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Parkinson disease and impulse control disorders: a review of clinical features, pathophysiology and management

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ABSTRACT

Impulse control disorders (ICDs) are a heterogeneous group of conditions involving repetitive, excessive and compulsive activities that interfere with life functioning. Examples are pathological gambling, compulsive shopping and hypersexuality. Over the last decade, ICDs have become increasingly recognised as being associated with Parkinson disease (PD), with the literature highlighting a link between dopamine replacement therapy and the development of ICDs. Patients who develop ICDs in the context of compulsive anti-Parkinsonian drug use are described as having dopamine dysregulation syndrome (DDS), which is associated with repetitive complex stereotyped behaviours called punding. Case–control and observational studies have further noted that patients with PD who develop ICDs are more likely to have younger-onset PD, a history of alcohol dependence, novelty-seeking personality traits and psychiatric co-morbidities. The pathophysiology of underlying mechanisms is not fully understood, but recent evidence suggests that dopaminergic drugs, particularly dopamine agonists, coupled with changes in reward pathways involving the ventral striatal and related circuitry, may play a role. Neuroimaging studies using positron emission tomography and functional MRI have provided valuable information in this area: patients with DDS have been found to show enhanced dopamine release in the ventral striatum, suggesting functional abnormalities in the mesolimbic networks. Management of ICDs in patients with PD can be challenging, as they may not be aware of a change in their behaviour or may conceal their symptoms to avoid embarrassment. Currently, there is no clear evidence of an optimal treatment. Management is based on a careful balance of dopaminergic drugs with control of the aberrant behaviour, supported by psychological interventions. This review aims to summarise the current literature on ICDs, their phenomenology, epidemiology, clinical features, pathophysiology and management.

Parkinson disease (PD) is a common neurodegenerative condition characterised by classic motor symptoms of bradykinesia, rigidity and tremor. In the last decade, impulse control disorders (ICDs) have emerged as an iatrogenic complication associated with dopaminergic replacement therapy used for treatment of PD.[1 2] The term ICD encompasses a group of psychiatric disorders that commonly involve pleasurable or hedonic behaviours that are performed repetitively and compulsively. Pathological gambling and hypersexuality are the most often published, although compulsive eating and compulsive shopping have also been documented. In patients with PD who develop ICDs with an addictive pattern of dopaminergic drug use, the condition is known as dopamine dysregulation syndrome (DDS). Emerging data suggest that certain groups of patients, such as those with a comorbid psychiatric history, young-onset PD, novelty-seeking traits and alcohol dependence, are more likely to develop ICDs during the course of PD treatment.[1 3] Once aberrant behaviours develop, patients may conceal their symptoms to prevent embarrassment, but consequences can be devastating to the individual and their families, often with financial and social implications. Management requires a supportive and logical approach, as patients may find it difficult to cope with the development of an unwanted behaviour with deterioration in their Parkinsonian symptoms. It is therefore important that clinicians have an understanding of this phenomenon, to aid early diagnosis, referral and optimal management.[4 5] This article aims to provide readers with an understanding of ICDs associated with PD, their clinical features, pathophysiology and management.

IMPULSE CONTROL DISORDERS

ICDs are described in the *Diagnostic statistical manual* (DSM IV-TR) as a group of psychiatric disorders characterised by a failure to resist an impulse, drive or temptation to perform an act that is harmful to the individual or to others.[4–6] They include a wide range of neurobehavioural disorders including pathological gambling, compulsive shopping, hypersexuality, compulsive eating, aggression, jealousy and phobias. As ICDs are a group of heterogeneous conditions, some have not been formally categorised. Conceptually, ICDs have been thought of as "behavioural addiction" and lie within a spectrum of disorders, with ICDs at one end and obsessive compulsive disorders at the other.[7]

Most research on ICDs has focused on pathological gambling. The DSM IV-TR gives a set of 10 criteria to aid diagnosis of pathological gambling; the presence of three of these criteria is suggestive of problem gambling, and the presence of five suggests a diagnosis of pathological gambling.[4–6] Several national surveys have examined the prevalence of pathological gambling as well as other ICDs. For example, the British Gambling Prevalence Survey 2007 documented a prevalence of problem gambling in the UK of 0.6%.[8] This compares with a prevalence estimate of 3% for problem gambling and 1% for pathological gambling in North America.[9] In other ICDs, compulsive

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buying is estimated to have a point prevalence of 5.8% in the USA.[10] Observational studies in the USA have also found a higher rate of ICDs in younger adults and lower rates in older adults.[11 12] Men are more likely to have intermittent explosive disorders, pathological gambling and hypersexuality, and women tend to exhibit compulsive buying.[13 14] Furthermore, a person can develop multiple ICDs, which may also occur with a broad range of other psychiatric disorders, such as alcohol dependence,[15] antisocial behaviour and major depression.[16 17]

The pathogenesis underlying ICDs is still unclear, but evidence from current research proposes that dysregulation of neurotransmitters such as dopamine and interaction of reward pathways involving dorsal striatal and related neurocircuitry may play a role in the development of ICDs.[18 19] Management options derived from studies focusing on pathological gambling support the role of psychiatric therapies, as well as mood-stabilisers and the opioid receptor antagonist, naltrexone.[20 21] Patients with ICDs and co-occurring psychiatric disorders tend to have a poorer treatment outcome than those with ICDs alone.[22]

ASSOCIATION OF ICDS WITH PD

In the last decade, emerging evidence from case series and case–control studies has highlighted an association between ICDs and PD, as well as other neurological disorders such as restless legs syndrome.[2 23] A range of ICDs have been reported in patients with PD, including compulsive eating,[24] pathological gambling,[24 25] compulsive shopping[26] and hypersexuality.[27] The association was initially suggested on the basis of rarely reported clinical observations, but, more recently, case reports and larger studies have linked the development of ICDs with dopaminergic replacement therapy,[24] and observational studies have suggested that ICDs in the setting of PD are more likely to occur in men with early-onset PD who misuse dopaminergic drugs.[28]

Prevalence of ICDs in patients with PD

The prevalence of ICDs in patients with PD ranges from 5.9% to 13.7%, with a point prevalence of ~4%.[29 30] The prevalence rises to 14% for patients taking dopamine agonists, compared with 0.7% for patients taking levodopa alone.[29] In particular:

- the lifetime prevalence of pathological gambling in patients with PD ranges from 3% to 8% in contrast with North American prevalence estimates of 0.42%–2.5%[2 13 16 23 30 31]
- the lifetime prevalence of hypersexual behaviour for patients with PD taking dopamine agonists is 7.2%[3]
- compulsive shopping in patients with PD has been reported as 0.4%–1.5%, in contrast with a higher North American prevalence estimate of 5.8%.[3 10 30]

It should be noted that these figures were obtained in specialist PD clinics, and the prevalence of ICD in the general population of patients with PD may have been underestimated. Patients may also hesitate to acknowledge symptoms or are less likely to be present in the clinic. The extent to which ICDs co-occur with other psychiatric disorders that are observed in association with PD (eg, dementia) has not been systematically evaluated.

DOPAMINE DYSREGULATION SYNDROME

The co-occurrence of ICDs and PD in the context of compulsive medication is known as DDS (box 2).[28 32] The prevalence of DDS in patients attending specialist PD centres is about 3–4%.[28] Patients with DDS have been found to be taking higher levodopa equivalent daily doses (LEDD) of dopaminergic drugs than their counterparts who do not have DDS.[33] Patients develop an addictive pattern of dopamine replacement therapy (DRT) use, where they may request larger doses of dopaminergic drugs at relatively early stages or self-escalate these drugs against their clinician's advice. Patients may also describe a perceived ineffectiveness of drugs and typically identify avoidance of the Parkinsonian "off" periods. As treatment continues, severe drug-induced dyskinesias occur along with socially harmful behaviours. Patients with DDS devote a great deal of time to complex and frequent drug regimens, and any attempt by the doctor to reduce the dose is met with resistance. The pattern of inappropriate dopaminergic drug use in patients with ICDs often resembles that of addiction to psychostimulants.

Punding, previously reported in cocaine addicts,[34] is a particular behavioural disturbance associated with DDS with an estimated prevalence of 1.4–14% in specialist clinics.[35] This term describes complex stereotyped behaviours characterised by an intense fascination with an excessive, repetitive activity, such as handling, examining or sorting through common objects, grooming, hoarding and engagement in extended monologues devoid of content.[36 37] The behaviour may be associated with the patients' hobbies or interest, and activities can include drawing, writing and computer cataloguing.[38] The effects of punding have been reported as soothing and are associated with an intense curiosity. While involved in their chosen activity, punders withdraw into themselves, and become irritable when distracted from their tasks. Punders are normally aware of the inappropriate nature of the behaviour, but do not abandon it. Although punding has been considered by some as a form of obsessive compulsive disorder, in contrast with obsessive compulsive disorder, which is usually preceded by anxiety and distress, punders tend to perform the repetitive, meaningless acts calmly.[39]

CLINICAL FEATURES OF PATIENTS WITH PD WHO HAVE ICDS

The occurrence of ICDs in only a subset of patients with PD suggests that specific groups of patients are susceptible to developing ICDs during the course of the disease, particularly during treatment with a dopamine agonist. As such, identifying

Box 1 Diagnostic criteria of dopamine dysregulation syndrome (DDS)[32]

- Parkinson disease with documented L-dopa responsiveness.
- Need for increasing doses of dopamine replacement therapy (DRT) in excess of those normally required to relieve Parkinsonian symptoms and signs.
- Pattern of pathological use: expressed need for increased DRT in the presence of excessive and significant dyskinesias despite being "on", drug-hoarding or drug-seeking behaviour, unwillingness to reduce DRT, absence of painful dystonias.
- Impairment of social or occupational functioning: violent behaviour, loss of friends, absence from work, loss of job, legal difficulties, difficulties with family.
- Development of hypomania, manic or cyclothymic affective syndrome in relation to DRT.
- Development of a withdrawal state characterised by dysphoria, depression, irritability and anxiety on reducing the level of DRT.
- Duration of disturbance of at least 6 months.

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clinical factors associated with the development of ICDs may allow us to distinguish patients at increased risk, to prompt specific screening and monitoring of such patients.

Evidence has been derived from small case series and observational studies, some of which had no control groups. Nonetheless, they point towards several common clinical features, which provide useful considerations for the clinician. These include young age of onset of PD, impulsive traits, history of alcohol dependence and comorbid psychiatric history, which are discussed below.

Early-onset PD

Patients who develop PD at a younger age are more likely to develop ICDs, particularly during treatment with dopamine agonists.[3 29] Patients with PD who developed pathological gambling were found to be 9 years younger at the onset of their Parkinsonian symptoms (mean age 49 years versus 58 years in a group of 286 patients without pathological gambling).[5] In another study sampling 272 patients with idiopathic PD, 6.6% were found to have one or more ICDs (pathological gambling, compulsive sexual behaviour, compulsive shopping), with 4.0% having an active ICD.

Novelty-seeking personality traits

Novelty-seeking personality traits are characterised by exploratory approach behaviours, excitement derived from novel situations, impulsivity and rapid decision-making. In two separate case–control studies with small samples, the prevalence of these traits was found to be higher in patients with PD taking dopaminergic drugs who had pathological gambling, hypersexuality and compulsive medication use than in matched healthy controls and control PD patients.[5 23] In addition, novelty-seeking personality traits were found to be significant predictors for the development of DDS[5] and pathological gambling in patients with PD.[23]

History of alcoholism

Pathological gambling and compulsive medication use in PD have been associated with a personal or immediate family history of alcohol use, which was found to be an independent predictive factor for development of pathological gambling with dopamine agonists.[5 23 26 40] However, published observational studies on adult twins have suggested that there may be some common genetic ground between pathological gambling and alcohol dependence, and it was observed that up to 42% of gamblers also manifest symptoms of alcohol dependence.[15 41] Therefore, further prospective case–control studies are required to establish the relationship between specific ICDs and alcohol dependence.

Comorbid psychiatric history

Patients with PD with a history of psychiatric disorders are thought to be more susceptible to developing ICDs, especially in the context of DRT. This is supported by a small observational study in patients with PD and ICDs where the rates of comorbid psychiatric diagnosis were found to be higher in the ICD group,[1] and also the observation that higher rates of psychiatric comorbidity and depression were found in non-PD populations with pathological gambling.[42] In addition, both patients with PD and controls with ICDs had higher Geriatric Depression Scale values, although the precise relationship with occurrence of abnormal behaviour is still unclear. Furthermore, antidepressants are often used in the treatment of ICDs, and there is increasing evidence that impulsivity and depression may be associated with low serotonin function, resulting in an imbalance between dopamine and serotonin neurotransmission, although no clinical studies have shown that antidepressants are effective treatment options for this group of patients.[43] Subtle symptoms of depressed mood, appetite changes, irritability and disinhibition were also more likely to be present in the ICD group.[1] There is a further suggestion that a family history of psychiatric illness may also be associated with the development of ICD in patients with PD. This is illustrated by a prospective study of pathological gambling and medication association in PD, which found that, in three out of 10 patients with PD and ICDs, there was a psychiatric history in the first-degree relatives, whereas none of 286 patients with PD without pathological gambling had this feature.[29] However, the data on clinical features have come from case series and case–control studies with small numbers of patients, and more objective methods are necessary to derive a precise relationship between development of ICDs and comorbid psychiatric history in patients with PD.

PATHOPHYISOLOGY

The observation that a patient with PD can develop multiple ICDs suggests some common underlying mechanisms, which could be attributed to the drugs used to treat PD, the pathophysiology of PD, or a combination of these. This section aims to examine the relationship between dopaminergic drugs and ICD development, followed by the neuroanatomical areas thought to be involved in reward-seeking behaviours.

Role of dopaminergic drugs in the development of ICDs

Early case series noted the onset of ICD behaviours co-occurring with the initiation of, or increase in, dopamine agonist medication, and a remission of symptoms with the reduction or cessation of dopaminergic medication,[25 26] although these studies did not take into account the differences in prescribing practice. In more recent studies that systematically assessed drug association of patients with PD and ICDs in comparison with control PD subjects, pathological gambling, hypersexuality and compulsive shopping were strongly associated with the use of dopamine agonist as a class, but not with any specific agonists.[2 3] In addition, total LEDD (calculated for dopamine agonists and levodopa) was found to be increased in association with ICDs overall, but this finding was not uniform across ICDs and has not been shown to predict the presence of an ICD.[2]

A further observation that supports the role of dopaminergic drugs in the development of ICDs is its occurrence in other neurological patient populations for whom these agents are used, such as restless legs syndrome.[44–46] For example, a survey of 70 patients with idiopathic restless legs syndrome treated with one or more dopaminergic drugs found that 7% noted a change in gambling behaviour and 6% reported an increased urge to gamble and an increase in time spent gambling after the use of dopaminergic medication.[47] This finding suggests that it is the drug rather than the pathogenesis of PD that causes ICD development.

The use of dopaminergic drugs may contribute to the development of ICDs by several mechanisms. Firstly, they may interfere with the endogenous physiological pattern of dopamine release and cause excess stimulation of dopamine receptors, resulting in aberrant activity of the neuroanatomical regions involved. Secondly, exogenous dopaminergic stimulation may enhance the shift from goal-directed behaviours to

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stimulus response or habit formation, and chronic stimulation may result in neuronal sensitisation of ventral or dorsal striatal areas leading to behavioural sensitisation (the latter point will be discussed in the next section under Neuronal sensitisation).

Specific dopamine receptor subtypes may be involved. Dopamine D3 receptors (DRD3) are predominantly expressed in ventral areas of the striatum, and their function is involved in reward, emotional and cognitive processes.[48] The relative binding affinities of D3 to D1 or D2 receptors differs between dopamine agonists, and interaction between anti-Parkinsonian drugs and dopamine receptors may lead to the development of ICDs in PD.[1] This theory is supported by an animal study in which related L-dopa administration resulted in ectopic induction of DRD3 receptors in the dorsal striatum, a process that could be responsible for the development of behavioural sensitisation.[49] Moreover, pramipexole and ropinirole are two non-ergot dopamine agonists widely used in patients with PD which have tropism for D3 receptors found in the nucleus accumbens and olfactory tubercle. Pathological gambling and compulsive behaviours are associated with dysfunction of these frontal subcortical regions, suggesting a link between specific dopamine receptors and development of aberrant behaviours.[50] However, the observation of withdrawal symptoms when levodopa is stopped in non-Parkinsonian patients, such as those with a wrong diagnosis, further supports the view that it is the drug rather than the underlying dopaminergic state that leads to the symptoms of ICDs.[51]

Neuronal sensitisation

The diagnostic criteria for ICDs overlap with the diagnosis of drug addiction (DSM IV-TR), and several studies have noted similar behaviours in these two groups. This suggests that proposed theories on drug dependence may be relevant to the pathophysiology of ICDs. To illustrate, Everitt and Robbins[52] postulated that drug-seeking actions, like habits, start out as explicit behaviours (with an initial hedonistic phase), but can become implicit, automatic or overlearned stimulus responses in pathological behaviours that engage the dorsal striatum. This observation, called behavioural sensitisation (increase in behavioural drug effects with repeated exposure) occurs with psychostimulants, particularly with high or escalating doses and intermittent administration, and is associated with neuronal changes in the nucleus accumbens and prefrontal cortex.[53] In addition, aberrant prefrontal cortex functioning, seen in drug misuse, may also be associated with loss of cognitive inhibitory control over prepotent tendencies, resulting in impulsive behaviours.

Another study postulates that drugs of misuse may alter the natural reward processes involving the nucleus accumbens and ventral striatal circuitry.[34] Augmentation of this system by dopaminergic drug intake is thought to cause ''addictive'' effects of these drugs termed ''incentive sensitisation'', a theory proposed by Robinson and Berridge,[54 55] and later supported by evidence from neuroimaging.[4]

Evidence from neuroimaging studies

Functional imaging studies using single photon emission computed tomography (SPECT), functional MRI (fMRI) and positron emission tomography (PET) have provided valuable insight into the neuroanatomy and neurobiology involved in the development of ICDs. Although most studies have been performed in pathological gamblers or healthy subjects, their findings have provided useful information on the pathophysiology of ICDs in patients with PD.

Subjects with pathological gambling have been reported to show reduced activation in the ventral striatal and ventromedial prefrontal cortex in response to reward-related tasks in two separate fMRI studies.[56 57] A further fMRI study observed that, when viewing gambling cues, subjects with pathological gambling showed relatively decreased activity in brain regions involved in impulse regulation (frontal, paralimbic and limbic brain structures) compared with controls.[58] These data are complemented by a PET study with fluorodeoxyglucose on 32 pathological gamblers who showed increased glucose metabolic rates in the orbitofrontal cortex and medial frontal cortex compared with normal controls.[59] Therefore, the temporal changes in activation and metabolism in response to gambling cues may be due to impaired dopaminergic neurocircuitry involved in reward processing. However, connectivity within the dopaminergic circuitry is complex and depends on the balance between D1 and D2/3 receptor stimulation. To illustrate, a PET study in rats showed that a decreased concentration of D2 and D3 receptors in the nucleus accumbens predicted higher rates of cocaine self-administration, supporting the suggestion of neurobehavioural susceptibility to the addiction process.[60] Similarly, the development of ICDs in patients with PD may be due to the interaction between dopamine receptor dysregulation and dopaminergic medication.

In addition, SPECT and PET neuroimaging have provided useful information on the functional neuroanatomy involved in pathological gambling and DDS in patients with PD. In a study using SPECT with technetium-99m, gamblers with PD were found to show significant overactivity in brain areas involved in reward and impulse control, namely basal ganglia, hippocampus, amygdale and insula, suggesting functional abnormalities in the mesolimbic network.[61] Our group conducted a study using PET and [^{11}C]raclopride, a tracer that specifically binds to D2 receptors, to image dopaminergic function of eight patients with DDS compared with eight PD control patients. A two-scan PET protocol was used to calculate the difference in dopamine release from a baseline withdrawal (off drug) state to after an oral dose of levodopa. We found enhanced levodopa-induced ventral striatal dopamine release in the DDS group compared with PD controls. In addition, the sensitised ventral striatal dopamine neurotransmission produced by levodopa in the DDS cohort correlated with self-reported compulsive drug ''wanting'' but not drug ''liking'', even when the effects of the drug became unpleasant. This behavioural change was related to punding. The study further suggests a link between sensitisation of ventral striatal circuitry to compulsive drug use and that the ventral striatum and its circuitry are postulated to mediate a specific reward system called ''incentive salience''. Repeated drug use sensitises the brain reward systems to the drug and its effects. Although the patient becomes tolerant to the effect of the drug, it is compulsively craved even when the pleasurable effect decreases.[28 62] In addition, the behaviour of punding with other drug-induced stereotypes suggests a relationship to plastic changes in the ventral striatum and related neuronal circuits and reward mechanisms.[63 64] Another study using PET with $H_2{}^{15}O$ techniques showed that monetary reward is associated with increased activation in the dopaminergic mesolimbic pathways in normal controls, but these areas failed to activate in patients with PD.[65]

The evidence from different studies indicates that several mechanisms interplay to trigger the onset of ICDs in susceptible patients with PD, and further research is required to establish

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the exact underlying mechanisms that predispose people to the development of these neuropsychiatric complications.

MANAGEMENT OF ICDS IN PATIENTS WITH PD

Management of this patient group presents many challenges for the clinician. Firstly, affected patients may not be aware of their symptoms as an aberrant behaviour or its associations with their PD treatment. If recognised, patients may conceal their symptoms to avoid stigmatisation. Once the problem is identified by the medical team, treatment requires careful readjustment of dopaminergic medication to balance their parkinsonian symptoms with control of the aberrant behaviour. In all cases, management should follow a stepwise multidisciplinary team approach tailored to the individual patient.

This section reviews the literature on management of ICDs in PD, but it is noteworthy that the evidence comes from empirical data and case reports, as there have been no clinical trials to identify efficacious treatments for ICDs in PD, and only in the last few years have small randomised trials of ICDs in general been performed. In addition, there are currently no drugs that are approved by the Food and Drug Administration for the treatment of any of the formal ICDs.

Patient education and identification of susceptible individuals

Levodopa and dopamine agonists remain effective treatments for the symptoms of PD despite the association of DRT with the development of ICDs. However, patients and their carers should be warned of the potential risks of aberrant behaviours before initiation of medication. The media has helped to highlight this through reports of several cases of patients developing ICDs as a result of dopaminergic medication, with litigations against clinicians and pharmaceutical companies.[66] In addition, the British National Formulary has documented pathological gambling, hypersexuality and binge eating as side effects of dopamine agonists, and it is therefore prudent that clinicians advise patients of these potential occurrences.[67]

Identifying susceptible patients for closer follow-up and monitoring can help to prevent the negative effects for the affected individual. Typically, people are ashamed or embarrassed about these behaviours and often will not broach the subject without prompting or direct screening. For example, clinicians should bear in mind that patients with PD who develop ICDs are likely to have younger-onset PD, with a history of alcohol dependence, comorbid psychiatric history and novelty-seeking traits. In addition, early severe dyskinesias (occurring 12–24 months into treatment) may serve as a red flag. Pharmacists can provide drugs in blister packs, and family members can help to supervise medication.[33]

Pharmacological management

In patients with compulsive medication use or who take high doses of DRT, a decrease in dosage or stepwise elimination of medication may reduce the unwanted behaviour. However, patients can experience withdrawal symptoms or a deterioration of their motor symptoms, and this may prove difficult for those with compulsive medication use, as they have an excessive preoccupation with their dosing regimens. Switching to a different class of dopamine agonist may cause a relapse of ICDs. Therefore, close monitoring and a multidisciplinary approach to treatment should be encouraged, and behavioural therapies are receiving empirical support in non-PD populations.[68 69]

There is limited evidence to support the use of drugs found to be useful in the treatment of ICDs for patients without PD, and the reader should be aware of the publication bias concerning the use of psychiatric drugs for patients with PD and ICDs, as no objective clinical studies on treatment have been carried out in this group. Limited double-blind, placebo controlled studies in patients without PD have shown an improvement in pathological gambling with selective serotonin reuptake inhibitors such as fluoxetine and paroxetine, as well as opioid antagonists.[70–72] Case reports have described resolution of hypersexuality in patients with PD and ICD treated with olanzapine or quetiapine coupled with either agonist or levodopa,[72] but further clinical studies on patients with PD and ICDs are required to clarify the effects of these drugs.

Surgical intervention

Deep brain stimulation (DBS) has been performed with various results on patients with young-onset PD who also have DDS or ICD. A study of five patients with DDS showed no improvement after DBS of the subthalamic nucleus.[73 74] In another study, patients with DDS underwent DBS, and their DDS was resolved or dramatically improved.[75] Arduoin *et al*[76] reported an improvement in well-screened patients with PD with pathological gambling after bilateral subthalamic nucleus DBS. However, symptomatic improvements in ICDs coincided with a reduction in DRT, although subthalamic nucleus DBS has been postulated to have a direct effect on the reward-seeking brain circuitry.[77] Other case reports have documented development or deterioration of ICDs after surgery,[30 78 79] and preoperative DDS or ICDs may even be a risk factor for postoperative suicide attempts.[79] Results from surgical interventions are conflicting, and further research is required before surgical options can be recommended as a potential treatment.

Main messages

- The estimated prevalence of impulse control disorders (ICDs) is 6–7% in patients with Parkinson disease (PD). However, the prevalence of ICDs is higher in patients who take dopamine agonist than patients who take levodopa alone.
- ICDs identified in patients with PD are mainly concerned with gambling, sex, shopping and eating.
- Dopamine dysregulation syndrome (DDS) refers to the co-occurrence of compulsive medication use and ICDs in patients with PD, and patients can develop motor stereotypy called punding.
- Among patients with PD, specific clinical features—including young age, novelty-seeking personality features, history of alcohol dependence, comorbid psychiatric history—have been found to be associated with ICDs and DDS.
- Treatments of ICD mainly involve reduction of dopaminergic drugs and engaging family or carers.

Current research questions

- To uncover neurobiological mechanisms underlying impulse control disorders in association with Parkinson disease, using positron emission tomography and fMRI techniques.
- To increase our understanding of the prevalence and treatment of ICDs by robust case–control and longitudinal studies.

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CONCLUSIONS AND FUTURE DIRECTIONS

DRT effectively relieves motor symptoms in patients with PD, but may lead to development of ICDs in some cases. In susceptible patients with PD, neurobehavioural processes and sensitisation of the brain dopamine system mediating reward is thought to cause ICDs and DDS. This can result in a wide range of aberrant behaviours, such as pathological gambling and compulsive eating and shopping. Patients and their carers should be warned of the potential risks of aberrant behaviours before initiation of medication. Management includes reduction of the causative drug, regular monitoring and support.

Further studies are required to establish the extent of the risk of developing ICDs and its correlation with dopaminergic medication in PD, and to improve our understanding of this group of neurobehavioural disorders.

MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AFTER THE REFERENCES)

1. Impulse control disorders

A. Can be resisted
B. Are not performed repetitively
C. Include compulsive sexual behaviours in their formal diagnostic criteria
D. Can develop in patients with PD

2. Regarding diagnosis of DDS

A. Patients are responsive to levodopa therapy
B. Patients tend to take less medication than required to relieve their symptoms
C. Patients can develop mood affective disorder
D. Punding is not an associated behaviour

3. Development of ICDs in patients with PD

A. Has an estimated prevalence of 6%
B. Is thought to be due to changes in the ventral striatal circuitry
C. Changes in dopamine receptors D2 and D3 are implicated in its pathophysiology
D. Chronic dopaminergic replacement in PD can result in a sensitisation effect by influencing reward learning and cognition that is not necessary for development of addictive disorders

4. Regarding clinical features of patients with PD who develop ICD

A. They are less likely to be taking dopamine agonists
B. Patients tend to develop PD at a younger age
C. Previous psychiatric history is an independent variable that predicts development of ICD during treatment for PD
D. Several ICDs can co-exist in patients with PD

5. Management of patients with PD and ICD

A. Deep brain stimulation has been tried for treatment of ICD
B. It is not necessary to warn all patients of risks before starting treatment with dopamine agonists
C. Dopaminergic medication should be reduced if patients develop an ICD during treatment
D. Patients may relapse if their dopaminergic medication is increased again after their ICD has been controlled

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Answers

1. (A) F; (B) F; (C) F; (D) T
2. (A) T; (B) F; (C) T; (D) F
3. (A) T; (B) T; (C) T; (D) T
4. (A) F; (B) T; (C) T; (D) T
5. (A) T; (B) F; (C) T; (D) T

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