Impulse Control Disorders in Parkinson’s Disease in a South Indian cohort

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DECLARATION

I, Dr. Pournamy Sarathchandran, hereby declare that the project in this book was undertaken by me under the supervision of the faculty, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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The candidate, Dr. Pournamy Sarathchandran, has carried out the project under report.

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Bowing before the blessings of Almighty.....

Dr Pournamy Sarathchandran
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**Introduction**

Impulse control disorders (ICDs) are defined as a failure to resist an impulse, drive or temptation to perform an act that is harmful to the person or others (Driver-Dunckley et al., 2003). ICDs and related behaviors (ICDRB) are increasingly found to be associated with dopamine replacement therapy (DRT) in patients with Parkinson’s disease (PD), particularly dopamine agonist (DA) (Driver-Dunckley et al. 2003; Seedat et al., 2000). The role of L-DOPA is controversial and amantadine was recently reported to be associated with pathological gambling, compulsive buying and sexual behavior. Common ICDs in PD include compulsive eating, pathological gambling, compulsive shopping and hypersexuality. Compulsive eating is characterized by eating greater amounts of food than is necessary to alleviate hunger, leading to harmful weight gain (Nirenberg et al., 2006). Pathological gambling is defined as failure to resist gambling impulses despite severe personal, family, or vocational consequences (DSM IV-TR). Compulsive shopping is an uncontrollable excessive buying of goods that can lead to psychological distress and substantial debt (Dittmar et al., 2005). In the absence of any validated scales of hypersexuality, the features that used to detect this behavioral disorder are increased preoccupation with sexual thoughts, excessive demands for sex from partners, increased use of pornography, seeking out prostitutes, engaging in exhibitionism and paraphilia (Lim SY et al., 2008). Compulsive anti-parkinsonian drug use or dopamine dysregulation syndrome (DDS) is sometimes associated with the
development of ICDs in Parkinson’s disease (PD), even though it is included as a complication of long-term dopaminergic therapy in advanced stages (O’Sullivan et al. 2009). Though considered to lie outside the ICD spectrum, punding or repetitive, complex, stereotyped behavior (Evans et al. 2004) has features of compulsions and is often associated with DDS (Evans et al. 2009).

Majority of studies on ICD in PD have been on pathological gambling (Crockford D, Avanzi M et al., 2006, Santangelo G et al., 2009) and most of the reports on prevalence of combined ICD are based on retrospective, medical database review, self reported-screening questionnaire or phone interview (Crockford D et al., 2008; Voon et al., 2006; Fahn W et al., 2009). Studies on combined ICDs that were structured/semistructured and involved psychiatric and clinician interviews of patients and family members are limited (Santangelo G et al., 2009; Grosset KA et al., 2006; Lee JY et al., 2009; Weintraub D et al., 2009; Pontone G et al., 2006). In a recent large multicentre study conducted in North America (Weintraub et al), the combined frequency of ICD in PD patients on DRT was reported to be 13.6%. There are only few previous studies on ICDs in PD from Asian countries. A Chinese study involving self-reported questionnaire followed by telephonic interview by movement disorder specialist found a low prevalence of ICDs of 3.5% when compared to western studies (Fahn et al., 2009). Another Chinese study using a semi structured interview found a prevalence of 7.1% (Auyeng et al., 2011). In a large Korean multicentre study, the reported
prevalence of ICRBs was 10.1% among the 1167 patients studied (Lee J Y et al., 2011).

The contradictory reports about the role of the dose of dopaminergic drugs and the use of L-DOPA as risk factors for ICD could be due to a possible interaction of a specific pharmacological trigger with intrinsic neurobiological vulnerability factors (Weintraub et al., 2006). There could be genetic factors that determine susceptibility to develop ICDs with DRT. The DOMINION study Part I (Weintraub et al., 2010) identified between-country differences in ICD frequencies. The authors reported that ICDs occurred more frequently in USA than Canada even after adjusting for confounding variables.

We undertook this prospective, single-centre, clinic-based, cross sectional study using a direct, structured interview of PD patients by a team consisting of psychiatrist, movement disorder specialist and a medical social worker. The aim was to examine the frequency, patterns and risk factors of ICD in a sample of Indian PD population and to look at the effect of socio-cultural factors if any, which might influence it. The cost of dopamine agonists influences the frequency of their use in Indian patients and many receive L-DOPA monotherapy, thereby providing an opportunity to examine the risk of ICD in them. We covered a broad area of impulsive/compulsive behavioral disorders to examine if different frequencies and behavioral patterns of ICD emerged. In India, gambling is prohibited and economic and cultural factors could potentially influence the manifestation or reporting of many of these disorders. Additionally, we examined the
impact of ICRB on the quality of life (QOL) of PD patients. There are no previous studies which have looked at the effect of ICDs on QOL of PD patients. A control group of healthy volunteers were also included to assess the frequency of ICD in the apparently normal population. These behaviors have different levels of severity but it causes great distress to the patient as well as family and it interferes with social, financial, or occupational functioning. Hence it is important to identify them at the early and treat appropriately.
Review of Literature

Parkinson’s disease (PD) is a neurodegenerative disorder that prominently affects motor function, resulting in bradykinesia, rigidity, postural instability, and resting tremor. Parkinson’s disease, however, may also cause non motor manifestations, including problems with cognition, mood and behavior. As Parkinson’s disease symptoms are largely due to a loss of dopamine-secreting neurons, pharmacologic dopamine-replacement therapy (DRT) is the cornerstone of Parkinson’s disease treatment, and is generally effective at restoring function. Over time, however, a proportion of Parkinson’s disease patients receiving DRT develop motor complications (ie, fluctuations in mobility and drug-induced dyskinesias) from non physiological, pharmacologic stimulation of dopamine receptors. Increasingly, data support the possibility that antiparkinsonian drugs provoke non motor complications including Parkinson’s disease-related compulsive behaviors possibly, through similar mechanisms.

Core motor symptoms of Parkinson’s disease arise from loss of dopaminergic neurons in the substantia nigra pars compacta and ventral tegmental area, leading to dopamine deficiency in the striatum. While basal ganglia pathways are known to regulate movement, non motor circuits include the dorsolateral prefrontal cortex, which regulates executive function; the lateral orbitofrontal cortex, which modulates socially
appropriate behavior and mood; and the anterior cingulate cortex, which initiates activity and maintains interest. Dopamine activates striatal neurons within the direct pathway via dopamine (D) 1-type receptors and inhibits those of the indirect pathways via D2-type receptors. Some research suggests that while cortical centers initiate goal-directed activities, the basal ganglia facilitate contextually appropriate behaviors (via the direct pathway) and suppress counter-productive behaviors (via the indirect pathway).

Perturbations of dopamine neurotransmission within basal ganglia circuitry may give rise to compulsive behaviors, including forms of drug addiction. Dopaminergic neurons are activated by unanticipated, motivationally relevant stimuli—both appetitive and aversive (Horvitz JC, 2000). Therefore, dopamine appears to regulate responsiveness to novel or salient environmental events and provides a means for reinforcing or correcting behavior based upon the reward value of such events. Within the D2-type receptor family are D3 receptors, which reside within the ventral striatum and govern non motor circuits. These receptors become dysregulated both in persons with Parkinson’s disease and in those with drug addictions, and the altered sensitivity of dopaminergic reward circuits within the ventral striatum may underlie DRT-related compulsions (Volkow ND et al., 2007).

Impulse control disorders (ICDs) are defined as a failure to resist an impulse, drive or temptation to perform an act that is harmful to the person or others (Driver-Dunckley et al., 2003).
Compulsive eating is characterized by eating greater amounts of food than is necessary to alleviate hunger, leading to harmful weight gain (Nirenberg et al., 2006). This finding contrasts with the typical progression of PD where patients experience weight loss, probably resulting from increased energy expenditure due to parkinsonism or dyskinesia. Reduced food intake due to poor appetite as a result of decreased gastrointestinal motility, peripheral dopaminergic side effects of medication, olfactory deficit, depression, disturbance of hypothalamic regulation of appetite and motor difficulties in eating due to limb or bulbar dysfunction are other proposed reasons of weight loss.

Pathological gambling is defined according to DSM-IV as persistent and recurrent maladaptive gambling behavior as indicated by features such as preoccupation with gambling; increasing amounts of money; unsuccessful attempts to control; restlessness or irritability when cutting down; lying to others about gambling; jeopardizing relationships, work, or education; and relying on others for money (at least five criteria required). “Problem gambling” describes behavior that meets some but not full diagnostic criteria for pathological gambling, and “disordered gambling” refers to the combination of these two groups.

Compulsive buying is defined by the presence of repetitive impulsive and excessive buying of goods that are not needed and may lead to financial stress. (Dittmar et al., 2005). Persons with compulsive buying often describe an increasing urge or anxiety that can have a sense of completion only when a purchase is made. Some investigators
believe that compulsive shoplifting (kleptomania) may be closely related (Holden, C.et al., 2001).

Hypersexuality was the earliest recognized PD related ICD. In the absence of any validated scales of hypersexuality, the features that used to detect this behavioral disorder are increased preoccupation with sexual thoughts, excessive demands for sex from partners, increased use of pornography, seeking out prostitutes, engaging in exhibitionism and paraphilia (Lim SY et al., 2008).

Punding was first described in psychostimulant addicts. There is a continuum of punding behavior ranging from excessive “hobbyism” to prolonged, disabling highly stereotyped ritualistic behavior. Activities are highly influenced by gender and, in Western societies, are reported to include collecting or hoarding items, cleaning, repairing things, gardening, writing and categorizing information, artistic drawing or craft-making, singing or playing a musical instrument, playing cards, fishing, and excessive computer and Internet use.

Punders may neglect their physiological needs, such as sleep, hunger, and thirst, as well as their social responsibilities. They may or may not retain insight regarding the inappropriateness of their behavior. Some patients report the activity as soothing and may become irritated when interrupted; others report no joy or satisfaction in their activities or even becoming agitated while carrying out the activity (Evans et al., 2009).

Compulsive anti-parkinsonian drug use or dopamine dysregulation syndrome (DDS) is sometimes associated with the development of ICDs in PD, even though it is included as a complication of long-term dopaminergic therapy in advanced stages (O’Sullivan et
Impulse Control Disorders in Parkinson’s disease

DDS refers to the compulsive use of dopaminergic medications well beyond the dose needed to optimally control motor disability and in the face of a mounting number of harmful physical, psychiatric, and social sequelae. Disability due to DDS may improve with medication reductions but there is an enduring tendency for the individual to relapse. Impulsive aggression is often encountered in individuals with DDS in the context of aggressive demands for medications or sexual intercourse. During the on or high phase, these patients may go on ‘‘walkabout’’ where they become restless and develop akathisia with an urge to walk or travel. Self-injury ideation/behavior and hypomanic behavior may occur during episodes of excessive medication use. Studies particularly highlight the link with total dopamine agonist use but also levodopa (L-dopa) use (especially when given in combination)(Weintraub et al., 2006). ICDs are under recognized in routine clinical practice. Systematic prevalence estimates for common ICDs in treated PD patients are around 14.0% and increase to 17.1% in patients on dopamine agonists (Voon V et al.,2006; Wentraub D et al., 2008; Weiss HD et al., 2006). Univariate analysis in different studies has also found younger age, longer PD duration, history of ICD symptoms prior to development of PD, amantadine use, unmarried status, and family history of gambling problems to be associated with the presence of an ICD

Epidemiology of ICDs

Voon et al. reported a 6.1% lifetime prevalence of ICDs (pathological gambling, hypersexuality, compulsive shopping, or a combination) in PD patients (Voon, V et al.,2006). A further study, which included compulsive eating in addition to these three
behavioral features, found a combined prevalence of 14% during the course of PD (Giladi et al., 2007). In a recent large multicentre study conducted in North America (DOMINION study Part-I), (Wientraub et al., 2010), the combined frequency of ICD in PD patients on DRT was reported to be 13.6%; between-country differences in ICD frequencies were also identified. Among the two previous Asian studies, a Chinese study (Fahn W et al., 2009) using a self-reported questionnaire followed by telephonic interview by the specialist, found a low frequency of ICDs (3.5%) and a large Korean multicentre study found a higher frequency (10.1%) (Lee JY et al., 2009).

ICDs appear to be more common in treated PD patients than in the general population, although few studies have addressed this issue. Giladi et al. found a prevalence of 14% in PD patients versus 0% in age- and sex-matched healthy control subjects.

**Risk factors for ICDs**

In PD patients, ICDs are associated with younger age (or at least younger age at PD onset). The association between disinhibitory psychopathologies and younger age could reflect an age-related susceptibility to impulsivity or compulsivity, greater plasticity in the younger brain’s neurotransmitter response, differences in PD biology, or medication prescribing practices. Younger patients are prone to developing dyskinesia and motor fluctuations, and dopamine agonists are promoted in younger patients to delay these complications.

Gender also plays a role in the prevalence as well as expression of disinhibitory psychopathologies. ICDs occur more commonly in men, especially hypersexuality.
Impulse Control Disorders in Parkinson’s disease (Giladi, N et al., 2007). Some authors reported that compulsive eating was “considerably more common in women” (Nirenberg et al., 2006). There is a high degree of correlation among personality traits variably labeled as “novelty seeking” and “impulsive sensation seeking” and incidence of ICDs in PD patients (Voon V et al., 2007).

There is a strong association between dopamine agonist therapy and ICDs. In one study the prevalence of ICDs on dopamine agonist therapy was 13.7%, versus 0.7% on L-dopa monotherapy (Voon et al., 2006). The association between dopamine agonist therapy and ICDs has been attributed to excessive or aberrant activation of the mesolimbic dopaminergic system, which under physiological conditions mediates the response to natural rewards. Most studies particularly implicate pramipexole, a dopamine agonist with relative selectivity for the dopamine D3 receptor subtype (10 times more potent at the D3 than at the D2 receptor) (McKeon A et al., 2007; Dodd, M.L et al., 2005). The D3 receptor is expressed mainly in discrete brain areas belonging or related to the limbic system, whereas D1 and D2 receptors are widely expressed in all major dopaminceptive areas.

Studies on the epidemiological and molecular genetics of behavioral addictions in non-PD populations have focused on pathological gambling. A significantly higher frequency of pathological gambling among first degree relatives of pathological gamblers has been reported than that in first-degree relatives of control subjects (8.3% versus 2.1%) (Bearn J et al., 2004). In a large twin investigation of pathological gambling, inherited factors accounted for 54% of the report of two or more symptoms
of pathological gambling. A high frequency (9.5%–16.7%) of compulsive buying in relatives of compulsive buyers has also been reported, but the studies were small and lacked control groups (O’Sullivan, S.S et al., 2007).

ICDs overlap with major depressive disorder, anxiety, and other psychiatric disorders (Goudriaan, A.E et al., 2004; Pietrzak, R.H. et al, 2007). Whether this overlap is due to the stress of coping with a chronic illness or boredom is unclear. Whether depression is causative in these patients is also unknown. ICDs have been triggered by the emergence of depression after STN DBS (Ardouin, C et al., 2006).

**Diagnosis and management**

Patients and families may not suspect drug treatment as a causal factor and therefore not report behavioral changes. The mean latency of onset of pathological gambling from dopamine agonist initiation has been estimated to be 23 months (Gallagher, D.A et al., 2007). Even with direct questioning, patients may deny these behaviors. Up to 75% of PD patients with active ICDs may go undetected by treating clinicians (Weintraub, D et al., 2006). The potential for ICDs and related behaviors should be routinely discussed with patients, and family members should be involved in these discussions whenever feasible. However, some patients may reveal these behaviors only to their physician privately for fear of repercussions from family members. Particular attention should be given to patients receiving dopamine agonist therapy and/or higher doses of L-dopa. Other warning signs that may aid in identifying patients at higher risk include being male, a history of depression, a personal or family history of substance dependence, younger age at PD onset, or early emergence of dyskinesia (Silveira-Moriyama, L et al.,
It should be discreetly but carefully inquired about patients’ activities and pastimes, and recent change in behaviour needs to be assessed carefully.

Once diagnosed, non pharmacological measures may be tried, such as involving the family, restricting money (e.g., canceling credit cards, appointing a financial guardian), discontinuing internet access or installing firewalls against internet pop-ups and gambling sites, requesting to be on the casino-banned list, shopping with a relative or friend (the presence of a person without compulsive buying may help curb the tendency to overspend), participating in self-help groups (e.g., Gamblers, Debtors, or Overeaters Anonymous), addiction counseling, psychotherapy or marriage counseling, and finding meaningful ways to spend leisure time. Circumstances of temptation should be avoided wherever possible. ICDs may tend to reduce once identified and when greater attention is focused on them; getting patients to be more aware of their behaviors may function as a covert cognitive behavioral therapy and has documented benefits in non-PD pathological gambling (Petry, N.M et al., 2001). ICDs often resolve with discontinuation or reduction of dopamine agonist therapy (Weintraub, D. et al., 2006; Nirenberg, M.J. et al., 2006). Reduction in L-dopa dose may also be required. Mamikonyan et al, report resolution of ICDs without compromising motor symptom control if the balance is shifted away from dopamine agonist to L-dopa therapy, without altering the intake of total daily L-dopa equivalents (Mamikonyan, E., et al., 2008). Although no therapy provides more powerful antiparkinsonian effects than L-dopa, patients sometimes experience significant motor worsening with dopamine agonist reduction, despite a concomitant increase in L-dopa. This effect may relate to the longer action of dopamine
agonists than that of L-dopa, or agonists may aid “cross-sensitization” to L-dopa (Evans, A.H et al., 2008). Many patients find worsening of motor symptoms more acceptable than the ICD (Tyne, H.L et al., 2004). Some authors have reported resolution after switching dopamine agonists (e.g., from pramipexole or pergolide to ropinirole or from pramipexole to pergolide), (Nirenberg, M.J. et al., 2006; Gallagher, D.A et al., 2007). But this experience is not uniform, equivalent doses are not necessarily used and there is no convincing evidence to date that any specific agonist has a lower risk with respect to ICDs.

However, ICDs and punding may sometimes be resistant to dopaminergic medication reduction (Kurlan, R. 2004) and the prognosis for DDS, which often occurs later in the course of PD, is generally poor with a high rate of relapse (Lawrence, A.D et al., 2003). In a small open label study, topiramate (a drug with multiple mechanisms of action) was used to treat seven PD patients with pathological gambling, hypersexuality, compulsive buying, and compulsive eating with “impressive” results (Bermejo, P.E. 2008). Cyproterone (an anti testosterone therapy) may be considered for severe hypersexuality (Quinn, N.P et al., 1983). Comorbid disorders should be treated, such as associated depression or mania that may sometimes act to trigger a recurrence of disinhibitory psychopathologies. SSRIs are typically first choice for the treatment of depression in PD patients (Weintraub, D et al, 2005) and may also lead to improvements in anxiety (Menza, M., H. et al., 2004).
Psycho-social Impact of ICDS

Reports highlight the potentially devastating psychological, social, legal, and/or economic consequences of ICDs, including divorce, bankruptcy, and attempted suicide in PD patients (Garcia, R.F et al., 2007; Smeding, H.M.M et al., 2007; Merims, D et al., 2008). Lawrence, A.J et al, reported that pathological gamblers lost an average of $129,000 (Lawrence, A.J et al., 2007). Recent studies have shown that the quality of life is adversely affected by the presence of ICDs.
Objectives

The frequency of impulse control disorders in PD patients in Indian population has not been assessed yet. There are no previous studies which have examined the independent effect of ICDs on Quality of Life of patients. Hence we undertook the study with the following objectives.

1. To find out the frequency and pattern of impulse control disorders in a cohort of South Indian PD patients and to compare it with healthy control population.
2. To identify the risk factors associated with ICD in patients with Parkinson’s disease.
3. To assess the impact of impulse control disorders on the quality of life (QOL) of PD patients.
Methods

This is a prospective, single-centre, clinic-based, cross-sectional study using a direct, structured interview of PD patients by a team consisting of psychiatrist, movement disorder specialist and a medical social worker. A cross-sectional prospective study was designed to include patients, who were diagnosed with PD by an experienced movement disorder specialist, based on UKPD society Brain Bank Criteria (Hughes). Patients attending the movement disorders clinic in our university hospital setting were selected. In every clinic (average attendance of 30 PD patients), 5 patients were screened who were the 5 odd number cases and if found eligible, recruited in the study. All demographic and clinical data were collected and verified with the medical records when necessary. Only patients who had received at least one year of DRT and whose treatment had not been modified in the clinic based on prior reporting of ICD were included. Only current medications and their doses were recorded. Patients who scored less than 24 in MMSE in the clinic screening visit were excluded. The modified Hoehn and Yahr staging was done by the movement disorder specialist in the clinic visit. All patients were informed of the aim of the study and all patients provided written informed consent and the study was approved by the institutional ethics committee.

A detailed clinical psychiatric interview was conducted within the 2 weeks following the screening visit. All interviews were conducted in the drug-On state to minimize patient discomfort. UPDRS III in “On” state was measured before the interview. All patients and the spouses (available in 301 cases, 4 were widowed and living with children. In the latter case, the adult offspring with whom the patient lived was also
interviewed) were then interviewed by psychiatrist by direct interview and diagnosis of ICD (current or premorbid) and other behavioral disorders were made. The psychiatrist was blinded to the drugs prescribed to the patients. Each patient underwent a single psychiatry interview, first alone and then with the spouse. The nature of tools and the objective were explained to the patient and family. They were familiarized with the questionnaire. After the screening and self rating assessments, a detailed history assessing the premorbid personality, family history of gambling and ICD was taken. After a detailed psychiatry interview, the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision, DSM IV-RT) or other operational criteria were applied in relevant areas to confirm the diagnosis of ICD that was identified using the screening tools. The key relative was also interviewed for corroborating the details given by the patient. The differences and inconsistencies in the versions and doubts of both patients and family were addressed and consistency achieved. A medical social worker trained for research work in PD interviewed the patients and family to collect the QOL scores. The Impulsive Disorders Interview and quality of life assessments were done by the same team on 250 healthy controls who were the friends or non biological family members of the patients. All controls were interviewed and examined to ensure that they had no neurological disorders.
Measurements

The Jay Modified Minnesota Impulsive Disorders Interview (MIDI) was used for screening for ICD (Christenson GA). If there was a positive response to the gateway question ($\geq 1$) for the five ICRB modules (compulsive buying, compulsive gambling, compulsive sexual behavior, compulsive eating and punding behavior) then, the remaining questions were applied. DSM IV-RT was used for the diagnosis of pathological gambling ($\geq 5$ out of maximum 10 scores) and compulsive eating. Hypersexuality was diagnosed using operational diagnostic criteria of Hypersexuality (Voon V 2006). McElroy’s criteria (A+B+C) was used for compulsive shopping (McElroy’s), operational criteria for punding (Evans et al), provisional criteria was used for diagnosing dopamine dysregulation syndrome (Giovanni). Impulsivity was diagnosed using Barratt impulsivity scale (BIS-II) (Patton et al). BIS-II consists of 30 questions assessing I order factors (a) attention (b) cognitive instability (c) motor (d) perseverance (e) self control and (f) cognitive complexity. The II order factors were (1) attentional impulsiveness (a+b), (2) motor impulsiveness (c+d) and (3) non planning compulsiveness (e+f). The total impulsiveness score was calculated as the sum of attentional impulsiveness, motor impulsiveness, non-planning impulsiveness. The Eysenck personality inventory (adapted form of 56 questions) was used to assess extroversion (score $>13$) and neuroticism (score $>9$) (Eysenck et al., 1958).
Beck’s depression inventory was used for depression (0-9 no depression, 10-18 = mild, 19-30 = moderate, > 30 = severe depression). Hamilton Anxiety and Depression Scale (HADS) was used for diagnosing anxiety (score > 7 positive for anxiety). PDQ39 was used for assessing QOL (ref). Levodopa equivalent daily dosages were calculated using the formula: 100 mg of regular levodopa = 133 mg of controlled release levodopa = 1 mg of pramipexole = 5 mg of ropinirole = 1 mg of rasagiline = 100 mg of amantadine = 0.33 x L DOPA dose of entacapone (Claire L et al., 2010)
Statistical Analysis

All data were analyzed using SPSS version 16. Student’s t-test was used for comparison of clinical characteristics between PD patients with and without ICDs. Mann Whitney test was used for comparison of various scores between the groups. Association between drug use and incidence of ICDs was calculated using odds ratios. Multiple logistic regression analysis was performed to adjust dopamine agonist use for various confounding variables. The threshold level for statistical significance was established at $P = 0.05$

For secondary analyses, variables associated with the presence of an ICD in univariate analyses with a $P < 0.1$ (uncorrected for multiple comparisons) were entered into stepwise logistic regression models to determine the independent effects of the different correlates.
Results

A total of 305 patients (220 men 85 women) with ages ranging from 24 to 84 years (mean =59±10.1 years) participated in the study. The mean age of onset of symptoms was 50.4 years (17-81 years; SD=10.8). The mean PD duration was 7.62 years (range 0.5-29 years; SD=4.9). The Male-female ratio was 2.47:1. Right-side motor symptom onset of PD was noted in 160/305 cases (52.46%).

Of the 305 patients, 255 (83.6%) had sporadic PD, whereas 50 (16.4%) had a positive family history of PD (≥ two members besides the proband affected in three generations). Early-onset PD (onset <45 years of age) was noted in 82 (26.9%). The mean years of education was 11.2 (range 5-23; SD = 4.2). Of the 305 patients, 282 (92.5%) were married and living with their spouse.
Table 1. Demographic and clinical characteristics of all patients and those with and without ICDs

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=305)</th>
<th>With ICD (n=96)</th>
<th>Without ICD (n=209)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at study (years)</td>
<td>59±10.1</td>
<td>54.6 ± 9.9</td>
<td>59.6 ± 9.8</td>
</tr>
<tr>
<td>Age at onset of disease (years)</td>
<td>50.45± 10.8</td>
<td>46.6 ± 10.3</td>
<td>52.2 ± 10.6</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>7.6 ±4.9</td>
<td>8.2 ± 4.9</td>
<td>7.3 ± 4.8</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.2 ± 4.2</td>
<td>11.07 ± 3.8</td>
<td>11.3 ± 4.4</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>71.1</td>
<td>72.9</td>
<td>70.3</td>
</tr>
<tr>
<td>Right sided onset of symptoms</td>
<td>52.5</td>
<td>55.2</td>
<td>51.2</td>
</tr>
<tr>
<td>Hoehn and Yahr stage in “Off”</td>
<td>3.1± 1.1</td>
<td>3.3± 1.1</td>
<td>2.9± 1.1</td>
</tr>
<tr>
<td>Hoehn and Yahr stage in “On”</td>
<td>1.9±0.5</td>
<td>2.0± 0.5</td>
<td>1.9± 0.5</td>
</tr>
<tr>
<td>UPDRS III “On”</td>
<td>18.5± 8.8</td>
<td>18.7 ±9.2</td>
<td>18.5± 8.8</td>
</tr>
<tr>
<td>% with motor fluctuations</td>
<td>70.5</td>
<td>78.1</td>
<td>67.0</td>
</tr>
<tr>
<td>High income category (%)</td>
<td>70.8</td>
<td>70.9</td>
<td>70.8</td>
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<tr>
<td>% with current alcoholism</td>
<td>12.5</td>
<td>30%</td>
<td>40%</td>
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<tr>
<td>% with current smoking</td>
<td>6.56%</td>
<td>55%</td>
<td>29.8%</td>
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<tr>
<td>Extrovertism (%)</td>
<td>56.7</td>
<td>42.7</td>
<td>43.5</td>
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<tr>
<td>Neurotic personality (%)</td>
<td>74.4</td>
<td>84.4</td>
<td>69.9</td>
</tr>
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</table>
Treatment characteristics of the patients

Of the 305 patients, 244 were on levodopa (80.6%) of which 142 were on levodopa monotherapy. Of the 61 patients who were not on levodopa, 46 were on a single dopamine agonist. Fifteen patients were not on either levodopa or dopamine agonist. Ten of them were on rasagiline and five, on anticholinergics alone. One hundred and forty nine patients (54.9%) received dopamine agonist treatment (23 were on ropinirolo and 126, on pramipexole). Thirty seven patients were on pramipexole monotherapy at the time of the study and none were on ropinirolo monotherapy. None were on more than one dopamine agonist or any other agonist. Forty four patients were on amantadine and 81 on anticholinergics, along with dopaminergic drugs.

The mean dose of pramipexole in the whole group was 2.61 ± 1.45mg mean duration of DA use of 2.41 ± 2.02years. The LEDD in pramipexole treated group was 572.81 ± 341.75mg. Twenty three patients were on ropinirolo, the mean dose of ropinirolo was 3.9 ± 2.6mg and mean duration of treatment was 3.9 ± 2.8 years. The mean LEDD was 567.1 ±341.5mg. There was no difference in the LEDD between pramipexole and ropinirolo treated patients.
Table 2. Treatment characteristics of all patients and those with and without ICDs

<table>
<thead>
<tr>
<th></th>
<th>Total n=305</th>
<th>With ICD n =96</th>
<th>Without ICD n=209</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa dose (mg)</td>
<td>329.1 ± 233.3</td>
<td>373.4 ± 268.5</td>
<td>326.2 ± 231.9</td>
</tr>
<tr>
<td>Levodopa treatment duration (years)</td>
<td>4.1 ± 4.3</td>
<td>5.0 ± 4.6</td>
<td>4.1 ± 4.3</td>
</tr>
<tr>
<td>Pramipexole dose (mg)</td>
<td>2.8± 1.4</td>
<td>1.54 ± 1.7</td>
<td>1.0 ± 1.5</td>
</tr>
<tr>
<td>Pramipexole duration (years)</td>
<td>2.6± 1.9</td>
<td>1.37± 1.8</td>
<td>0.88± 1.7</td>
</tr>
<tr>
<td>Ropinirole dose (mg)</td>
<td>3.9± 2.6</td>
<td>1.0 ± 2.02</td>
<td>0.4 ± 1.4</td>
</tr>
<tr>
<td>Ropinirole duration (years)</td>
<td>3.9± 2.8</td>
<td>0.9 ± 2.2</td>
<td>0.4 ± 1.4</td>
</tr>
<tr>
<td>LEDD (mg)</td>
<td>455.4 ± 64.1</td>
<td>590 ± 364.8</td>
<td>448± 280</td>
</tr>
<tr>
<td>Antidepressant use (%)</td>
<td>28.9</td>
<td>38.9</td>
<td>24.4</td>
</tr>
</tbody>
</table>

ICD- Impulse control disorder; LEDD- Levodopa equivalent daily dose
Frequency and patterns of ICDs in PD

Of the 305 patients, 96 (31.6%) were diagnosed to have at least one ICD. Punding was present in 48 (15.7%), compulsive buying in 25 (8.2%), compulsive eating in 24 (7.8%), hypersexuality in 16 (5.2%) and pathological gambling in 14 (4.6%). Ten patients (3.3%) had compulsive medication use. Two or more ICDs were seen in 23 (7.5%) patients. Subsyndromal hypersexuality was seen in 13 (4.3%) and hobbyism in 16 (5.2%). Premorbid ICD was seen in 20 (6.6%) which exacerbated after starting dopaminergic replacement therapy (DRT) in 13.

Table 3 Frequencies of ICDs in PD cohort

<table>
<thead>
<tr>
<th>Type of ICD</th>
<th>No (%) Total=305</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punding</td>
<td>48 (15.7%)</td>
</tr>
<tr>
<td>Compulsive buying</td>
<td>25 (8.2%)</td>
</tr>
<tr>
<td>Compulsive eating</td>
<td>24 (7.8%)</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td>16 (5.2%)</td>
</tr>
<tr>
<td>Compulsive Medication Use</td>
<td>10 (3.3%)</td>
</tr>
<tr>
<td>Subsyndromal hypersexuality</td>
<td>13 (4.3%)</td>
</tr>
<tr>
<td>Hobbyism</td>
<td>16 (5.2%)</td>
</tr>
</tbody>
</table>
FIGURE 1 FREQUENCY OF INDIVIDUAL ICDs IN PD COHORT

- Punding: 15.4%
- Compulsive buying: 8.2%
- Compulsive eating: 7.8%
- Hypersexuality: 5.2%
- Pathological gambling: 4.6%
ICD in the control subjects

Of the 234 controls, 36 (15.38%) were diagnosed to have ICD based on DSM IV. The most common was compulsive buying (11.1%), followed by punding (5.6%), hypersexuality (1.7%), compulsive eating (1.7%) and pathological gambling (0.8%).

FIGURE - 2. FREQUENCY OF ICDS IN CONTROL POPULATION
**Risk factors for any ICD**

Univariate analysis showed that patients with ICD were younger at the time of the study ($P < 0.001$), had younger age of onset of motor symptoms ($P < 0.001$), had higher Hoehn and Yahr stage ($P = 0.007$) and experienced motor fluctuations ($P = 0.04$).

**FIGURE -3. RELATION OF MOTOR SYMPTOMS WITH INCIDENCE OF ICDS**
Table 4. Patient and Parkinson’s disease related risk factors for incidence of ICDs

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Total n=305</th>
<th>With ICD n=96</th>
<th>Without ICD n=209</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at study in years</td>
<td>59±10.1</td>
<td>54.6 ± 9.5</td>
<td>59.6 ± 9.8</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Age at onset in years</td>
<td>50.45±</td>
<td>46.6 ±</td>
<td>52.2 ± 10.6</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Duration of disease in years</td>
<td>7.6 ±4.9</td>
<td>8.2 ± 4.9</td>
<td>7.3 ± 4.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.2 ± 4.2</td>
<td>11.07 ± 3.8</td>
<td>11.3 ± 4.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>71.1</td>
<td>72.9</td>
<td>70.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Right sided onset (%)</td>
<td>52.5</td>
<td>55.2</td>
<td>51.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Mean Hoehn and Yahr in “Off”</td>
<td>3.1± 1.1</td>
<td>3.3± 1.1</td>
<td>2.9± 1.1</td>
<td>0.007*</td>
</tr>
<tr>
<td>Hoehn and Yahr stage in “On”</td>
<td>1.9±0.5</td>
<td>2.0± 0.5</td>
<td>1.9± 0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>UPDRSIII “On”</td>
<td>18.5± 8.8</td>
<td>18.7± 9.2</td>
<td>18.5± 8.8</td>
<td>0.7</td>
</tr>
<tr>
<td>% with motor fluctuations</td>
<td>70.5</td>
<td>78.1</td>
<td>67.0</td>
<td>0.04*</td>
</tr>
<tr>
<td>High income (%)</td>
<td>70.8</td>
<td>70.9</td>
<td>70.8</td>
<td>0.8</td>
</tr>
<tr>
<td>% with current alcoholism</td>
<td>12.5</td>
<td>30%</td>
<td>40%</td>
<td>0.1</td>
</tr>
<tr>
<td>% with current smoking</td>
<td>6.56%</td>
<td>55%</td>
<td>29.8%</td>
<td>0.01*</td>
</tr>
</tbody>
</table>
Psycho behavioural factors

Patients with ICD had more anxiety \((P = 0.03)\) when compared with patients with no ICD and the healthy control population. They also had a trend towards having more depression \((p=0.05)\).
Patients with a neurotic personality was more likely to have incidence of ICDs compared to extrovertic personality ($P = 0.007$) as assessed by the neuropsychiatric inventory.

Patients with impulse control disorders were found to have higher scores in the Barrett’s Impulsivity Score. These scores were higher in total scores ($P < 0.001$) and sub scores of attentional ($P < 0.001$), motor ($P < 0.001$) and non-planning impulsiveness ($P < 0.001$).

**Table-5. Psycho behavioral factors of patients with and without ICDs**

<table>
<thead>
<tr>
<th></th>
<th>Total n=305</th>
<th>With ICD n=96</th>
<th>Without ICD n=209</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety (%)</td>
<td>29.5%</td>
<td>37.5%</td>
<td>25.8%</td>
<td>0.03*</td>
</tr>
<tr>
<td>Depression (%)</td>
<td>49.7%</td>
<td>57.9%</td>
<td>45.9%</td>
<td>0.05*</td>
</tr>
<tr>
<td>Neurotic personality (%)</td>
<td>74.4</td>
<td>84.4</td>
<td>69.9</td>
<td>0.007*</td>
</tr>
<tr>
<td>Barret’s impulsivity score (total)</td>
<td>60.1 ± 16.1</td>
<td>69.5 ± 16.5</td>
<td>55.8 ± 13.9</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Attentional impulsiveness</td>
<td>16.3 ± 4.6</td>
<td>18.7 ± 4.7</td>
<td>15.1 ± 4.0</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Motor impulsiveness</td>
<td>22.0 ± 5.8</td>
<td>25.0 ± 5.7</td>
<td>20.6 ± 5.3</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Non-planning impulsiveness</td>
<td>21.8 ± 6.8</td>
<td>25.7 ± 7.1</td>
<td>20.0 ± 5.8</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

ICD- Impulse control disorder; *$= P < 0.05$
Treatment related characteristics

The patients with ICDs were on a higher dose of pramipexole ($P = 0.003$), had longer duration of pramipexole use ($P = 0.03$), were on a higher dose of ropinirole ($P = 0.006$), had longer duration of ropinirole use ($P = 0.004$), and were on higher LEDD ($P < 0.001$). There was no association of ICD with the use of levodopa ($P = 0.1$). There was also no significant difference between the use of DA alone or in combination with levodopa ($P = 0.06$). No difference was found between the groups who received or did not receive trihexyphenidyl, amantadine or entacapone.

Table -6 Treatment characteristic of PD patients with and without ICD

<table>
<thead>
<tr>
<th></th>
<th>Total n=305</th>
<th>With ICD n =96</th>
<th>Without ICD n=209</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-dopa dose (mg)</td>
<td>329.1 ± 233.3</td>
<td>373.4 ± 268.5</td>
<td>326.2 ± 231.9</td>
<td>0.1</td>
</tr>
<tr>
<td>L-dopa Rx duration (years)</td>
<td>4.1 ± 4.3</td>
<td>5.0 ± 4.6</td>
<td>4.1 ± 4.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Pramipexole dose (mg)</td>
<td>2.8± 1.4</td>
<td>1.54 ± 1.7</td>
<td>1.0 ± 1.5</td>
<td>0.003*</td>
</tr>
<tr>
<td>Pramipexole duration(years)</td>
<td>2.6± 1.9</td>
<td>1.37± 1.8</td>
<td>0.88± 1.7</td>
<td>0.03*</td>
</tr>
<tr>
<td>Ropinirole dose (mg)</td>
<td>3.9± 2.6</td>
<td>1.0 ± 2.02</td>
<td>0.4 ± 1.4</td>
<td>0.006*</td>
</tr>
<tr>
<td>Ropinirole duration(years)</td>
<td>3.9 ±2.8</td>
<td>0.9 ± 2.2</td>
<td>0.4 ± 1.4</td>
<td>0.004*</td>
</tr>
<tr>
<td>LEDD (mg)</td>
<td>455.4 ± 64.1</td>
<td>590 ± 364.8</td>
<td>448± 280</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Antidepressant use (%)</td>
<td>28.9</td>
<td>38.9</td>
<td>24.4</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

Rx= Treatment
**Multivariate Analysis**

On multivariate analysis (Table 4), only treatment with DA was associated with higher incidence of ICD \((P = 0.005, \ OR = 2.03\ CI = 1.09-2.33)\). The odds ratio for treatment with pramipexole was 2.02 \((P = 0.003, \ CI = 1.21-3.34)\) and for ropinirole, 2.76 \((P = 0.006, \ CI = 1.39-5.48)\). DA dose, duration of DA use and LEDD were found to have no significant effect on the frequency of ICDs.

**Table-7. Treatment related Risk factors for the development of any ICD**

<table>
<thead>
<tr>
<th></th>
<th>ICD (N=96)</th>
<th>No ICD (N=208)</th>
<th>OR (CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa use</td>
<td>78</td>
<td>166</td>
<td>1.2 (0.6-2.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Pramipexole use</td>
<td>45</td>
<td>64</td>
<td>2.02 (1.21-3.34)</td>
<td>0.003*</td>
</tr>
<tr>
<td>Ropinirole use</td>
<td>20</td>
<td>19</td>
<td>2.8 (1.39-5.47)</td>
<td>0.006*</td>
</tr>
<tr>
<td>Levodopa + DA</td>
<td>56</td>
<td>48</td>
<td>3.14 (1.8-5.5)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Anticholinergic use</td>
<td>36</td>
<td>59</td>
<td>1.5 (0.9-2.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Amantadine use</td>
<td>15</td>
<td>27</td>
<td>1.2 (0.6-2.5)</td>
<td>ns</td>
</tr>
</tbody>
</table>

ICD- Impulse control disorder; OR- Odd’s ratio; CI- Confidence Interval; DA- Dopamine agonist; *= P < 0.05
Risk factors for individual ICDs

Punding

Punding showed a trend to be more frequent in women (63.8% women vs. 36.2% men; \( P = 0.05 \)). Punding was significantly associated with the onset of PD motor symptoms on the left side (60.5% vs. 39.6%; \( P = 0.03 \)) and neurotic personality trait (\( P = 0.03 \)).
Hypersexuality

Hypersexuality showed a trend to be higher in men (31.4% vs. 3.8%; $P = 0.05$). It was also associated with depression ($P = 0.002$) and the use of antidepressants ($P = 0.003$). Patients with hypersexuality had higher attentional impulsiveness ($P = 0.04$) but not motor ($P = 0.7$) or non-planning impulsiveness ($P = 0.2$).

FIGURE-7. GENDER DISTRIBUTION IN HYPERSEXUALITY (males* > females)
Compulsive Buying

Compulsive buying was associated with younger age at the time of study ($P = 0.01$) and impulsivity ($P < 0.0001$), including subsets of attentional impulsiveness ($P < 0.0001$), motor impulsiveness ($P = 0.003$) and non-planning impulsiveness ($P < 0.0001$).

Compulsive eating

Compulsive eating was associated with (1) higher LEDD ($P = 0.01$), (2) more advanced disease by Hoehn and Yahr staging in “off” ($P = 0.02$) and (3) higher levodopa responsiveness, reflected by a lower Hoehn and Yahr stage in “on” ($P = 0.004$).

Compulsive medication overuse

No risk factor was identified for this ICD.
Table-8. Patient and PD characteristics of patients with individual ICDs

<table>
<thead>
<tr>
<th></th>
<th>Punding</th>
<th>Hypersexuality</th>
<th>Compulsive eating</th>
<th>Compulsive buying</th>
</tr>
</thead>
<tbody>
<tr>
<td>H &amp; Y –OFF</td>
<td>0.2</td>
<td>0.8</td>
<td>0.2</td>
<td>0.33</td>
</tr>
<tr>
<td>H &amp; Y - ON</td>
<td>0.2</td>
<td>0.3</td>
<td>0.05</td>
<td>0.74</td>
</tr>
<tr>
<td>BIS Total</td>
<td>0.55</td>
<td>0.4</td>
<td>0.74</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>BIS-attentional</td>
<td>0.14</td>
<td>0.3</td>
<td>0.72</td>
<td>&lt;0.000*</td>
</tr>
<tr>
<td>BIS-motor</td>
<td>0.83</td>
<td>1</td>
<td>0.79</td>
<td>0.003*</td>
</tr>
<tr>
<td>BIS-Non planning</td>
<td>0.58</td>
<td>0.2</td>
<td>0.75</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.8</td>
<td>0.07</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Depression</td>
<td>0.5</td>
<td>0.003*</td>
<td>0.2</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Table -9. Treatment characteristics of patients with individual ICDs

<table>
<thead>
<tr>
<th></th>
<th>Pundin g</th>
<th>Hypersexuality</th>
<th>Compulsive Eating</th>
<th>Compulsive buying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ldopa dose</td>
<td>0.5</td>
<td>0.6</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Ldopa durn</td>
<td>0.4</td>
<td>0.7</td>
<td>0.5</td>
<td>0.06</td>
</tr>
<tr>
<td>Prami dose</td>
<td>0.2</td>
<td>0.1</td>
<td>0.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Prami durn</td>
<td>0.09</td>
<td>0.4</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Ropinirole dose</td>
<td>0.4</td>
<td>0.9</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Ropi durn</td>
<td>0.8</td>
<td>0.5</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>LEDD</td>
<td>0.5</td>
<td>0.3</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Pacitane</td>
<td>0.5</td>
<td>0.9</td>
<td>0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Amantadine</td>
<td>0.7</td>
<td>0.4</td>
<td>0.7</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Quality of life in PD patients with ICD

The total quality of life (p<0.01) and emotional (p=0.002), stigma (p=0.01) and communication domains (p=0.05) were worse in patients with any ICD. Patients with hypersexuality had less impairment of QOL (p=0.02) and in the communication subscore (p=0.01) when compared to patients without this ICD. Patients with compulsive buying showed less impairment in the social support domain (p=0.001) than those without. QOL was less impaired in bodily discomfort domain (p=0.04) in those with compulsive eating. Patients who had compulsive medication use experienced less severe social stigma (p=0.04).
Table-10. Quality of life in PD patients with ICD

<table>
<thead>
<tr>
<th></th>
<th>Total n=305</th>
<th>With ICD n =96</th>
<th>Without ICD n=209</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDQ 39 Summary Index</td>
<td>47.8 ± 25.5</td>
<td>51.9 ± 26.1</td>
<td>45.9 ± 25.1</td>
<td>0.04*</td>
</tr>
<tr>
<td>Mobility subscore</td>
<td>37.2 ± 23.7</td>
<td>38.3 ± 23.4</td>
<td>36.6 ± 23.8</td>
<td>0.5</td>
</tr>
<tr>
<td>ADL subscore</td>
<td>34.5 ±22.4</td>
<td>37.1 ±22.8</td>
<td>33.3 ±22.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Emotional subscore</td>
<td>31.5 ± 23.0</td>
<td>37.5 ± 24.3</td>
<td>28.7 ± 21.9</td>
<td>0.002*</td>
</tr>
<tr>
<td>Stigma subscore</td>
<td>30.9 ± 48.9</td>
<td>33.8 ± 26.4</td>
<td>29.7±57.6</td>
<td>0.01*</td>
</tr>
<tr>
<td>Social support</td>
<td>11.5 ±18.8</td>
<td>26.8 ± 19.5</td>
<td>10.5 ± 18.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>28.8 ± 42.4</td>
<td>27.6 ± 18.6</td>
<td>29.4 ± 49.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Communication</td>
<td>23.9 ±20.6</td>
<td>27.4 ± 22.1</td>
<td>22.2 ± 19.77</td>
<td>0.05</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>33.9±22.3</td>
<td>33.5 ± 22.2</td>
<td>34.1±22.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>

ICD- Impulse control disorder; ADL: Activities of daily living; QOL- Quality of life.
* = P < 0.05
Table – 11. Quality of life as per PDQ 39 scores with individual ICDs

<table>
<thead>
<tr>
<th>QOL subscores</th>
<th>Punding</th>
<th>Hypersexuality</th>
<th>Compulsive eating</th>
<th>Compulsive buying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility</td>
<td>0.15</td>
<td>0.03*</td>
<td>0.84</td>
<td>0.9</td>
</tr>
<tr>
<td>ADL</td>
<td>0.06</td>
<td>0.25</td>
<td>0.75</td>
<td>0.8</td>
</tr>
<tr>
<td>Emotional</td>
<td>0.89</td>
<td>0.08</td>
<td>0.85</td>
<td>0.1</td>
</tr>
<tr>
<td>Stigma</td>
<td>0.19</td>
<td>0.18</td>
<td>0.58</td>
<td>0.2</td>
</tr>
<tr>
<td>Social support</td>
<td>0.46</td>
<td>0.29</td>
<td>0.20</td>
<td>0.001*</td>
</tr>
<tr>
<td>Cognitive</td>
<td>0.82</td>
<td>0.44</td>
<td>0.74</td>
<td>0.9</td>
</tr>
<tr>
<td>Communication</td>
<td>0.10</td>
<td>0.02</td>
<td>0.89</td>
<td>0.7</td>
</tr>
<tr>
<td>Bodily discomfort</td>
<td>0.82</td>
<td>0.09</td>
<td>0.04*</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* = P < 0.05
Discussion

This is the first Asian study on the frequency of ICDs and related behaviors and the risk factors associated with them that were detected using a structured, direct psychiatric interview in PD patients and their family members and involved a multidisciplinary team. We found a relatively higher frequency (31.6%) of ICDs in this sample, and 7.5% of them had two or more ICDs. The common ICDs in the order of frequency were punding (15.4%), compulsive buying (8.2%), compulsive eating (7.8%) and hypersexuality (5.2%). Pathological gambling was less common (4.6%) and compulsive medication use was the least (3.3%). Additionally, we also identified the sub-syndromic hypersexuality (4.3%) and hobbyism (5.2%) in this cohort. Premorbid ICDs were seen in 6.6%, which exacerbated after taking dopamine replacement therapy in the majority (65% of those with premorbid ICD). By univariate analysis multiple risk factors were found to be associated with ICDs such as younger age, young-onset PD, more severe motor disability, presence of motor fluctuations, higher anxiety scores, exposure to dopamine agonists, higher LEDD, longer duration of treatment, neurotic personality and greater impulsivity. However, multivariate analysis revealed that current dopamine agonist use was the only risk factor in patients with ICDs. Our study did not demonstrate any significant association of ICDs with the use of levodopa monotherapy or the use of amantadine or anticholinergics.

Though limited by the small numbers in the different categories of ICDs, the risk factor profile for the individual ICDs (comparison of those with any specific ICD with those with ICDs excluding the specific ICD) showed different patterns for each of the ICDs.
Punding was associated with left sided onset of motor symptoms and a neurotic personality. Hypersexuality was more common in patients with depression and with worse attentional and non-planning impulsiveness. Compulsive buying was commoner in younger patients and those with higher levels of impulsivity. Compulsive eating was associated with higher LEDD and a higher levodopa-responsiveness of the motor disability. It was observed that family members of the patients did not discourage punding behavior and hobbyism and even favored them while actively discouraging compulsive buying, gambling and hypersexuality. This may have influenced the higher frequency of detection of punding in this sample. The risk factor profile of individual ICDs in the DOMINION studies shows a different pattern (Weintraub D et al., 2010, Voon V et al., 2011). They found that compulsive shopping and compulsive sexual behavior were associated with higher levodopa doses, pathological gambling and compulsive shopping with more novelty-seeking behavior and compulsive shopping with greater exploratory excitability. In their study patients with pathological gambling were older, compulsive sexual behavior was more in men, while compulsive buying and binge eating less in them. Differences in sample sizes, population characteristics and method of assessment of ICDs may explain these differences.

In contrast to a previous study (Weintraub D et al., 2006), pre-morbid ICD was not found to be a major risk factor for the development of ICDs and this observation is similar to the DOMINION Part I study.

The frequency of ICDs identified in the current study is higher than most previous reports (Table 12). An important reason for this difference could be that unlike many
of the previous studies, the current study addressed a wider spectrum of ICDs and used a comprehensive method of assessment. The DOMINION Part I study which used a semi-structured interview (compulsive buying, pathological gambling, compulsive eating and hypersexuality) detected a lower frequency of 20.5% in the North American population. Two recent studies (Lee JY et al., 2010; Auyeung M et al., 2011) that also used a semi structured interview found lower frequencies ranging from 7% to 10.1%. Our results compare more with a Finnish study (Jouts J et al., 2012) and a Malaysian study (Lim SY et al 2011) in which the overall frequency was 34.8% even though the ICDs in both the studies were not confirmed by direct psychiatric interview. Besides a higher detected rate, through these results we also infer that socio-cultural and economic factors may not influence the detection and accurate reporting of these disorders if the methodology used is direct and comprehensive.

Another significant reason for the variable frequencies of ICDs in different populations could be the existence of genetic susceptibility factors for the development of ICDs. Dopaminergic function-related genes such as A2/A2 or A1/A2 genotypes of D2 receptors, are implicated in higher impulsiveness and drug abuse (Blum K et al., 1995). Along the same line, D4 receptor polymorphism was found to be associated with pathological gambling (Castro I et al., 1997) and D3 receptor p.S9G and GRIN2B c.366C>G variations are identified risk factors for ICDs (Lee JY et al., 2009). A recent genetic association analysis in a Korean cohort of 404 patients with Parkinson’s disease showed a trend towards association of HTR2A c.102T allele which is presumably linked to higher serotonin receptor expression in patients with ICD (Lee JY et al.,
Intrinsic differences in the occurrence of such genetic polymorphisms may influence dopaminergic signaling and explain some of these racial differences in the frequency of ICDs in PD.

The frequency and pattern of ICDs in the healthy control population was different from PD patients. In them, the most frequent type was compulsive buying (11.1%), followed by punding (5.6%), hypersexuality (1.7%), compulsive eating (1.7%) and pathological gambling (0.80%). As gambling is prohibited in India, we could not get a true picture of the frequency of this behavior in our population. Giladi et al. in Israeli population reported the prevalence of ICDs to be 14% in PD patients versus 0% in age- and sex-matched healthy control subjects (Giladi et al., 2007). The lifetime prevalence of pathological gambling in the non-PD population in the United States and Canada was estimated to be 1.6% in a meta-analysis of 119 prevalence studies estimates (Shaffer HJ et al., 1999). Our study shows that the incidence of ICDs in the general population in India is higher than the Western population. Another new finding in the current study was that QOL was worse in patients with ICDs, irrespective of the type of ICD, particularly in the domains of emotion, stigma and communication.
Table 12. Comparison of frequencies of ICDs in studies that applied structured/semistructured psychiatric interview

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<tr>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ICD</td>
<td>31.6 (include punding)</td>
<td>13.6 (exclude punding)</td>
<td>10.1 (exclude punding)</td>
<td>7 (includes punding)</td>
<td>3.53 (include punding)</td>
</tr>
<tr>
<td>Compulsive buying</td>
<td>8.2</td>
<td>5.7</td>
<td>2.5</td>
<td>0.4</td>
<td>-</td>
</tr>
<tr>
<td>Compulsive eating</td>
<td>7.8</td>
<td>4.3</td>
<td>NA</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td>7.5</td>
<td>3.5</td>
<td>2.8</td>
<td>3.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Pathological gambling</td>
<td>1.45</td>
<td>5</td>
<td>1.3</td>
<td>6.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Punding</td>
<td>15.4</td>
<td>NA</td>
<td>4.2</td>
<td>-</td>
<td>0.3</td>
</tr>
<tr>
<td>Comp. medication over use</td>
<td>3.27</td>
<td>NA</td>
<td>NA</td>
<td>-</td>
<td>0.6</td>
</tr>
<tr>
<td>≥2 ICDs</td>
<td>7.5</td>
<td>7.2</td>
<td>2.9</td>
<td>3.7</td>
<td>NA</td>
</tr>
<tr>
<td>Premorbid ICD</td>
<td>6.6</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

ICD- Impulse control disorder
**Conclusion**

This study reveals a relatively higher frequency of ICDs in an Indian PD cohort when compared with the Western or East Asian PD patients. The study highlights the need for a structured psychiatric interview to identify various impulse control and related behaviors.

More investigations into the genetic susceptibility factors for ICD needs to be undertaken; more prudent use of dopamine agonists in vulnerable populations and periodic screening for the presence of ICDs in them is also warranted.

ICDs have a negative impact on the quality of life of Parkinson’s disease patients.
BIBLIOGRAPHY


ANNEXURES

Impulse Control Disorders in Parkinson’s Disease in a South Indian cohort

**PROFORMA**

Name
Current age  Sex
Hospital no:
Address

Telephone no:
Occupation
Income
(Economic status / monthly family income)
Marital status  married/ divorced/separated/bachelor)
Age of onset of disease
Duration of disease
Type of PD (sporadic/familial)
Side of onset:
**Medications**

Levodopa (dose, duration) :
Levodopa + agonist (dose, duration) :
Levodopa + amantadine (dose, duration) :
Agonist only (dose, duration) :
Levodopa + agonist + (artane or amantadine) :
Others (dose, duration) :

LEDD :

**Stage of disease**

H&Y (On) :
H&Y (Off) :
UPDRS III (ON) :

**PREMORBID HABITS**

Alcohol - YES/NO

Years of Alcohol Intake

Occasional/Moderate/Severe/ dependent

Smoking - YES/NO

Panchewing-YES/NO
MMSE:

Baseline personality (Personality Inventory): Neurotic/Extrovert

Beck’s Depression rating:

HADS:

mMDI:

1. Compulsive buying: Positive/ negative Score:
2. Pathological gambling: Positive/negative Score:
3. Hyper sexuality: Positive/ negative Score:
4. Compulsive eating: Positive/ negative Score:
5. Punding: Positive/ negative Score:

Barrett’s Impulsivity Score:
Mini-Mental State Examination (MMSE)

Patient’s Name: ____________________________ Date: ____________

**Instructions:** Ask the questions in the order listed. Score one point for each correct response within each question or activity.

<table>
<thead>
<tr>
<th>Maximum Score</th>
<th>Patient’s Score</th>
<th>Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td></td>
<td>“What is the year? Season? Date? Day of the week? Month?”</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>“Where are we now: State? County? Town/city? Hospital? Floor?”</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient’s response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials: __________</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>“I would like you to count backward from 100 by sevens.” (93, 86, 79, 72, 65, …) Stop after five answers. Alternative: “Spell WORLD backwards.” (D-L-R-O-W)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>“Earlier I told you the names of three things. Can you tell me what those were?”</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>“Repeat the phrase: ‘No ifs, ands, or buts.’”</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>“Take the paper in your right hand, fold it in half, and put it on the floor.” (The examiner gives the patient a piece of blank paper.)</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>“Please read this and do what it says.” (Written instruction is “Close your eyes.”)</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>“Make up and write a sentence about anything.” (This sentence must contain a noun and a verb.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>“Please copy this picture.” (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)</td>
</tr>
<tr>
<td>30</td>
<td>TOTAL</td>
<td></td>
</tr>
</tbody>
</table>

(Adapted from Rovner & Folstein, 1987)
Jay Modified Minnesota Impulsive Disorders Interview (mMIDI)

Module 1: Buying Disorder Screen
1. Do you or others think that you have a problem with buying things too often or with spending too much money? □ Yes (score = 1), complete Questions 2 and 3 below □ No (score = 0), end this module and go to the next module

2. Do you ever experience an irresistible urge or uncontrollable need to buy things or mounting tension that can only be relieved by buying?

No Rarely Occasionally Frequently

3. Has problem buying led to social, marital, family financial or work problems or caused you to experience significant distress?

No Rarely Occasionally Frequently

Module 2: Compulsive Gambling
1. Do you gamble? □ Yes (score = 1), complete Questions 2 and 5 below □ No (score = 0), end this module and go to the next module

2. Do you or others think that you have ever had a problem with gambling?

No Rarely Occasionally Frequently

3. Have you ever felt guilty about the way you gamble or what happens when you gamble?

No Rarely Occasionally Frequently
4. Have you been preoccupied with gambling or obtaining money to gamble?

<table>
<thead>
<tr>
<th>Score</th>
<th>No</th>
<th>Rarely</th>
<th>Occasionally</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
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<td>2</td>
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<tr>
<td>3</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

5. Have you gambled larger amounts of money or over longer period of time than you intended to?

<table>
<thead>
<tr>
<th>Score</th>
<th>No</th>
<th>Rarely</th>
<th>Occasionally</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>3</td>
<td></td>
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</tbody>
</table>

**Module 3: Compulsive Sexual Behaviour Screen**

1. Do you or others that you know think that you have a problem with being overly preoccupied with some aspect of your sexuality or being overly sexually active?

- Yes (score = 1), complete Questions 2 and 4 below
- No (score = 0), end this module and go to the next module

2. Do you have repetitive sexual fantasies which you feel are out of your control or cause you distress?

<table>
<thead>
<tr>
<th>Score</th>
<th>No</th>
<th>Rarely</th>
<th>Occasionally</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Do you have repetitive sexual urges which you feel are out of your control or cause you distress?

<table>
<thead>
<tr>
<th>Score</th>
<th>No</th>
<th>Rarely</th>
<th>Occasionally</th>
<th>Frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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</tbody>
</table>

4. Do you engage in repetitive sexual behavior which you feel is out of control or causes you distress?

<table>
<thead>
<tr>
<th>Score</th>
<th>No</th>
<th>Rarely</th>
<th>Occasionally</th>
<th>Frequently</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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<tr>
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</tbody>
</table>
Module 4: Compulsive Eating Screen

1. Do you or others that you know think that you have a problem with being, overly preoccupied with food or actively overeating?
   ☐ Yes (score = 1), complete Questions 2 and 4 below
   ☐ No (score = 0), end this module and go to the next module

2. Do you have repetitive fantasies about eating which are out of your control or cause you distress?
   0  1  2  3
   No Rarely Occasionally Frequently

3. Do you have repetitive urges to eat which you feel are out of your control or cause you distress?
   0  1  2  3
   No Rarely Occasionally Frequently

4. Do you engage in constant or overly frequent eating which you feel is out of control or causes you distress?
   0  1  2  3
   No Rarely Occasionally Frequently

Module 5: Punding Behaviour Screen

1. Do you find yourself fascinated with or performing repetitive and/or mechanical tasks such as taking apart and putting back together simple mechanical objects, or picking at oneself, or sorting and arranging common objects?
   ☐ Yes (score = 1), complete Questions 2 and 4 below
   ☐ No (score = 0), end this module and go to the next module

2. Do you collect things such as rocks, coins or books and line them up together?
   0  1  2  3
   No Rarely Occasionally Frequently
3. Do you disassemble mechanical things such as doorknobs, watches, radios or other objects and then re-assemble them?

0 1 2 3
No Rarely Occasionally Frequently

4. Do you find performing such repetitive tasks comforting?

0 1 2 3
No Rarely Occasionally Frequently

5. Do you get frustrated if you are unable to perform such repetitive tasks?

0 1 2 3
No Rarely Occasionally Frequently

6. Have you ever taken amphetamines?

0 1 2 3
No Rarely Occasionally Frequently
Diagnostic Criteria for Various Impulse-Control Disorders

Diagnostic Criteria for Pathological Gambling (DSM IV)

A. Persistent and recurrent maladaptive gambling behavior as indicated by five or more of the following:

1. Is preoccupied with gambling (eg preoccupied with reliving past gambling experiences, handicapping or planning the next venture, or thinking of ways to get money with which to gamble)

2. Needs to gamble with increasing amounts of money in order to achieve the desired excitement

3. Has repeated unsuccessful efforts to control, cut back or stop gambling

4. Is restless or irritable when attempting to cut down or stop gambling

5. Gambles as a way of escaping from problems or of relieving a dysphoric mood (eg, feelings of helplessness, guilt, anxiety, depression)

6. After losing money gambling, often returns another day to get even (“chasing” one’s losses)

7. Lies to family members, therapist or others to conceal the extent of involvement with gambling

8. Has committed illegal acts such as forgery, fraud, theft, or embezzlement to finance gambling

9. Has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling

10. Relies on others to provide money to relieve a desperate financial situation caused by gambling

B. The gambling behavior is not better accounted for by a manic episode
Proposed Diagnostic Criteria for Hedonistic Homeostatic Dysregulation Syndrome Due to DRT Misuse (Giovannoni et al., 2000)

A. Parkinson’s disease with documented levodopa responsiveness

B. Need for increasing doses of DRT in excess of those normally required to relieve Parkinsonian symptoms and signs

C. Pattern of pathological use: expressed need for increased DRT in the presence of excessive and significant dyskinesias despite being “on,” drug-hoarding or drug-seeking behavior, unwillingness to reduce DRT, or absence of painful dystonias

D. Impairment in social or occupational functioning: fights, violent behavior, loss of friends, absence from work, loss of job, legal difficulties, arguments, or difficulties with family

E. Development of hypomanic, manic, or cyclothymic affective syndrome in relation to DRT

F. Development of a withdrawal state characterized by dysphoria, depression, irritability, and anxiety on reducing the level of DRT

G. Duration of disturbance of at least 6 months

Proposed Diagnostic Criteria for Compulsive Buying (McElroy et al 1994)

A. Maladaptive preoccupation with buying or shopping, or maladaptive buying or shopping impulses or behavior, as indicated by at least one of the following:
   1. Frequent preoccupation with buying or impulses to buy that is/are experienced as irresistible, intrusive and/or senseless
   2. Frequent buying of more than can be afforded, frequent buying of items that are not needed, or shopping for longer periods of time than intended

B. The buying preoccupations, impulses, or behaviors cause marked distress, are time-consuming, significantly interfere with social or occupational functioning or result in financial problems (eg, indebtedness or bankruptcy)

C. The excessive buying or shopping behavior does not occur exclusively during periods of hypomania or mania
Proposed Diagnostic Criteria for Pathological Hypersexuality (Voon Vet al., 2006)

A. The sexual thoughts or behaviors are excessive or an atypical change from baseline marked by one or more of the following:

1. Maladaptive preoccupation with sexual thoughts
2. Inappropriately or excessively requesting sex from spouse or partner
3. Habitual promiscuity
4. Compulsive masturbation
5. Telephone sex lines or pornography
6. Paraphilias

B. The behavior must have persisted for at least one month

C. The behavior causes at least one of the following:

1. Marked distress
2. Attempts to control thoughts or behavior are unsuccessful or result in marked anxiety or distress
3. Are time consuming
4. Interfere significantly with social or occupational functioning

D. The behavior does not occur exclusively during periods of hypomania or mania

E. If all criteria except C are fulfilled, the disorder is subsyndromal
Eysenck Personality Inventory

1. Does your mood often go up and down?
2. Do you take much notice of what people think?
3. Are you a talkative person?
4. If you say you will do something, do you always keep your promise no matter how inconvenient it might be?
5. Do you ever feel ‘just miserable’ for no reason?
6. Would being in debt worry you?
7. Are you rather lively?
8. Were you ever greedy by helping yourself to more than your share of anything?
9. Are you an irritable person?
10. Would you take drugs which may have strange or dangerous effects?
11. Do you enjoy meeting new people?
12. Have you every blamed someone for doing something you knew was really your fault?
13. Are your feelings easily hurt?
14. Do you prefer to go your own way rather than act by the rules?
15. Can you usually let yourself go and enjoy yourself at a lively party?
16. Are all your habits good and desirable ones?
17. Do you often feel ‘fed-up’?
18. Do good manners and cleanliness matter much to you?
19. Do you usually take the initiative in making new friends?
20. Have you ever taken anything (even a pin or button) that belonged to someone else?
21. Would you call yourself a nervous person?
22. Do you think marriage is old-fashioned and should be done away with?
23. Can you easily get some life into a rather dull party?
24. Have you ever broken or lost something belonging to someone else?
25. Are you a worrier?
26. Do you enjoy co-operating with others?
27. Do you tend to keep in the background on social occasions?
28. Does it worry you if you know there are mistakes in your work?
29. Have you ever said anything bad or nasty about anyone?
30. Would you call yourself tense or ‘highly strung’?
31. Do you think people spend too much time safeguarding their future with savings and insurance?
32. Do you like mixing with people?
33. As a child were you every cheeky to your parents?
34. Do you worry too long after an embarrassing experience?
35. Do you try not to be rude to people?
36. Do you like plenty of bustle and excitement around you?
37. Have you ever cheated at a game?
38. Do you suffer from ‘nerves’?
39. Would you like other people to be afraid of you?
40. Have you ever taken advantage of someone?
41. Are you mostly quiet when you are with other people?
42. Do you often feel lonely?
43. Is it better to follow society’s rules than go your own way?
44. Do other people think of you as being very lively?
45. Do you always practice what you preach?
46. Are you often troubled about feelings of guilt?
47. Do you sometimes put off until tomorrow what you ought to do today?
48. Can you get a party going?
Hospital Anxiety and Depression Scale (HADS)

Patients are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. The questions relating to anxiety are marked "A", and to depression "D". The score for each answer is given in the right column. Instruct the patient to answer how currently describes their feelings.

A  I feel tense or 'wound up':

Most of the time 3
A lot of the time 2
From time to time, occasionally 1
Not at all 0

D  I still enjoy the things I used to enjoy:

Definitely as much 0
Not quite so much 1
Only a little 2
Hardly at all 3
A I get a sort of frightened feeling as if something awful 
bout to happen:

Very definitely and quite badly 3
Yes, but not too badly 2
A little, but it doesn't worry me 1
Not at all 0

D I can laugh and see the funny side of things:

As much as I always could 0
Not quite so much now 1
Definitely not so much now 2
Not at all 3

A Worrying thoughts go through my mind:

A great deal of the time 3
A lot of the time 2
From time to time, but not too often 1
Only occasionally 0
D I feel cheerful:

Not at all 3
Not often 2
Sometimes 1
Most of the time 0

A I can sit at ease and feel relaxed:

Definitely 0
Usually 1
Not Often 2
Not at all 3

D I feel as if I am slowed down:

Nearly all the time 3
Very often 2
Sometimes 1
Not at all 0
A  I get a sort of frightened feeling like 'butterflies' in the stomach:

Not at all 0
Occasionally 1
Quite Often 2
Very Often 3

D  I have lost interest in my appearance:

Definitely 3
I don't take as much care as I should 2
I may not take quite as much care 1
I take just as much care as ever 0

A  I feel restless as I have to be on the move:

Very much indeed 3
Quite a lot 2
Not very much 1
Not at all 0
D  I look forward with enjoyment to things:

As much as I ever did  0
Rather less than I used to  1
Definitely less than I used to  2
Hardly at all  3

A  I get sudden feelings of panic:

Very often indeed  3
Quite often  2
Not very often  1
Not at all  0

D  I can enjoy a good book or radio or TV program:

Often  0
Sometimes  1
Not often  2
Very seldom  3

Scoring: Add the As = Anxiety. Add the Ds = Depression
0-7 = Normal    8-10 = Borderline abnormal    11-21 = Abnormal

Reference: Zigmond and Snaith (1983)
Beck Depression Inventory

<table>
<thead>
<tr>
<th>1. Sadness</th>
<th>6. Punishment Feelings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  I do not feel sad.</td>
<td>0  I don't feel I am being punished.</td>
</tr>
<tr>
<td>1  I feel sad much of the time.</td>
<td>1  I feel I may be punished.</td>
</tr>
<tr>
<td>2  I am sad all the time.</td>
<td>2  I expect to be punished.</td>
</tr>
<tr>
<td>3  I am so sad or unhappy that I can’t stand it.</td>
<td>3  I feel I am being punished.</td>
</tr>
</tbody>
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<thead>
<tr>
<th>2. Pessimism</th>
<th>7. Self-Dislike</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  I am not discouraged about my future.</td>
<td>0  I feel the same about myself as ever.</td>
</tr>
<tr>
<td>1  I feel more discouraged about my future than I used to be.</td>
<td>1  I have lost confidence in myself.</td>
</tr>
<tr>
<td>2  I do not expect things to work out for me.</td>
<td>2  I am disappointed in myself.</td>
</tr>
<tr>
<td>3  I feel my future is hopeless and will only get worse.</td>
<td>3  I dislike myself.</td>
</tr>
</tbody>
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<table>
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<tr>
<th>3. Past Failure</th>
<th>8. Self-Criticalness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  I do not feel like a failure.</td>
<td>0  I don’t criticize or blame myself more than usual.</td>
</tr>
<tr>
<td>1  I have failed more than I should have.</td>
<td>1  I am more critical of myself than I used to be.</td>
</tr>
<tr>
<td>2  As I look back, I see a lot of failures.</td>
<td>2  I criticize myself for all of my faults.</td>
</tr>
<tr>
<td>3  I feel I am a total failure as a person.</td>
<td>3  I blame myself for everything bad that happens.</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>4. Loss of Pleasure</th>
<th>9. Suicidal Thoughts or Wishes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  I get as much pleasure as I ever did from the things I enjoy.</td>
<td>0  I don’t have any thoughts of killing myself.</td>
</tr>
<tr>
<td>1  I don’t enjoy things as much as I used to.</td>
<td>1  I have thoughts of killing myself, but I would not carry them out.</td>
</tr>
<tr>
<td>2  I get very little pleasure from the things I used to enjoy.</td>
<td>2  I would like to kill myself.</td>
</tr>
<tr>
<td>3  I can’t get any pleasure from the things I used to enjoy.</td>
<td>3  I would kill myself if I had the chance.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Guilty Feelings</th>
<th>10. Crying</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  I don’t feel particularly guilty.</td>
<td>0  I don’t cry anymore than I used to.</td>
</tr>
<tr>
<td>1  I feel guilty over many things I have done or should have done.</td>
<td>1  I cry more than I used to.</td>
</tr>
<tr>
<td>2  I feel quite guilty most of the time.</td>
<td>2  I cry over every little thing.</td>
</tr>
<tr>
<td>3  I feel guilty all of the time.</td>
<td>3  I feel like crying, but I can’t.</td>
</tr>
</tbody>
</table>
### Impulse Control Disorders in Parkinson’s disease

#### 11. Agitation
- **0** I am no more restless or wound up than usual.
- **1** I feel more restless or wound up than usual.
- **2** I am so restless or agitated that it’s hard to stay still.
- **3** I am so restless or agitated that I have to keep moving or doing something.

#### 12. Loss of Interest
- **0** I have not lost interest in other people or activities.
- **1** I am less interested in other people or things than before.
- **2** I have lost most of my interest in other people or things.
- **3** It’s hard to get interested in anything.

#### 13. Indecisiveness
- **0** I make decisions about as well as ever.
- **1** I find it more difficult to make decisions than usual.
- **2** I have much greater difficulty in making decisions than I used to.
- **3** I have trouble making any decisions.

#### 14. Worthlessness
- **0** I do not feel I am worthless.
- **1** I don’t consider myself as worthwhile and useful as I used to.
- **2** I feel more worthless as compared to other people.
- **3** I feel utterly worthless.

#### 15. Loss of Energy
- **0** I have as much energy as ever.
- **1** I have less energy than I used to have.
- **2** I don’t have enough energy to do very much.
- **3** I don’t have enough energy to do anything.

#### 16. Changes in Sleeping Pattern
- **0** I have not experienced any change in my sleeping pattern.
- **1a** I sleep somewhat more than usual.
- **1b** I sleep somewhat less than usual.
- **2a** I sleep a lot more than usual.
- **2b** I sleep a lot less than usual.
- **3a** I sleep most of the day.
- **3b** I wake up 1–2 hours early and can’t get back to sleep.

#### 17. Irritability
- **0** I am no more irritable than usual.
- **1** I am more irritable than usual.
- **2** I am much more irritable than usual.
- **3** I am irritable all the time.

#### 18. Changes in Appetite
- **0** I have not experienced any change in my appetite.
- **1a** My appetite is somewhat less than usual.
- **1b** My appetite is somewhat greater than usual.
- **2a** My appetite is much less than before.
- **2b** My appetite is much greater than usual.
- **3a** I have no appetite at all.
- **3b** I crave food all the time.

#### 19. Concentration Difficulty
- **0** I can concentrate as well as ever.
- **1** I can’t concentrate as well as usual.
- **2** It’s hard to keep my mind on anything for very long.
- **3** I find I can’t concentrate on anything.

#### 20. Tiredness or Fatigue
- **0** I am no more tired or fatigued than usual.
- **1** I get more tired or fatigued more easily than usual.
- **2** I am too tired or fatigued to do a lot of the things I used to do.
- **3** I am too tired or fatigued to do most of the things I used to do.

#### 21. Loss of Interest in Sex
- **0** I have not noticed any recent change in my interest in sex.
- **1** I am less interested in sex than I used to be.
- **2** I am much less interested in sex now.
- **3** I have lost interest in sex completely.
Barratt Impulsivity Scale: BIS-11

Below are the 30 personal statements of the Barratt Impulsiveness Scale as listed in Patton et al. (1995). Each is rated on a 1 (rarely/never) to 4 (always/almost always) scale. The scoring on items 4, 5, 13, 14, 15, 16, 17, 19, 20, 21, and 26 is reversed (4 (rarely/never) to 1 (always/almost always)).

1. I “squirm” at plays or lectures.
2. I am restless at the theater or lectures.
3. I don’t “pay attention."
4. I concentrate easily.
5. I am a steady thinker.
6. I act “on impulse."
7. I act on the spur of the moment.
8. I buy things on impulse.
9. I make up my mind quickly.
10. I do things without thinking.
11. I spend or charge more than I earn.
12. I am happy-go-lucky.
13. I am a careful thinker.
15. I am self-controlled.
16. I plan trips well ahead of time.
17. I plan for job security.
18. I say things without thinking.
19. I like to think about complex problems.
20. I like puzzles.


22. I am more interested in the present than the future.

23. I get easily bored when solving thought problems.

24. I change residences.

25. I change jobs.

26. I am future oriented.

27. I can only think about one problem at a time.

28. I often have extraneous thoughts when thinking.

29. I have “racing” thoughts.

30. I change hobbies.