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ORIGINAL PAPER

Dopaminergic Medication in Parkinson's Disease and Problem Gambling

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Abstract Studies on Parkinson's disease patients on dopaminergic medication report elevated rates of problem gambling. Results suggest changes in gambling behaviour are associated with the commencement and termination of dopaminergic medication implying a direct causal relationship. However, previous reports have not controlled for possible factors independent of dopamine medication contributing to the onset of problem gambling. This study aimed to explore the temporal relationships between problem gambling and dopamine medication taking into account premorbid gambling risk factors in a sample of Parkinson's disease patients. Twenty patients with Parkinson's disease meeting criteria for moderate risk or problem gambling were compared to twenty patients with Parkinson's disease who did not meet such criteria. The cross-sectional research design compared between group qualitative and quantitative differences. Participants completed an in-depth interview and timeline follow back, and battery of psychometric measures assessing impulsivity, gambling status, affective states, and obsessionality. Results revealed a complex and varied temporal relationship between dopaminergic medication onset and gambling. A small number of participants manifested excessive gambling following dopaminergic medication, with some ceasing on reduction in dosage or change in agonist class. Many demonstrated a range of individual and situational characteristic similar to problem gamblers in the general population, and in older adults with gambling problems. The obtained results provide a better understanding of the role of dopaminergic medication in problem gambling. Such findings have theoretical relevance to the reward deficiency model of gambling and have implications for the treatment of pathological gambling in PD and the general community.

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Introduction

Parkinson's disease is a progressive, complex and disabling neurological disorder characterised by significant degeneration of dopamine producing neuronal cells (Jankovic 2008). Currently there is no effective treatment; rather, drug regimes attempt to temporarily replenish or mimic dopamine in the brain to ameliorate symptoms (Fung et al. 2001).

Recent studies of patients suffering Parkinson's disease treated with dopamine agonists and/or Levodopa medication (dopaminergic medication) have reported elevated rates of impulsive behaviour/disorders including pathological gambling, hypersexuality, compulsive shopping/buying, and binge eating (Weintraub et al. 2010; Crockford et al. 2008; Dodd et al. 2005; Driver-Dunckley et al. 2003; Gschwandtner et al. 2001). With respect to gambling, prevalence studies suggest that up to 9.3 % of Parkinson's disease patients on dopamine replacement medication met criteria for problem and pathological gambling; a rate significantly higher than the reported general population rate of 1–2 % (Crockford et al. 2008; Voon et al. 2006b).

A recent cross-sectional study examined the frequency of four reward-seeking behaviours (problem/pathological gambling, compulsive sexual behaviour, compulsive buying, and binge-eating disorder) in 3,090 Parkinson's disease patients (Weintraub et al. 2010). Over 13 % of the sample met criteria for at least one impulse control disorder with gambling 5 %, compulsive sexual behaviour 3.5 %, compulsive buying 5.7 %, and binge eating disorder in 4.3 % being represented. Furthermore, 3.9 % met criteria for two or more impulse control disorders. These results were consistent with earlier findings reported by Bodi et al. (2009), Evans et al. (2009), and Crockford et al. (2008).

Crockford et al. (2008) administered the Canadian Problem Gambling Index (CPGI; Ferris and Wynne 2001) to a sample of 140 Parkinson's patients to determine the prevalence rates and severity of gambling problems in this population. Results revealed a 12-month problem gambling prevalence rate of 3.6 %, and pathological gambling, 5.7 %, giving a combined total of 9.3 %. Other similar studies have reported disparate figures, for example, 0.05 % (Driver-Dunckley et al. 2003), 2.6 % (Weintraub et al. 2006), 3.4 % (Voon et al. 2006a), 4.4 % (Grosset et al. 2006), 6.1 % (Avanzi et al. 2005), and 7 % (Lu et al. 2006).

Few studies to date have controlled for additional possible factors independent of medication that may contribute to appetitive/impulsive behaviours in Parkinson's disease. Significantly, problem and pathological gambling behaviours occur in only a small subset of Parkinson's disease patients despite the widespread use of dopaminergic medication (Grosset et al. 2006; Weintraub et al. 2006; Lu et al. 2006; Voon et al. 2006a, b). Previous research has identified a number of individual factors such as high novelty seeking traits, personal or immediate family history of alcohol use disorders, mood disturbances, impaired planning, and a prior history of impaired impulse control behaviours as variables associated with the development of pathological gambling and other impulse control disorders in Parkinson's disease (Djamshidian et al. 2011; Voon et al. 2006a, b; Crockford et al. 2008; Bodi et al. 2009).

Impulse control problems in Parkinson's disease may have theoretical relevance to the reward deficiency model of addiction and pathological gambling. Previously, it has been postulated that dopamine synaptic release stimulates a number of dopamine receptors resulting in increased feelings of wellbeing and stress reduction (Blum et al. 2000). This process has been described as a "reward cascade". However, when dopamine deficits create an ineffective cascade effect, individuals tend to experience anxiety, anger, low self-esteem and aversive behaviours (Raylu and Oei 2002; Blum et al. 2000). These individuals may engage in compulsive activities (i.e., gambling) or drug use to temporarily restore dopaminergic levels reduce aversive mood states (Sunderwirth and Milkman 1991). To date, this model has only been applied to individuals with certain genetic variants rather than disease-induced dopamine deficits.

The observation of a functional relationship between commencement and termination of dopaminergic medication and onset and cessation of gambling behaviour respectively, has led to the suggestion of a causal relationship between these two conditions (Dodd et al. 2005; Driver-Dunckley et al. 2003; Gschwandtner et al. 2001; Djamshidian et al. 2011). However, the detailed temporal sequence of the relationship remains largely unknown with previous researchers ignoring potential alternative explanations (independent of dopaminergic medication) that may account for the onset of problem gambling, for example, attempts cope with depression and stress following diagnosis (emotional escape), uncertainty of the future and anxiety over financial security (erroneous beliefs that gambling represents a rapid source of additional income), or diagnosis exacerbating a pre-existing vulnerability to gambling.

The current study was designed to investigate putative factors independent of medication that may contribute or exacerbate problem gambling behaviours. It was hypothesised that (1) The onset and cessation of problem gambling would emerge in parallel with the commencement and termination of dopaminergic agonist and/or Levodopa medication regimes, and (2) That non-medication external or intra-psychic pre-morbid and/or concurrent factors can be identified as possible alternative explanations to dopaminergic action accounting for manifest increased gambling in a proportion of such patients.

Method

Participants

Forty patients with Parkinson's disease and on dopaminergic medication participated in this study. Of the sample, 57.5 % (n = 23) were recruited from a population of patients already attending a university research clinic, 27.5 % (n = 11) through local support groups for Parkinson's disease, 10 % (n = 4) from gambling counseling services, and 5 % (N = 2) through a community health centre.

Inclusion criteria included (1) a diagnosis of Parkinson's disease as determined by a neurologist or physician specialising in movement disorders, (2) adherence to a medication regime of one or more dopaminergic therapies (Bromocriptine, Cabergoline, Pergolide, Pramipexole, Rotigotine), Levodopa therapy (Carbidopa/Levodopa, Carbidopa/Levodopa/Entacapone, Levodopa/Benserazide), or a combination of these pharmaceutical treatments, (3) increased gambling while taking dopamine replacement therapy (PG_PD), or no change in gambling while taking dopamine replacement therapy (NG_PD).

Exclusion criteria included significant cognitive deficits based on the Addenbrooke's Cognitive Examination-Revised assessment (ACE-R; Mioshi et al. 2006); however, on the

basis of assessment scores and corroborated by information from spouses, no participants were excluded for reasons of cognitive impairment. No patients were excluded on the basis of a current episode of mania or psychosis.

Twenty participants meeting criteria for problem gambling or moderate risk gambling subsequent to Parkinson's disease diagnosis (PG_PD) were matched to a comparable group of twenty participants with Parkinson's disease who did not meet such criteria (NG_PD) on the Problem Gambling Severity Index assessing gambling status (Ferris and Wynne 2001). The groups did not differ significantly on gender, age, age of onset, duration of disease (date of diagnosis to interview date calculated in years), or disease severity as categorised by the Hoehn and Yahr staging system (H&Y scale; Hoehn and Yahr 1967). Using a compromised power analysis it was recommended a sample size of 20 in each condition in order to sufficiently determine significant differences. Using a one-tailed *t* test for independent samples with a predicted large effect size of D = 0.8 would provide a critical t ratio of 1.273 (df, 38) to give a power value of 1-β error probability of 0.89. This was considered sufficient to determine group differences for the purposes of this mixed qualitative and quantitative study.

Procedure and Design

Patients who reported an increase in their gambling behaviours or urges since commencing dopaminergic medication, and obtained PGSI scores within the moderate risk or problem gambling (Ferris and Wynne 2001) were allocated to the PD_PG sample. Patients who reported no change to their gambling behaviour or urges, and scored within the non-problem range on the PGSI were allocated to the comparison sample NG_PD.

Participants were administered a battery of questionnaires and completed a semi-structured interview as described below. Accuracy of medication and disease severity was verified in 92.5 % of participants (n = 37) by confirming prescriptions with existing clinic databases, reports from GP or treating physician, family informant and/or community nurses.

Measures

Participants were administered the following battery of psychometric and semi-structured interview schedules.

Problem Gambling Severity Index (PGSI; Ferris and Wynne 2001): This 9-item subscale of the Canadian Problem Gambling Index (Ferris and Wynne 2001) was used to determine the presence and severity of problem gambling. Each item is scored along a 4-point Likert Scale: Never (0), sometimes (1), most of the time (2), and almost always (3). Total scores range from 0 to 27, with higher scores indicating greater risk of problem gambling. Cut-off scores adhered to those used in original validation of the PGSI: 0 = non-problem gamblers, 1–2 = low risk gambler, 3–7 = moderate risk gambler and 8–27 = problem gambler. The instrument has a demonstrated a test–retest reliability and Cronbach's alpha scores indicating good internal consistency and stability (Ferris and Wynne 2001).

Gambling Treatment Outcome Monitoring System (GAMTOMS; Stinchfield and Winters 1996): This measure was used to elicit demographics, clinical and treatment history, recent gambling behaviours including gambling frequency for each game and gambling debt/loss. The measure incorporates the South Oaks Gambling Screen (SOGS: Lesieur and Blume 1987), DSM-IV (American Psychiatric Association 2000), Behaviour and Symptom Identification Scale (BASIS-32: Eisen 1996) and the Gambling Timeline Follow-back

(G-TLFB: Weinstock et al. 2004). The G-TLFB instrument incorporates the use of calendars and memory aids to determine specific days and amounts of money gambled over a specified time period.

UPPS-P Impulsive Behaviour Scale (UPPS-P; Lynam et al. 2006; Whiteside and Lynam 2001): This instrument was used to assess personality traits and premorbid risk factors that have been associated with pathological gambling. The UPPS-P is a 59-item self-report measure designed to assess five impulsivity-related traits: Negative Urgency, Premeditation (lack of), Perseverance (lack of), Sensation Seeking, and Positive Urgency. Negative Urgency assesses an individual's tendency to give into strong impulses, specifically when accompanied by negative emotions such as depression, anxiety, or anger and Positive Urgency assesses an individual's tendency to give into impulses under conditions of high positive affect. The five scales have good convergent validity across assessment method and good discriminant validity from each other (Cyders and Smith 2007). Average internal consistencies ranged from 0.83 to 0.94 in the current study. Test–retest reliabilities over a three-month period ranged from 0.62 to 0.81 (Smith et al. 2007).

Hospital Anxiety Depression Scales (HADS; Zigmund and Snaith 1983): This is a widely used 14-item self-report scale designed to briefly measure current anxiety and depressive symptomatology in non-psychiatric hospital and general medical patients. The HADS excludes somatic symptoms of depression and anxiety which may overlap with motor and non-motor Parkinson's disease manifestations (Zigmund and Snaith 1983; Rodriguez-Blazquez et al. 2009). Internal consistencies (Cronbach's alphas) are excellent at 0.80–0.93 for anxiety and 0.81–0.90 for depression subscales (Hermann 1996). Retest reliability shows a high correlation, $r > 0.80$, after up to 2 weeks (Hermann 1996) and 0.72 over a period of 1.69 months (Savard et al. 1998).

Questionnaire for Impulsive–Compulsive Disorders in Parkinson's Disease (QUIP; Weintraub et al. 2009): This measure was used to assess the presence of Impulse Control Disorders (ICDs) such as gambling, hypersexuality, excessive spending or buying, binge or compulsive eating, punding, hobbyism, and the Dopamine Dysregulation Syndrome. It is a brief 30-item screening questionnaire that provides a dichotomous choice (yes or no) as a response for each question. The discriminant validity of the QUIP was high for each disorder or behaviour (gambling = 0.95, sexual behaviour = 0.97, buying = 0.87, eating = 0.88, punding = 0.78, hobbyism = 0.93, walkabout = 0.7) (Weintraub et al. 2009).

Minnesota Impulsive Disorders Interview (MIDI; Christenson et al. 1994): This instrument was used to further identify concurrent impulse control disorders and impaired impulse control. The MIDI is a 119 instrument and was modified to include other impulsive and compulsive behaviours adapted from published literature regarding the presence of ICDs in Parkinson's disease patients. Although widely used in published research, to date there is very limited data regarding the MIDI's validity and reliability that has been published (Albrecht et al. 2007).

Padua Inventory-Washington State University Revision (PI-WSUR, Burns et al. 1996; Sanavio 1988): This inventory was used to measure levels of obsessive and compulsive symptoms as possible premorbid risk factors contributing gambling problems. The PI-WSUR contains 39-items rated on a five-point Likert scale. Internal consistency for the PI-WSUR total score were reported to be excellent by (Burns et al. 1996) (Cronbach's alpha = 0.92), and for the subscales was fair to good with alphas ranging from 0.77 to 0.88. Test–retest reliability is reported to be good at 0.76 for the PI-WSUR total score and ranged from 0.61 to 0.84 for the subscales over a 6- to 7-month interval (Burns et al. 1996).

Addenbrooke's Cognitive Examination Revised (ACE-R; Mioshi et al. 2006) and Mini Mental State Examination (MMSE; Folstein et al. 1975) was administered to assess various

cognitive domains such as memory, language, visuo-spatial components, and verbal fluency. The ACE-R has been reported to have high internal consistency; good construct validity and high sensitivity (Komadina et al. 2011).

S*emi Structured Interview* (derived from Steele and Blaszczynski 1998) was used to obtain detailed information about all gambling behaviours (e.g., preferred forms of activities, frequency, betting patterns, accumulated losses, etc.), gambling history including early and peak gambling behaviours, degrees of preoccupation, urges and self-control, cognitions and appraisals of gambling, family history of addiction, psychosocial impact of gambling, and any treatment or attempts to cease or reduce their gambling. The interview also assessed current family and social relationships, academic and work status/history, and social functioning.

Information was elicited on current and previous mental health concerns (both diagnosed/treated and undiagnosed/untreated), self-perceived changes in coping abilities and strategies, and substance consumption.

Additional questions were included to address impact of Parkinson's disease including prescribed medications, estimates of disease duration, disease severity, history of medication treatment, and participant's view of their functioning and coping skills.

The temporal relationship between each variable of interest and onset of problem gambling was carefully delineated on the timeline. The allocation of participants into each category was done through inter-ratings by the authors until consensus was achieved.

Results

Demographics of the samples are described in Table 1. The groups did not differ significantly on gender, age, age of onset, duration of disease (date of diagnosis to interview date in years), or disease severity as categorised by the Hoehn and Yahr staging system.

A Chi square test for independence was nearing significance χ^2 (1, $n = 40$) = 0.30, $p = 0.058$, $\phi = -0.30$ between employment status (medical retirement and planned retirement/employment) and condition (PG_PD and NG_PD).

Medication and dosage for PD_PG and NG_PD groups are described in Table 2 and includes information regarding PG_PD medication during their period of gambling and NG_PD at time of interview.

Changes in Gambling and Dopaminergic Medication

Gambling and Medication Onset

Within 6 months of commencement of dopaminergic medication, 80 % (n = 16) of PG_PD reported an increase in gambling behaviour (i.e., frequency and amount spent), 10 % (n = 2) an increase in urge to gamble but denied increases in behaviours, and 10 % (n = 2) revealed pre-existing gambling problem prior to the commencement of medication. Therefore, 90 % of PG_PD sample identified a noticeable increase in their gambling behaviours and urges after commencing medication. Within this 90 % of PG_PD who increased their gambling, PGSI scores fell within 80 % problem gambling (n = 16) and 20 % (n = 4), the moderate risk gambling range.

While on dopaminergic (DA) medication, PGSI scores for NG_PD indicated 20 % (n = 4) experienced decrease in their gambling behaviour, and 80 % reported no change in

Table 1 Demographic characteristic of participants (n = 40)

	PG_PD (n = 20)	NG_PD (n = 6)
Male/female	15/5	15/5
Mean age [mean (SD)]	64.5 (8.0)	67.6 (6.3)
Disease duration (years)	1–20	3–19
Mean (SD)	8 (5.0)	7.9 (4.2)
Age of onset (years)	40–79	48–76
Mean (SD)	56.4 (9.0)	59.4 (7.8)
Disease severity	1–4	1–4
H&Y staging scale [mean (SD)]	2.7 (0.9)	2.3 (0.9)
Marital status (n)		
Married/partnered	16	17
Divorced/separated	3	2
Widowed	1	1
Single	0	0
Employment status (n)		
Full-time/part-time/voluntary	2	6
Planned retirement/never employed	5	7
Medically retired	13	7

their gambling behaviour and urges. All participants in this sample fell within the non-problem range after DA medication was introduced.

The PGSI data was not normally distributed so nonparametric tests were utilised. To explore the between group difference regarding changes in gambling, as measured by PGSI, Mann–Whitney *U* tests were used to compare PG_PD and NG_PD PGSI scores for time points: (1) PGSI score pre-DA medication, (2) PGSI score on DA medication, and (3) PGSI completed at time of interview. Table 3 provides the mean and standard deviations for PGSI scores for each of these time points.

Wilcoxon Signed Rank Test was conducted to assess trends in gambling behavior across time periods (pre-DA, During DA, Interview) for both groups. See Fig. 1 for diagrammatic display of temporal sequence.

A Wilcoxon Signed Rank Test revealed a statistical increase in PGSI scores for the time between pre-DA and during DA for PG_PD, $z = -3.72$, $p < 0.001$, with a large effect size ($r = 0.59$). The median score of PGSI increased from pre-DA ($Md = 0$) to during DA ($Md = 17.5$). There was no significant change in PGSI scores for NG_PD across the same time period, $z = -1.6$, $p = 0.11$. A Wilcoxon Signed Rank Test revealed a statistical decrease in PGSI scores for the time period during DA and time of interview for PG_PD, $z = -3.51$, $p < 0.001$, with a large effect size ($r = 0.55$). The median score of PGSI decreased from during DA ($Md = 17.5$) to interview ($Md = 1.5$). There was no significant change in PGSI scores for NG_PD, $z = 0.0$, $p = 1.0$.

Gambling and Medication Offset

At the time of interview, 80 % of PG_PD (n = 16) changed the dosage, class or type of dopaminergic medication, and within this group 30 % (n = 6) had ceased gambling behaviours, and 50 % (n = 10) had decreased gambling behaviours. Examining the 20 %

Table 2 Medication for Parkinson's Disease patients meeting criteria for problem gambling (PG_PD) (n = 20) when gambling, and Parkinson's disease patients not meeting criteria for problem gambling (NG_PG) (n = 20) at time of interview

	PD patients meeting criteria for problem gambling (n = 20)	PD patients not meeting criteria for problem gambling (n = 20)
Dopamine agonist		
Cabergoline (n)	10	8
Min Dose (mg)	4.00	0.50
Max Dose (mg)	6.00	4.00
Mean (SD)	4.40 (0.84)	2.81 (1.46)
Monotherapy/adjunct L'dopa (n)	0/10	1/7
Pramipexole—immediate release (n)	6	4
Min dose (mg)	0.38	0.75
Max dose (mg)	800.00	200.00
Mean (SD)	384.48 (419.06)	51.69 (98.89)
Monotherapy/adjunct L'dopa (n)	0/6	0/4
Pramipexole—extended release (n)	0	7
Min dose (mg)	–	0.15
Max dose (mg)	–	600.00
Mean (SD)	–	87.24 (226.11)
Monotherapy/adjunct L'dopa (n)	0/0	0/7
Pergolide (n)	1	0
Min dose (mg)	4.00	–
Max dose (mg)	4.00	–
Mean (SD)	4.00	–
Monotherapy/adjunct L'dopa (n)	0/1	0
Bromocriptine (n)	1	0
Min dose (mg)	7.00	–
Max dose (mg)	7.00	–
Mean (SD)	7.00	–
Monotherapy/adjunct L'dopa (n)	0/1	0
Levodopa		
Carbidopa/levodopa (n)	1	1
Min dose (mg)	375.00	75.00
Max dose (mg)	375.00	75.00
Mean (SD)	–	–
Levodopa/benserazide (n)	1	0
Min dose (mg)	250.00	–
Max dose (mg)	250.00	–
Mean (SD)	250.00	–

(n = 4) of the PG_PD who had not changed DA medication, half these participants (n = 2) reported ongoing problem gambling while the other half (n = 2) reported a decrease or cessation of gambling behaviours. According to PGSI scores at time of

Table 3 Mean and standard deviation PGSI scores at pre-DA, during DA and interview

PGSI scores	PD patients meeting criteria for problem gambling (n = 20)	PD patients not meeting criteria for problem gambling (n = 20)	*z* scores
Before DA medication [*M* (*SD*)]	3.50 (5.39)	1.35 (3.64)	1.99*
During DA medication [*M* (*SD*)]	15.95 (8.5)	0 (0)	−3.73**
Time of interview [*M* (*SD*)]	5.6 (6.90)	0 (0)	−3.51**

* $p < 0.05$; ** $p < 0.01$

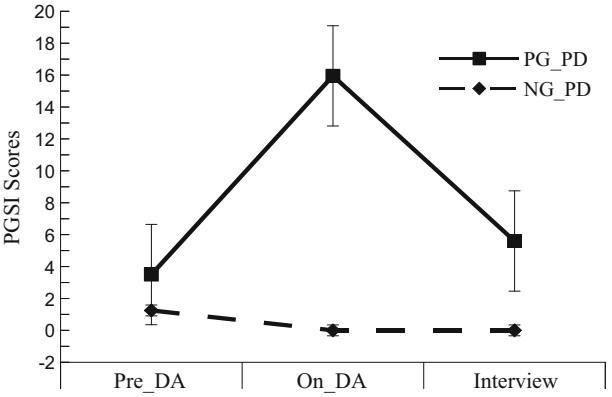

Fig. 1 Mean scores for PGSI by Parkinson's disease patients with gambling problems (PG_PD) (n = 20) and no gambling problems (NG_PD) (n = 20) across periods prior to dopaminergic medication, while taking dopaminergic medication, and time of interview. *Error bars* represent the standard error of the mean

interview, 45 % (n = 9) reported non-problem, 15 % (n = 3) reported low risk, 10 % (n = 2), moderate risk, and 30 % (n = 6) reported continued problem gambling.

Finally, in regard to reducing and/or abstaining from gambling, 70 % of PG_PD (n = 14) sought treatment for their gambling behaviours during DA treatment or after change/cease DA, including a combination of therapy/counselling (n = 12), Gamblers Anonymous meetings (n = 2), self-exclusion (n = 2), and other methods such as limiting opportunity to access money or visit venues (n = 13).

Premorbid Gambling

Chi square tests for independence were conducted to compare the two groups on severity and regularity of pre-morbid gambling. Retrospective rated PGSI scores demonstrated gambling severity across participant's lifespan before DA medication. In the PG_PD group, 65 % (n = 13) engaged in non-problem to low risk, 10 % (n = 2) moderate risk, and 25 % (n = 5), problem gambling. NG_PD retrospective PGSI scores before DA medication included 85 % (n = 17) who were within non-problem to low risk, 10 % (n = 2) moderate risk, and 5 % (n = 1) with periods of problem gambling. A Chi square test for independence was conducted to compare the proportion of PG_PD and NG_PG within non-problem, moderate risk, and problem gambling prior to DA medication. No significant results were found.

In regards to regular gambling behavior, frequency analysis indicated that 55 % (n = 11) of PG_PD and 30 % of NG_PD (n = 6) participated in regular gambling (i.e., at least once per week) before taking dopaminergic medication. A Chi square test for independence (with Yates Continuity Correction) indicated no significant association for regular gambling between PG_PD and NG_PD before commencement of DA medication, χ^2 (1, $n = 40$) = 1.64, $p = 0.20$, $\phi = 0.25$.

Other Risk Factors

Risk factors independent of dopaminergic medication were explored for both groups. A combination of *t* tests and Mann–Whitney *U* test were utilized based on normality of data distribution. Results are displayed in Table 4.

Age of PD onset, disease duration, and disease severity were identified as risk factors for PG; however, there were no significant differences between groups for these variables.

Between group differences in impulsivity traits, depression anxiety, obsessive and compulsive traits were assessed. Significant differences were found for negative urgency UPPS-P scores between the PG_PD ($M = 27.40$, SD = 6.68) and NG_PD ($M = 21.85$, SD = 6.69) groups; t (38) = −2.62, $p = 0.012$. The magnitude of mean differences (mean difference = −5.56, 95 % CI −1.27 to −1.27) was small (eta squared = 0.15). This finding indicates PG_PD participants reported elevated tendency to act rashly in response to distress (negative urgency) compared to NG_PD. In addition PG_PD participants had significantly greater positive urgency scores ($M = 27.90$, SD = 8.54) compared to the NG_PD ($M = 19.45$, SD = 4.57) sample; t (38) = −3.90, $p = 0.0001$. The effect size was close to medium (eta squared = 2.9).

An independent samples *t* test was conducted to compare the UPPS-P (lack of) premeditation scores for PG_PD and NG_PD. Results indicated PG_PD ($M = 21.95$, SD = 5.09) reported significantly greater problems with lack of planning compared to participants who have had no change in gambling ($M = 18.45$, SD = 3.39); t (38) = −2.57, $p = 0.014$ with a small effect size (eta squared = 0.15). Similarly, PG_PD participants obtained greater scores on the UPPS-P (lack of) perseverance scores; gambling ($M = 21.00$, SD = 3.92) compared to NG_PD ($M = 17.80$, SD = 4.19); t (38) = −2.50, $p = 0.017$ with a small effect size (eta squared = 0.14).

A Mann–Whitney *U* test revealed no significant difference for UPPS-P sensation seeking scores; PG_PD ($Md = 29.0$, $n = 20$ and NG_PD ($Md = 27.5$, $n = 20$), $U = 175$, $z = -0.66$, $p = 0.51$, $r = -0.10$.

A Mann–Whitney *U* test found no significant difference in depression scores for PG_PD ($Md = 6.0$, $n = 20$) and NG_PD ($Md = 3.5$, $n = 20$, $U = 126$, $z = -2.02$, $p = 0.04$. An independent samples *t* test compared anxiety scores between groups and found a significant difference in scores between PG_PD ($M = 7.3$, SD = 4.17) and NG_PD ($M = 4.9$, SD = 2.36); t (38) = −2.24, $p = 0.031$. The magnitude of the differences in the means was small (eta squared = 0.12).

An independent *t* test showed significant reduced scores for total scores for obsessive and compulsive traits on the Padua Inventory for PG_PD ($M = 8.40$, SD = 6.55) compared to NG_PD ($M = 14.05$, SD = 8.13); t (38) = 2.42, $p = 0.020$ (eta squared = 0.13). Mann–Whitney *U* tests were conducted on the other OCD traits (dressing, checking, obsessional thoughts and obsessional impulse to harm self and others) and there was no significant difference between PD_PG and NG_PD on these subscales.

The semi structured interview revealed 75 % of PG_PD experienced significant stressors (e.g., relationship discord, personal or family member's ill health or injury,

Table 4 Premorbid risk factors to gambling for PG and NG_PD

	PD patients meeting criteria for problem gambling (n = 20) *M (SD)* *Md (n)*	PD patients not meeting criteria for problem gambling (n = 20) *M (SD)* *Md (n)*	df	*t* *z*
Age of onset (years)	$M = 56.35$ (8.98)	$M = 59.4$ (7.75)	38	$t = 1.15$
Disease duration (years)	$Md = 7.0$ (n = 20)	$Md = 7.0$ (n = 20)	–	$z = -0.16$
Disease severity (H&Y stage)	$Md = 2.75$ (n = 20)	$Md = 2.25$ (n = 20)	–	$z = -1.04$
Negative urgency (UPPS-P)	$M = 27.40$ (6.68)	$M = 21.85$ (7.75)	38	$t = -2.62$*
Positive urgency (UPPS-P)	$M = 27.90$ (8.54)	$M = 19.45$ (4.57)	38	$t = -3.90$**
Planning (lack) (UPPS-P)	$M = 21.95$ (5.09)	$M = 18.45$ (3.39)	38	$t = -2.57$*
Perseverance (lack) (UPPS-P)	$M = 21.00$ (3.92)	$M = 17.8$ (4.19)	–	$t = -2.50$*
Sensation seeking (UPPS-P)	$Md = 29.0$ (n = 20)	$Md = 27.5$ (n = 20)	–	$z = -0.66$
Depression (HADS)	$Md = 6.0$ (n = 20)	$Md = 3.5$ (n = 20)	–	$z = -2.02$*
Anxiety (HADS)	$M = 7.3$ (4.17)	$M = 4.9$ (2.36)	38	$t = -2.24$*
Obsessive compulsive total (PI-WSUR)	$M = 8.40$ (6.55)	$M = 14.05$ (8.13)	38	$t = 2.42$*

* $p < 0.05$; ** $p < 0.01$

financial concerns, employment difficulties) very close in time before or after commencing the medication compared to 25 % of the NG_PD patients who reported similar stressors. A Chi square test of independence assessed the relation between the presence of significant life stressors and the onset of gambling problems while on DA. The relation between these variables was significant, χ^2 (2, $n = 40$) = 6.5, $p = 0.39$, $\phi = 0.40$.

Higher rates of other impulse control disorders were found to be prevalent among the PG_PD participants (see Table 5).

Although the other impulse control disorders were found to be at the clinical level for the PG_PD participants, there was evidence of elevated impulse disorders among the NG_PD that did not reach clinical significance.

Qualitative Results

Categories of Gambling

In total, eight different categories were classified based on specific variables and characteristics. These are described in detail below. There were four PG_PD categories and four NG_PD categories, each accounting for different proportions of the data set. The grouping of participants into categories were completed by two separate raters, and then re-rated again by the same two raters to achieve consensus. See Tables 5, 6, and 7 for patient demographic characteristics of each category.

Category One: Established Relationship Between Changes in Gambling After Commencement of Dopaminergic Medications Participants reported a clear increase of gambling behaviour and urges within 3 months of commencement of dopaminergic medication. There was no regular gambling (i.e., once a week) prior to diagnosis of Parkinson's. PGSI scores prior to dopamine medication were within non-problem or low risk range which increased to moderate risk to problem gambling after commencement of dopaminergic medication. Finally, there was no evidence or other individual or situational

Table 5 Percentage of PG_PD and NG_PD meeting criteria for clinical and elevated impaired impulse control behaviours other than gambling

	Percentage of PG_PD reporting impaired impulse control behaviours (n = 20)	Percentage of NG_PD reporting impaired impulse control behaviours (n = 20)
Hypersexuality		
Clinical	30	5
Elevated	10	35
Compulsive shopping		
Clinical	25	5
Elevate	5	5
Computer/internet usage		
Clinical	30	0
Elevated	5	20
Dopamine dysregulation syndrome		
Clinical	15	0
Elevated	5	10
Punding/hobbyism		
Clinical	30	5
Elevated	10	15
Binge eating		
Clinical	10	5
Elevated	20	5
Explosive anger		
Clinical	0	0
Elevated	5	0

factors reported that may have contributed or better explain the development of problem gambling in these participants. Five participants were allocated to Category One.

The following case study demonstrates the relationship between dopaminergic medication and onset of problem gambling.

Case Study The 64 years old male was diagnosed with Parkinson's disease in 2003 at age 56 years. At time of interview his disease severity indicated bilateral involvement without impairment of balance. He was medically retired at age 56 years because of his functioning within the workplace and reduced social/physical activities.

He first gambled in his twenties and described electronic gaming machines (EGMs) as "mindless". His PGSI scores prior to diagnosis of Parkinson's disease indicated that he fell in the non-problem range. He reported a subtle increase in urge to gamble within 1–2 months after receiving the diagnosis of Parkinson's disease, and commencing and titrating Madopar (Levodopa and Benserazide) to 62.5 mg four times per day, and dopamine agonist Permax (Pergolide Mesylate) 3 mg per day. From 2003, he started to gamble small amounts on EGMs in the company of his wife or friends. During this three-year period his gambling increased to playing EGMs three times per week when he was alone, and his PGSI scores fell in the moderate risk range.

He believes his gambling became a significant problem in 2006 after changing dopamine agonist from Permax to Sifrol and began gambling five to seven times per week. He

Table 6 Demographic characteristic of participants allocated to categories one to four (N = 20)

	Category 1 (n = 5)	Category 2 (n = 6)	Category 3 (n = 7)	Category 4 (n = 2)
Male/female (%)	4/1 (80/20)	5/1 (83/17)	4/3 (57/43)	2/0 (100/0)
Age (years old) [mean (SD)]	55–73 63.2 (7.4)	51–67 60.3 (5.9)	59–77 66.6 (7.0)	62–84 73.0 (15.6)
Disease duration (years) [Mean (SD)]	4–10 7.4 (2.3)	3–17 10 (5.7)	1–20 7.3 (6.5)	4–8 6.0 (2.8)
Age of onset (years old) [mean (SD)]	45–69 55.4 (9.0)	40–61 50.5 (7.0)	52–67 59.0 (5.6)	55–79 67.0 (17.0)
Disease severity	2–3	2–4	1–4	3.5–4
H&Y Staging Scale [mean (SD)]	2.30 (0.5)	2.8 (0.8)	2.8 (1.3)	3.8 (0.35)
Marital status (n)				
Married/partnered	4	6	6	0
Divorced/separated	1	0	1	1
Widowed	0	0	0	1
Single	0	0	0	0
Employment status (n)				
Full–time/part-time/voluntary	0	0	3	0
Planned retirement/never employed	1	1	2	1
Medically retired	4	5	2	1

raised concerns about his gambling behaviour and medication and his treating neurologist changed his medication to Madopar (Levodopa/Benserazide) 62.5 mg four times per day and Stalevo (Levodopa/Carbidopa/Entacapone) 200/50/150 mg five times per day. He also completed a self-exclusion application at his local gaming venues, reduced access to his bankcards and car in an attempt to decrease opportunities to gamble. At the time of the interview in 2011, he had abstained from gambling but admitted the urge to gambling persisted.

Category Two: Probable Relationship Between Changes in Gambling After Commencement of Dopaminergic Medications Participants reported an increase in gambling behaviours and urges within 3 months after commencing anti-Parkinsonian medication. In contrast to Category One, other factors independent of the medication potentially influencing or contributing to changes in gambling were reported. These included periods of regular premorbid gambling, ineffective coping skills, mental illness, and increased accessibility to gambling venues (Petry 2005; Potenza and Hollander 2002; Blaszczynski and Nower 2002). Six participants were allocated to Category Two.

The following case demonstrates an association between commencement of dopaminergic medication and onset or increase in gambling with other factors possibly contributing/exacerbating changes in gambling.

Case Study Aged 50 years time of the interview, he was diagnosed with Parkinson's disease 47 years. His current disease stage was classified bilateral involvement without impairment. He reported considerable anxiety about the diagnosis and prognosis of Parkinson's disease.

He first gambled aged 22 years old and gradually increased time and money spent to the extent that at age 40 years, he played EGMs at least weekly. He estimated he was within

Table 7 Demographic characteristic of participants allocated to categories five to eight (N = 20)

	Category 5 (n = 6)	Category 6 (n = 11)	Category 7 (n = 1)	Category 8 (n = 2)
Sex: male/female (%)	5/1 (83/17)	6/5 (55/45)	1/0 (100/0)	2/0 (100/0)
Age (years old) [mean (SD)]	61–73 66.2 (3.8)	55–79 66.0 (6.6)	73 –	76–77 76.5 (0.7)
Disease duration (years) [mean (SD)]	3–14 8.0 (3.6)	3–19 8 (5.0)	12 –	5–7 6.0 (1.4)
Age of onset (years old) [mean (SD)]	50–63 58.2 (5.2)	48–76 50.5 (7.0)	61 –	69–72 70.5 (3.5)
Disease severity	1.5–3	1–4	2.5	3–4
H&Y Staging Scale [mean (SD)]	2.25 (0.5)	2.2 (1.1)	–	3.5 (0.71)
Marital status (n)				
Married/partnered	5	11	1	0
Divorced/separated	0	0	0	0
Widowed	0	0	0	1
Single	1	0	0	1
Employment (n)				
Full-time/part-time/voluntary	2	3	1	0
Planned retirement/never employed	1	5	0	1
Medically retired	3	3	0	1

the low to moderate risk. At age 47 years old, at time of diagnosis with Parkinson's disease, he commenced Sinemet (Carbidopa/Levodopa) 125 mg three times per day, and began playing EGMs three to four times per week. He also commenced visiting the casino to play table games with friends. His gambling continued to increase, and by age 49, estimated he was spending between $1,000 and $5,000 per week. His PGSI scores fell in the high end of problem gambling range. Around this time his medication regime had been changed to Sifrol 1 mg (Pramipexole- Extended Release) and Stalevo (Levodopa/Carbidopa/Entacapone) 200 mg three times per day. At this time he was also experiencing significant stress at work and stated he reacted to this situation with anger and aggression. He noted his anger and depression at work coincided with increased urges to gamble.

At time of interview he disclosed the problem to his treating neurologist and agreed to change his medication regime. In addition, he was considering self-exclusion from the casino and local gambling venues and reducing access to his back accounts.

Category Three: Possible Relationship Between Changes in Gambling After Commencement of Dopaminergic Medications Participants reported some increase of gambling behaviour and urges within a period of 6 months after commencement, increase or new combination of anti-Parkinsonian medication. A number of other factors reported via the semi-structured interview represented plausible alternative explanations to dopaminergic medication as contributing to his problem gambling. Seven participants were allocated to Category Three.

The following case study demonstrates the temporal relationship between dopaminergic medication and changes in gambling behaviours; however, there are possible alternative explanations for the behaviour change.

Case Study The female participant was 61 years at time of assessment and was diagnosed with Parkinson's disease 7 months prior to interview. Her disease severity was unilateral with minimal or no functional disability. She was diagnosed with breast cancer and underwent mastectomy surgery the same month as she received the diagnosis of Parkinson's disease. She was commenced on Sinemet (Carbidopa/Levodopa) 100/25 mg and had followed directions to titrate her does up to three tablets per day.

She first gambled at age 24 years on EGMs, and continued to gamble occasionally on horse betting at the Totalisator Agency Board (TAB: Off track betting). Between ages 39 and 43 years she abstained from all EGM gambling; however, she continued wagering on horses. She subsequently experienced marital conflict and two marriage breakdowns, which led to an increase in her EGM gambling and betting as a way to escape feelings of loneliness. She scored in the problem gambling range.

She reported a noticeable increase in gambling since commencing and titrating Sinemet (Carbidopa/Levodopa) 100/25 mg describing an urge "to keep going". Over six-months the amount spent on gambling increased from $500 to $2,000 weekly. Her PGSI score (Ferris and Wynne 2001) had increased to the high end of the problem gambling range. At time of interview, she planned to discuss her recent increase in gambling with her neurologist and considered seeking counseling.

Category Four: Unlikely Relationship Between Changes in Gambling After Commencement of Dopaminergic Medications Participants reported frequent and large sums of money spent on gambling concurrent with dopaminergic medication; however, further questioning revealed these behaviours were present premorbid and did not increase since commencing medication. In addition, these participants reported PGSI scores retrospectively rated for the 12 months prior to commencing anti-Parkinsonian medication within the moderate risk range.

Case Study The participant was 62 years old at time of interview, and was diagnosed with Parkinson's disease at age 55. His disease stage indicated a severe disability but he was still able to walk and stand unassisted.

He first gambled on EGM at age 15 with friends with his behaviour gradually escalating to his early forties where he played EGMs weekly and purchasing twice weekly lottery tickets. Around age 52, 3 years before commencement of dopaminergic medication, his EGM gambling increased to a daily frequency spending up to $2,000 per session. In 2005, 2 years after diagnosis and commencement of Cabaser (0.5 titrated to 4 mg), he medically retired which lead to marked decrease in his income. As a result his gambling also decreased. He reported the change in dopamine agonist medication in 2009 from Cabaser 4 mg to Sifrol (Pramipexole) Immediate Release 250 mcg three times daily, Stalevo (Levodopa/Carbidopa/Entacapone) 200/50/200 mg three times daily, and Sinemet (Carbidopa/Levodopa) 100/25 mg twice daily "made it easier not to gamble"; however that same year he was legally declared bankrupt and he reduced EGM gambling to once a week. He had also commenced therapy with a gambling counselor. He identified boredom as a trigger to gamble, and utilised free transport to the gaming venues in order to gain social contact and stimulation. At the time of interview he was gambling at least weekly. His self-report PGSI score remained in the moderate risk range before, and during dopamine agonist medication regime.

Category Five: Non-gambler, No Change After Dopaminergic Medication Commenced The criterion for Category Five was restricted to a maximum of two small gambling bets across their lifetime and PGSI scores of zero. Six participants were allocated to this category.

Category Six: Some Non-problem Gambling, No Change (or Decrease) After Dopaminergic Medication Commenced Participants reported instances of non-problem gambling prior to dopaminergic medication, and no changes in gambling preferences or increase in gambling behaviours (i.e., frequency or amount spent) after commencement of dopaminergic medication. PGSI scores never exceeded low risk. Eleven participants were allocated to Category Six.

Category Seven: Some Non-problem Gambling, Some Increase After Dopaminergic Medication Commenced Participants reported an increase in gambling behaviours after their diagnosis of Parkinson's disease. This increase of gambling occurred 12 months after commencing or changing dopaminergic medication and fell within the non-problem range. One participant was allocated to Category Seven.

Category Eight: Significant Previous Gambling History, No Change (or Decrease) After Dopaminergic Medication Commenced Participants reported a history of premorbid moderate risk to problem gambling, but fell within the non-problem or low risk range in the 12 months prior to diagnosis and dopaminergic medication. Two participants were allocated to Category Eight.

Discussion

This study confirms and extends findings from prior work reporting an association between dopamine agonist and/or dopamine replacement therapy (including Levodopa medication) and an increased risk of developing impulse control disorders (Weintraub et al. 2010; Crockford et al. 2008; Voon et al. 2006a, b). However, the findings of the present study demonstrated such relationships vary in strength and across a spectrum of associations rather than in a dichotomous fashion.

The majority of participants experiencing gambling problems reported a decrease or cessation in behaviours gambling following a change or termination of dopamine agonist medication. At face value, these results would support the hypothesis and previous findings of full or partial remission of impulse control behaviours after the discontinuation or decrease of dopamine agonist (Mamikonyan et al. 2008; Drapier et al. 2006). However, on closer inspection, many participants were still experiencing gambling problems after significant adjustments to medication regime, albeit to a lesser severity. The lag between medication reduction and gambling reduction could be attributed to selectivity for receptors subtypes, half life, and metabolism that vary between different dopamine agonists and patients themselves. However, examination of the participants' timelines reveals many participants struggled with gambling for months after adjustments to medication regime. Furthermore, over two thirds of the participants experiencing gambling problems on dopaminergic medication also implemented gambling reduction strategies such as therapy/counselling, self exclusion and limiting opportunity to access money or gambling venues.

The commencement of medication and emergence of gambling behaviours were clearly associated in a small subset of Parkinson's disease patients. It appears once problem gambling behaviours have been activated, the influences of different aspects of gambling addiction such as distorted beliefs and cognitions, reward and reinforcement, neurotransmitter dysregulation, and psychological vulnerabilities serve to exacerbate and maintain problems.

The second hypothesis was only partly supported. There was no significant association between regular gambling statuses prior to the diagnosis of Parkinson's disease. This

finding is consistent with previous research that indicated the majority of Parkinson's disease patients with problem gambling had never gambled or only participated in low risk gambling before the onset of dopamine agonist therapy (Djamshidian et al. 2011).

The results demonstrated a relationship between severity of premorbid gambling and subsequent gambling on dopaminergic medication. Participants who did develop gambling problems reported more severe premorbid gambling compared to those not experiencing an increase in gambling, and supports similar findings by Weintraub et al. (2006) and Weintraub et al. (2010). Therefore, the severity of premorbid gambling rather than regular engagement has been identified as risk factor for problem or pathological gambling in the context of dopaminergic medication.

There was no difference found between the two groups on age, age of onset, disease duration, or disease severity. These findings were not consistent with previous research (Singh et al. 2007; Voon et al. 2007; Ceravolo et al. 2010) but may reflect specific demographic characteristic and prescribing practices of the different studies. Longer disease duration and disease severity in Parkinson's disease indicates a greater reduction in dopamine levels and potentially greater levels of dopaminergic medication; however, the non-significant results between groups may highlight the subtle differences between dopamine neurotransmitters and pathways involved in dopamine reward pathway (nucleus accumbens) and the motor circuit (operating predominantly via the putamen). These findings are consistent with the claim of Voon and Fox (2007) that Parkinson's disease related neurobiological features do not play a primary role in the development of gambling but do interact with individual vulnerability to increase susceptibility. Moreover, regarding age as a risk factor, recent research has demonstrated an increase in gambling behaviour in adults over the age of 51 years in the general population and is commensurate with the age range of the current sample. Nower and Blaszczynski (2008) identified older adults as a distinct subgroup of problem gamblers whose gambling behaviour is likely to be linked to situational factors.

It was noted that the PD_PG group overall appeared to exhibit a higher exposure/dose history to dopamine agonists than the NG_PG group. It is not clear why these participants were on such medication regimes but it could be speculated that PG worsening is a dose-dependent concern, or alternatively, there some thing about the PD in the patients with more PG risk, that makes them more refractory to DA agonist treatment resulting in higher prescribed doses of medication.

In relation to other risk factors, it was found that certain impulsivity traits such as negative urgency, positive urgency, lack of planning and lack perseverance as measured on the UPPS scale were more frequently reported in participants who developed gambling problems. Similar findings were reported by Evans et al. (2005), Ceravolo et al. (2010), and Voon et al. (2007), and is also consistent with research on personality traits associated with pathological gambling in the general population (Raylu and Oei 2002; Petry et al. 2005; Potenza and Hollander 2002). Alternatively impulsive traits demonstrated by some Parkinson's disease patients may actually be a direct effect of mania induced by the dopaminergic treatment (Lauterbach 2004) or due to disinhibited behaviours and cognitive impairment. There were no differences between the two groups on sensation seeking traits and this finding may be explained by common non-motor features of Parkinson's disease, such as apathy which is correlated with mesolimbic dopaminergic denervation (Voon et al. 2011). It is also possible that this neurobiology may have influenced this personality characteristic within the current sample (Pandya et al. 2008). Evans et al. (2005) also found a positive relationship between low sensation seeking and Parkinson's disease.

Depression is commonly associated with problem gambling in the general population; however, there was no significant difference in depression scores between the gambling and non-gambling sample. Depression is also one of the most common non-motor symptoms of Parkinson's disease and many participants, in both samples, reported taking adjunct antidepressant medication. There is a lack of controlled studies on antidepressant therapy in Parkinson's' disease and very limited systematic research into the efficacy of dopaminergic medication on depression (Lemke et al. 2004). Anxiety symptoms also commonly occur in Parkinson's disease patients and have been associated with fluctuations in medication status (Pandya et al. 2008). Anxiety symptoms were found to be more elevated in participants who gambled compared to those participants that did not gamble. This is consistent with gambling literature that identifies a positive relationship between gambling behaviours and increased levels of anxiety as an outcome (Blaszczynski and Nower 2002).

It was further predicted that premorbid stressors such as relationship difficulties and forced retirement would act as risk factors in the development of problem gambling in Parkinson's disease patients. Almost two thirds of the sample experiencing gambling problems on dopaminergic medication reported they were medically retired due to the physical and cognitive impact of Parkinson's disease compared to only one third of the non-gambling sample. Blaszczynski and Nower (2002) identified a cohort of problem gamblers in the general population who were emotionally vulnerable as a result of psychosocial stressors and biological factors, and utilised gambling primarily to relieve aversive mood states by providing escape or arousal. Access and opportunity to attend gambling venues is another factor to consider in regards to medically retired patients. These participants noted relatively easy access to Internet gambling and EGMs in local hotel and sports clubs as a means to relieve boredom and increase stimulation.

Three quarters of the gambling sample described experiencing significant stressors very close in time before or after commencing the medication compared to one quarter of the non-gambling group. Stress included subjective distress about relationship, family, work and financial concerns. Poor coping skills and limited social supports combined with psychosocial stressors are considered significant contributors to the development and maintenance of problem gambling (Blaszczynski and Nower 2002). Studies have shown electronic gambling machine players, particularly women, gamble to combat loneliness, feelings of social isolation, and other psychiatric problems, all factors reported in the current sample (Nower and Blaszczynski 2008). Once gambling behaviours are initiated as an ineffective coping strategy, a habitual pattern of gambling and dependence was likely formed which further contributed to this relationship and financial concerns. It was earlier concluded the experimental sample yielded a higher severity of premorbid gambling history, which suggests gambling had previously been used as an emotional escape or arousal. This finding lends support to the dopamine reward deficiency model (Blum et al. 1996) given that gambling for these participants represented a means to cope with aversive moods and affective states both prior and during dopamine replacement therapy.

Over half of the Parkinson's disease patients who participated in gambling also engaged in other dopamine stimulating behaviours, compared to only one quarter of control sample and is consistent with previous research (Weintraub et al. 2010; Singh et al. 2007). The current finding supports previous postulations by Voon and Fox (2007); that over-dosing parts of the striatum that are less dopamine depleted (e.g., nucleus accumbens) drives the impulse control problems. Alternative interpretations include reduced dopamine in the limbic structures act as motivation to engage in multiple reward seeking activities (e.g., hypersexual behaviour, compulsive buying, binge eating) rather than relying on one

behaviour (i.e., gambling) to temporarily restore dopamine neurotransmitter (Sunderwirth and Milkman 1991). This finding can be interpreted as further speculative evidence for the Reward Deficiency Model (Blum et al. 1996).

There are a number of limitations in this investigation that are important to consider. Firstly, the relatively small sample size may limited the statistical analysis options and reduce the available power of the quantitative results; however, the major aim of the present study was to explore the temporal relationship between onset of gambling and Parkinson's disease unlike other studies in this area that had larger sample sizes. The current study should be viewed as a preliminary investigation of factors not previously considered or masked by large prevalence studies.

Participants could not provide sufficient accurate data regarding exact time periods between commencement of medication and commencement of problem gambling consequently limiting options for valid analyses. The use of retrospective data was also potentially problematic due to subjective bias, mistaken memory or misrepresentation. The reliance on self-report bias was minimised because information was frequently corroborated with spouses, family member, and clinic database and health care providers. More work using longitudinal and prospective designs is recommended so demographic impacts, shared aetiology, and natural courses of these behaviours can be more fully elucidated.

The current study has implications for the management of Parkinson's disease patients identified with gambling and other impaired impulse control behaviour. It has been suggested that dopaminergic medication may precipitate the problem gambling, and repeated excessive gambling may lead to multiple biological, social and psychological consequences. It is these variables that then reinforce and maintain the gambling behaviours rather than the exclusive influence of dopaminergic treatment. Physicians prescribing dopamine agonists should take into consideration external and intra-psychic factors that may require some form of intervention to prevent relapse or onset of gambling problems that emerge independently of the effects of medication. Titrating dosage or changing medication may not be effective in preventing episodes of gambling.

The critical findings of the study should help change clinical practice. One of the most significant findings is the influence of factors independent of dopaminergic medication. Therefore, treatment for gambling problems need to address these factors and cannot rely on cessation of medication alone. Cognitive behaviour therapy has been shown to be an effective treatment approach for problem gambling because of the importance given to the client's cognitions and underlying beliefs (Sharpe and Tarrier 1993). Alternative activities such as appropriate volunteer work or other distractions such as hobbies should be encouraged especially for those who are medically retired and at risk to use gambling for entertainment and relief of boredom. It is recommended clinicians provide education and information to patients and caregivers about the risks and warning signs of problem gambling and other impaired impulse behaviours in the context of dopaminergic medication. In addition, patients should be routinely screened for gambling behaviours before commencement of dopaminergic medication, and at all subsequent appointments, especially after commencing, increasing, and/or modify anti-Parkinsonian medication regime.

In conclusion, gambling problems are associated with dopaminergic medication in a small number of Parkinson's disease patients. This temporal relationship was shown to vary in strength and there was limited evidence to conclude a direct causal relationship without intervening factors. These factors include individual characteristics, such as premorbid impaired impulse control behaviors, impulsivity traits, anxiety and aversive emotions, and ineffective coping strategies, as well as situational factors, such as relationship stressors, forced medical retirement, and limited social supports. These individual

and situational factors are similar to problem gamblers in the general population and more specifically in older adults with gambling problems. The results contribute further to understanding gambling based on dopamine reward mechanisms and the reward deficiency model. Finally, the critical findings of the study should lead to changes in clinical practice for the prevention and treatment for potential gambling problems within this specific population.

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