The prevalence and clinical characteristics of pathological gambling in Parkinson’s disease: an evidence-based review

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Abstract

Large prospective studies in the USA and Canada have estimated the prevalence of pathological gambling (PG) in the general population at 0.43% and 1% respectively. Studies using equivalent methodology in patients with Parkinson’s disease (PD) have reported markedly higher prevalence rates. A total of 1032 patients with PD have been included in clinical studies in North America, Great Britain and Italy. Of these, 3.2% met diagnostic criteria for PG. The prevalence of PG was found to be higher in men than in women with PD, although the difference was not statistically significant. A younger age at onset of PD, increased novelty-seeking behaviour and a history of alcohol misuse have been found to be associated with PG in this population. Pathological gambling has been associated with dopamine agonist use, and the prevalence of the association has been found to be 5.7% in patients with PD. Although the literature suggests a high incidence of psychiatric co-morbidity, particularly depression and other impulse control disorders, this is yet to be confirmed by case-control studies.

KEY WORDS: dopamine, gambling, impulse control disorders, Parkinson’s disease, prevalence

Introduction

Pathological gambling (PG) is a well recognised disorder characterised by persistent and progressive gambling despite negative consequences of the behaviour and/or the desire to quit (1). In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) it is classed as an impulse control disorder (ICD) along with pathological buying, hypersexual behaviour, pyromania, trichotillomania, and intermittent explosive disorder (1). Although commonly portrayed as non-pharmacological or behavioural addictions (2), ICDs probably have a high degree of neurobiochemical overlap with pharmacological addictions.

Parkinson’s disease (PD), although conventionally considered a movement disorder, has become one of a growing number of conditions that bridge the divide between neurology and psychiatry (3). There is evidence suggesting that the majority of PD patients exhibit psychiatric symptoms and that these can precede the onset of motor symptoms by many years (4). An association between PG and medication for PD was first reported in 2000 (5), although it initially attracted little scientific interest (6). However, a handful of unfortunate cases leading to multi-million dollar lawsuits against pharmaceutical companies brought it to the attention both of the legal profession and the media (7).

The first studies estimating the prevalence of PG were retrospective and their results inconsistent. Driver-Dunkley et al. (8) reported a prevalence of 0.05% (n=1884) whereas Molina et al. (5) found a much higher prevalence, 4.8% (n=250). In 2004, Giovannoni et al. (9) described a condition in which patients self-escalating their dosage of dopamine replacement therapy developed multiple motor and behavioural disturbances. Behavioural manifestations of this ‘dopamine dysregulation syndrome’ (DDS) included punding (repetitive, purposeless behaviours), hypersexuality, compulsive shopping, eating disorders, and PG (9-11). Although the literature indicates that PG most commonly occurs in subjects on prescribed medication regimes, it has been suggested to be secondary to self-escalation of dose in some cases (12). The past few years have seen much interest in this field, with numerous papers investigating the prevalence, clinical characteristics and, most recently, neurobiochemistry of this phenomenon (13). This systematic review focuses on the prevalence and clinical characteristics of PG in patients with idiopathic PD.

Methods

To determine the prevalence of PG in patients with PD, the Medline, Embase and Pyscinfo databases were searched using the terms ‘Parkinson’ and ‘gambling’. All entries published before October 2009 were examined for relevance. To be included, prevalence studies had to have used systematic screening methods and interview-based diagnosis based on PG diagnostic criteria. It was felt that this approach would, as far as possible, guarantee sets of results comparable both to each other and to those obtained from the general population using similar
methodologies. No additional literature was identified using alternative search terms, by scanning paper references, or in recent editions of relevant journals. Of the studies identified in this way, five were excluded from the prevalence estimates; these included the two retrospective studies mentioned previously (5,8). In addition, a published letter by Lu et al. (14) is widely cited in the literature but does not contain sufficient raw data for analysis. Pontone et al. (15) found that four out of 100 PD patients under 65 years of age screened positive for PG and although this is, in many ways, a useful study, it was felt that the age restriction applied by the authors would, in view of the younger age of PG patients reported elsewhere (16,17), probably result in an overestimation of prevalence. Finally, another recent study (18) was not included because it did not distinguish between problem gambling and PG. Case-control data on the clinical characteristics and factors associated with PG in patients with PD is limited. Using the same search strategy, papers were identified that compared PD patients with and without PG. One additional study was identified which investigated a variety of factors that might be associated with PG (19). All the prevalence studies included also contained limited analyses of this sort.

Prevalence of pathological gambling in the general population

Prevalence studies in PD have tended not to include controls but have instead relied on previous estimates from the general population. In 2001, Shaffer and Hall (20) published a meta-analysis of 66 prevalence studies conducted in North America. Level 3 gambling lifetime prevalence was reported at 1.9% and one-year active prevalence at 1.5%. Level 3 gambling is described as clinical disordered gambling and is similar to PG as defined by the DSM-IV. The 2005 US National Epidemiological Study (n=43092) reported a prevalence of 0.42% in the general adult population (21). Participants were assessed by structured interview based on DSM-IV criteria. A very similar methodology (n=1030) found a 1% prevalence in Canada (22).

Four studies met the inclusion criteria for this review, all published in 2006 and involving patients from tertiary care clinics (12,16,17,23). Table I summarises their main results. Voon et al. (16) used a patient-rated screening questionnaire (the South Oaks Gambling Screen) and psychiatrist interviews based on DSM-IV criteria. They reported a three-month active prevalence of 1.7% but a markedly higher lifetime prevalence of 3.4%. The lifetime prevalence in patients taking dopamine agonists (DAs), alone or in combination, was 7.2%. None of the 150 patients on levodopa monotherapy developed PG.

In Italy, Avanzi et al. (12) compared two-month prevalence data from 98 patients with PD and from 392 age-and sex-matched controls without PD. They also used the South Oaks Gambling Screen and DSM-IV diagnosis. They found a significantly higher (p=0.00001) prevalence in the patients than in the controls (6.1% vs 0.25%). These data produced an odds ratio of 25.6, or 16.6 if the two patients with DDS were excluded from analysis. Five patients who developed PG following treatment were on DAs, of whom one was on levodopa monotherapy.

Grosset et al. (17), over a period of three months, employed a semi-structured interview based on DSM-IV criteria in six West Scotland movement disorder clinics. Of 388 patients using anti-Parkinson drugs, 17 met the criteria for PG. All of these were on DAs and they accounted for 7.8% of all the patients on DAs.

Weintraub et al. (23) administered the Modified Minnesota Impulsive Disorders Interview (MIDI) to patients who screened positive for ICDs. Screening was systematic but unstructured. The MIDI is based on DSM-IV criteria and includes questions aimed at identifying various ICDs, including PG.

Across all studies, 34 of 1055 patients (3.2%) met diagnostic criteria for a diagnosis of PG. The population was 62% male (n=654) with sex data unavailable for one patient. Voon et al. (16) did not publish sex data for active prevalence, although lifetime prevalence did not differ between sexes. Calculations based on the other three

Table I - Results from the four studies meeting our search criteria on the prevalence of pathological gambling in Parkinson’s disease

<table>
<thead>
<tr>
<th>Country</th>
<th>PG diagnostic criteria</th>
<th>Sample size</th>
<th>Active PG frequency</th>
<th>Number taking DAs</th>
<th>Active PG frequency on DAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avanzi et al. (12)</td>
<td>Italy</td>
<td>DSM-IV</td>
<td>98</td>
<td>6 (6.1%)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Voon et al. (16)</td>
<td>Canada</td>
<td>DSM-IV</td>
<td>297</td>
<td>5 (1.7%)</td>
<td>139</td>
</tr>
<tr>
<td>Grosset et al. (17)</td>
<td>Scotland</td>
<td>DSM-IV</td>
<td>388</td>
<td>17 (4.4%)</td>
<td>218</td>
</tr>
<tr>
<td>Weintraub et al. (23)</td>
<td>USA</td>
<td>MIDI</td>
<td>272</td>
<td>6 (2.2%)</td>
<td>137</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>1055</td>
<td>34 (3.2%)</td>
<td>494</td>
</tr>
</tbody>
</table>

Abbreviations and symbols: PG= pathological gambling; DAs=dopamine agonists; DSM=Diagnostic and Statistical Manual of Mental Disorders; MIDI=Modified Minnesota Impulsive Disorders Interview. *The study by Avanzi et al. (12) could not be included in this estimate.
studies (12,17,23) found the prevalence of PG to be 4.2% in males and 3.2% in females. No study found statistically significant differences in sex distribution although this is quite possibly a consequence of low statistical power.

**Association with medications**

In three of the studies (16,17,23), 32 of the 559 (5.7%) patients taking DAs as part of their medication regime were diagnosed with PG. The study by Avanzi et al. (12) had to be excluded from this calculation as it did not provide a sufficiently detailed breakdown of drug classes. All the case-control studies showed a strong association with DAs as a class, but not with any particular drug (12,16,17,23). The results of an early retrospective study showed a high level of pramipexole use amongst gamblers (24), but this finding has since been attributed to the study population (14).

Three of the studies included in this review examined dose relationships (12,16,17). Two of these (12,16) found no association with DA dose although the third found an association with pramipexole dose (17).

**Clinical characteristics**

Voon et al. (19) compared 21 idiopathic PD patients with PG and 42 controls with PD and no compulsive behaviours. Pathological gambling was found to be associated with a younger age at PD onset, higher novelty seeking (NS), medication-induced mania or hypomania, impaired planning, and personal or immediate family history of alcohol misuse. Age at PD onset, NS scores and personal/family alcohol misuse accounted for 62% of the variance in a logistic regression model. Observations were based on previously validated patient-rated questionnaires and extensive clinical interview (19). Grosset et al. (17) also found that pathological gamblers had a significantly younger age at PD onset. Both studies noted that a greater preference for DA prescriptions in younger patients is potentially confounding (17,19).

Case reports have identified many patients with comorbid psychiatric conditions although in case-control designs no significant associations have been demonstrated. Neither Voon et al. (19) nor Avanzi et al. (12) found PG to be associated with depression. However in the latter study, 50% of the PD patients with PG were depressed versus 29% of the PD patients without PG (12). The absence of significance may be a consequence of the small size of the PG populations in these studies. Case reports can provide some of the most useful information for the clinician. Dodd et al. (24) described 11 patients seen in their movement disorders clinic, highlighting two different patterns of PG onset: seven patients developed PG within three months of DA initiation or dose escalation, whereas in the other four patients symptoms took between 12 and 30 months to appear. In parallel with PG, six of the patients developed other behavioural problems such as compulsive eating, excessive alcohol intake, compulsive buying, and hypersexuality. In the eight cases in which follow up was available, both PG and other behavioural problems resolved after discontinuation of DA therapy. The time to resolution varied, ranging from 48 hours to six months; in six patients resolution took less than a month (24). Several other reports have verified the effectiveness of withdrawing DA, although this strategy is not universally effective (12,25,26). Inevitably, it will often compromise the treatment of the motor symptoms of PD. Deep brain stimulation may prove to be an effective solution in some cases. Ardouin et al. (27) describe resolution of PG in seven patients following subthalamic nucleus (STN) stimulation surgery for disabling motor fluctuations. It seems likely that this result was facilitated by the marked dose reduction possible post-surgery, but there may also have been a direct effect on the STN. Evidence supporting other treatment options is highly anecdotal; the use of money restriction, support groups, and computer safeguards has been described in case reports, although generally as adjuvant measures (12,24,26).

**Discussion**

On the basis of the studies reviewed, it seems likely that PG is under-diagnosed in PD. Two prevalence studies observed that less than half of the patients who met diagnostic criteria for PG had this recorded in their notes (17,23). Increased awareness of the problem since 2006 may now be leading to better detection rates. According to what is described in case reports, partners or doctors often become aware of patients’ gambling problems only after they have sustained substantial losses. And the losses reported vary dramatically: from token ones to millions of dollars (7,17,24). The mean loss reported by the 10 patients included in Voon et al.’s prevalence study (16) was $129,000. The type of gambling reported also varies considerably and may reflect local availability. Slot machines emerge as the primary type in a third of published cases, with casino gambling, lottery/scratch cards, internet gambling and horse/greyhound racing accounting for most of the rest (28). This is consistent with a preference for repetitive, low-skill activities with high reward uncertainty. Online gambling appears to be on the rise and has been attributed to increased access to the internet (26). Clearly, online gambling, which does not involve travelling anywhere, would particularly suit subjects with motor disability due to PD. Robust evidence supports a higher prevalence of PG in patients with PD, especially those taking DAs, than in the general population. It is apparent that a subset of patients with PD shows an increased susceptibility to PG but whether this vulnerability is PD-specific or representative of an underlying susceptibility in the general population is unclear. Voon et al. (19), albeit in a preliminary study, suggest that some of the factors associated with PG may be inherent traits while others are related to the presence of PD or DAs. Their methodology involved comparing patients with current PG with those who had remitted after withdrawal of treatment. Impulsivity scores were relatively impaired in current gamblers compared with both non-gamblers and those who had remitted, which suggests they are ‘state-related’ i.e. related to the presence of DAs/PD. Novelty seeking, on the other hand, was found to be ‘trait-related’, i.e. an inherent difference unaffected by the presence of DAs/PD.
There is indirect evidence that PD may even be protective against PG. General population studies have associated PG with high levels of novelty seeking (29) characterised by exploratory-type behaviours, excitement in novel situations, rapid decision-making and extravangance (30). On the other hand, PD has been associated with low levels of novelty-seeking behaviour (31), accompanied by thoughtful, careful decision-making and a calm temperament (30). There is no evidence that untreated PD patients have an increased rate of PG and it is worth considering that PD patients are almost unique in terms of their long-term exposure to DAs. However PG has also been associated with DAs in another context: the treatment of restless legs syndrome due to multiple sclerosis (32). Evidence suggests that DAs are the key to PG exposure, the role of PD itself remaining unclear; potentially it could be contributory, protective or entirely independent.

Our review of the current evidence on this issue has some limitations. Exactly how much more prevalent PG is in PD versus the general population is difficult to judge due to major differences in population characteristics, but also minor methodological differences, between studies. Only one study included in this review compared PD patients to an age-/sex-matched non-PD control group (12).

Variations of PG prevalence with age and sex are well documented in the general population, in which the condition is more common in men and rates decrease with age (20,21). With reference to sex, two of the uncontrolled studies had predominantly male samples (16,23), which may have contributed to the increased prevalence they reported. Sex-specific prevalence rates calculated from three studies (12,18,23) support this, with the rate in men being slightly higher than that in women (6% versus 5%).

All the prevalence studies identified involved PD patients in tertiary care clinics, who are probably representative of more complicated cases. In particular, they may be prone to co-morbidities, such as several psychiatric disorders, that are independently associated with PG and PD (4,29). Although the data currently available on the prevalence of PG cannot be generalised to the wider PD population, a higher level of suspicion in all PD cases is clearly warranted.

References


