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Punding in non-demented Parkinson's disease patients: Relationship with psychiatric and addiction spectrum comorbidity

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ABSTRACT

Punding is a stereotyped behavior characterized by an intense fascination with a complex, excessive, non-goal oriented, repetitive activity, associated with dopaminergic replacement therapy (DRT) in patients affected by Parkinson's disease (PD) and with dopamine agonists in several conditions. We studied 25 PD patients with punding behaviors, and compared them to 130 PD controls. The psychiatric evaluation included: the Snaith-Hamilton Pleasure Scale (SHAPS); the SCales for Outcomes in PArkinson's disease-Psychiatric Complications (SCOPA-PC); the Barratt Impulsiveness Scale, Version 11 (BIS-11); the Mood Disorder Questionnaire; the Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale (HARS). The occurrence of impulse control disorders (ICDs) was diagnosed through a psychiatric interview. Significantly more punding patients (96% vs. 68%; $p < 0.01$) were in treatment with DA agonists, receiving significantly higher DA agonists levodopa equivalent daily dose (LEDD). Punding behaviors were found to be associated with psychiatric comorbidity, particularly with psychosis and bipolar disorder. In addition, higher anhedonic symptoms were reported by punders. High rate of co-occurring addictive behaviors (pathological gambling, hedonistic homeostatic dysregulation) and ICDs were found. In conclusion, presented data confirm that DRT, in a subset of PD patients, is strongly associated with addiction-like behavioral issues. Punding shares similarities with addictive behaviors and is associated to other psychiatric symptoms involving dopamine system alterations.

1. Introduction

Punding is a stereotyped behavior characterized by an intense fascination with a complex, excessive, non-goal oriented, repetitive activity. The most common causes of punding are dopaminergic replacement therapy in patients affected by Parkinson's disease (PD) [12, 43] and psychostimulants addiction [11, 39]. Also, it was reported as a symptom of dementia [30], brainstem stroke [28], bipolar disorder [34], as well as a complication during treatment with dopamine agonists in other clinical conditions [2, 48]. The prevalence rates of punding behaviors in PD samples lie within the range 0.34–4.2% [52]. Patients' awareness of punding might be poor, as punding commonly occurs without subjective distress [13]. Though the consolidated role of dopaminergic stimulation [5, 49], the occurrence of punding in only a subset of PD patients suggests that intrinsic features play a role in its pathogenesis [38], so that it arises from a complex interaction between pharmacological and nonpharmacological clinical features.

The pathophysiology of punding is still unclear. It has been hypothesized that it may be related to plastic changes in the dorsal and ventral striatal structures, including the nucleus accumbens [20], and linked to psychomotor stimulation and reward mechanisms [22, 29]. It is likely that these conditioned neurobiological responses reflect corticostriatal and corticomesencephalic glutamatergic adaptations, reinforced by the permissive action of accumbens [19, 46]. Clinical and epidemiological features aside the role of the D1 and D2 receptors further strengthen the view of a common pathophysiological process shared by addiction, dyskinesias and stereotypies [14, 33, 46]. The premise of habit models is that, even though the behavior is initially goal-directed, eventually there is a progression to a form of automatic behavior in which voluntary control is lost [9, 12].

The aim of present study is to assess psychiatric and addiction-spectrum comorbidity in a sample of PD patients with punding, with respect to PD controls, to investigate clinical factors associated and influencing its onset and severity.

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2. Material and methods

Patients were recruited among outpatients with a diagnosis of PD according to UK Brain Bank criteria [15], seen at the Movement Disorders clinic of the "A. Gemelli" Hospital in Rome, Italy from January to September 2012. Exclusion criteria were: any history of neurological illness other than PD; possible or probable dementia according to clinical diagnostic criteria [7]; mental retardation; inability to provide an informed consent.

We studied 25 PD patients with punding behaviors, and compared them to 100 PD controls. Punding was diagnosed according to Punding Rating Scale [12]. All patients underwent a thorough clinical evaluation. We collected information on clinical variables (age at onset, disease duration, side of symptoms' onset, educational level, motor complications of therapy such as motor fluctuations and dyskinesia) and on individual daily medications. All patients underwent a clinical interview in which sleep history was gathered to assess the presence of REM behavioral disorder – RBD – before and after PD diagnosis [27]. Dopamine replacement treatments were expressed in terms of Levodopa Equivalent Daily Dose (LEDD). We assessed hedonic tone using the Snaith-Hamilton Pleasure Scale (SHAPS) [40]. The psychiatric evaluation included: the SCales for Outcomes in PArkinson's disease-Psychiatric Complications (SCOPA-PC) [44], to assess psychotic and compulsive symptoms; Barratt Impulsiveness Scale, Version 11 (BIS-11) [31]; the Mood Disorder Questionnaire, to assess the presence of bipolar disorders [18]; the Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Rating Scale (HARS).

The occurrence of impulse control disorders (ICDs) and Addictive Behaviors was diagnosed with a psychiatric interview. Pathological Gambling (PG) was diagnosed according to DSM-V criteria; hypersexuality according to Voon's criteria [47]; Compulsive Shopping according to McElroy's criteria [26]; Binge Eating according to DSM-V; Hedonistic Homeostatic Dysregulation according to criteria proposed by Giovannoni et al. [16].

Patients were tested in the morning in their "medication-on" condition. They all agreed to enter the study and sign a consent form according to the Declaration of Helsinki.

2.1. Statistical analysis

Statistical analysis was conducted using SPSS 13.0. Dichotomous data were compared by χ^2-test using the Fisher or the Yates corrections as appropriate. Continuous data were expressed as means ± standard deviation and compared by one-way analysis of variance (ANOVA) and Student *t*-test. Not normally distributed variables were compared using non-parametric testing (Mann-Whitney test). Pearson's correlation coefficient was used to assess relationships between continuous data. Significance was set at $p < 0.05$.

3. Results

Socio-demographic characteristics and clinical data of the samples are illustrated in Table 1. No differences in gender, age, education level, disease duration and severity were found between groups. Though not statistically significant, an earlier age of onset was found in Punding Group as compared with PD-controls. Also, punders were more likely to experience REM behavior disorder (RBD) (56% vs. 37%, $p < 0.05$).

Twenty-four out of 25 (96%) punding patients were in treatment with DA agonists, compared to 68% in PD-controls ($p < 0.01$), and received significantly higher DA agonists LEDD (Table 1). Lower antidepressant use was found in the punding group (4% vs. 20%; $p < 0.05$).

Compared to PD controls, patients with punding scored significantly higher on the SCOPA-PC, particularly in paranoid ideation and compulsivity items (Table 2). They had higher levels of impulsivity, higher SHAPS scores, and higher incidence of bipolar disorder as measured by MDQ. No other significant differences emerged when comparing groups, in particular depressive and anxiety symptoms were comparable across groups.

Table 1
Sociodemographic characteristics in non-demented PD patients with and without punding behaviors.

	PD + punding	PD controls	Statistical analysis
N	25	130	
Punding Rating Scale	12.1 (4.6)	–	
Gender	15 M (60%)	67 (52%)	NS
Age (years)	65 (8.9)	67.2 (9.4)	NS
Education (years)	8.8 (4)	10.6 (4.8)	NS
Age of onset	56.9 (9)	60.3 (9.4)	NS ($p = 0.09$)
Disease duration (years)	8.1 (4.2)	6.9 (5.4)	NS
UPDRS III score (on)	19.3 (8.7)	20 (8.1)	NS
Dyskinesias	6 (24%)	17 (13%)	NS
REM behavior disorder	**14 (56%)**	46 (37%)	$p < 0.05$
Pharmacological treatment			
L-Dopa	21 (84%)	94 (72%)	NS
DA agonists	**24 (96%)**	89 (68%)	$p < 0.01$
Amantadine	2 (8%)	7 (5%)	NS
Antipsychotics	3 (12%)	15 (12%)	NS
Antidepressants	**1 (4%)**	26 (20%)	$p < 0.05$
iMAO	6 (24%)	34 (26%)	NS
iCOMT	3 (12%)	16 (12%)	NS
LEDD			
LEDD levodopa	464.3 (271.6)	431.2 (393.7)	NS
LEDD DA agonists	**186.3 (92.2)**	130.5 (114.7)	$p < 0.05$
LEDD total	650.6 (278.4)	561.7 (414.4)	NS

Abbreviations: UPDRS: Unified Parkinson's Disease Rating Scale; iMAO: Monoaminoxydase Inhibitors; iCOMT: Catechol-O-methyltransferase Inhibitors; LEDD: Levodopa Equivalent Daily Dose.

According to diagnostic criteria, 40% (n = 10) of punding subjects had at least one ICD, as compared to 17% (n = 22) of PD controls ($p < 0.01$). In particular, 5 out of 25 punding patients fulfilled the diagnostic criteria for PG (20% vs. 2%, $p < 0.0001$). Finally, higher hypersexuality and HHD rates were observed in the punding-group as compared to controls (Table 2).

4. Discussion

The main finding of this study is the report of a high rate of neuropsychiatric comorbidities in PD patients with punding, as compared to PD controls. Punding behaviors were found to be associated with

Table 2
Psychiatric assessment and addiction-spectrum comorbidity in non-demented PD patients with and without punding.

	PD + punding (n = 25)	PD controls (n = 130)	Statistical analysis
Psychiatric assessment			
HDRS	9.1 (5.6)	10 (7.2)	NS
HARS	8.2 (5.4)	8.6 (7.3)	NS
SCOPA-PC	**4.3 (2.8)**	2.6 (2.3)	$p < 0.001$
Paranoid ideation	**0.6 (0.8)**	0.3 (0.5)	$p < 0.05$
Compulsive behaviors	**1.8 (1.7)**	0.6 (0.9)	$p < 0.0001$
MDQ	**2 (8%)**	0 (0%)	$p < 0.01$
BIS-11 total score	**67.2 (11.2)**	61.4 (9.7)	$p < 0.01$
Attentional impulsivity	15.6 (3.8)	14 (3.7)	$p = 0.05$
Motor impulsivity	**23.5 (5)**	20.8 (4.2)	$p < 0.01$
Non-planning impulsivity	28.1 (5.3)	26.6 (5.5)	NS
SHAPS score	**1.56 (1.6)**	1.02 (1.17)	$p < 0.05$
Anhedonia (SHAPS > 2)	**7 (28%)**	16 (12%)	$p < 0.05$
Addiction-spectrum comorbidity			
Pathological gambling	**5 (20%)**	3 (2%)	$p < 0.0001$
Hypersexuality	**9 (36%)**	16 (12%)	$p < 0.01$
Binge eating	5 (20%)	20 (15%)	NS
Compulsive buying	1 (4%)	4 (3%)	NS
HHD	**2 (8%)**	0 (0%)	$p < 0.01$
Any ICD	**10 (40%)**	22 (17%)	$p < 0.01$

Abbreviations: HDRS: Hamilton Depression Rating Scale; HARS: Hamilton Anxiety Rating Scale; SCOPA-PC: SCales for Outcomes in PArkinson's disease-Psychiatric Complications; MDQ: Mood Disorders Questionnaire; BIS-11: Barratt Impulsiveness Scale; HHD: Homeostatic Hedonistic Dysregulation.