DBS, Shotbolt et al (2008) found an increased prevalence of DDS and ICDs than in previous estimates by the clinic. The researchers concluded that younger patients with dyskinesia are increasingly likely to be referred for DBS, however this is the group most associated with ICDs and DDS. Given the possible benefits and risks, the role of DBS in such patients requires further exploration.

Psychological and psychosocial management

Methods of psychological and psychosocial management may be related to specific symptomatology. An example might be to encourage the patient with DDS to attend self-help groups, such as Gamblers Anonymous or Overeaters Anonymous. Other types of interventions may include attending addiction or marriage counselling. Families can be encouraged to employ practical measures to manage behaviour, including limiting credit cards, restricting Internet access or installing restrictions to gambling and casino websites. Additionally, it is important to enlist the carers, GPs and pharmacists to manage medication reduction strategies.

Psychosocial treatments, including cognitive behavioural therapy, have been shown to have value in the treatment of impulse control disorders (O’Sullivan et al, 2007) and include approaches to build insight and provide education about the syndrome. Other strategies include handling control of finances to carers, and teaching problem-solving and communication techniques. To help reduce the burden on carers, cognitive behavioural therapy and psychosocial education have been useful in managing Parkinson’s disease patients with DDS (Secker and Brown, 2005). Difficulties in accessing these types of services remain, as they are not readily available in primary care, and access to specialist services can be difficult due to long waiting times.

The Parkinson’s Disease Society, in conjunction with King’s College London, has funded a major randomized controlled study into ICDs and DDS, the ICaDDS study (Brown et al, 2008). The study aims to provide psychological and educational interventions directly to the patient. It includes a specialist care package involving a 12–16 week nurse-led intervention, including cognitive behavioural therapy, psychosocial education and motivational interviewing as an adjunct to routine care (Brown et al, 2008).

Conclusions

Within the past 10 years there has been an emerging body of evidence recognizing DDS in Parkinson’s disease associated with impulse control disorders, particularly in younger patients with early-onset disease. The syndrome results in major psychosocial effects on quality of life, and the financial and social well-being of patients and carers. The first line of treatment of the syndrome is generally medication rationalization. Although this can be effective, it is not without its difficulties, particularly in terms of increased motor problems and concordance issues.

KEY POINTS

- Dopamine dysregulation syndrome (DDS) is characterized by a compulsive and escalating pattern of dopaminergic medication use, which is disproportionate to the degree of immobility experienced in ‘off’ states in patients with Parkinson’s disease
- Typically, the development of symptoms of DDS is associated with early-onset disease
- Within the past 10 years, there has been an emerging body of evidence recognizing DDS in Parkinson’s disease and its association with impulse control disorders
- Although the first line of symptom management is usually medication reduction, there is a growing recognition that psychosocial interventions can be effective

Conflicting evidence around the effectiveness of deep brain stimulation suggests that this intervention has a long way to go before it is recognized as a viable option in the management of this patient group. There is growing interest in psychological and psychosocial approaches to the treatment of this patient group. In the absence of existing randomized controlled trials to provide evidence of the effectiveness of such approaches, the results of the ICaDDS study are eagerly anticipated.

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