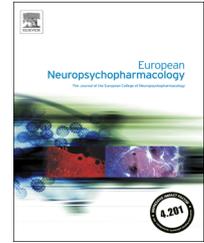




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# Sociodemographic, neuropsychiatric and cognitive characteristics of pathological gambling and impulse control disorders NOS in Parkinson's disease

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## Abstract

Despite of previous evidence supporting the association between impulse control disorder (ICD) and several demographic, clinical and therapeutic features in Parkinson's disease (PD), the relationships between pathological gambling (PG) or other variants of ICD (ICD-NOS) and specific neuropsychiatric or cognitive domains are not entirely defined.

In this study, 155 PD patients without dementia or cognitive impairment underwent: i. the ICD diagnoses, using the Questionnaire for Impulsive-Compulsive Disorders, ii. the mood and anxiety disorders diagnoses, according to the DSM-IV-TR criteria, and iii. a comprehensive battery for measuring severity of psychopathology and neuropsychology domains. Patients were divided in those with pathological gambling (PG), ICDs not otherwise specified (ICD-NOS), or the lack of ICD (No-ICD). There was a progression in age and age at onset from the younger PG subjects throughout ICD-NOS to No-ICD. PG and ICD-NOS subjects had longer disease duration and were taking significantly higher dosages of antiparkinsonian drugs than No-ICD ones. PG subjects had significantly higher severity of depressive and anxious symptoms with respect to the other 2 groups. Both PG and ICD-NOS subjects suffer from increased severity of psychotic symptoms than No-ICD ones. The 3 groups did not differ in any cognitive measure.

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Our results support the concept that the different sociodemographic and neuropsychiatric profiles of PD patients are associated with different ICDs. Moreover, we clearly demonstrate the lack of relationship between ICD and cognitive performances in undemented PD patients.

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## 1. Introduction

The inability to resist an impulse, drive, or temptation to perform an act that is harmful to the person or others, defined as “impulse control disorder” (ICD), interferes with major areas of life functioning. Originally, ICD pertained to a variety of aberrant behaviors, including pathological gambling (PG), compulsive shopping, hypersexuality and binge eating. Within this context, however, a distinction between PG and other variants of ICD (ICD-NOS), was initiated in the Diagnostic and Statistical Manual of Mental Disorders, IV Edition-Text Revision (DSM-IV-TR) (APA, 2000) and defined in the 5th Edition of the DSM (DSM-5) that categorizes PG within the “Addiction and Related Disorders” section (APA, 2013).

ICDs have been identified in subjects suffering from Parkinson's disease (PD) (Leeman and Potenza, 2011; Weintraub, 2009) with significantly higher prevalence than general population (Avanzi et al., 2006; Voon et al., 2007). Given the severe negative impact of ICDs on personal, social and economic activities, a great deal of scientific attention has focused recently on the identification of risk factors for this neuropsychiatric complication of PD. Despite of consistent evidence for the association between ICDs and multiple demographic, clinical and therapeutic traits in PD (Isaias et al., 2008; Voon et al., 2007, 2010, 2011; Weintraub et al., 2010), several issues remain unclear, particularly with respect to differences of neuropsychiatric profile between PG and ICD-NOS. Thus, the co-morbidity between depression and anxiety and PG (Avanzi et al., 2006; Gallagher et al., 2007; Santangelo et al., 2013) as well as the links between diverse variants of ICDs and psychotic symptoms in PD patients (Housden et al., 2010) are still incompletely defined. Moreover, the possible relationships between ICDs and cognitive dysfunction in PD are even more controversial (Bentivoglio et al., 2013; Housden et al., 2010; Pettorruso et al., 2014; Siri et al., 2010; Vitale et al., 2011; Weintraub et al., 2010).

Given these premises, the primary aim of the present study was two-fold: first, to clarify the differences of neuropsychiatric profile of PD patients with PG as compared to those with ICD-NOS or without ICD (No-ICD) by means of a comprehensive approach based on both categorical (psychiatric diagnosis formulated following a formal psychiatric interview) and continuous (rating scales) classifications; second, to investigate the relationships between aberrant behaviors and specific cognitive functions in PD patients by using a complete neuropsychological battery. To avoid confusion caused by the global cognitive impairment, we excluded patients with clear dementia or even mild cognitive impairment.

We hypothesized that specific features and severity of neuropsychiatric profile could differentiate among PG, ICD-NOS and No-ICD. Conversely, we postulated the lack of difference of cognitive functions among the three conditions.

## 2. Experimental procedures

### 2.1. Participants and study design

The study was carried out on 155 PD patients aged between 35 and 80 years, diagnosed according to the criteria by Gelb et al. (1999). Participants were recruited consecutively during scheduled visits at the Outpatient Services for Movement Disorders of the “Fondazione Santa Lucia, IRCCS” and the “Sapienza Università di Roma - Ospedale Sant'Andrea”, between January 2011 and December 2012. Three neurologists with expertise in PD (FEP, CP and CaC) were in charge of diagnosis and selection of patients. The protocol was approved by the Ethical Committee of the “Fondazione Santa Lucia, IRCCS” and each subject signed an informed consent before enrollment. All patients were under stable dopaminergic therapy for at least 2 months before enrollment. Dopamine replacement therapy was calculated as daily levodopa equivalents. In the case of dopamine agonists, the following conversion table was applied: 100 mg levodopa=1 mg pramipexole=5 mg ropinirole=5 mg rotigotine. Within each group, the number (and %) of subjects receiving antidepressant, benzodiazepines and/or antipsychotic therapy was calculated. Overall disease severity was staged according to the modified Hoehn and Yahr (H&Y) scale (Hoehn and Yahr, 1967). The Unified Parkinson's Disease Rating Scale - part III (UPDRS-III) (Fahn et al., 1987) was used to evaluate motor disability.

Exclusion criteria were as follows: i. Co-morbidity with major medical illnesses. ii. Co-morbidity with primary neurological disorders such as stroke, Alzheimer's disease, head trauma with loss of consciousness, and others. iii. Mini-Mental State Examination (MMSE) score (Folstein et al., 1975) <26. iv. Diagnosis of PD-dementia according to the clinical diagnostic criteria of the Movement Disorder Society (Emre et al., 2007) using an extensive neuropsychological battery (see Section 2.2). v. Diagnosis of schizophrenia or bipolar disorder prior to the onset of motor symptoms. A diagnosis of major or minor depression before the onset of parkinsonism was not considered an exclusion criterion in view of the established role of depression as prodromal non-motor symptom of PD (Pellicano et al., 2007) as well as risk factor for subsequent development of ICD (Gallagher et al., 2007; Santangelo et al., 2013). Similarly, previous history of drug dependence or abuse was not considered an exclusion criterion. vi. CT or MRI evidence of significant focal cerebral abnormalities suggested a secondary nature of parkinsonism.

All subjects were submitted to a structured psychiatric interview (SCID-P) (First et al., 2002) for the identification of psychiatric disorders according to the DSM-IV-TR criteria (APA, 2000). A senior research psychiatrist (GS) made all psychiatric diagnoses. Symptoms of ICD were identified by means of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) (Weintraub et al., 2009) while the formal diagnosis of ICD was based on the DSM-IV-TR criteria. Patients were divided into 3 groups (i.e. PG, ICD-NOS and No-ICD). As mentioned earlier, the subdivision between PG and ICD-NOS was based upon previous results suggesting different psychopathologic (Gallagher et al., 2007; Pettorruso et al., 2014) and cognitive (Pettorruso et al., 2014; Vitale et al., 2011) profiles, as well as on the categorical difference between PG and ICD-NOS initiated in the DSM-IV-TR and is defined in the DSM-5 (APA, 2013). In the case of multiple ICDs, the presence of PG drove inclusion of subject into the PG subgroup.

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