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Review

Pathological gambling in Parkinson's disease. A comprehensive review

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ABSTRACT

Pathological gambling (PG) and other Impulse Control Disorders (ICDs), such as hypersexuality, compulsive eating and buying, are often reported in Parkinson's disease (PD). The prevalence of PG is 2.2%–7% in treated PD patients, which is higher than the background population rate. As other non motor symptoms in PD, PG is frequently under-reported by patients and caregivers and may be under-recognized by the treating physicians.

Factors associated with PG include male sex, younger age or younger age at PD onset, personal or family history of substance abuse or ICD, a personality profile characterized by impulsiveness, and treatment with dopamine agonists (DA) more than with levodopa (L-dopa). The DA effect seems to be a class effect and not specific for any DA.

Neurofunctional studies suggest that medication-induced downregulation of frontostriatal connections and upregulation of striatum might combine to induce impulsive behavior. A dysfunction of fronto-subcortical circuits in PD patients with PG is also supported by neuropsychological findings of impaired executive control and monitoring abilities.

Management of ICDs in PD is complex, and until now only discontinuation and/or tapering of DA treatment seem to be an effective management strategy for ICDs in PD. There is no empirical evidence supporting the use of psychiatric drugs for PG such as antipsychotics and antidepressants. Data regarding the effect of deep brain stimulation (DBS), particularly of subthalamic nucleus, on PG and ICDs in PD are still limited and sometimes conflicting since improvement of PG or new onset of PG after surgery have been reported.

1. Introduction

Pathological gambling (PG) is a behavioral disorder characterized by persistent and recurrent maladaptive gambling that can have devastating psychosocial consequences for the person involved and her/his family [1]. Point and lifetime prevalence rates of PG in general population are reported to be as high as 1.4% and 5.1%, respectively, but they seem to increase progressively with the spread of legalized gambling [2].

PG is considered as an impulse control disorder (ICD) that combines impulsive and compulsive features, namely repetitive gambling and impaired inhibition of this negative behavior [3]. Neuroimaging and neuropsychological studies found an association between PG and abnormalities in the prefrontal cortex and subcortico-cortical networks projecting to the frontal cortex [4–6]. Current neurobiological research highlighted both an abnormal functioning of mesolimbic structures and an altered neurotransmitter regulation of the 'reward pathways' in the brain of pathological gamblers [4], particularly of the neurotransmitter dopamine.

As it will be described below, PG is largely more frequent in patients affected by Parkinson's disease (PD) than in the general population. Alteration of dopaminergic transmission in both PG and PD might support common pathophysiologic mechanisms and some clinical overlap of the two conditions. Traditionally, PG has been considered as a side effect of dopamine agonists (DA) treatment in PD [7–9]. However, since only a small proportion of patients treated with DA develop PG and/or other ICDs, we will argue that DA medication can trigger these non motor symptoms in PD patients with specific individual predisposing factors.

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In the present paper we will offer an overview of the most recent advances in the study of clinical, neuropsychological, behavioral, neurofunctional and genetic correlates of PG in PD. Finally, the management of PG in PD will also be reviewed.

2. Prevalence of PG in PD

The prospective PG prevalence (either current or anytime during PD) in a tertiary PD clinic has been reported to vary from 2.2% to 7% (Table 1); such percentages are higher than those reported in general population (see above) and become also higher if one considers "problem gambling" (not clinically relevant gambling behavior). As evident in Table 1, prevalence rates in Caucasian samples [7–13] tend to be higher than those reported in Asian countries [14–17]. This divergence might depend on cultural and ethnic differences [14] (e.g., reluctance to admit presence of PG, availability of legalized gambling, lower DA usage in Asian countries than in Caucasian populations), methodological differences (e.g., different diagnostic criteria or assessment methods), or genetic differences (e.g., variable occurrence of genetic polymorphisms among Caucasians and Asians). However, significant discrepancies in prevalence rates of problem/pathological gambling can be found even between two Caucasians populations (i.e., US and Canadian patients; [7]), thus highlighting that differences among PD populations have not been fully elucidated.

Apart from ethnic and cultural factors, one source for variability in prevalence rates of PG in PD seems to be related to measures used for screening. As shown in Table 1, prevalence rates tend to be lower when diagnosis rests on self-administered questionnaires [8] than on informant-based interviews [9,10,12,13,18], as many patients have reduced insight into the social consequences of their behavior or conceal it from their families because of shame or denial [19]. Use of specifically devised and validated diagnostic tools administered to both patients and caregivers can likely reduce possible underestimation of PG, and of other ICDs in PD. Two such questionnaires have been developed in recent years: the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) [20] and the Parkinson's disease Dopamine Dysregulation Syndrome-Patient and Caregiver (DDS-PC) inventory [21]. Both screening tools have good clinometric properties. The QUIP has been proved to be a sensitive instrument for detection of ICD whether completed by a patient or informant [22]. Agreement between patient- and informant-reporting of any ICD behaviors on the QUIP was moderate to fair for individual ICDs, but was high for PG [23].

It is important to underline here that the assessment of prevalence rates during the disease course will likely provide valuable cues for comprehending the genesis of PG and other ICDs in PD. Two recent studies reported low prevalence of PG among newly diagnosed PD patients with rates (0.9% [24] and 1.2% [25]) similar to those reported in general population, whereas prevalence of at least one ICD was quite high (17.5% [24] and 20% [25]). Such findings would suggest that several factors contribute to development of ICDs in PD.

3. Clinical and behavioral features associated with PG in PD

In general population, older age, poor socioeconomic status, mental disorders (e.g. manic and depressive disorders) [26] and alcohol or substance use seem to be factors associated with development of disordered gambling (for a recent review, see Ref. [27]). Moreover, two personality traits seem to be associated with PG: high impulsivity (the tendency to react to internal or external stimuli with diminished regard to negative consequences of these reactions [28]) and high novelty seeking (an individual's tendency toward excitement in response to new stimuli or cues for potential rewards, leading to frequent exploratory activity in pursuit of such experiences), which appears to be modulated by dopaminergic transmission in the ventral striatum [29,30]. Finally, pathological gamblers show high rates of other ICDs, particularly compulsive buying, compulsive sexual behavior and intermittent explosive disorder [31–33].

In PD patients, PG occurs in relation to DA and L-dopa treatment (see below the "PD therapy and management of PG" section), but some of the abovementioned factors seem to be associated to development of PG. In particular, male gender, young age at onset of PD, previous personal or family history of gambling problems, alcohol and/or substance abuse have been found to increase risk for developing PG [28,34–40]. In a recent prospective study, patient-specific risk factors for ICDs including greater usage of caffeine and cigarettes, motor complications, and higher peak dopamine agonist dosage have been identified [41].

Moreover in PD patients (see Table 2), as in the general population, novelty seeking and high impulsivity were associated with PG [36,38,39,42,43]. In particular, Voon et al. [43] reported that PG patients had greater impulsive choice with higher reward magnitudes reflecting the tendency toward immediate over delayed gratification.

Some studies tend to show higher aggressiveness, anxiety, irritability, disinhibition, obsessive compulsive features, medication-induced hypomania or mania in PD pathological gamblers than in non-gamblers [42–44], but these findings have not been confirmed

Table 1
Results of prevalence studies in PD patients with PG.

Authors	N. patients	Population	Prevalence (%)	Tools
Lu et al., 2006 [12]	200	Tertiary PD clinics	7 (PG alone)	Face-to-face interviews
Grosset et al., 2006 [13]	388	Tertiary PD clinics	4.4 (PG alone)	Semi-structured interview based on DSM-IV criteria
Voon et al., 2006 [8]	297	Tertiary PD clinics	3.4 (PG alone)	Modified SOGS
Avanzi et al., 2006 [10]	98	Tertiary PD clinics	6.1 (PG alone)	Interview based on DSMIV-TR; SOGS
Weintraub et al., 2006 [9]	272	Tertiary PD clinics	2.2 (active cases of PG)	Modified MIDI
Crockford et al., 2008 [11]	140	Tertiary PD clinics	9.8 (problem gambling: 3.6; PG: 5.7)	CPGI
Weintraub et al., 2010 [7]	3090	Tertiary PD clinics	5 (problem and pathological gambling)	Massachusetts gambling screen
Antonini et al., 2011 [24]	103	Tertiary PD clinics	0.9 (problem/pathological PG)	SOGS
Weintraub et al., 2013 [25]	168	Tertiary PD clinics	1.2 (problem/pathological PG)	QUIP
Asian countries				
Fan et al., 2009 [15]	400	Tertiary PD clinics	0.32 (PG alone)	Modified south oaks gambling screen (SOGS), interview based on DSM-IV-TR criteria for PG
Lee et al., 2010 [17]	1167	Tertiary PD clinics	1.3 (PG alone)	Minnesota impulsive disorders interview
Chiang et al., 2012 [14]	278	Tertiary PD clinics	1.49 (PG alone)	Interview based on DSM-IV-TR criteria for PG
Auyeung et al., 2011 [16]	213	Tertiary PD clinics	6.1 (PG alone)	Structured screening questionnaire

SOGS = South Oaks Gambling Screen; MIDI = Minnesota Impulsive Disorders Interview; CPGI = Canadian Problem Gambling Index; QUIP = Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease.

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