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Impulse control disorders in Parkinson's disease

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SUMMARY

Impulse control disorders (ICDs), a group of complex behavioral disorders, occur more commonly in Parkinson's disease (PD) patients than in the general population, with a reported prevalence up to 13.6% in some studies. The most common ICDs reported are pathological gambling (PG), hypersexuality (HS), compulsive shopping and compulsive eating. More than a quarter of the patients with ICDs have 2 or more behavioral addictions. These abnormal behaviors impair activities of daily living and have a negative impact on quality of life of patients and their families. As with many other non motor symptoms in PD, ICDs are frequently under-reported by patients and caregivers and may be under-recognized by the treating physicians. Treatment with dopamine agonists (DA) is the main risk factor for developing ICDs, and stimulation of mesolimbic D3 receptors by DA is thought to underlie their development. The DA effect seems to be a class effect and not specific for any DA. Levodopa can also induce ICDs but much less so than the DAs. The management of ICDs in PD is complex. Modifications in dopaminergic drug treatment are frequently necessary. In some cases alternative therapies such as atypical antipsychotics, antidepressants or deep brain stimulation if motor symptoms become incapacitating after adjustment of dopamine replacement therapy should be considered.

1. Introduction

The term *impulse control disorders* (ICDs), defines a group of complex behavioral disorders characterized by failure to resist an impulse or temptation to perform an act that is harmful to the individual or to others. ICDs are thought to occur more commonly in PD patients than in the general population [1]. They have recently been the focus of considerable interest because of their association with the use of dopaminergic treatment, in particular dopamine agonists (DA), also because their presence has a significant negative impact on the quality of life of patients and their families. As with many other non motor symptoms in PD, ICDs are frequently under-reported by patients and caregivers and may be under-recognized by the treating physician. Other neuropsychiatric problems occurring in PD that may be related to ICD include *dopamine dysregulation syndrome*, an addiction-like state marked by excessive dopaminergic medication use; *punding*, a fascination with meaningless movements or activities and *walkabout*, characterized by excessive wandering [2,3].

2. Epidemiology and risk factors

Reported prevalence rates of ICDs in PD vary considerably ranging from 6% in PD patients not receiving DA and 17% among those on DA treatment [4]. In one study assessing ICDs in 3090 PD patients, the DOMINION (Impulse Control Disorders in Parkinson's Patients Treated With Pramipexole and Other Agents) cross-sectional study [5], the 6-month ICD prevalence was 13.6%. The most common ICDs reported were pathological gambling (PG), with a prevalence of 5%, hypersexuality (HS) (3.6%), compulsive shopping (5.7%) and compulsive eating (4.3%). More than a quarter of the patients with ICDs had 2 or more other behavioral addictions [5].

DA treatment is the primary risk factor for ICD development in PD. Several studies support this association [6,7] and it is also clear from a number of studies and everyday clinical practice that withdrawal of the offending DA typically results in marked improvement in the ICD. In the above mentioned DOMINION study DA treatment was associated with a 2- to 3.5-fold increased odds of having an ICD. ICDs frequency was similar for pramipexole and ropinirole (17.7% vs 15.5%), suggesting that the association between DA and ICDs is a drug class relationship.

Additional variables independently associated with ICDs include male sex, mainly in HS and PG, younger age [5,8], being unmarried, current cigarette smoking, prior personal/family history of alcohol addiction or gambling problems, higher novelty seeking scores and impulse traits [8], a greater incidence of medication-induced hypomania/mania [8], an impaired planning [8], levodopa use [5], and amantadine (PG, HS and buying) [9].

An independent association between levodopa treatment and ICDs has been found [5]. In patients taking a DA, concurrent

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Table 1
Diagnostic criteria for pathological gambling (PG)[a]

A. Persistent and recurrent maladaptive gambling behavior as indicated by five or more of the following:
1. Is preoccupied with gambling (eg preoccupied with reliving past gambling experiences, handicapping or planning the next venture, or thinking of ways to get money with which to gamble)
2. Needs to gamble with increasing amounts of money in order to achieve the desired excitement
3. Has repeated unsuccessful efforts to control, cut back or stop gambling
4. Is restless or irritable when attempting to cut down or stop gambling
5. Gambles as a way of escaping from problems or of relieving a dysphoric mood (e.g., feelings of helplessness, guilt, anxiety, depression)
6. After losing money gambling, often returns another day to get even ("chasing" one's losses)
7. Lies to family members, therapist or others to conceal the extent of involvement with gambling
8. Has committed illegal acts such as forgery, fraud, theft, or embezzlement to finance gambling
9. Has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling
10. Relies on others to provide money to relieve a desperate financial situation caused by gambling
B. The gambling behavior is not better accounted for by a manic episode

[a] American Psychiatric Association, American Psychiatric Association Task Force on DSM-IV [11]. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. 4th ed. Washington, DC: American Psychiatric Association; 2000.

levodopa use increased the odds of an ICD by approximately 50%. While the relation between ICDs and DA therapy is not dose-related, in the case of levodopa only high dosages were also associated with ICDs [5].

3. Clinical manifestations

ICDs are under-recognized in clinical practice. Most patients do not spontaneously offer information about ICD behaviors, either because of shame or because they do not understand that it is related to PD and its treatment. Most common ICDs in PD are PG, HS, compulsive shopping and compulsive eating. Early detection of ICDs is crucial and all patients should be questioned directly about such behavior. A useful tool to detect ICDs can be the Questionnaire for Impulsive-Compulsive Disorders I Parkinson's Disease (QUIP-Current-Short), a validated quick screening questionnaire that when positive should be followed by a clinical directed interview [10].

Pathological gambling (PG): PG is defined as an inability to resist gambling impulses despite severe repercussion on personal, family or professional life. PG is persistent and recurrent maladaptive gambling with tolerance or withdrawal, maladaptive behaviors and consequences (risking significant relationships or employment, turning to others for financial assistance) (Table 1). The more frequent PG modes are slot machines, lottery scratch cards and bingo. PG occurs more frequently during the "on" period [12]. Cultural differences are thought to have a significant impact on prevalence rates and in Far Eastern countries PG prevalence is higher than in Asia [13]. Voon et al. [8] studied the factors associated with dopaminergic drug-related PG in PD. When compared with patients without, those with PG had younger age of onset, higher novelty seeking, a greater incidence of medication-induced hypomania/mania, an impaired planning and personal/family history of alcohol use disorders.

Hypersexual behavior (HS): HS typically entails an increase in premorbid sexual activities as well as an increase in the variety of sexual behaviors. In patients with HS the need for sexual behavior consumes so much money, time, concentration and energy that the patient describes himself as out of control. Intrusive unwanted paraphiliac thoughts prevent concentration on other life demands and are the source of anxiety. Orgasm does not produce satiety in the way it typically does for age mates [14]. HS occurs predominantly in males with relatively early-onset PD, patients with prior history of tobacco or alcohol addiction, and can be associated to other inappropriate behavior or psychotic symptoms [9,14]. HS is associated to treatment with DA alone (including apomorphine) or adjunctive to levodopa, selegiline and amantadine [9] although this last relation is controversial, as discussed below.

Compulsive shopping: This is defined as a maladaptive preoccupation with buying or shopping, or maladaptive buying or shopping impulses, frequent buying of more than can be afforded, items that are not needed, or shopping for longer periods of time than intended. The buying impulses cause marked distress, are time-consuming, interfere significantly with social or occupational functioning or result in financial problems [15].

Compulsive eating: Most frequent clinical presentations are an increase in the food intake dramatically in the setting of new-onset food cravings for carbohydrates, sweets, and/or salty foods; a new-onset binge eating, compulsively eating both larger portions of food at mealtimes and more frequent snacks throughout the day and tendency to compulsively snack or binge in the middle of the night. The consequence of this is an unintentional and undesired increase in the weight and body mass index [16]. Compulsive shopping and binge eating are more common in female PD patients whereas compulsive sexual behaviors have been more frequently reported in males [4,5] (Table 2).

Other symptoms associated with ICDs: Other neuropsychological disturbances such as novelty seeking and impulsivity have been associated with ICDs in PD. Their presence may vary depending on ICD type. Pathological gambling and compulsive shopping, for example, share similarities in higher novelty seeking and impulsive choice as compared with hypersexuality and binge eating. In another study, high scores in depression, anxiety and obsessive-compulsive symptoms have been reported in ICD PD patients [18]. Motor fluctuations are more common in patients with ICDs, and early and severe dyskinesias (within the first 12–24 months) have been considered a warning sign for the development of dopamine dysregulation syndrome or ICDs [13].

4. Pathophysiology of ICDs

A role for dopaminergic stimulation in the development of ICDs has been confirmed by several lines of evidence. Underlying pathological changes occurring in PD probably do not play a major role since ICDs are known to occur in other conditions treated with DA such as restless legs syndrome [19]. While dopaminergic mechanisms are important, not all patients taking dopaminergic drugs develop these behaviors and ICDs probably