Cognitive-Behavioral Therapy for Pathological Gambling in Parkinson's Disease: A Pilot Controlled Study

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Key Words

Parkinson's disease · Pathological gambling · Therapy response · Cognitive-behavioral therapy · Clinical features

results may provide guidance for obtaining accurate diagnostic information in pathological gamblers by properly identifying patients with specific needs that may be targeted with treatment.

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Abstract

Objectives: The main objective of this study was to compare the clinical characteristics and differences in response to treatment of two groups of pathological gamblers: with comorbid Parkinson's disease (PG + PD) and without (PG – PD). **Methods:** Clinical and psychopathological profiles and response to cognitive-behavioral treatment were assessed in 15 PG + PD and 45 PG – PD individuals consulting a specialized hospital Unit. **Results:** Statistically significant differences were observed between the two groups on a series of clinical variables. PG + PD patients were older and presented later onset of problematic gambling behaviors, lower alcohol consumption and higher bingo playing than PG – PD patients. No significant differences were noted in psychopathology except for lower measures of hostility in the PG + PD group. No statistical differences were detected between groups in terms of response to treatment. **Conclusion:** These

Introduction

Pathological gambling (PG), included as an impulse control disorder not elsewhere classified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [1], is characterized by a failure to resist the impulse, drive or temptation to perform an act that is harmful to the person or to others. Impulse control disorders share biopsychological vulnerabilities and clinical and psychopathological characteristics, expressed in the form of neuropsychological deficits [2, 3], personality traits, namely impulsivity or risk-taking [4], and psychopathological impairment [5]. In individuals with PG, higher impulsivity has been associated with specific subgroups of patients, severity of the disorder, poorer psy-

chological functioning, less effective coping skills and poorer treatment outcome [2, 6]. Furthermore, PG shows high comorbidity rates, especially with substance use disorders [7], affective and anxiety disorders, attention deficit hyperactivity disorder [8, 9], and personality disorders [10].

Impulse Control Disorders and Parkinson's Disease

Impulse control disorders are relatively common in Parkinson's disease (PD), with an estimated prevalence of 9.3% compared to 1.6% in the general population [11]. Furthermore, PG has been reported as a complication in the treatment of PD [12–14]. In fact, PG is one of several disturbances recognized to arise *de novo* in the context of PD treatment with dopaminergic medications [15, 16]. Other behaviors thought to be induced by this type of pharmacological treatment include the addictive use of dopamine replacement therapy, stereotyped behaviors, known as punding, and other impulse control disorders, such as hypersexuality, compulsive buying and compulsive eating. Although dopamine replacement therapy is thought to play a key role in the reward and incentive system, the fact that PG emerges in only a subset of individuals treated with dopaminergic drugs suggests an interaction with individual vulnerabilities. Younger age at PD onset [17, 18], personal and family history of alcohol abuse [19, 20] and impulsive and novelty-seeking personality traits [14] have been proposed as risk factors for the development of PG in PD. Although the pathophysiological mechanism whereby dopaminergic drugs may trigger PG in PD is not known, some studies are suggesting that this might be due to hyperfunction in specific brain areas, such as subthalamic and limbic region [21, 22], but also to greater release of dopamine in the ventral striatum [23].

Cognitive-Behavioral Therapy in PG and PD

Traditionally, PD has not only been associated with motor symptoms and cognitive deficits, but also with affective symptoms and behavioral deterioration along with the progression of the disease [24]. Although cognitive-behavioral therapy (CBT) has been demonstrated to be effective for treating PG [6, 25, 26] and for the management of depressive symptomatology in PD [27, 28], there is a lack of studies that focus on the use of CBT to treat PG in patients with PD. Testing nonpharmacological treatment for the management of impulse control disorders in PD is particularly important given that many PD patients with PG are reluctant or unable to decrease the dosage of their dopaminergic medication [29]. Thus, we

consider that comparing treatment responses of PD and non-PD patients with PG could inform best practices for the treatment of these complex disorders.

Aims of the Study

The specific goals of this research were threefold: (a) to assess clinical and psychopathological characteristics in individuals with and without PD who are pathological gamblers (PG + PD versus PG – PD); (b) to characterize differences in therapy response between PG – PD and PG + PD groups; (c) to assess the main predictors of developing PG + PD taking into account severity of the disorder, sociodemographical and psychometrical characteristics.

Hypotheses

Based on the few reports in the literature where clinical features of PD patients with PG were comparable to those described in clinical samples of PG [30], we hypothesized that the therapy response in both conditions would be similar.

Methods

Participants

Subjects were recruited for the study between September 2004 and February 2009. The initial sample included 1,182 PG patients consecutively admitted to the Pathological Gambling Unit at the University Hospital of Bellvitge. Individuals were excluded from the analyses if they had missing values in any of the relevant items ($n = 202$). Of the 980 remaining patients, 15 PG patients (1.47% of the total) presented PD and were included in the present study. For all of the PD patients, PD was a premorbid medical condition (development of PG after diagnosis of PD and initiation of dopamine replacement therapy). The selected patients had been referred to our specialized unit by neurologists and primary care physicians for treatment of PG. While in therapy, PD patients remained under the care of their physicians. Individuals were excluded from the analyses if they had missing values for any diagnostic items. To increase the statistical power, a pairwise matching comparison procedure, was used to form a comparison sample of 45 patients diagnosed with PG. Each participant was paired with a randomly selected patient with the same PG diagnosis (in our unit we see patients with other impulse control disorders and several forms of behavioral addictions), sex and type of therapy (specifically individual CBT). Randomization was performed by computer. All participants were diagnosed using DSM-IV criteria obtained through a semi-structured clinical interview (SCID-I), conducted by experienced psychologists and psychiatrists. The mean age of the whole sample was 46.2 years ($SD = 16.1$). The mean age at onset of the PG was 41.0 years ($SD = 15.9$), and the mean duration of the disorder was 5.0 years ($SD = 3.9$). All PG + PD patients were taking at least one dopamine agonist; of these, 14 patients started gambling after the onset of PD and the initial

tion of pharmacotherapy. The mean age at onset of pharmacotherapy for PD was 55.6 years (SD = 10.3).

This study was carried out in accordance with the latest version of the Declaration of Helsinki. The Ethics Committee of the University Hospital of Bellvitge approved the study, and informed consent was obtained from all participants.

Assessment

We developed a comprehensive battery of assessments to identify PG symptoms, general psychopathology, and personality. The battery included the South Oaks Gambling Screen (SOGS) [31], a 20-item diagnostic questionnaire that effectively discriminates between probable pathological gamblers, problematic gamblers, and non-problematic gamblers. A Spanish validation of this questionnaire [32] showed high reliability and validity: its test-retest reliability is 0.98 and internal consistency 0.94 (Cronbach's α), and its convergent validity with regard to DSM-III-R criteria for PG [33] was estimated as 0.92. Although SOGS has been used to define categories to identify recreational gamblers, subthreshold pathological gamblers and pathological gamblers, several studies have reported the use and utility of this test as an index of gambling severity [6, 34, 35].

Other instruments included were as listed below. (1) The Diagnostic questionnaire for PG according to DSM-IV criteria [36], in its Spanish adaptation by Jiménez-Murcia [37]. This 19-item questionnaire reflects the DSM-IV diagnostic criteria for PG. Reliability was estimated using a measure of internal consistency (Cronbach's α), which yielded the following values: 0.81 for the general population and 0.77 for a gambling treatment group. Convergent validity in comparison to the SOGS questionnaire was estimated as $r = 0.77$ for the general population and 0.75 for a gambling treatment group. (2) The Symptom Checklist-90 items-Revised (SCL-90-R) [38, 39], in its Spanish validation by González de Rivera [40], a widely used 90-item scale assessing self-reported psychological distress and psychopathology. The test is usually scored on nine primary symptom dimensions (comprising a total of 83 items): somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. (3) The Global Severity Index, which is the participant's mean score (using all the 90 items), is a widely used global index of distress. The Spanish validation of this scale shows good psychometric properties, with internal consistencies ranging from 0.81 to 0.90. Test-retest reliability ranged from 0.78 to 0.90. We obtained additional demographic information, including age, marital status, education, occupation, living arrangements and clinical relevant variables (namely age at onset, problem gambling, frequency, mean/bet size, and smoking status) via a semi-structured interview.

Procedure and Design

The patients filled in all the study questionnaires at the start of treatment at our Unit. Three experienced psychologists and psychiatrists (neuroscience master and doctorate level), with more than 15 years working in PG and specially trained in liaison psychology for treating chronic illnesses, completed the intake evaluation during two structured face-to-face interviews. As well as a comprehensive clinical and psychological evaluation (including the instruments mentioned previously) additional demographic data were also collected. The therapeutic approach and rationale was explained during these initial sessions, and therapeutic materi-

als were provided. Patients underwent a CBT intervention based on Sharpe and Tarrier's [41] integrative model, consisting of 16 weekly outpatient sessions (45 min each), whose structure and format was adapted to individual patient's needs. The main objective of the treatment was to teach patients to use CBT strategies so as to achieve complete abstinence from problem gambling. As described previously [6], the topics addressed included psychoeducation on the disorder, stimulus control, response prevention, cognitive restructuring, reinforcement and self-reinforcement, social skill training and relapse prevention techniques. Additionally, self-monitoring records about adherence, relapses, and achievement of intersession tasks were systematically collected during every treatment session. This treatment program and accompanying program materials have already been manualized and published in Spanish [42]. To fit the therapeutic needs of PD patients, we adapted our initial therapy model. Therefore, several topics were more emphasized in the PG + PD group than in the PG group. These included: psychoeducation about specific conditions, self-instructions and planning of alternative gratifying activities (e.g. interaction between dopaminergic drug therapy and gambling behavior, additional impulsive behaviors to take into account, how to cope with somatic chronic disease and how to deal with free time; see table 1).

Statistical Analysis

Statistical analysis was carried out with SPSS 15.0.1 for Windows. We assessed the number of treatment sessions; dropout and relapse during the 16-week intervention and total SOGS scores.

To establish the rate of dropout and relapse, we only considered the data from patients who completed treatment. Treatment dropout was defined as no therapy attendance for more than three sessions. Relapses were defined as any episode of gambling (commercial and non-commercial, involving a money bet) during the 16 weeks of treatment. Although both variables were not mutually exclusive, for the statistical analysis they have been considered separately. What was defined as poor performance was weak compliance with the treatment regimens, namely bringing the self-monitoring diaries to the weekly sessions and regularly attending the group meetings.

In the first step, clinical profiles (severity of PG measures and global psychopathology) were compared through Mann-Whitney tests for patients diagnosed with PG and those with PG and PD. In addition, the specific predictive accuracy of PD on clinical outcomes was measured with the change in R^2 coefficient obtained in hierarchical multiple regressions, entering the patient's age in the first step and the presence of PD in the second step. In the second step, the risk (cumulative incidence) of therapeutic outcomes (presence of relapses and dropouts) was obtained and compared for patients diagnosed with PG and PG with PD through logistic regressions adjusted for age. The goodness-of-fit was valued with Hosmer-Lemeshow's test, and the discriminative accuracy with the area under the ROC curve (AUC).

Finally, survival analysis techniques were used to model the rate of relapses and dropouts during the 16 sessions of treatment (over 4 months). Survival functions adjusted for sex, age and severity of PG (SOGS total score) were obtained and compared for patients with PG alone or PG with PD. Next, a multiple Cox's regression valued the specific contribution of patient's age and sex, severity of PG (SOGS score) and the presence of PD to the relapse and dropout rates. Global predictive accuracy was measured with the R^2 with Atkinson estimation [43].

Table 1. Detailed schedule of the CBT sessions

Session	Main topics	Objectives	Task
1–2	<ul style="list-style-type: none"> – Rationale and psychoeducation – Exploring mood/mental state examination – Psychoeducation about specific PD conditions (medication check and possible effects) 	<ul style="list-style-type: none"> – Providing information about the disorder/therapeutic process – Motivation and therapy adherence – Self-control strategies and gambling behavior – Maintaining and triggering factors of PG – PD-specific maintaining and triggering factors 	Set of worksheets and diaries for gambling behavior self-monitoring
3–4	<ul style="list-style-type: none"> – Stimulus control (money control, avoidance of risk situations, self-exclusion program, changing risky routes) – Symptoms review and behavioral changes 	<ul style="list-style-type: none"> – Promote gradual abstinence – Enhance mutual trust with cotherapists 	Use of the therapeutic worksheets, avoidance of the risk situations and use of receipts and expenses reminder
5–6	<ul style="list-style-type: none"> – Discussion of social or emotional issues – Planning of alternative gratifying activities – How to deal with free time 	<ul style="list-style-type: none"> – Explore difficulties, obstacles – Social skills training – Productive time management 	Set the hobbies planning, role playing and behavioral experiments
7–8	<ul style="list-style-type: none"> – Relapse prevention techniques – Exploring mood/mental state examination – Medical evaluation in collaboration with neurologist – Rationale of cognitive model 	<ul style="list-style-type: none"> – Generating alternative behaviors – Understanding relationship between cognitions, emotions and behaviors – Identification of specific risk situations – Analyzing presence of other impulse control behaviors 	Self-monitoring diaries Cognitive self-monitoring diaries
9–12	<ul style="list-style-type: none"> – Cognitive restructuring on illusions of control and magical thinking – Self-reinforcement – Reduce family participation in external control strategies and increasing self-control skills 	<ul style="list-style-type: none"> – Reinforcement of patient's social and economic achievements – Communication promotion – Discussion of vulnerability factors and similar aspects of thinking 	Self-monitoring diaries Cognitive self-monitoring diaries
13–14	<ul style="list-style-type: none"> – Cognitive restructuring – Patient-family communication styles – Self-instructions strategies – Solving problem techniques 	<ul style="list-style-type: none"> – Positive communication styles – Exploring risk behaviors 	Self-monitoring diaries Cognitive self-monitoring diaries
15–16	<ul style="list-style-type: none"> – Middle- to long-term relapse prevention techniques – Summary of treatment key points – Final discussion/feedback from patients/relatives – Future plans – Medical evaluation in collaboration with neurologist 	<ul style="list-style-type: none"> – Relapse prevention and future risk factors analysis – Discussion about future difficulties and relevance to keep full abstinence – Analyzing presence of other impulse control behaviors – How to cope with somatic chronic disease 	

In the PG + PD patients, several topics were more emphasized than in the PG individuals (in bold).

Results

Clinical and Sociodemographic Characteristics of the Sample

The between-group comparison (table 2) suggested an older age and older age at onset ($p < 0.0005$) in the PG + PD group, although duration of PG was similar in both groups ($p = 0.337$). No significant differences were found

in gender distribution ($p = 0.999$), educational level ($p = 0.076$) or alcohol and drug abuse ($p = 0.680$ and $p = 0.173$). The PG – PD group had higher percentages of smokers ($p < 0.0005$) and employment ($p = 0.001$) and a lower rate of divorce ($p = 0.014$) than the PG + PD group. Differences were also noted in the type of gambling problem, with significantly more bingo playing in the PG + PD group ($p = 0.042$).

Table 2. Clinical and sociodemographic characteristics of the sample

Sociodemographic and clinical characteristics	PG – PD (n = 45)	PG + PD (n = 15)	p value
Age, years ^a	40.7 ± 14.2	62.7 ± 8.5	<0.0005
Age at onset, years ^a	35.2 ± 13.6	57.8 ± 7.7	<0.0005
Duration, years ^a	5.0 ± 4.6	5.0 ± 0.8	0.337
Males, %	88.9	86.7	0.999
Employed, %	64.4	13.3	0.001
Education level, %			
University	8.9	0	0.076
Secondary	48.9	35.7	
Primary or less	42.2	64.3	
Civil status, %			
Divorced	2.2	21.4	0.014
Married	62.2	71.4	
Single/widow	35.6	7.1	
Smokers, %	81.4	14.3	<0.0005
Alcohol abuse, %	11.6	6.7	0.680
Other drug abuse, %	16.3	0	0.173
Machines, %	97.7	86.7	0.156
Bingos, %	9.1	36.4	0.042
Lotteries, %	9.1	9.1	1.000
Casinos, %	6.8	0	0.603
Cards, %	0	0	1.000
Bets, %	0	9.1	0.200
Internet, %	0	0	1.000
Other, %	0	9.1	0.200
Gambling episodes, %			
1	59.1	66.7	0.784
2	31.8	33.3	
≥3	9.1	0	
Personal income, EUR ^a	1,297 ± 627	1,209 ± 868	0.419
Family income, EUR ^a	2,346 ± 1,490	2,152 ± 1,145	0.597

p value with Mann-Whitney test for quantitative variables and exact χ^2 test for categorical features.

^a Values expressed as mean ± SD.

Psychopathological and Clinical Indices

Table 3 shows the results of the first step of clinical profile analysis (severity of PG measures and global psychopathology). No statistically significant differences were found between PG – PD and PG + PD in severity of the disorder (SOGS $p = 0.111$; DSM-IV $p = 0.299$) and psychopathologic profiles (SCL-90-R score, SOGS questionnaire, and Stinchfield's questionnaire), with the exception of higher scores on the Hostility Scale ($p = 0.005$) and Positive Symptom Total (number of self-reported symptoms, $p = 0.010$) for the PG – PD group.

Hierarchical multiple regressions (entering the patient's age in the first step and the presence of PD in the

Fig. 1. Survival functions for relapses (a) and dropout (b) adjusted for patient's sex, age and PG severity (SOGS score).

second step) revealed no significant associations between presence of PD, the rate of global psychopathology and severity of PG.

Table 4 shows that the risk of relapses was 24.4% for the PG – PD group and 41.7% for the PG + PD group, and the OR adjusted for patient's age was not statistically significant (OR = 5.26, $p = 0.088$). The risk of dropout was statistically equal for both diagnoses (28.9% for PG – PD and 33.3% for PG + PD, OR = 2.48, $p = 0.305$), as was the probability of low compliance with therapy (35.6% for PG – PD versus 33.3% for PG + PD, OR = 0.825, $p = 0.811$). Discriminative accuracy was moderate to low (AUC values between 0.57 and 0.66).

Survival Analyses for the Rate of Relapses and Dropouts

Figure 1 shows that the weekly rate of relapses and drop-out during the 16 sessions of treatment was higher for the PG + PD group. At the end of the first month, 25%

Table 3. Comparison between PG – PD and PG + PD of psychopathological and clinical outcomes at baseline

	PG – PD (n = 45)	PG + PD (n = 15)	M-W p	Hierarchical regressions Results obtained in the second step					R ² total
				B ^a	95% CI B	ΔR^2 ^a	p		
SOGS									
Total score	10.24 ± 2.9	8.73 ± 3.5	0.111	–0.457	–2.69; 1.78	0.003	0.684		0.086
DSM-IV									
Total score	7.18 ± 1.9	6.54 ± 2.0	0.299	–0.029	–1.49; 1.44	0.001	0.969		0.056
SCL									
Somatization	0.92 ± 0.7	0.98 ± 0.6	0.687	–0.067	–0.68; 0.54	0.001	0.826		0.017
Obsessive-compulsive	1.05 ± 0.7	0.74 ± 0.5	0.214	–0.27	–0.85; 0.30	0.018	0.339		0.032
Interpersonal sensitivity	0.89 ± 0.7	0.69 ± 0.6	0.517	–0.08	–0.70; 0.55	0.001	0.805		0.022
Depressive	1.37 ± 1.0	1.10 ± 0.7	0.517	–0.21	–1.03; 0.62	0.005	0.614		0.014
Anxiety	0.88 ± 0.7	0.94 ± 0.6	0.724	0.12	–0.52; 0.75	0.003	0.713		0.004
Hostility	0.81 ± 0.8	0.18 ± 0.2	0.005	–0.45	–1.10; 0.19	0.036	0.163		0.110
Phobic anxiety	0.35 ± 0.6	0.36 ± 0.5	0.779	0.048	–0.44; 0.54	0.001	0.844		0.002
Paranoid ideation	0.68 ± 0.7	0.82 ± 0.7	0.670	0.31	–0.33; 0.95	0.019	0.331		0.029
Psychotic	0.71 ± 0.6	0.59 ± 0.6	0.652	–0.06	–0.63; 0.52	0.001	0.842		0.009
GSI	0.93 ± 0.6	0.75 ± 0.5	0.685	–0.15	–0.86; 0.56	0.004	0.676		0.007
PSDI	1.86 ± 0.6	1.34 ± 0.8	0.053	–0.50	–1.04; 0.04	0.062	0.071		0.091
PST	42.2 ± 21.2	18.2 ± 23.8	0.010	–24.2	–44.1; –4.19	0.105	0.019		0.130

M-W = Mann-Whitney test; ΔR^2 = change in R² coefficient; GSI = Global Severity Index; PSDI = Positive Symptom Distress Index; PST = Positive Symptom Total. Values for PG – PD and PG + PD are expressed as mean ± SD.

^a Coefficient valuing the predictive value of the presence of PD.

Table 4. Predictive accuracy of PD on therapy outcomes

	PG – PD (n = 45)	PG + PD (n = 15)	Logistic regression adjusted for age				
			OR	95% CI for OR	p value	H-L	AUC
Relapses	24.4%	41.7%	5.26	0.78; 35.5	0.088	0.694	0.659
Dropout	28.9%	33.3%	2.48	0.43; 14.0	0.305	0.292	0.612
Poor compliance ^a	35.6%	33.3%	0.825	0.17; 3.97	0.811	0.005	0.573

H-L = Hosmer-Lemeshow's test for goodness of fit.

^a To be considered with caution due the lack of goodness of fit for this model.

Table 5. Predictive value of patient's profile on survival time to therapy outcomes

	Relapses (R ² = 6.4%)				Dropout (R ² = 6.5%)			
	B	p value	OR	95% CI for OR	B	p value	OR	95% CI for OR
Sex	–0.055	0.944	0.947	0.205; 4.37	–0.136	0.861	0.873	0.191; 3.99
Age	–0.038	0.159	0.963	0.913; 1.02	–0.040	0.097	0.961	0.916; 1.01
Severity of PG (SOGS)	–0.029	0.747	0.972	0.816; 1.16	–0.137	0.157	0.872	0.722; 1.05
Presence of PD	1.45	0.092	4.25	0.791; 22.9	0.866	0.272	2.38	0.508; 11.1

Results obtained through Cox regression models.

of PG + PD patients had reported relapses and 29% had dropped out of therapy, compared with corresponding figures of 11% and 9% in the PG – PD group.

Table 5 shows the Cox's regression results were not statistically different for the presence of PD and the rate of relapses (OR = 4.25, $p = 0.092$), entering the patient's sex, age and severity of PG (SOGS total score) simultaneously. No significant differences were found for the presence of PD and the rate of dropout (OR = 2.38, $p = 0.272$). Global predictive accuracy was low for both models (R^2 around 6.5%).

Discussion

The present study aimed to explore differences in clinical and psychopathological features and response to therapy between a group of individuals with PG + PD and a group with PG – PD. The therapeutic approach in PD has often privileged the treatment of motor aspects of disease, whereas non-motor aspects have received little attention from researchers. Although the literature stresses the contribution of non-pharmacological approaches such as CBT or psychosocial support in PD [17, 18, 44, 45], to our knowledge this is the first study that analyzed the effectiveness of CBT in PD with PG.

Clinical and Psychopathological Features in PG + PD and PG – PD

As reported above, most pathological gamblers in our sample were male; the main gambling problem was slot machines and bingo, and the mean problem duration was 5 years [46–49]. Compared to PG – PD, PG + PD patients showed lower rates of smoking and employment. The lower rate of employment is probably attributable to the older age and therefore a higher likelihood of retirement in the PG + PD group, while the differential pattern of substance use corroborates previous reports of a negative relationship between tobacco smoking and the development of PD [50, 51]. Moreover, a study of 498 subjects diagnosed with PG identified a negative relationship between age and the probability of tobacco use (younger, more likely to smoke) [52]. As such, the majority of studies with pathological gamblers observe a positive relationship between consumption of nicotine, alcohol and other substances and adolescence youth [53, 54].

Consistent with the view that the use of dopaminergic medications is associated with PG onset [15–18], gambling behavior in our sample appeared after the onset of treatment with dopaminergic treatment for PD in 15 pa-

tients. Our finding corroborates other reports that suggest that PG is a possible consequence of pharmacological treatment [55–57] and could explain the later age at onset of PG in this group. Normally, male pathological gamblers begin to gamble during their youth [58]. The first symptoms, and in fact the complete clinical profile, usually emerge earlier in life [59].

Interestingly, we did not find statistically significant between-group differences on indices of global psychopathology and severity of PG. The lack of difference could be linked to differences in the mean age of the sample and the age at onset of PG. However, the results of research in this area are contradictory. Some studies associate the later age at onset with higher psychopathology [59–62], but other authors have observed more medical and psychiatric problems in early-onset PG [59–61]. In our sample, the age factor may have been mitigated by the presence of pharmacological use as well as by variables related to the illness.

Therapy Response in PG + PD and PG – PD

Finally, accordingly to what we predicted in our study hypotheses, we observed that the presence of PD in PG was not related to treatment response. No significant differences were observed in any of the treatment variables explored. Beyond the statistical results and from a clinical point of view, the obtained response to treatment in both groups is in keeping with previous studies in PG, in which dropout rates between 30–50% are described [6, 63, 64] after standard CBT programs (6–16 weekly sessions plus follow-up, averaging 17 months after end of the treatment) [65]. Regarding relapses, some authors [65, 66] consider that a great number of patients with PG relapse at least once while attempting to quit gambling. As in other addictions, relapses in PG during treatment are frequent, with reported rates between 40 and 70% throughout the treatment follow-up period [67, 68]. Thus, our dropout and relapse rates closely match the percentages described in other studies, and lend support to the use of a CBT-based approach for treating PG in patients with PD, albeit with the expectation of a modest treatment response. Of note, pathological gamblers with PD may be very heterogeneous, ranging from cases that require only an adjustment in dopaminergic pharmacotherapy to resolve their gambling problem to cases that present associated factors of vulnerability such as impulsiveness, low tolerance of stress or low adaptation to PD and finally to cases who suffer comorbid psychiatric disorders (alcoholism, personality disorders, etc.) [69]. Several studies have found that the existence of comorbid disorders compli-

cates the evolution and severity of gambling problems [7, 8]. Most studies support the need to design treatment programs that include appropriate treatment strategies for comorbid disorders in order to ensure good treatment response [7, 69]. To maximize its effectiveness in PD patients, CBT should also be tailored to their particular needs (cognitive deficits such as difficulties with memory, attention and language and other comorbid psychiatric conditions) to decrease the risk of relapse and dropout during treatment.

Limitations

These results should be considered within the context of several limitations. First, the study's retrospective nature and the self-report data collection procedures may limit the validity of the findings, which are subject to the unreliability of individual recall and potential memory bias, especially in PG + PD patients. Second, the sample size in the present study was very small and could therefore have influenced the results. Third, the assessment procedures used did not allow for in-depth evaluation of comorbid disorders. Fourth, while the definition of relapse is heterogeneous in the addiction literature and has been considered in several different ways [68], the criteria of relapse used in our study are perhaps too strict, not allowing differentiation between patients who presented an isolated episode of relapse versus those who never really stopped gambling. Finally, although we used indirect

measures of adherence and compliance (namely frequency of attending therapy sessions and completing weekly homework, as shown in fig. 1), we did not assess our patients with any specific direct measures (e.g. self-reports).

Contributions

A major strength of this study are the specific characteristics of the selected sample. We assessed and compared clinical and psychopathological profiles as well as response to CBT in a group of PG individuals (with and without associated PD) who were treated consecutively at our specialized unit for PG disorder. In summary, although PG individuals (with and without PD) presented similar symptoms, as far as their gambling disorder was concerned, we found certain PD-specific clinical and psychopathological characteristics but also PD-specific treatment response. Our results support the use of CBT in PG patients, although the program must be adapted to their specific needs.

Acknowledgements

Partial financial support was received from Fondo de Investigación Sanitaria (PI081573), Ministerio de Ciencia e Innovación (PSI2011-28349) and AGAUR (2009SGR1554). CIBER Fisiopatología de la Obesidad y Nutrición and CIBER Salud Mental are supported by ISCIII. This work is part of the PhD thesis of Francesca I. Bove at the University of Barcelona (School of Medicine).

References

- 1 American Psychiatric Association: DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington, American Psychiatric Association, 2000.
- 2 Alvarez-Moya E, Jimenez-Murcia S, Aymami MN, Gomez-Peña M, Granero R, Santamaria J, Menchon JM, Fernandez-Aranda F: Subtyping Study of a Male Pathological Gambling Sample. *Can J Psychiatry* 2010;55:498–506.
- 3 Kertzman S, Vainder M, Vishne T, Aizer A, Kotler M, Dannon PN: Speed-accuracy tradeoff in decision-making performance among pathological gamblers. *Eur Addict Res* 2010;16:23–30.
- 4 Fernández-Aranda F, Jiménez-Murcia S, Álvarez-Moya EM, Granero R, Vallejo J, Bulik CM: Impulse control disorders in eating disorders: clinical and therapeutic implications. *Compr Psychiatry* 2006;47:482–488.
- 5 Kessler RC, Hwang I, LaBrie R, Petukhova M, Sampson NA, Winters KC, Shaffer HJ: The prevalence and correlates of DSM-IV Pathological Gambling in the National Comorbidity Survey Replication. *Psychol Med* 2008;38:1351–1360.
- 6 Jiménez-Murcia S, Álvarez-Moya EM, Granero R, Aymami MN, Gómez-Peña M, Jaurieta N, Bibiana S, Rodríguez-Martí J, Vallejo J: Cognitive-behavioral group treatment for pathological gambling: analysis of effectiveness and predictors of therapy outcome. *Psychother Res* 2007;17:544–552.
- 7 Lesieur HR, Blume SB: Evaluation of patients treated for pathological gambling in a combined alcohol, substance abuse and pathological gambling treatment unit using the Addiction Severity Index. *Br J Addict* 1991;86:1017–1028.
- 8 Ibanez A, Blanco C, Donahue E, Lesieur HR, Perez de Castro I, Fernandez-Piqueras J, Saiz-Ruiz J: Psychiatric comorbidity in pathological gamblers seeking treatment. *Am J Psychiatry* 2001;158:1733–1735.
- 9 Grall-Bronnec M, Wainstein L, Augy J, Bouju G, Feuillet F, Vénisse JL, Sébille-Rivain V: Attention deficit hyperactivity disorder among pathological and at-risk gamblers seeking treatment: a hidden disorder. *Eur Addict Res* 2011;17:231–240.
- 10 Bagby RM, Vachon DD, Bulmash E, Quilty LC: Personality disorders and pathological gambling: a review and re-examination of prevalence rates. *J Pers Disord* 2008;22:191–207.
- 11 Crockford D, Quickfall J, Currie S, Furtado S, Suchowersky O, el-Guebaly N: Prevalence of problem and pathological gambling in Parkinson's disease. *J Gambl Stud* 2008;24:411–422.
- 12 Grosset DG, Schapira AH: Timing the initiation of treatment in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2008;79:615.
- 13 Lader M: Antiparkinsonian medication and pathological gambling. *CNS Drugs* 2008;22:407–416.

- 14 Wolters E: Variability in the clinical expression of Parkinson's disease. *J Neurol Sci* 2008;266:197–203.
- 15 Weintraub D: Dopamine and impulse control disorders in Parkinson's disease. *Ann Neurol* 2008;64(suppl 2):S93–S100.
- 16 Claassen DO, van den Wildenberg WP, Ridderinkhof KR, Jessup CK, Harrison MB, Wooten GF, Wylie SA: The risky business of dopamine agonists in Parkinson disease and impulse control disorders. *Behav Neurosci* 2011;125:492–500.
- 17 Giladi N, Weitzman N, Schreiber S, Shabtai H, Peretz C: New onset heightened interest or drive for gambling, shopping, eating or sexual activity in patients with Parkinson's disease: the role of dopamine agonist treatment and age at motor symptoms onset. *J Psychopharmacol* 2007;21:501–506.
- 18 Verbaan D, van Rooden SM, Visser M, Marinus J, Emre M, van Hilten JJ: Psychotic and compulsive symptoms in Parkinson's disease. *Mov Disord* 2009;24:738–744.
- 19 Barnes GM, Welte JW, Hoffman JH, Tidwell MC: Gambling, alcohol, and other substance use among youth in the United States. *J Stud Alcohol Drugs* 2009;70:134–142.
- 20 Buzik O: Combination of gambling and alcohol addiction (in Russian). *Zh Nevrol Psikhiatr Im S S Korsakova* 2007;suppl 1:41–44.
- 21 Calandrella D, Antonini A: Pathological gambling in Parkinson's disease: disease related or drug related? *Expert Rev Neurother* 2011;11:809–814.
- 22 Rogers RD, Wielenberg B, Wojtecki L, Elben S, Campbell-Meiklejohn D, Schnitzler A: Deep brain stimulation of the subthalamic nucleus transiently enhances loss-chasing behaviour in patients with Parkinson's disease. *Exp Neurol* 2011;231:181–189.
- 23 Steeves TD, Miyasaki J, Zurowski M, Lang AE, Pellicchia G, Van Eimeren T, Rusjan P, Houle S, Strafella AP: Increased striatal dopamine release in Parkinsonian patients with pathological gambling: a [¹¹C] raclopride PET study. *Brain* 2009;132:1376–1385.
- 24 Blonder LX, Slevin JT: Emotional dysfunction in Parkinson's disease. *Behav Neurol* 2011;24:201–217.
- 25 Ladouceur R: Controlled gambling for pathological gamblers. *J Gambl Stud* 2005;21:49–59.
- 26 Toneatto T, Ladouceur R: Treatment of pathological gambling: a critical review of the literature. *Psychol Addict Behav* 2003;17:284–292.
- 27 Dobkin RD, Allen LA, Menza M: Cognitive-behavioral therapy for depression in Parkinson's disease: a pilot study. *Mov Disord* 2007;22:946–952.
- 28 Dobkin RD, Menza M, Bienfait KL: CBT for the treatment of depression in Parkinson's disease: a promising nonpharmacological approach. *Expert Rev Neurother* 2008;8:27–35.
- 29 Bharmal A, Lu C, Quickfall J, Crockford D, Suchowersky O: Outcomes of patients with Parkinson disease and pathological gambling. *Can J Neurol Sci* 2010;37:473–477.
- 30 Shapiro MA, Chang YL, Munson SK, Jacobson CE, Rodriguez RL, Skidmore FM, Okun MS, Fernandez HH: The four As associated with pathological Parkinson disease gamblers: anxiety, anger, age, and agonists. *Neuropsychiatr Dis Treat* 2007;3:161–167.
- 31 Lesieur HR, Blume SB: The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. *Am J Psychiatry* 1987;144:1184–1188.
- 32 Echeburúa E, Báez C, Fernández J, Páez D: South Oaks Gambling Screen (SOGS): Spanish validation (in Spanish). *Análisis Modif Conducta* 1994;20:769–791.
- 33 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 3, revised (DSM-III-R). Washington, American Psychiatric Association, 1987.
- 34 Stinchfield R: Reliability, validity, and classification accuracy of the South Oaks Gambling Screen (SOGS). *Addict Behav* 2002;27:1–19.
- 35 Cox BJ, Kwong J, Michaud V, Enns MW: Problem and probable pathological gambling: considerations from a community survey. *Can J Psychiatry* 2000;45:548–553.
- 36 Stinchfield R: Reliability, validity, and classification accuracy of a measure of DSM-IV diagnostic criteria for pathological gambling. *Am J Psychiatry* 2003;160:180–182.
- 37 Jiménez-Murcia S, Stinchfield R, Alvarez-Moya E, Jaurrieta N, Bueno B, Granero R, Aymamí MN, Gómez-Peña M, Martínez-Giménez R, Fernández-Aranda F, Vallejo J: Reliability, validity, and classification accuracy of a Spanish translation of a measure of DSM-IV diagnostic criteria for pathological gambling. *J Gambl Stud* 2009;25:93–104.
- 38 Derogatis LR: SCL-90-R. Administration, Scoring and Procedures Manual. Baltimore, Clinical Psychometric Research, 1990.
- 39 Derogatis LR: SCL-90-R. Cuestionario de 90 síntomas-Manual. Madrid, TEA ediciones, 2002.
- 40 González de Rivera JL: Version española del 90 Symptoms Check List Revised (SCL-90-R). Madrid, TEA ediciones, 2001.
- 41 Sharpe L, Tarrier N: Towards a cognitive-behavioural theory of problem gambling. *Br J Psychiatry* 1993;162:407–412.
- 42 Jiménez-Murcia S, Aymamí-Sanromá MN, Gómez-Peña M, Álvarez-Moya EM, Vallejo J: Protocols de tractament cognitivoconductual pel joc patològic i d'altres addiccions no tòxiques. Barcelona, Hospital Universitari de Bellvitge, Departament de Salut, Generalitat de Catalunya, 2006.
- 43 Atkinson RC: Tax incentives and research. *Science* 1980;208:449.
- 44 Ehmann TS, Beninger RJ, Gawel MJ, Riopelle RJ: Coping, social support, and depressive symptoms in Parkinson's disease. *J Geriatr Psychiatry Neurol* 1990;3:85–90.
- 45 Thanvi BR, Munshi SK, Vijaykumar N, Lo TC: Neuropsychiatric non-motor aspects of Parkinson's disease. *Postgrad Med J* 2003;79:561–565.
- 46 Breen RB, Zimmerman M: Rapid onset of pathological gambling in machine gamblers. *J Gambl Stud* 2002;18:31–43.
- 47 Shaffer HJ, Vander Bilt J, Hall MN: Gambling, drinking, smoking and other health risk activities among casino employees. *Am J Ind Med* 1999;36:365–378.
- 48 Tavares H, Zilberman ML, el-Guebaly N: Are there cognitive and behavioural approaches specific to the treatment of pathological gambling? *Can J Psychiatry* 2003;48:22–27.
- 49 Wood RT, Griffiths MD: The acquisition, development and maintenance of lottery and scratchcard gambling in adolescence. *J Adolesc* 1998;21:265–273.
- 50 Kandinov B, Giladi N, Korczyn AD: Smoking and tea consumption delay onset of Parkinson's disease. *Parkinsonism Relat Disord* 2009;15:41–46.
- 51 Morens DM, Davis JW, Grandinetti A, Ross GW, Popper JS, White LR: Epidemiologic observations on Parkinson's disease: incidence and mortality in a prospective study of middle-aged men. *Neurology* 1996;46:1044–1050.
- 52 Jiménez-Murcia S, Granero-Pérez R, Fernández-Aranda F, et al: Comorbilidad del juego patológico: variables clínicas, personalidad y respuesta al tratamiento. *Rev Psiquiatr Salud Ment* 2009;2:178–189.
- 53 Gupta R, Derevensky JL: Adolescent Gambling Behavior: A Prevalence Study and Examination of the Correlates Associated with Problem Gambling. *J Gambl Stud* 1998;14:319–345.
- 54 Stinchfield R, Winters KC: Pathological Gambling. A Clinical Guide to Treatment. Arlington, American Psychiatric Publishing, 2004.
- 55 Fujimoto K: Pathological gambling and Parkinson disease. *Brain Nerve* 2008;60:1039–1046.
- 56 Imamura A, Uitti RJ, Wszolek ZK: Dopamine agonist therapy for Parkinson disease and pathological gambling. *Parkinsonism Relat Disord* 2006;12:506–508.
- 57 Stamey W, Jankovic J: Impulse control disorders and pathological gambling in patients with Parkinson disease. *Neurologist* 2008;14:89–99.
- 58 Raylu N, Oei TP: Pathological gambling. A comprehensive review. *Clin Psychol Rev* 2002;22:1009–1061.
- 59 Burge AN, Pietrzak RH, Molina CA, Petry NM: Age of gambling initiation and severity of gambling and health problems among older adult problem gamblers. *Psychiatr Serv* 2004;55:1437–1439.

- 60 Lesieur HR, Blume SB: Characteristics of pathological gamblers identified among patients on a psychiatric admissions service. *Hosp Community Psychiatry* 1990;41:1009–1012.
- 61 Lynch WJ, Maciejewski PK, Potenza MN: Psychiatric correlates of gambling in adolescents and young adults grouped by age at gambling onset. *Arch Gen Psychiatry* 2004;61:1116–1122.
- 62 Jimenez-Murcia S, Alvarez-Moya EM, Stinchfield R, Fernandez-Aranda F, Granero R, Aymami N, Gomez-Pena M, Jaurieta N, Bove F, Menchon JM: Age of onset in pathological gambling: clinical, therapeutic and personality correlates. *J Gambl Stud* 2010;26:235–248.
- 63 Melville KM, Casey LM, Kavanagh DJ: Psychological treatment dropout among pathological gamblers. *Clin Psychol Rev* 2007;27:944–958.
- 64 Dunn K, Delfabbro P, Harvey P: A preliminary, qualitative exploration of the influences associated with drop-out from cognitive-behavioural therapy for problem gambling: an Australian perspective. *J Gambl Stud* 2012;28:253–272.
- 65 Pallesen S, Mitsem M, Kvale G, Johnsen BH, Molde H: Outcome of psychological treatments of pathological gambling: a review and meta-analysis. *Addiction* 2005;100:1412–1422.
- 66 Oei TPS, Gordon LM: Psychosocial factors related to gambling abstinence and relapse in members of gamblers anonymous. *J Gambl Stud* 2008;24:91–105.
- 67 Hodgins DC, el-Guebaly N: Retrospective and prospective reports of precipitants to relapse in pathological gambling. *J Consult Clin Psychol* 2004;72:72–80.
- 68 Ledgerwood DM, Petry NM: What do we know about relapse in pathological gambling? *Clin Psychol Rev* 2006;26:216–228.
- 69 Grant JE, Kim SW: Comorbidity of impulse control disorders in pathological gamblers. *Acta Psychiatr Scand* 2003;108:203–207.