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ORIGINAL PAPER

# Prevalence of Problem and Pathological Gambling in Parkinson's Disease

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**Abstract** Pathological gambling (PG) has been identified in patients with Parkinson's disease (PD) treated with dopamine agonists suggesting that dysregulation of brain dopaminergic activity may contribute to the development of gambling problems. The current study was undertaken to further establish the prevalence of problem and PG in patients with PD, identify any clinical correlates, and determine if psychiatric or substance use co-morbidity contributes to the increased prevalence of problem and PG. A cross-sectional survey of 140 serially recruited moderate to severe PD patients was undertaken utilizing the Canadian Problem Gambling Index, Alcohol Use Disorders Identification Test, Drug Abuse Screening

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Test, Beck Depression Inventory, Beck Anxiety Inventory, and Mini-Mental State Exam augmented by chart review, completed over an 8 month period. The 12 month prevalence of problem and PG in PD was 9.3% compared to 1.6% in the general population within a comparably aged sample. The increased prevalence of problem and PG in the PD group was related to dopamine agonist use and younger age, but not co-morbidity. Most subjects with problem and PG reported their gambling increased after being diagnosed with PD and starting treatment. The results suggest that brain dopaminergic activity is involved in the underlying neurobiology of problem and PG.

**Keywords** Parkinson's disease · Pathological gambling · Dopamine agonists · Co-morbidity · Prevalence

## Introduction

Pathological gambling (PG) is characterized by persistent and progressive gambling behavior despite negative consequences and/or the desire to quit (American Psychiatric Association 2000). In the general population, the prevalence of PG has been estimated at 1–2% (Shaffer and Hall 2001), with an additional 3–5% considered at risk for problem gambling (defined as acknowledging problems related to gambling but not meeting criteria for PG) (Petry 2005).

Prior case reports and series reported an association between PG and the use of dopamine agonists (DA) (Dodd et al. 2005; Driver-Dunckley et al. 2003). Several recent studies have further substantiated an increased prevalence of PG in treated Parkinson's disease (PD) patients and have attempted to clarify the association of PG to DA use (Avanzi et al. 2006; Grosset et al. 2006; Voon et al. 2006b; Weintraub et al. 2006). Voon et al. 2006b reported a lifetime prevalence of PG in a tertiary care PD clinic to be 3.4% (with a higher lifetime prevalence of 7.2% in PD patients treated with any DA) and a three-month active prevalence of 1.7% based on the South Oaks Gambling Screen (SOGS) self-report followed by an interview using DSM-IV criteria. They found PG to be associated with earlier onset of PD and DA use in general, but not to particular DA subtypes or levodopa equivalent daily dose. Prevalence estimates were not compared to an age-matched, non-patient sample. Weintraub et al. (2006) found that of a tertiary care sample, 2.2% reported current PG and a 2.6% prevalence of PG during the course of PD via the modified Minnesota Impulsive Disorders Interview (MIDI) based on DSM criteria. They also found a dose–dependent relationship between total levodopa equivalent daily dose and PG as well as elevated rates of other impulse control problems. Grosset et al. (2006) sampled patients from six movement disorder clinics over 3 months. Among 388 PD patients on antiparkinsonian medications with no history of PG, 4.4% developed DSM-IV PG, all of which were on DA (representing 8% of PD patients on DA). All studies involved patients from tertiary care movement disorder centers potentially prone to sampling complex patients with a greater potential for co-morbidity. The Weintraub et al. study also predominantly sampled men; as PG is more common in men (Potenza et al. 2001), the reported increased prevalence of PG may be related to the sample studied. Avanzi et al. (2006) attempted to address these concerns via comparing 2 month prevalence data from 98 PD patients in their movement disorder program to 392 age and sex matched general practice patients without PD. They found 6.1% of the PD group met the DSM-IV-TR criteria for PG, compared to only 0.25% of the general practice group. This increased

prevalence found was not related to levadopa equivalent daily dose, a specific DA (but DAs in general), or depression.

Research to date, however, lacks the systematic assessment of problem and PG in PD patients using structured instruments employed in community epidemiologic samples. Such assessments would allow for the adequate comparison of prevalence rates in similar age groups, to ascertain if the prevalence of problem and PG is greater than normally expected in PD patients based on general population trends for this age group. For example, population rates of PG have been found to decline with advancing age (Ladouceur et al. 2005; Petry 2005). As PG is associated with significant psychiatric co-morbidity including mood, anxiety, and substance use disorders (Crockford and el-Guebaly 1998; Ladouceur et al. 2005; Potenza et al. 2001) that may directly contribute to its development (Crockford and el-Guebaly 1998), co-morbidity should be accounted for if pharmacologic treatments are to be considered as potentially causative. Reports to date have identified co-morbid psychiatric symptoms, histories, and treatments in many of the PD patients identified as having PG (Dodd et al. 2005; Molina et al. 2000; Voon et al. 2006a, b). While the report by Avanzi et al. (2006) suggests no statistically significant relationship between PG and depression, 50.0% of the PD patients with PG vs. 29.3% of PD patients without PG were identified as depressed by having Beck Depression Inventory (BDI) scores >20. Further systematic study is therefore required to ensure that co-morbidity does not influence the prevalence rates of problem and PG in treated PD patients.

The present study was completed to (1) determine the prevalence of problem and PG in patients treated for PD compared to general population trends for this demographic age group; (2) investigate clinical correlates (e.g., relationship with PD medications) of problem gambling in PD patients, and; (3) determine how problem gambling in this group is associated with psychiatric or substance use co-morbidity. We hypothesized that problem and PG would be greater in patients treated for PD compared to population estimates, and that the increased prevalence is independent of psychiatric and substance use co-morbidity.

## Method

### Subjects

Participants consisted of 140 serially recruited patients with clinical diagnoses of idiopathic PD from the University of Calgary Movement Disorder Clinic, recruited over an 8 month span (April to December, 2005) seen in Calgary, Medicine Hat and Lethbridge, Alberta. Non-demented patients (Folstein Mini-Mental Status Exam [MMSE] >26/30) with moderate to severe PD, determined by the Hoehn and Yahr (1967) in the off state were identified and referred by their treating neurologists (with expertise in PD) during new intakes or follow-up visits (mean Hoehn and Yahr score 3.07, SD 0.66). Subjects were not sought outside of this context to avoid possible recruitment bias of patients who gamble. All 140 identified subjects completed the survey with no subjects refusing to participate. Some eligible patients may have refused to participate when seen and referred by the neurologist or not been identified, but this data was not recorded, preventing its analysis (and was reported to be very minimal by the referring neurologists). The final sample of 140 represents approximately 90% of the moderate to severe PD patients seen at our clinic during the data collection phase of the study.

## Procedure and Measures

Identified subjects were administered the instruments described below and their medical records were reviewed for pertinent data. All subjects provided voluntary written informed consent prior to their inclusion in the study, which was reviewed and approved by the University of Calgary Conjoint Ethics and Review Board.

To determine the prevalence of problem and PG, the Canadian Problem Gambling Index (CPGI) (Ferris and Wynne 2001; Ladouceur et al. 2005) was administered by a trained research assistant. The CPGI is a validated and comprehensive screening instrument for problem and PG designed to examine various aspects of gambling behavior and potential co-morbidity (Ferris and Wynne 2001). Demographic information and the extent of involvement (types of games, frequency of play, amount spent) in gambling activities over the last 12 months were identified by questions from the CPGI. A 'core' of nine questions in the CPGI comprised the Problem Gambling Severity Index (PGSI) to quantify the severity of gambling (Ferris and Wynne 2001). The SOGS threshold score indicative of probable PG has been correlated with that of the PGSI (Ferris and Wynne 2001). Two questions were added to the CPGI to assess onset of gambling behavior in relation to onset of PD and its treatment.

Patients also completed the BDI (Beck et al. 1961) and Beck Anxiety Inventory (BAI) (Beck et al. 1988) as indices of depressive and anxiety symptomatology, both of which are often co-morbid with PG and PD (Crockford and el-Guebaly 1998; Glosser 2001). The BAI has been used in studies with PD patients and validated to standardized rating scales (Harrison et al. 2000; Shulman et al. 2001), while the BDI has been empirically validated (Leentjens et al. 2000) in this population. The Alcohol Use Disorders Identification Test (AUDIT) was included to screen for alcohol use disorders (Bohn et al. 1995; Schmidt et al. 1995), and has been validated in a variety of healthcare settings (Daeppen et al. 2000; Philpot et al. 2003; Reinert and Allen 2002). The Drug Abuse Screening Test (DAST), expanded to include prescription drugs, was given as a validated instrument to screen for the presence of drug use disorders (Gavin et al. 1989). Patients without a recently documented cognitive assessment were administered the Folstein Mini-Mental Status Exam (MMSE) (Folstein et al. 1975). All patients scored 27 or higher on the MMSE and thus none were excluded on this basis.

## Data Analysis

Prevalence of problem and PG in the PD sample was compared to Canadian population data from a comparable peer group (described below). Cross-sectional analysis of the PD sample was conducted to identify socioeconomic, historical, biomedical, and psychological features that are associated with increasing risk of a gambling disorder within this group. PD subjects were categorized according to their gambling status and level of risk as defined by the PGSI: non-gambler (not gambled at all in last year), non-problem gambler (gambled in last year, PSGI score $= 0$), low-risk gambler (PSGI $= 1$ or 2), and moderate risk/problem gambler (PSGI $\geq 3$). Approximate 95% confidence intervals (CI) around the prevalence estimates of problem gambling were constructed (Slevin 2004). For statistical comparisons, the non-problem (NP) and low-risk (LR) gambler categories were combined (NP/LR), as were the moderate risk and problem gambler categories (indicative of problem and PG, respectively). *t*-test (continuous variables) and chi-square analyses compared groups across socioeconomic (current age, gender, marital status, annual income, years of

education), gambling history (age started gambling, average money spent on gambling, total number of gambling activities in last year, average duration of gambling per session), biomedical (years with PD, years on DA, DA dosage, Hoehn & Yahr score), and psychological (BDI, BAI, AUDIT, DAST & MMSE) dimensions.

## Results

Demographics of the sample are described in Table 1. Typical for PD patients, the sample was older (age range: 44–88 years), married, well educated and retired. Nearly the entire sample was treated with levodopa and a large majority was taking DA, the most common agent being pramipexole. Mean scores on the psychiatric and substance use co-morbidity tests demonstrated an absence of depression, anxiety, or drug/alcohol use. Thirty-three percent of the sample ($N = 46$) had been previously treated for a mood or anxiety disorder ($N = 35$; 25%) or was currently taking an antidepressant ($N = 23$; 16%). No differences were found between this group and patients with no history of mental health treatment ($N = 94$) in terms of PGSI score [1.0 (SD = 3.7) vs. 1.3 (SD = 4.7); $t = 0.46$, $P > .05$] or PGSI category (7% vs. 11% were moderate risk or problem gamblers; $\chi^2 = 0.86$, $P > .05$). The groups also showed no differences in Hoehn and Yahr score, gender, age, or total dollars spent on gambling in the past year (all $P$s $> .05$). None of the PD patients met criteria for bipolar disorder, were treated with mood stabilizers or had their gambling behavior relate to a hypomanic or manic episode.

Acknowledging that clinical and community samples are difficult to compare, prevalence rates for the continuum of gambling behavior from the PD sample were compared to that in the general population sample aged 45 years and older ($N = 27848$) derived from the Canadian Community Health Survey–Mental Health and Well-being public use file

**Table 1** Sample characteristics ($N = 140$)

| Characteristic | % or mean, SD |
|---|---|
| Age | 67.6, SD 9.5 |
| Gender, % men | 62 |
| Marital status, % married | 75 |
| Education, % post-secondary | 66 |
| Employment, % retired | 69 |
| Medications | |
| l-dopa equivalents (mg) | 707.7, SD 402.0 |
| Pramipexole, % taking | 58 |
| Ropinirole, % taking | 24 |
| Pergolide, % taking | 5 |
| Bromocriptine, % taking | 1 |
| Levodopa, % taking | 99 |
| Comorbidities | |
| Drug abuse screening test score | 0.03, SD 0.17 |
| Beck depression inventory score | 9.5, SD 7.4 |
| Beck anxiety inventory score | 11.5, SD 8.1 |
| Alcohol use disorders identification test score | 2.0, SD 1.94 |
| Past mood disorder (%) | 24% |

(CCHS-1.2) (Statistics Canada 2003). Fewer subjects in the PD sample compared to the community sample reported no gambling in the last 12 months (13.5% vs. 49.2%). However, when combined with non-problem gambling behavior the two groups were not markedly different [87.8% (95% CI = 81.3–92.8%) vs. 95.9% (95% CI = 95.4–96.0%)]. The prevalence of problem and PG in the PD sample was over five times greater than that in the community sample [9.3% (95% CI = 5.0–15.4%) vs. 1.3% (95% CI = 1.2–1.5%)].

Table 2 compares PD patients with problem and PG to the NP/LR PD patients. There was no significant difference between either group on measures of depression, anxiety, alcohol or other substance use. Severity of PD was also not significantly different between groups. The gender split was comparable across groups, but subjects in the problem and PG group were significantly younger (61.8 vs. 68.7 years, $P < 0.05$). The groups did not differ in the rate of PD-related neurological problems (dyskinesia, hallucinations; $P > 0.05$ for all chi-square analyses). The CPGI identified that electronic gaming machines (EGMs) were played significantly more both inside (62% vs. 9.3%, $P < 0.001$) and outside of casinos (85% vs. 23%, $P < 0.001$) in the problem and PG group compared to the NP/LR group. More subjects in the problem and PG group reported gambling to win money (23% vs. 15%, $P < 0.001$) or for excitement (39% vs. 17%, $P < 0.001$), with fewer subjects in the problem and PG group gambling for entertainment (8% vs. 28%, $P < 0.001$). The problem and PG group also spent more money on average per year on gambling ($4039.30 ± 5937.70 vs. $242.20 ± 1114.60 in the NP/LR group, $P < 0.001$).

Problem and PG was not found to be associated with the use of a particular DA, nor was there a significant correlation with the total levodopa equivalent daily dose. However, significantly greater numbers of problem and PG subjects were on DAs (92% vs. 65%, $P < 0.05$) with 12.4% of PD patients with problem and PG being on a DA. In the NP/LR group, 11 patients (10.2%) reported that their gambling increased following being diagnosed with PD, whereas nine patients (69%) of the problem and PG group reported this ($P < 0.001$), with 7/9 of these patients reporting increased gambling after starting medication for PD.

No significant differences in DAST, BDI, BAI, and AUDIT scores were detected between the NP/LR and the problem and PG groups. Scores for both groups were in the normative range for all measures, except the BDI, which was in the mildly depressed range (>8, <15).

## Discussion

This study confirms and extends findings from prior work identifying an increased prevalence of problem and PG in patients with treated idiopathic PD (Voon et al. 2006b). The 12 month prevalence of problem gambling was 3.6% and PG was 5.7%, for a total of 9.3%. The prevalence of PG found is similar to the 6.1% reported by Avanzi et al. (2006) and 4.4% reported by Grosset et al. (2006), while slightly higher than the 3.4% reported by (Voon et al. 2006b) and 2.6% reported by Weintraub et al. (2006).

Despite essentially the entire PD sample being on dopamine replacement and/or DA, the presence of problem or PG occurred in the minority of patients and was related to DA use in general rather than DA subtype or total levodopa equivalent daily dose. It has been suggested that pramipexole is more likely to be associated with the development of PG (Dodd et al. 2005; Szarfman et al. 2006), however, we did not find this. Our findings are consistent with that of (Voon et al. 2006b) and Avanzi et al. (2006) who also did not find an association to DA subtype or levadopa equivalent daily dose to PG. Although

**Table 2** Comparison of non-problem/low-risk gambler and moderate risk/problem gambler subtypes across demographic, gambling characteristics, and medication use

| | Non-problem/low-risk gambler ($n = 108$)[a] % ($n$) or mean, SD | Moderate risk/problem gambler ($n = 13$) % ($n$) or mean, SD | Non-gambler ($n = 18$) % ($n$) or mean, SD | $\chi^2$ or ANOVA ($F$-value) |
|---|---|---|---|---|
| Age | 68.7, SD 9.1 | 61.8, SD 7.6[a] | 66.4, SD 11.9 | 3.25* |
| Gender, % men | 63 | 69 | 50 | 1.45 |
| Hoehn and Yahr score | 3.1, SD 0.7 | 3.4, SD 0.5 | 2.8, SD 0.6 | 2.77 |
| Gambling last 12 months | | | | |
| Instant win/ scratch tickets | 31 | 46 | NA | 1.29 |
| Lottery tickets | 57 | 62 | | 0.12 |
| Bingo | 9 | 15 | | 0.49 |
| Cards with family/ friends | 11 | 23 | | 1.53 |
| EGMs outside casinos | 9.3 | 62 | | 25.04** |
| EGMs inside casinos | 23 | 85 | | 20.97** |
| Casino games except EGMs | 13 | 8 | | 0.29 |
| Horse racing | 7 | 15 | | 1.34 |
| Total amount spent on gambling (CAN$) | 242.2, SD 1114.6 | 4039.3, SD 5937.7 | NA | 2.30* |
| Main reason to gamble | | | | |
| Win money | 15 | 23 | NA | 5.05** |
| Entertainment | 28 | 8 | | |
| Excitement | 17 | 39 | | |
| Other | 40 | 31 | | |
| Gambling in relationship to onset of PD | | | | |
| Same or more before diagnosed with PD | 90 | 31 | NA | 29.32** |
| Increased after diagnosed with PD | 10 | 69 | | |
| Medication use | | | | |
| Ropinirole, % taking | 19 | 54 | 28 | 7.91* |
| Bromocriptine, % taking | 0.9 | 7.7 | 0 | 4.09 |
| Pergolide, % taking | 3.7 | 7.7 | 11 | 2.02 |

**Table 2** continued

| | Non-problem/low-risk gambler ($n = 108$)[a] % ($n$) or mean, SD | Moderate risk/problem gambler ($n = 13$) % ($n$) or mean, SD | Non-gambler ($n = 18$) % ($n$) or mean, SD | $\chi^2$ or ANOVA ($F$-value) |
|---|---|---|---|---|
| Pramipexole, % taking | 56 | 62 | 67 | 0.81 |
| Sinemet, % taking | 98 | 92 | 100 | 2.35 |
| l-dopa equivalents (mg) | 712.9, SD 395.9 | 602.3, SD 355.4 | 775.0, SD 471.5 | 0.70 |
| Any dopamine agonist, % | 65 | 92 | 78 | 4.73 |
| Comorbidities | | | | |
| DAST | 0.04, SD 0.19 | 0.00 | 0.00 | 0.58 |
| BDI | 9.6, SD 7.4 | 11.5, SD 8.4 | 5.5, SD 4.4 | 2.47 |
| BAI | 11.8, SD 8.3 | 10.3, SD 4.8 | 9.5, SD 8.3 | 0.75 |
| AUDIT | 2.1, SD 2.0 | 2.1, SD 2.1 | 1.1, SD 1.5 | 2.10 |

EGM–electronic gaming machine, DAST–Drug Abuse Screening Test, BDI/BAI–Beck Depression/Anxiety Inventory, AUDIT–Alcohol Use Disorders Identification Test

[a] Moderate-problem gamblers < non-problem/low-risk gambler groups ($P < .05$)

* $P < .05$. ** $P < .01$

Weintraub et al. (2006) found an association to levadopa equivalent daily dose, differences may relate to disparity in the severity of PD symptoms between studies, where our study group was more severe than that in the Weintraub et al. (2006) study and more like the Voon et al. (2006b) study.

Another possible and more likely explanation is that all studies identified only small numbers of problem and PG subjects, making differences found in prevalence rates between studies highly probable. We attempted to compensate for limitations in statistical power by expanding the definition of problematic gambling beyond PG alone, to also include problem gamblers so that we would report on a comparable number of subjects with problem and PG to prior work (Dodd et al. 2005; Driver-Dunckley et al. 2003; Voon et al. 2006b; Weintraub et al. 2006). While we feel this inclusion is clinically and methodologically relevant, it may contribute to higher total prevalence rates seen in our study. The small number of PD patients with problem or PG would make it difficult to find significant differences between agents. If such differences were present, they would be difficult to replicate from study to study. Different DA may still be more prone than others to be associated with problem and PG, especially those that may preferentially act on D3 receptors related to their primary localization in the extended dopamine reward pathway (O'Brien and Gardner 2005), but this currently cannot be determined definitively.

The prevalence of problem and PG in the current study is five times greater in moderate to severe PD patients compared to similarly aged individuals in the general Canadian population, recognizing that clinical and community samples are difficult to compare. The presence of any gambling behavior in the PD sample was also slightly higher than that found in the community (86.5% vs. 75.8%). Random selection of PD subjects and a comparison group derived from a patient population rather than a community-based cohort would have been better in retrospect, however, the large difference found in the prevalence rates of

problem and PG is difficult to dismiss as being a product of selection bias, especially when considering the consistency of findings across various studies. Furthermore, the high rate found in PD patients is contrary to the age trend for PG within the general population (Petry 2005). The slightly greater presence of any gambling behavior may represent sub-clinical manifestations of impulse control problems with the use of dopaminergic agents or the underlying neurologic abnormalities associated with PD or both.

Younger age was associated with problem and PG in our patient sample where subjects with problem and PG were on average 7 years younger than non-problem gamblers. Younger age was also identified as a key demographic risk factor in the (Voon et al. 2006b) and Grosset et al. (2006) studies. Problem and PG were also more likely to report the onset of gambling problems after being diagnosed and treated for PD, as well as more likely to play EGMs compared to non-disordered gamblers. The increased prevalence of problem and PG was not related to other demographic factors, severity of PD, or psychiatric/substance use co-morbidity.

It remains possible that the increased prevalence of problem and PG in PD patients could still partly relate to selection bias. Patients who seek treatment are typically more symptomatic and at higher risk for the presence of psychiatric co-morbidity (el-Guebaly 1995). The study purposely selected subjects with moderate to advanced PD to ensure that diagnoses were unambiguous and that all subjects would be on dopaminergic agents. Although individuals with PD are at increased risk for both medical and psychiatric co-morbidity (Henderson et al. 1992; Shulman et al. 2001), rates of concurrent mental health problems, including mood and substance use disorders, were comparable in the disordered and non-disordered gambling groups. In fact, the severity of psychiatric co-morbidity was uniformly low across the entire sample. Hence, the elevated rates of problem and PG detected cannot be attributed to the influence of co-morbid addictions or mental illness. In addition, the rural and serial sampling was purposely added to reduce the potential for treatment setting or referral bias potentially influencing results. With the measures taken, selection bias appears unlikely suggesting that the increased prevalence rates are related to the underlying neurobiology of PD and its pharmacologic treatment rather than other variables.

Our assessment examined the 12 month prevalence of gambling problems without consideration of lifetime rates. Some patients with prior gambling problems may have gone undetected, lowering the reported prevalence. We were aware of at least one patient in treatment for PG at the time of the survey that scored "0" on the PGSI because he was abstinent for over 12 months. This finding highlights the limitation of single point-in-time survey estimating procedures.

Although most patients reported some non-problematic gambling prior to the onset of their PD, the majority of problem and PG patients reported their problem and PG developed after being diagnosed with PD. This was particularly the case after starting on dopaminergic treatments, suggesting these agents contributed to the gambling behavior in the context of their underlying brain pathology. Dopaminergic systems in the brain have been implicated in the pathophysiology of both PD and PG (Bergh et al. 1997). Gambling tasks (Breiter et al. 2001) and monetary rewards (Elliott et al. 2000; O'Doherty et al. 2001) have been reported to activate mesocorticolimbic brain regions representative of the extended dopamine reward pathway (Kalivas 2001). Such activation may result in monetary rewards being deemed as salient for persistent behavioral choice (Zink et al. 2004) thereby linking cues to rewarding events for behavioral persistence (Crockford et al. 2005). DA may result in the development of problem and PG via excessive mesocorticolimbic pathway activation, potentially resulting in salience being inappropriately and overly attributed to the monetary rewards of gambling. In all likelihood, given that the majority of

treated PD patients did not develop problem or PG, certain PD patients may be at more risk for developing problem and PG over other patients.

In addition to the potential differences in dopaminergic agents already discussed and the degree/severity of underlying neuropathology, those persons with prior non-problematic gambling behavior as found in our study, may be predisposed to developing problem and PG on dopaminergic agents, especially the DA, as gambling has already been selected as a behavior. This may help explain why patients did not also develop substance use disorders as dysregulation of the extended dopamine reward pathways has also been implicated (Kalivas and Volkow 2005). In addition to substance use being less socially acceptable compared to gambling, patients may have avoided mixing substances with their medications for fear of worsening their cognition and neurologic status.

Future work should examine prospective data rather than rely upon retrospective self-report data to assess for presence, onset and change in gambling behaviors. Potential psychiatric co-morbidity should be also be better identified and characterized by the use of structured clinical interviews like the Mini-International Neuropsychiatric Interview (MINI) (Pinninti et al. 2003; Sheehan et al. 1998) or the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I) (First et al. 2001) as the use of self-report instruments does not identify prior significant symptoms that could potentially relate to the development of problem and PG and clinical diagnoses often underestimate or misclassify psychiatric diagnoses (Endicott 2001, Shear et al. 2000). Structured clinical interviews are also needed to further confirm the presence of problem and PG, as well as other impulse control problems, such as eating, shopping, spending and sexual behaviors like the Voon et al., Weintraub et al., and Pontone et al. (Pontone et al. 2006; Voon et al. 2006a; Weintraub et al. 2006) studies due to their reported association with DA. Subjects may have been more prone to attribute their escalation in gambling problems to their PD and its treatment via retrospective reporting bias as self-report questionnaires can overestimate the prevalence of PG (Ladouceur et al. 2005).

In conclusion, this study found that patients with PD treated with dopamine replacement or DA have a prevalence of problem and PG that is significantly greater than expected based on comparison to that in the community, not attributable to PD severity or co-morbidity. The findings confirm those from previous reports suggesting that dysregulation of brain dopaminergic activity in the context of underlying neuropathology appear to contribute to the development and persistence of problem and PG. It also suggests that all patients with PD should be screened for the presence of gambling behaviors as well as problem or PG initially, and then be followed prospectively for its potential emergence or worsening, particularly in younger patients, those with gambling experience, and when treatment is altered.

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## References

American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington DC: American Psychiatric Association.

Avanzi, M., Baratti, M., Cabrini, S., Uber, E., Brighetti, G., & Bonfa, F. (2006). Prevalence of pathological gambling in patients with Parkinson's disease. *Movement Disorders, 21*, 2068–2072. doi: 10.1002/mds.21072.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology, 56*, 893–897. doi:10.1037/0022-006X.56.6.893.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 561–571.

Bergh, C., Eklund, T., Sodersten, P., & Nordin, C. (1997). Altered dopamine function in pathological gambling. *Psychological Medicine, 27*, 473–475. doi:10.1017/S0033291796003789.

Bohn, M. J., Babor, T. F., & Kranzler, H. R. (1995). The alcohol use disorders identification test (AUDIT): validation of a screening instrument for use in medical settings. *Journal of Studies on Alcohol, 56*, 423–432.

Breiter, H. C., Aharon, I., Kahneman, D., Dale, A., & Shizgal, P. (2001). Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron, 30*, 619–639. doi:10.1016/S0896-6273(01)00303-8.

Crockford, D. N., & el-Guebaly, N. (1998). Psychiatric comorbidity in pathological gambling: a critical review. *Canadian Journal of Psychiatry, 43*, 43–50.

Crockford, D. N., Goodyear, B., Edwards, J., Quickfall, J., & el-Guebaly, N. (2005). Cue-induced brain activity in pathological gamblers. *Biological Psychiatry, 58*, 787–795. doi:10.1016/j.biopsych.2005.04.037.

Daeppen, J. B., Yersin, B., Landry, U., Pecoud, A., & Decrey, H. (2000). Reliability and validity of the alcohol use disorders identification test (AUDIT) imbedded within a general health risk screening questionnaire: results of a survey in 332 primary care patients. *Alcoholism, Clinical and Experimental Research, 24*, 659–665. doi:10.1111/j.1530-0277.2000.tb02037.x.

Dodd, M. L., Klos, K. J., Bower, J. H., Geda, Y. E., Josephs, K. A., & Ahlskog, J. E. (2005). Pathological gambling caused by drugs used to treat Parkinson disease. *Archives of Neurology, 62*, 1377–1381. doi:10.1001/archneur.62.9.noc50009.

Driver-Dunckley, E., Samanta, J., & Stacy, M. (2003). Pathological gambling associated with dopamine agonist therapy in Parkinson's disease. *Neurology, 61*, 422–423.

el-Guebaly, N. (1995). Substance use disorders and mental illness: the relevance of comorbidity. *Canadian Journal of Psychiatry, 40*, 2–3.

Elliott, R., Friston, K. J., & Dolan, R. J. (2000). Dissociable neural responses in human reward systems. *The Journal of Neuroscience, 20*, 6159–6165.

Endicott, J. (2001). Good diagnoses require good diagnosticians: collecting and integrating the data. *American Journal of Medical Genetics, 105*, 48–49. doi:10.1002/1096-8628(20010108)105:1<48::AID-AJMG1057>3.0.CO;2-M.

Ferris, J., & Wynne, H. (2001). *The Canadian Problem Gambling Index: final report*. In. Ottawa: Canadian Centre on Substance Abuse.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2001). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders*. Research Version New York: Biometrics Research: New York State Psychiatric Institute.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189–198. doi:10.1016/0022-3956(75)90026-6.

Gavin, D. R., Ross, H. E., & Skinner, H. A. (1989). Diagnostic validity of the drug abuse screening test in the assessment of DSM-III drug disorders. *British Journal of Addiction, 84*, 301–307. doi:10.1111/j.1360-0443.1989.tb03463.x.

Glosser, G. (2001). Neurobehavioral aspects of movement disorders. *Neurologic Clinics, 19,* 535–551. doi:10.1016/S0733-8619(05)70033-5.

Grosset, K. A., Macphee, G., Pal, G., Stewart, D., Watt, A., Davie, J., et al. (2006). Problematic gambling on dopamine agonists: Not such a rarity. *Movement Disorders, 21*, 2206–2208. doi:10.1002/mds.21110.

Harrison, J. E., Preston, S., & Blunt, S. B. (2000). Measuring symptom change in patients with Parkinson's disease. *Age and Ageing, 29*, 41–45. doi:10.1093/ageing/29.1.41.

Henderson, R., Kurlan, R., Kersun, J. M., & Como, P. (1992). Preliminary examination of the comorbidity of anxiety and depression in Parkinson's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences, 4*, 257–264.

Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression and mortality. *Neurology, 17*, 427–442.

Kalivas, P. W. (2001). Drug addiction: to the cortex and beyond!. *The American Journal of Psychiatry, 158*, 349–350. doi:10.1176/appi.ajp.158.3.349.

Kalivas, P. W., & Volkow, N. D. (2005). The neural basis of addiction: a pathology of motivation and choice. *The American Journal of Psychiatry, 162*, 1403–1413. doi:10.1176/appi.ajp.162.8.1403.

Ladouceur, R., Jacques, C., Chevalier, S., Sevigny, S., & Hamel, D. (2005). Prevalence of pathological gambling in Quebec in 2002. *Canadian Journal of Psychiatry, 50*, 451–456.

Leentjens, A. F., Verhey, F. R., Luijckx, G. J., & Troost, J. (2000). The validity of the Beck depression inventory as a screening and diagnostic instrument for depression in patients with Parkinson's disease. *Movement Disorders, 15*, 1221–1224. doi:10.1002/1531-8257(200011)15:6<1221::AID-MDS1024>3.0.CO;2-H.

Molina, J. A., Sainz-Artiga, M. J., Fraile, A., Jimenez-Jimenez, F. J., Villanueva, C., Orti-Pareja, M., et al. (2000). Pathologic gambling in Parkinson's disease: a behavioral manifestation of pharmacologic treatment? *Movement Disorders, 15*, 869–872. doi:10.1002/1531-8257(200009)15:5<869::AID-MDS1016>3.0.CO;2-I.

O'Brien, C. P., & Gardner, E. L. (2005). Critical assessment of how to study addiction and its treatment: human and non-human animal models. *Pharmacology & Therapeutics, 108*, 18–58. doi:10.1016/j.pharmthera.2005.06.018.

O'Doherty, J., Kringelbach, M. L., Rolls, E. T., Hornak, J., & Andrews, C. (2001). Abstract reward and punishment representations in the human orbitofrontal cortex. *Nature Neuroscience, 4*, 95–102. doi:10.1038/82959.

Petry, N. M. (2005). *Pathological Gambling: Etiology, Comorbidity, and Treatment*. Washington, DC: American Psychological Association.

Philpot, M., Pearson, N., Petratou, V., Dayanandan, R., Silverman, M., & Marshall, J. (2003). Screening for problem drinking in older people referred to a mental health service: a comparison of CAGE and AUDIT. *Aging & Mental Health, 7*, 171–175. doi:10.1080/1360786031000101120.

Pinninti, N. R., Madison, H., Musser, E., & Rissmiller, D. (2003). MINI international neuropsychiatric schedule: clinical utility and patient acceptance. *European Psychiatry, 18*, 361–364. doi:10.1016/j.eurpsy.2003.03.004.

Pontone, G., Williams, J. R., Bassett, S. S., & Marsh, L. (2006). Clinical features associated with impulse control disorders in Parkinson disease. *Neurology, 67*, 1258–1261. doi:10.1212/01.wnl.0000238401.76928.45.

Potenza, M. N., Kosten, T. R., & Rounsaville, B. J. (2001). Pathological gambling. *Journal of the American Medical Association, 286*, 141–144. doi:10.1001/jama.286.2.141.

Reinert, D. F., & Allen, J. P. (2002). The alcohol use disorders identification test (AUDIT): a review of recent research. *Alcoholism, Clinical and Experimental Research, 26*, 272–279.

Schmidt, A., Barry, K. L., & Fleming, M. F. (1995). Detection of problem drinkers: the alcohol use disorders identification test (AUDIT). *Southern Medical Journal, 88*, 52–59.

Shaffer, H. J., & Hall, M. N. (2001). Updating and refining prevalence estimates of disordered gambling behaviour in the United States and Canada. *Canadian Journal of Public Health, 92*, 168–172.

Shear, M. K., Greeno, C., Kang, J., Ludewig, D., Frank, E., Swartz, H. A., et al. (2000). Diagnosis of nonpsychotic patients in community clinics. *The American Journal of Psychiatry, 157*, 581–587. doi:10.1176/appi.ajp.157.4.581.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The mini-international neuropsychiatric interview (M.I·N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *The Journal of Clinical Psychiatry, 59*(Suppl 20), 22–33. quiz 34–57.

Shulman, L. M., Taback, R. L., Bean, J., & Weiner, W. J. (2001). Comorbidity of the nonmotor symptoms of Parkinson's disease. *Movement Disorders, 16*, 507–510. doi:10.1002/mds.1099.

Slevin, S. (2004). *Statistical Analysis of Epidemiologic Data Toronto*. ON: Oxford University Press.

Statistics Canada. (2003). *Canadian Community Health Survey (Cycle 1.2)-Mental Health and Well-being Ottawa*. ON: Statistics Canada.

Szarfman, A., Doraiswamy, P. M., Tonning, J. M., & Levine, J. G. (2006). Association between pathologic gambling and parkinsonian therapy as detected in the Food and Drug Administration Adverse Event database. *Archives of Neurology, 63*, 299–300. doi:10.1001/archneur.63.2.299-b. author reply 300.

Voon, V., Hassan, K., Zurowski, M., de Souza, M., Thomsen, T., Fox, S., et al. (2006a). Prevalence of repetitive and reward-seeking behaviors in Parkinson disease. *Neurology, 67*, 1112–1113.

Voon, V., Hassan, K., Zurowski, M., Duff-Canning, S., de Souza, M., Fox, S., et al. (2006b). Prospective prevalence of pathologic gambling and medication association in Parkinson disease. *Neurology, 66*, 1750–1752. doi:10.1212/01.wnl.0000218206.20920.4d.

Weintraub, D., Siderowf, A. D., Potenza, M. N., Goveas, J., Morales, K. H., Duda, J. E., et al. (2006). Association of dopamine agonist use with impulse control disorders in Parkinson disease. *Archives of Neurology, 63*, 969–973. doi:10.1001/archneur.63.7.969.

Zink, C. F., Pagnoni, G., Martin-Skurski, M. E., Chappelow, J. C., & Berns, G. S. (2004). Human striatal responses to monetary reward depend on saliency. *Neuron, 42*, 509–517. doi:10.1016/S0896-6273(04)00183-7.