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Impulse control disorders and related behaviors in Parkinson's disease: risk factors, clinical and genetic aspects and management

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Abstract

Purpose of review: To review recent findings and research directions on impulse control disorders and related behaviors (ICDRBs) in Parkinson's disease (PD).

Recent findings: Longitudinal studies found that prevalence increases during PD progression, incident ICDRBs being around 10% per year in patients treated with dopaminergic therapies. Screening tools and severity scales already developed have been validated and are available in several countries and languages. Main clinical risk factors include young age, male gender, type, doses and duration of the dopaminergic therapy, PD motor severity and dyskinesia, depression, anxiety, apathy, sleep disorders and impulsivity traits. Genetic factors are suspected by a high estimated heritability, but individual genes and variants remain to be replicated. Management of ICDRBs is centered on dopamine agonists decrease, with the risk to develop withdrawal symptoms. Cognitive behavioral therapy and subthalamic nucleus deep brain stimulation also improve ICDRBs. In the perspective of precision medicine, new individual prediction models of these disorders have been proposed, but they need further independent replication.

Summary: Regular monitoring of ICDRB during the course of PD is needed, particularly in subject at high risk of developing these complications. Precision medicine will require appropriate use of machine learning to be reached in the clinical setting.

Keywords: impulse control disorders, Parkinson's disease, dopamine agonists, dopamine replacement therapy, prediction medicine

Introduction

Impulse control disorders (ICDs) are behavioral disorders are common complication in Parkinson's disease (PD) treated by dopamine replacement therapies (DRT). Related behaviors, such as hobbyism and dopamine dysregulation syndrome (DDS), have also been reported. These disorders negatively impact the quality of life of the patients and caregiver [1].

This article reviews previous and recent findings on ICDs in PD regarding their frequency, phenomenology, screening tools, and risk factors (Figure 1). The current and future strategies to manage these behaviors are also discussed.

Definition and description of impulse control disorders

PD is a frequent neurodegenerative disorder, affecting over 6 million patients worldwide [2]. Apart from the characteristic motor symptoms of PD, a wide variety of non-motor symptoms have been described, among which impulse control disorders and related behaviors (ICDRBs). ICDRBs are characterized by impairment in behavioral self-control with a failure to resist an urge to an enjoyable activity, that can lead to harmful situations and interfere with various areas of daily life when performed excessively. Despite the possible negative consequences, the behaviors are repeated without control, defining those behaviors as impulsive and compulsive. ICDRBs have shown to negatively impact life and social-occupational functioning of PD patients and their caregivers [1,3–7]. Among available dopamine replacement therapies (DRTs), dopamine agonists (DA) are the main treatment and risk factor associated with the occurrence of ICDRBs.

Description of ICDRBs reported in PD

The wide variety of ICDRBs reported in PD are summarized in Table 1 and Figure 1.

The main ICDs are pathological gambling, binge eating, compulsive shopping and hypersexuality. Pathological gambling is defined as recurrent and persistent dysfunctional patterns of gambling behavior leading to clinically significant distress or impairment [8]. Binge eating is characterized by recurrent episodes of high food intake in a short span of time [8]. Compulsive shopping is defined as excessive shopping and buying behavior that leads to distress or impairment [9]. Hypersexuality is characterized by recurrently or persistently present sexual or erotic thoughts or fantasies and desire for sexual activity [8,10]. Repetitive behaviors such as, punding, hobbyism, walkabouts and hoarding and, as in DDS, the compulsive use of DRT medication, have also been described as related behaviors [11–16]. Punding results in repetitive, purposeless behaviors focused on specific activities or motor tasks such as unnecessary repetitive home repair or assembling and disassembling objects repetitively. Hobbyism pertains to more complex repetitive behaviors such as arts, sports or online gaming. Walkabouts are excessive, aimless wanderings. In hoarding, patients collect a large number of items with little objective value, without being able to discard them, leading to impaired living conditions.

Assessment and diagnosis

Given their potentially devastating consequences, prompt identification of these disorders is important, especially as the patients may not be aware, or hide, their behaviors. Several screening tools and scales have been developed to screen, diagnose or assess severity of ICDs in PD (Table 1).

The Movement Disorder Society Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) includes an item entitled *Features of dopamine dysregulation syndrome* in the part assessing non-motor aspects of experiences of daily living (part I) [17]. This single item encompasses impulse control disorders, DDS, hobbyism, and punding.

The Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) was developed as a screening instrument for ICDRBs, structured to be consistent with diagnostic criteria as described in the fourth edition of Diagnostic and Statistical Manual (DSM) of Mental Disorders [18]. Its three sections focus on (i) the four most common ICDs, (ii) punting and hobbyism, and (iii) compulsive medication use. A rating scale version of the QUIP, the QUIP-RS, assess their frequency [19] and has been validated in several countries [20–22]. The QUIP can be used for screening for ICDRBs, while the QUIP-RS can be used for both screening and severity rating of ICDRBs [23].

The Ardouin Scale of Behavior in PD (ASBPD) consists of eighteen items addressing psychological and behavioral symptoms, grouped in four parts: general psychological evaluation, apathy, non-motor fluctuations and hyperdopaminergic behaviors [24]. This scale was validated in comparison to other scales and is particularly useful for the assessment of the severity across the range of ICDRBs [23,25].

The Scale for Outcomes in PD – Psychiatric Complications is a screening and severity scale with a 7-item questionnaire [26]. Each item score ranges from 0 (no symptom) to 3 (severe symptoms). Two items are related to ICD: one for compulsive shopping and pathological gambling, and another for hypersexuality [23]. This scale is only recommended for the evaluation of these three ICDRBs [23].

The Minnesota Impulsive Disorders Interview (MIDI) was originally developed in 2008 for the diagnosis of compulsive buying, trichotillomania, kleptomania, pyromania, intermittent explosive disorder, pathological gambling, and compulsive sexual behavior [27,28]. The original version was revised to match the changes made in the fifth edition of the DSM of Mental Disorders [27]. This semi-structured interview is used to assess the impulsive aspect of a compulsive behavior.

This large number of screening tools and scales may introduce heterogeneity in the assessment of ICDRBs in PD, which is already inherently high because of socio-cultural differences. So far, the QUIP-RS seems the most prominent tool given its validation in several languages. For severity rating across the range of ICBs, the QUIP-RS and the ASBPD are recommended [23]. Further testing of established scales against gold standard diagnostic criteria is required for all individual ICDRBs in PD, in the perspective of studies focusing on a specific subtype of ICD for instance, and such as the South Oaks Gambling Screen (SOGS) for gambling.

Frequency

ICDRBs are common in PD, the prevalence ranging from 14 to 33% in cross-sectional and longitudinal studies [3,29–36]. The prevalence increases during disease progression, incident ICDRBs being around 10% per year in patients treated with DRT [29,37]. The frequency and severity seem higher in specific subpopulations such as PD patients with *Parkin* mutations or *GBA* variants [38,39]. A recent review focused on the geographical analysis of ICD prevalence in PD, in regards to the socio-cultural aspects that may influence their occurrence [40]. The overall prevalence in European and American countries (20.8%) was significantly higher than in Asian countries (12.8%). The relative frequency of each subtype of ICDs also varied across countries. Binge eating was reported as the most frequent in European countries and American states, followed by hypersexuality and compulsive buying; whereas hypersexuality seems the most frequent in Asian countries, followed by pathological gambling. Studies in Turkey and India reported very low pathological gambling prevalences [41,42], possibly explained by the fact that gambling is prohibited in Turkey and heavily restricted in India.

Regarding ICD-related behaviors, less characterized, prevalence data are scarcer. Punding prevalence rates vary from 1.4% to 14% [12,13,43] depending on the clinical profile

of patients such as higher dosage of treatment. The prevalence of hoarding has been estimated at 12.2%, although in a specialized PD clinic, hence possibly overestimated [44]. DDS prevalence rate has been reported at 2.3% [45].

Pharmacological, clinical and genetic risk factors

Many risk factors of ICDs in PD have been reported, including demographic, PD-related, pharmacological and genetic risk factors.

Pharmacological variables

DRT, especially dopamine agonists (DA), has been strongly associated with ICDs. Ever use, longer cumulative duration, and higher cumulative dose of DAs have been correlated with ICDs [29]. Lifetime average daily dose and duration of treatment by DA were reported as independently associated with ICDs with significant dose-effect relationships [29,33,34,46]. The six DA approved by the US FDA (pramipexole, ropinirole, bromocriptine, cabergoline, rotigotine, and apomorphine) have all been associated with ICDs [47]. The strongest associations were reported for DA with a preferential affinity for D2-like receptors (D2 and D3 receptors) [48], and were higher with oral short-lasting DA than oral long-lasting or transdermal DA suggesting that pharmaceutical formulation and delivery route may also be important [49,50]. To a lesser extent, associations with levodopa [36,46] and amantadine [36] have been reported. Associations of ICDRBs with zonisamide, istradefylline, monoamine oxidase inhibitors but also antidepressants and sleep inductors were also suggested [33,35,51]. ICDRBs have been reported in drug-naïve PD patients with the same prevalence as in the general population, and in patients with restless leg syndrome (RLS) treated by DA [52–56], suggesting that ICDRBs are not related to PD only, but rather to the DRTs. The lack of association found between a PD genetic risk score and ICDRBs in PD supports this hypothesis [57].

Demographic features

A younger age, younger age at PD onset and male sex have been associated with ICDRBs [36,45,46,58–60]. Differences between sexes depending on ICDRBs subtypes were observed, with women developing more compulsive buying and eating disorders and men developing more pathological gambling and hypersexuality disorders [61,62], although the same differences have been reported in the general population [63]. A personal pre-PD history of an ICD and personal or family history of substance abuse are also risk factors for ICDRBs [64].

Personality traits

The most associated personality trait is impulsivity, with studies reporting higher impulsivity scores [64,65] and greater choice impulsivity [65]. PD patients with ICDs show a higher level of neuroticism and lower levels of agreeableness and conscientiousness [58], particularly among PD patients with pathological gambling [66] or hypersexuality [10]. Such patients are also reported to have ineffective coping skills [67], premorbid personality (novelty seeking and harm avoidance) [60], and anxiety [68].

Psychiatric disturbances

Symptoms and a history of depression [58,62,64,66,69–72], and a history of or higher scores of anxiety [10,46,64,72,73] have been reported as associated with ICDs. A recent study reported that the majority of PD patients with ICDs also suffered from clinically significant apathy and more than a third of apathetic PD patients suffered from ICDs [74].

Cognition

The relationship between ICDRBs and cognitive decline is not clear yet. A recent study reported higher prevalence and severity of all ICDRBs in PD patients with dementia than without dementia [75] whereas others reported less common ICDs in PD demented patients, but they were older, and less treated by DAs [59].

Worse set-shifting and reward-related decision-making were reported in PD patients with ICDs [70]. They may show different neuropsychological profiles depending on ICD subtype, with distinct dysexecutive or memory impairments [13,76]. But these alterations may be reversible modifications, only subsequent to DRT use [77,78].

Sleep disturbances

PD patients with ICDs have been reported to have an increased prevalence of sleep disturbances, including worse sleep efficiency, RLS symptoms, and daytime sleepiness [46,79–82]. Recent results suggest a common phenomenology of urge to move between RLS and ICDs [83]. PD patients with RLS develop more ICD, especially compulsive eating disorders, and show a different psycho-behavioral profile with more hyperdopaminergic behaviors on the ASBPD scale [82]. A strong association has been reported between ICDs, especially pathological gambling, and rapid eye movement sleep behavior disorder (RBD) both in early PD and longitudinally [68,82,84–88], although some recent findings did not reproduce this association [88,89].

PD-related factors

Several PD-related factors have been associated with ICDs such as younger age at PD onset [46,58,61,90], longer disease duration [46,58,61], and higher motor impairment [34,58,73]. A negative association between motor fluctuations or dyskinesias and ICDs has been reported [87], but others reported a positive association between dyskinesia and ICDs [91]. A higher

MDS-UPDRS Part I score, assessing non-motor disturbances of daily living, was reported [65,92], but one of the MDS-UPDRS Part I items concerns DDS.

Genetic data

Heritability of ICDRBs was estimated at 50-60% both in non PD twin studies and PD studies [93,94].

Studies reporting associations of genetic variants with ICDs in PD usually performed candidate gene analyses. Associations were reported with variants in genes encoding receptors or enzymes from dopamine, norepinephrine, serotonin, glutamate and opioid pathways in PD: *DAT1* [95], *DRD1* [96,97], *DRD2* [93,97], *DRD3* [98–100], *DDC* [93,101], *GRIN2B* [97,100], *HTR2A* [93,102], *OPRK1* [93], *ANKK1* [103], *OPRM1* [95], and *SLC22A1* [104] and in the general population [105]. Several of these associations were not always confirmed [95,106], most of these studies being underpowered in PD and without independent replication. The reader can refer to a recent review for a more extensive list of variants investigated in ICDRBs [107].

Exome sequencing suggests genes implicated in signaling pathways linked to G protein-coupled receptors such as the “Adenylate cyclase activating” pathway could participate to genetic susceptibility to ICDs in PD [108].

Management

There is no specific pharmacological agent approved for the management of ICDRBs [107]. Nonetheless, several strategies to manage these disorders have been investigated.

Since DA use is the most important risk factors to develop ICDRBs in PD, a common approach is to reduce the dose or withdraw DA use, with reports suggesting ICDRB resolution or improvement after a few weeks to several months [1,78,109,110]. DA withdrawal may

however have significant drawbacks, including DA withdrawal syndrome with anxiety and depression [111], and may precipitate motor complications. Some patients may require low doses of DA over a large span of time to prevent psychological disorders, but persistence of ICDRBs also occur [112].

Pharmacological agents, including naltrexone [113], citalopram [114], amantadine, and atomoxetine [115,116], have been trialed with modest results and no definitive demonstration of efficacy.

Cognitive behavioral therapy has been investigated to manage ICDRBs, with encouraging results. A randomized controlled trial reported improvement in ICDRBs as well as anxiety and depression levels for 28 patients enrolled in a cognitive behavioral therapy in comparison to 17 wait-listed controls [117], who also demonstrated beneficial response to therapy six months later [118].

Subthalamic nucleus deep brain stimulation (STN-DBS) seems to possibly improve ICDRBs in most reported cases [119] and in prospective observational studies, possibly related to DA medication decrease [120–122]. Yet, worsening of ICDRBs, no change, and development of de novo ICDRBs after STN-DBS have also been reported [119,122].

Prediction

Given the difficulties to screen for ICDs in clinical practice, and the limited treatment strategies to manage ICDs in PD, developing predictive tools would be of great interest. Although risk factors are useful clinical clues, they still cannot reach prediction medicine level for individual risk prediction, which would require machine learning approaches, applied in a few recent studies.

Studies that investigated the predictability of ICDs in PD [93,96,101] trained and evaluated a logistic regression model with clinical and genetic variables as inputs, each in a

different cohort. Adding genetic variables input increased the predictive performance of the models.

These studies have important limitations as they included a single cohort in their analyses, and none of the studies performed cross-validation to evaluate the predictive performance of their models. The same dataset was used as the training set but also as the test set. The predictive performances of these models may thus be highly overestimated. None of the three studies evaluated the performance of their models on an independent replication cohort, which would help estimate the generalizability of the models. Some publicly available cohorts could be used in the next studies to train algorithms on one dataset and evaluated them on another dataset.

Conclusion

Since the first reports of ICDRBs in PD in the early 2000s, dedicated clinical cohorts allowed to determine the frequency and risk factors of ICDRBs, and screening tools and severity scales have been validated. Genetic liability of ICDRBs remains mostly unknown, and larger genetic association studies with independent replication are still needed. The clinical management of ICDRBs includes the decrease in DA use, cognitive behavioral therapy, and eventually STN-DBS. Preliminary studies have proposed predictive models of ICDRBs in the perspective of precision medicine development. Further discoveries on the pathophysiology and predictability of these disorders will likely integrate the use of deep-learning approaches to combine clinical and genetic risk factors for a potential application in the clinical setting.

Key points

- Impulse control disorders and related behaviors are frequent in Parkinson's disease, with an incidence estimated to 10% per year in patients treated with dopamine replacement therapy
- The main risks factors are the dose and duration of the dopamine replacement therapy, a younger age and male gender, motor and non-motor features of Parkinson's disease profile, and potential genetic factors that remain to be explored
- Management relies on the decrease of the dopamine agonist doses with the risk of withdrawal symptoms, cognitive behavioral therapy, and eventually deep brain stimulation in eligible patients
- Clinical-genetic models to predict patients at high risk of developing these disorders would be ideal, but are in need of further development with accurate deep-learning approaches and replication

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Figure legend

Figure 1. Overview of the frequency, screening tools, risk factors, clinical and genetic aspects, management and predictive models of impulse control disorders and related behaviors in Parkinson's disease.

Abbreviations: ASBPD, Ardouin scale of behavior in Parkinson's disease; DD, disease duration; ICDs, impulse control disorders; ICDRBs, impulse control disorders and related behaviors; MAO, monoamine oxidase; MDS-UPDRS, Movement Disorders Society revision of the unified Parkinson's disease rating scale; MIDI, Minnesota impulsive disorders interview; PD, Parkinson's disease; QUIP, questionnaire for impulsive-compulsive disorders in Parkinson's disease; QUIP-RS, questionnaire for impulsive-compulsive disorders in Parkinson's disease – rating scale; RBD, rapid eye moment sleep behavior disorder; RLS, restless leg syndrome; SCOPA, scales for outcomes in Parkinson's disease; SOGS, South Oaks gambling screen; STN-DBS, subthalamic nucleus deep brain stimulation.

References

1. Weintraub D, Claassen DO: **Impulse Control and Related Disorders in Parkinson's Disease**. *Int Rev Neurobiol* 2017, **133**:679–717.
2. GBD 2016 Parkinson's Disease Collaborators: **Global, regional, and national burden of Parkinson's disease, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016**. *Lancet Neurol* 2018, **17**:939–953.

*Report of the worldwide global burden of Parkinson's disease between 1990 and 2016 with determination trends of evolution and influencing factors. Through a systematic analysis of epidemiological studies, global, regional, and country-specific prevalence and years of life lived with disability for Parkinson's disease were estimated from 1990 to 2016.

3. Phu AL, Xu Z, Brakoulias V, Mahant N, Fung VSC, Moore GD, Martin A, Starcevic V, Krause M: **Effect of impulse control disorders on disability and quality of life in Parkinson's disease patients**. *J Clin Neurosci Off J Neurosurg Soc Australas* 2014, **21**:63–66.
4. Mamikonyan E, Siderowf AD, Duda JE, Potenza MN, Horn S, Stern MB, Weintraub D: **Long-term follow-up of impulse control disorders in Parkinson's disease**. *Mov Disord Off J Mov Disord Soc* 2008, **23**:75–80.
5. Erga AH, Alves G, Tysnes OB, Pedersen KF: **Impulsive and compulsive behaviors in Parkinson's disease: Impact on quality of and satisfaction with life, and caregiver burden**. *Parkinsonism Relat Disord* 2020, **78**:27–30.
6. Leroi I, Harbshettar V, Andrews M, McDonald K, Byrne EJ, Burns A: **Carer burden in apathy and impulse control disorders in Parkinson's disease**. *Int J Geriatr Psychiatry* 2012, **27**:160–166.
7. Gulunay A, Cakmakli GY, Yon MI, Ulusoy EK, Karakoc M: **Frequency of non-motor symptoms and their impact on the quality of life in patients with Parkinson's disease: a prospective descriptive case series**. *Psychogeriatr Off J Jpn Psychogeriatr Soc* 2020, **20**:206–211.
8. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*. American Psychiatric Association; 2013.
9. Black DW: **A review of compulsive buying disorder**. *World Psychiatry* 2007, **6**:14–18.
10. Sachdeva J, Harbshettar V, Barraclough M, McDonald K, Leroi I: **Clinical profile of compulsive sexual behaviour and paraphilia in Parkinson's disease**. *J Park Dis* 2014, **4**:665–670.
11. Giovannoni G, O'Sullivan JD, Turner K, Manson AJ, Lees AJ: **Hedonistic homeostatic dysregulation in patients with Parkinson's disease on dopamine replacement therapies**. *J Neurol Neurosurg Psychiatry* 2000, **68**:423–428.

12. Evans AH, Katzenschlager R, Paviour D, O'Sullivan JD, Appel S, Lawrence AD, Lees AJ: **Punding in Parkinson's disease: its relation to the dopamine dysregulation syndrome.** *Mov Disord Off J Mov Disord Soc* 2004, **19**:397–405.
13. Hinkle JT, Perepezko K, Mills KA, Pontone GM: **Attentional dysfunction and the punding spectrum in Parkinson's disease.** *Parkinsonism Relat Disord* 2021, **84**:23–28.
14. Warren N, O'Gorman C, Lehn A, Siskind D: **Dopamine dysregulation syndrome in Parkinson's disease: a systematic review of published cases.** *J Neurol Neurosurg Psychiatry* 2017, **88**:1060–1064.
15. Barbosa P, Djamshidian A, Lees AJ, Warner TT: **The Outcome of Dopamine Dysregulation Syndrome in Parkinson's Disease: A Retrospective Postmortem Study.** *Mov Disord Clin Pract* 2018, **5**:519–522.
16. Cilia R, Siri C, Canesi M, Zecchinelli AL, De Gaspari D, Natuzzi F, Tesesi S, Meucci N, Mariani CB, Sacilotto G, et al.: **Dopamine dysregulation syndrome in Parkinson's disease: from clinical and neuropsychological characterisation to management and long-term outcome.** *J Neurol Neurosurg Psychiatry* 2014, **85**:311–318.
17. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stern MB, Dodel R, et al.: **Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results.** *Mov Disord Off J Mov Disord Soc* 2008, **23**:2129–2170.
18. Weintraub D, Hoops S, Shea JA, Lyons KE, Pahwa R, Driver-Dunckley ED, Adler CH, Potenza MN, Miyasaki J, Siderowf AD, et al.: **Validation of the questionnaire for impulsive-compulsive disorders in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2009, **24**:1461–1467.
19. Weintraub D, Mamikonyan E, Papay K, Shea JA, Xie SX, Siderowf A: **Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale.** *Mov Disord Off J Mov Disord Soc* 2012, **27**:242–247.
20. Choi JH, Lee JY, Cho JW, Ko SB, Ahn TB, Kim SJ, Cheon SM, Kim JS, Kim YJ, Ma HI, et al.: **Validation of the Korean Version of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease Rating Scale.** *J Clin Neurol Seoul Korea* 2020, **16**:245–253.
21. Marques A, Vidal T, Pereira B, Benchetrit E, Socha J, Pineau F, Elbaz A, Artaud F, Mangone G, You H, et al.: **French validation of the questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIP-RS).** *Parkinsonism Relat Disord* 2019, doi:10.1016/j.parkreldis.2019.02.026.
22. Probst CC, Winter LM, Möller B, Weber H, Weintraub D, Witt K, Deuschl G, Katzenschlager R, van Eimeren T: **Validation of the questionnaire for impulsive-compulsive disorders in Parkinson's disease (QUIP) and the QUIP-rating scale in a German speaking sample.** *J Neurol* 2014, **261**:936–942.

23. Evans AH, Okai D, Weintraub D, Lim S-Y, O'Sullivan SS, Voon V, Krack P, Sampaio C, Post B, Leentjens AFG, et al.: **Scales to assess impulsive and compulsive behaviors in Parkinson's disease: Critique and recommendations.** *Mov Disord Off J Mov Disord Soc* 2019, **34**:791–798.

* Review from the Movement Disorder Society on the screening tools and severity scales to assess impulse control disorders in Parkinson's disease, including recommendations on which tools to use for diagnostic screening and severity rating.

24. Ardouin C, Chéreau I, Llorca P-M, Lhommée E, Durif F, Pollak P, Krack P, groupe évaluation comportementale de la maladie de Parkinson: **[Assessment of hyper- and hypodopaminergic behaviors in Parkinson's disease].** *Rev Neurol (Paris)* 2009, **165**:845–856.
25. Rieu I, Martinez-Martin P, Pereira B, De Chazeron I, Verhagen Metman L, Jahanshahi M, Ardouin C, Chéreau I, Brefel-Courbon C, Ory-Magne F, et al.: **International validation of a behavioral scale in Parkinson's disease without dementia.** *Mov Disord Off J Mov Disord Soc* 2015, **30**:705–713.
26. Visser M, Verbaan D, van Rooden SM, Stiggelbout AM, Marinus J, van Hilten JJ: **Assessment of psychiatric complications in Parkinson's disease: The SCOPA-PC.** *Mov Disord Off J Mov Disord Soc* 2007, **22**:2221–2228.
27. Chamberlain SR, Grant JE: **Minnesota Impulse Disorders Interview (MIDI): Validation of a structured diagnostic clinical interview for impulse control disorders in an enriched community sample.** *Psychiatry Res* 2018, **265**:279–283.
28. Grant JE: *Impulse Control Disorders: A Clinician's Guide to Understanding and Treating Behavioral Addictions.* WW Norton and Company; 2008.
29. Corvol J-C, Artaud F, Cormier-Dequaire F, Rascol O, Durif F, Derkinderen P, Marques A-R, Bourdain F, Brandel J-P, Pico F, et al.: **Longitudinal analysis of impulse control disorders in Parkinson disease.** *Neurology* 2018, **91**:e189–e201.

* One of the first study with a longitudinal analysis of impulse control disorders in Parkinson's disease showing that almost half of PD patients experience impulse control disorders after five years of follow-up.

30. Voon V, Napier TC, Frank MJ, Sgambato-Faure V, Grace AA, Rodriguez-Oroz M, Obeso J, Bezard E, Fernagut P-O: **Impulse control disorders and levodopa-induced dyskinesias in Parkinson's disease: an update.** *Lancet Neurol* 2017, **16**:238–250.
31. Marković V, Stanković I, Petrović I, Stojković T, Dragašević-Mišković N, Radovanović S, Svetel M, Stefanova E, Kostić V: **Dynamics of impulsive-compulsive behaviors in early Parkinson's disease: a prospective study.** *J Neurol* 2020, **267**:1127–1136.
32. Prange S, Danaila T, Laurencin C, Caire C, Metereau E, Merle H, Broussolle E, Maucort-Boulch D, Thobois S: **Age and time course of long-term motor and nonmotor complications in Parkinson disease.** *Neurology* 2019, **92**:e148–e160.

33. Perez-Lloret S, Rey MV, Fabre N, Ory F, Spampinato U, Brefel-Courbon C, Montastruc J-L, Rascol O: **Prevalence and pharmacological factors associated with impulse-control disorder symptoms in patients with Parkinson disease.** *Clin Neuropharmacol* 2012, **35**:261–265.
34. Bastiaens J, Dorfman BJ, Christos PJ, Nirenberg MJ: **Prospective cohort study of impulse control disorders in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2013, **28**:327–333.
35. Kon T, Ueno T, Haga R, Tomiyama M: **The factors associated with impulse control behaviors in Parkinson's disease: A 2-year longitudinal retrospective cohort study.** *Brain Behav* 2018, **8**:e01036.
36. Weintraub D, Koester J, Potenza MN, Siderowf AD, Stacy M, Voon V, Whetteckey J, Wunderlich GR, Lang AE: **Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients.** *Arch Neurol* 2010, **67**:589–595.
37. Smith KM, Xie SX, Weintraub D: **Incident impulse control disorder symptoms and dopamine transporter imaging in Parkinson disease.** *J Neurol Neurosurg Psychiatry* 2016, **87**:864–870.
38. Morgante F, Fasano A, Ginevrino M, Petrucci S, Ricciardi L, Bove F, Crisculo C, Moccia M, De Rosa A, Sorbera C, et al.: **Impulsive-compulsive behaviors in parkin-associated Parkinson disease.** *Neurology* 2016, **87**:1436–1441.
39. Amami P, De Santis T, Invernizzi F, Garavaglia B, Albanese A: **Impulse control behavior in GBA-mutated parkinsonian patients.** *J Neurol Sci* 2020, **421**:117291.
40. Parra-Díaz P, Chico-García JL, Beltrán-Corbellini Á, Rodríguez-Jorge F, Fernández-Escandón CL, Alonso-Cánovas A, Martínez-Castrillo JC: **Does the Country Make a Difference in Impulse Control Disorders? A Systematic Review.** *Mov Disord Clin Pract* 2021, **8**:25–32.

* Systematic review of the impact of the country on impulse control disorders in Parkinson's disease, reporting different profiles in different geographical areas, which may be attributable to genetic, socio-economical, cultural or political influences in the phenomenology of these disorders.

41. Kenangil G, Ozekmekçi S, Sohtaoglu M, Erginöz E: **Compulsive behaviors in patients with Parkinson's disease.** *The Neurologist* 2010, **16**:192–195.
42. Sarathchandran P, Soman S, Sarma G, Krishnan S, Kishore A: **Impulse control disorders and related behaviors in Indian patients with Parkinson's disease.** *Mov Disord* 2013, **28**:1901–1902.
43. Miyasaki JM, Al Hassan K, Lang AE, Voon V: **Punding prevalence in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2007, **22**:1179–1181.

44. O'Sullivan SS, Djamshidian A, Evans AH, Loane CM, Lees AJ, Lawrence AD: **Excessive hoarding in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2010, **25**:1026–1033.
45. Kim J, Kim M, Kwon DY, Seo W-K, Kim JH, Baik JS, Koh S-B: **Clinical characteristics of impulse control and repetitive behavior disorders in Parkinson's disease.** *J Neurol* 2013, **260**:429–437.
46. Pontieri FE, Assogna F, Pellicano C, Cacciari C, Pannunzi S, Morrone A, Danese E, Caltagirone C, Spalletta G: **Sociodemographic, neuropsychiatric and cognitive characteristics of pathological gambling and impulse control disorders NOS in Parkinson's disease.** *Eur Neuropsychopharmacol J Eur Coll Neuropsychopharmacol* 2015, **25**:69–76.
47. Grall-Bronnec M, Victorri-Vigneau C, Donnio Y, Leboucher J, Rousselet M, Thiabaud E, Zreika N, Derkinderen P, Challet-Bouju G: **Dopamine Agonists and Impulse Control Disorders: A Complex Association.** *Drug Saf* 2018, **41**:19–75.
48. Moore TJ, Glenmullen J, Mattison DR: **Reports of pathological gambling, hypersexuality, and compulsive shopping associated with dopamine receptor agonist drugs.** *JAMA Intern Med* 2014, **174**:1930–1933.
49. Rizos A, Sauerbier A, Antonini A, Weintraub D, Martinez-Martin P, Kessel B, Henriksen T, Falup-Pecurariu C, Silverdale M, Durner G, et al.: **A European multicentre survey of impulse control behaviours in Parkinson's disease patients treated with short- and long-acting dopamine agonists.** *Eur J Neurol* 2016, **23**:1255–1261.
50. Antonini A, Chaudhuri KR, Boroojerdi B, Asgharnejad M, Bauer L, Grieger F, Weintraub D: **Impulse control disorder related behaviours during long-term rotigotine treatment: a post hoc analysis.** *Eur J Neurol* 2016, **23**:1556–1565.
51. Carbutaru S, Eisinger RS, Ramirez-Zamora A, Bassan D, Cervantes-Arriaga A, Rodriguez-Violante M, Martinez-Ramirez D: **Impulse control disorders in Parkinson's: Sleep disorders and nondopaminergic associations.** *Brain Behav* 2018, **8**:e00904.
52. Schreglmann SR, Gantenbein AR, Eisele G, Baumann CR: **Transdermal rotigotine causes impulse control disorders in patients with restless legs syndrome.** *Parkinsonism Relat Disord* 2012, **18**:207–209.
53. Hankin C, Lee D, Garcia-Borreguero D, Wang Z: **Increased Risk for New-Onset Psychiatric Adverse Events in Patients With Newly Diagnosed Primary Restless Legs Syndrome Who Initiate Treatment With Dopamine Agonists: A Large-Scale Retrospective Claims Matched-Cohort Analysis.** *J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med* 2019, **15**:1225–1232.
54. Voon V, Schoerling A, Wenzel S, Ekanayake V, Reiff J, Trenkwalder C, Sixel-Döring F: **Frequency of impulse control behaviours associated with dopaminergic therapy in restless legs syndrome.** *BMC Neurol* 2011, **11**:117.

55. Tippmann-Peikert M, Park JG, Boeve BF, Shepard JW, Silber MH: **Pathologic gambling in patients with restless legs syndrome treated with dopaminergic agonists.** *Neurology* 2007, **68**:301–303.
56. Cornelius JR, Tippmann-Peikert M, Slocumb NL, Frerichs CF, Silber MH: **Impulse control disorders with the use of dopaminergic agents in restless legs syndrome: a case-control study.** *Sleep* 2010, **33**:81–87.
57. Ihle J, Artaud F, Bekadar S, Mangone G, Sambin S, Mariani LL, Bertrand H, Rascol O, Durif F, Derkinderen P, et al.: **Parkinson's disease polygenic risk score is not associated with impulse control disorders: A longitudinal study.** *Parkinsonism Relat Disord* 2020, **75**:30–33.

* First study investigating the association between a Parkinson's disease genetic risk score and impulse control disorders in Parkinson's disease; no significant association was found.

58. Callesen MB, Weintraub D, Damholdt MF, Møller A: **Impulsive and compulsive behaviors among Danish patients with Parkinson's disease: prevalence, depression, and personality.** *Parkinsonism Relat Disord* 2014, **20**:22–26.
59. Poletti M, Logi C, Lucetti C, Del Dotto P, Baldacci F, Vergallo A, Ulivi M, Del Sarto S, Rossi G, Ceravolo R, et al.: **A single-center, cross-sectional prevalence study of impulse control disorders in Parkinson disease: association with dopaminergic drugs.** *J Clin Psychopharmacol* 2013, **33**:691–694.
60. Jesús S, Labrador-Espinosa MA, Adarmes AD, Méndel-Del Barrio C, Martínez-Castrillo JC, Alonso-Cánovas A, Sánchez Alonso P, Novo-Ponte S, Alonso-Losada MG, López Ariztegui N, et al.: **Non-motor symptom burden in patients with Parkinson's disease with impulse control disorders and compulsive behaviours: results from the COPPADIS cohort.** *Sci Rep* 2020, **10**:16893.
61. Lee J-Y, Kim J-M, Kim JW, Cho J, Lee WY, Kim H-J, Jeon BS: **Association between the dose of dopaminergic medication and the behavioral disturbances in Parkinson disease.** *Parkinsonism Relat Disord* 2010, **16**:202–207.
62. Joutsa J, Martikainen K, Vahlberg T, Kaasinen V: **Effects of dopamine agonist dose and gender on the prognosis of impulse control disorders in Parkinson's disease.** *Parkinsonism Relat Disord* 2012, **18**:1079–1083.
63. Marinus J, Zhu K, Marras C, Aarsland D, van Hilten JJ: **Risk factors for non-motor symptoms in Parkinson's disease.** *Lancet Neurol* 2018, **17**:559–568.
64. Voon V, Sohr M, Lang AE, Potenza MN, Siderowf AD, Whetteckey J, Weintraub D, Wunderlich GR, Stacy M: **Impulse control disorders in Parkinson disease: a multicenter case-control study.** *Ann Neurol* 2011, **69**:986–996.
65. Sáez-Francàs N, Martí Andrés G, Ramírez N, de Fàbregues O, Álvarez-Sabín J, Casas M, Hernández-Vara J: **[Clinical and psychopathological factors associated with impulse control disorders in Parkinson's disease].** *Neurol Barc Spain* 2016, **31**:231–238.

66. Gescheidt T, Majerová V, Menšíková K, Dušek L, Czekóová K, Kotková P, Kaňovský P, Roth J, Bareš M: **ID 16 – Impulse control disorders in young-onset patients with Parkinson’s disease: Cross-sectional study seeking associated factors with regard of personal characteristics.** *Clin Neurophysiol* 2016, **127**:e70.
67. Olley J, Blaszczyński A, Lewis S: **Dopaminergic Medication in Parkinson’s Disease and Problem Gambling.** *J Gamb Stud* 2015, **31**:1085–1106.
68. Cao R, Chen X, Xing F, Xie C, Hu P, Wang K: **Cross-sectional and longitudinal associations between probable rapid eye movement sleep behavior disorder and impulse control disorders in Parkinson’s disease.** *Eur J Neurol* 2020, **27**:757–763.
69. Vela L, Martínez Castrillo JC, García Ruiz P, Gasca-Salas C, Macías Macías Y, Pérez Fernández E, Ybot I, Lopez Valdés E, Kurtis MM, Posada Rodriguez IJ, et al.: **The high prevalence of impulse control behaviors in patients with early-onset Parkinson’s disease: A cross-sectional multicenter study.** *J Neurol Sci* 2016, **368**:150–154.
70. Martini A, Dal Lago D, Edelstyn NMJ, Grange JA, Tamburin S: **Impulse Control Disorder in Parkinson’s Disease: A Meta-Analysis of Cognitive, Affective, and Motivational Correlates.** *Front Neurol* 2018, **9**:654.

* Systematic review with meta-analysis of the evidence for an association between impulse control disorders in Parkinson’s disease and cognitive, affective, and motivational abnormalities, reporting associated with worse set-shifting and reward-related decision-making, and increased depression, anxiety, anhedonia, and impulsivity.

71. Pontone G, Williams JR, Bassett SS, Marsh L: **Clinical features associated with impulse control disorders in Parkinson disease.** *Neurology* 2006, **67**:1258–1261.
72. Auyeung M, Tsoi TH, Tang WK, Cheung CM, Lee CN, Li R, Yeung E: **Impulse control disorders in Chinese Parkinson’s disease patients: the effect of ergot derived dopamine agonist.** *Parkinsonism Relat Disord* 2011, **17**:635–637.
73. Leroi I, Andrews M, McDonald K, Harbisetar V, Elliott R, Byrne EJ, Burns A: **Apathy and impulse control disorders in Parkinson’s disease: a direct comparison.** *Parkinsonism Relat Disord* 2012, **18**:198–203.
74. Scott BM, Eisinger RS, Burns MR, Lopes J, Okun MS, Gunduz A, Bowers D: **Co-occurrence of apathy and impulse control disorders in Parkinson disease.** *Neurology* 2020, **95**:e2769–e2780.

* Study highlighting the high co-occurrence of apathy and impulse control disorders in Parkinson’s disease and challenging the concept of apathy and impulse control disorders as opposite ends of a spectrum.

75. Martínez-Martin P, Wan YM, Ray Chaudhuri K, Schrag AE, Weintraub D: **Impulse control and related behaviors in Parkinson’s disease with dementia.** *Eur J Neurol* 2020, **27**:944–950.

76. Vitale C, Santangelo G, Trojano L, Verde F, Rocco M, Grossi D, Barone P: **Comparative neuropsychological profile of pathological gambling, hypersexuality, and compulsive eating in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2011, **26**:830–836.
77. Siri C, Cilia R, Reali E, Pozzi B, Cereda E, Colombo A, Meucci N, Canesi M, Zecchinelli AL, Tesei S, et al.: **Long-term cognitive follow-up of Parkinson's disease patients with impulse control disorders.** *Mov Disord Off J Mov Disord Soc* 2015, **30**:696–704.
78. Lee J-Y, Jeon B, Koh S-B, Yoon WT, Lee H-W, Kwon OD, Kim JW, Kim J-M, Ma H-I, Kim H-T, et al.: **Behavioural and trait changes in parkinsonian patients with impulse control disorder after switching from dopamine agonist to levodopa therapy: results of REIN-PD trial.** *J Neurol Neurosurg Psychiatry* 2019, **90**:30–37.

* Study investigating the replacement of dopamine agonists with an equivalent dose of levodopa/carbidopa slow-release formulation for PD subjects with impulse control disorders, and reporting alleviated impulse control disorders in PD patients leading to improvement in daily activities but no improvement in neuropsychiatric traits associated with ICD after the 12-week therapy.

79. Antonini A, Barone P, Bonuccelli U, Annoni K, Asgharnejad M, Stanzione P: **ICARUS study: prevalence and clinical features of impulse control disorders in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 2017, **88**:317–324.
80. O'Sullivan SS, Loane CM, Lawrence AD, Evans AH, Piccini P, Lees AJ: **Sleep disturbance and impulsive-compulsive behaviours in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 2011, **82**:620–622.
81. Scullin MK, Sollinger AB, Land J, Wood-Siverio C, Zanders L, Lee R, Freeman A, Goldstein FC, Bliwise DL, Factor SA: **Sleep and impulsivity in Parkinson's disease.** *Parkinsonism Relat Disord* 2013, **19**:991–994.
82. Marques A, Figorilli M, Pereira B, Derost P, Debilly B, Beudin P, Vidal T, Durif F, Fantini ML: **Impulse control disorders in Parkinson's disease patients with RLS: a cross sectional-study.** *Sleep Med* 2018, **48**:148–154.
83. Marques A, Figorilli M, Lambert C, Pereira B, Vidal T, Montplaisir J, Durif F, Fantini ML: **The urge to move: From restless legs syndrome to impulse control disorders in Parkinson's disease.** *J Sleep Res* 2020, doi:10.1111/jsr.13127.

* Study investigating the “urge” to move through the suggested immobilization test supporting the diagnosis of restless leg syndrome, and reporting significantly higher score for PD subjects with impulse control disorders than those without.

84. Fantini ML, Macedo L, Zibetti M, Sarchioto M, Vidal T, Pereira B, Marques A, Debilly B, Derost P, Ulla M, et al.: **Increased risk of impulse control symptoms in Parkinson's disease with REM sleep behaviour disorder.** *J Neurol Neurosurg Psychiatry* 2015, **86**:174–179.

85. Fantini ML, Figorilli M, Arnulf I, Zibetti M, Pereira B, Beudin P, Puligheddu M, Cormier-Dequaire F, Lacomblez L, Benchetrit E, et al.: **Sleep and REM sleep behaviour disorder in Parkinson's disease with impulse control disorder.** *J Neurol Neurosurg Psychiatry* 2018, **89**:305–310.
86. Fantini ML, Durif F, Marques A: **Impulse Control Disorders in REM Sleep Behavior Disorder.** *Curr Treat Options Neurol* 2019, **21**:23.
87. Ramírez Gómez CC, Serrano Dueñas M, Bernal O, Araoz N, Sáenz Farret M, Aldinio V, Montilla V, Micheli F: **A Multicenter Comparative Study of Impulse Control Disorder in Latin American Patients With Parkinson Disease.** *Clin Neuropharmacol* 2017, **40**:51–55.
88. Fantini ML, Fedler J, Pereira B, Weintraub D, Marques A-R, Durif F: **Is Rapid Eye Movement Sleep Behavior Disorder a Risk Factor for Impulse Control Disorder in Parkinson Disease?** *Ann Neurol* 2020, **88**:759–770.

* Study suggesting that probable rapid eye movement sleep behavior disorder is not clearly associated with impulse control disorders in Parkinson's disease.

89. Baig F, Kelly MJ, Lawton MA, Ruffmann C, Rolinski M, Klein JC, Barber T, Lo C, Ben-Shlomo Y, Okai D, et al.: **Impulse control disorders in Parkinson disease and RBD: A longitudinal study of severity.** *Neurology* 2019, **93**:e675–e687.

* Study investigating the severity of impulse control disorders in Parkinson's disease using a relatively large cohort with longitudinal follow-up, reporting association with dopamine agonist use, motor complications, and apathy but not rapid eye movement sleep behavior disorder.

90. Ye Z, Hammer A, Camara E, Münte TF: **Pramipexole modulates the neural network of reward anticipation.** *Hum Brain Mapp* 2011, **32**:800–811.
91. Biundo R, Weis L, Abbruzzese G, Calandra-Buonaura G, Cortelli P, Jori MC, Lopiano L, Marconi R, Matinella A, Morgante F, et al.: **Impulse control disorders in advanced Parkinson's disease with dyskinesia: The ALTHEA study.** *Mov Disord Off J Mov Disord Soc* 2017, **32**:1557–1565.
92. Rodríguez-Violante M, González-Latapi P, Cervantes-Arriaga A, Camacho-Ordoñez A, Weintraub D: **Impulse control and related disorders in Mexican Parkinson's disease patients.** *Parkinsonism Relat Disord* 2014, **20**:907–910.
93. Kraemmer J, Smith K, Weintraub D, Guillemot V, Nalls MA, Cormier-Dequaire F, Moszer I, Brice A, Singleton AB, Corvol J-C: **Clinical-genetic model predicts incident impulse control disorders in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 2016, **87**:1106–1111.
94. Eisen SA, Lin N, Lyons MJ, Scherrer JF, Griffith K, True WR, Goldberg J, Tsuang MT: **Familial influences on gambling behavior: an analysis of 3359 twin pairs.** *Addict Abingdon Engl* 1998, **93**:1375–1384.

95. Cormier-Dequaire F, Bekadar S, Anheim M, Lebbah S, Pelissolo A, Krack P, Lacomblez L, Lhommée E, Castrioto A, Azulay J-P, et al.: **Suggestive association between OPRM1 and impulse control disorders in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2018, **33**:1878–1886.

* Study suggesting a novel association of the opioid receptor gene OPRM1 with impulse control disorders and related behaviors in Parkinson's disease and confirming a previous association with DAT1.

96. Erga AH, Dalen I, Ushakova A, Chung J, Tzoulis C, Tysnes OB, Alves G, Pedersen KF, Maple-Grødem J: **Dopaminergic and Opioid Pathways Associated with Impulse Control Disorders in Parkinson's Disease.** *Front Neurol* 2018, **9**.

97. Zainal Abidin S, Tan EL, Chan S-C, Jaafar A, Lee AX, Abd Hamid MHN, Abdul Murad NA, Pakarul Razy NF, Azmin S, Ahmad Annuar A, et al.: **DRD and GRIN2B polymorphisms and their association with the development of impulse control behaviour among Malaysian Parkinson's disease patients.** *BMC Neurol* 2015, **15**:59.

98. Castro-Martínez XH, García-Ruiz PJ, Martínez-García C, Martínez-Castrillo JC, Vela L, Mata M, Martínez-Torres I, Feliz-Feliz C, Palau F, Hoenicka J: **Behavioral addictions in early-onset Parkinson disease are associated with DRD3 variants.** *Parkinsonism Relat Disord* 2018, **49**:100–103.

99. Krishnamoorthy S, Rajan R, Banerjee M, Kumar H, Sarma G, Krishnan S, Sarma S, Kishore A: **Dopamine D3 receptor Ser9Gly variant is associated with impulse control disorders in Parkinson's disease patients.** *Parkinsonism Relat Disord* 2016, **30**:13–17.

100. Lee J-Y, Lee EK, Park SS, Lim J-Y, Kim HJ, Kim JS, Jeon BS: **Association of DRD3 and GRIN2B with impulse control and related behaviors in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2009, **24**:1803–1810.

101. Jesús S, Periñán MT, Cortés C, Buiza-Rueda D, Macías-García D, Adarmes A, Muñoz-Delgado L, Labrador-Espinosa MÁ, Tejera-Parrado C, Gómez-Garre MP, et al.: **Integrating genetic and clinical data to predict impulse control disorders in Parkinson's disease.** *Eur J Neurol* 2021, **28**:459–468.

* Study investigating the predictability of impulse control disorders in Parkinson's disease, using clinical and genetic data as input of a logistic regression model.

102. Lee J-Y, Jeon BS, Kim H-J, Park S-S: **Genetic variant of HTR2A associates with risk of impulse control and repetitive behaviors in Parkinson's disease.** *Parkinsonism Relat Disord* 2012, **18**:76–78.

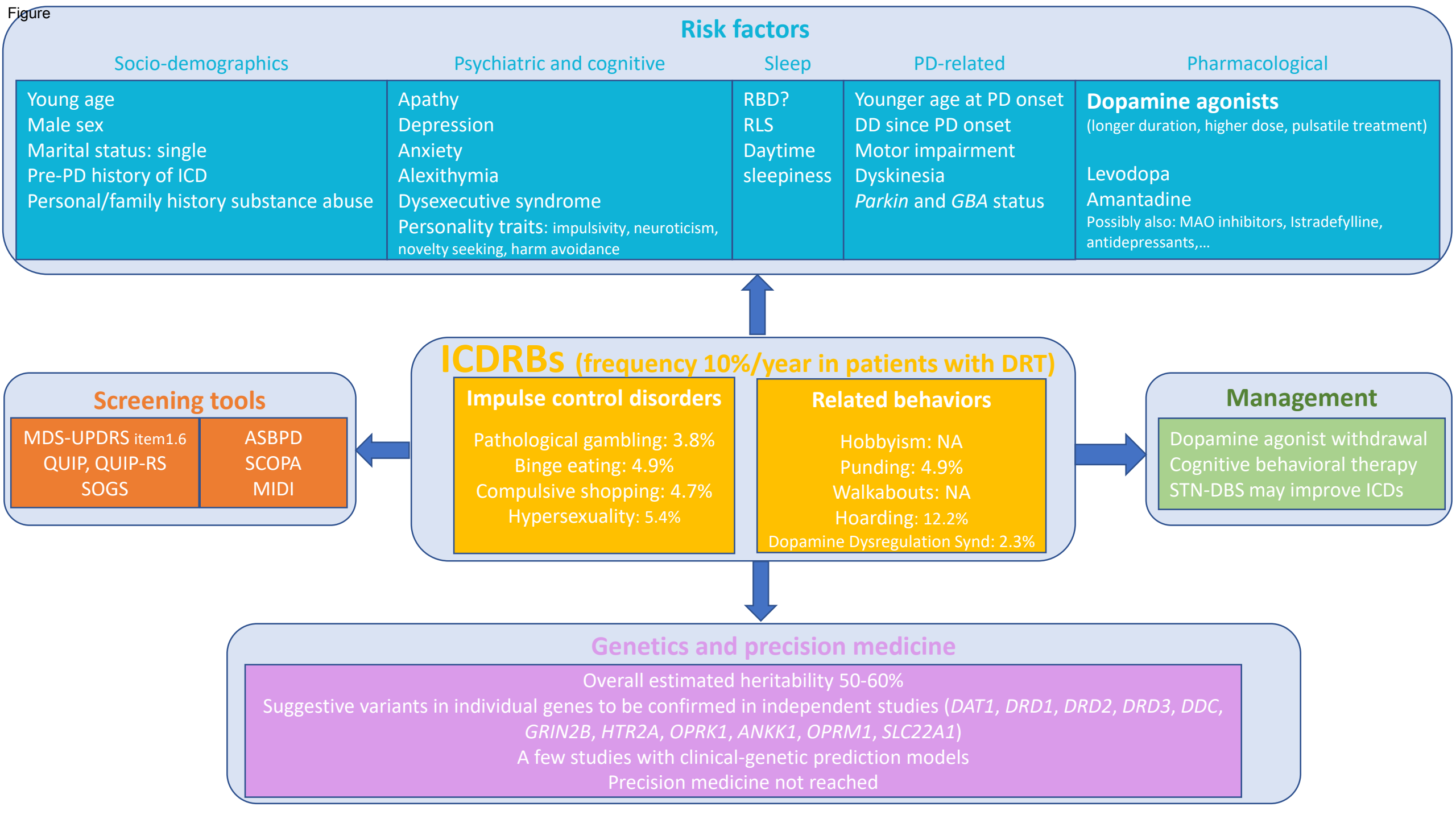
103. Hoenicka J, García-Ruiz PJ, Ponce G, Herranz A, Martínez-Rubio D, Pérez-Santamarina E, Palau F: **The addiction-related gene ANKK1 in Parkinsonian patients with impulse control disorder.** *Neurotox Res* 2015, **27**:205–208.

104. Redenšek S, Flisar D, Kojović M, Gregorič Kramberger M, Georgiev D, Pirtošek Z, Trošt M, Dolžan V: **Dopaminergic Pathway Genes Influence Adverse Events Related to Dopaminergic Treatment in Parkinson's Disease.** *Front Pharmacol* 2019, **10**:8.
105. Cormier F, Muellner J, Corvol J-C: **Genetics of impulse control disorders in Parkinson's disease.** *J Neural Transm Vienna Austria 1996* 2013, **120**:665–671.
106. Vallelunga A, Flaibani R, Formento-Dojot P, Biundo R, Facchini S, Antonini A: **Role of genetic polymorphisms of the dopaminergic system in Parkinson's disease patients with impulse control disorders.** *Parkinsonism Relat Disord* 2012, **18**:397–399.
107. Kelly MJ, Baig F, Hu MT-M, Okai D: **Spectrum of impulse control behaviours in Parkinson's disease: pathophysiology and management.** *J Neurol Neurosurg Psychiatry* 2020, **91**:703–711.
108. Prud'hon S, Bekadar S, Rastetter A, Guégan J, Cormier-Dequaire F, Lacomblez L, Mangone G, You H, Daniau M, Marie Y, et al.: **Exome Sequencing Reveals Signal Transduction Genes Involved in Impulse Control Disorders in Parkinson's Disease.** *Front Neurol* 2020, **11**:641.
- * Study investigating new pathways for impulse control disorders in Parkinson's disease and suggesting that genes implicated in the signaling pathways linked to G protein-coupled receptors participate to the genetic susceptibility to impulse control disorders in Parkinson's disease.
109. Mamikonyan E, Siderowf AD, Duda JE, Potenza MN, Horn S, Stern MB, Weintraub D: **Long-term follow-up of impulse control disorders in Parkinson's disease.** *Mov Disord* 2008, **23**:75–80.
110. Nirenberg MJ, Waters C: **Compulsive eating and weight gain related to dopamine agonist use.** *Mov Disord* 2006, **21**:524–529.
111. Okai D, Samuel M, Askey-Jones S, David AS, Brown RG: **Impulse control disorders and dopamine dysregulation in Parkinson's disease: a broader conceptual framework.** *Eur J Neurol* 2011, **18**:1379–1383.
112. Ávila A, Cardona X, Martín-Baranera M, Bello J, Sastre F: **Impulsive and compulsive behaviors in Parkinson's disease: a one-year follow-up study.** *J Neurol Sci* 2011, **310**:197–201.
113. Papay K, Xie SX, Stern M, Hurtig H, Siderowf A, Duda JE, Minger J, Weintraub D: **Naltrexone for impulse control disorders in Parkinson disease: a placebo-controlled study.** *Neurology* 2014, **83**:826–833.
114. Ye Z, Altena E, Nombela C, Housden CR, Maxwell H, Rittman T, Huddleston C, Rae CL, Regenthal R, Sahakian BJ, et al.: **Selective serotonin reuptake inhibition modulates response inhibition in Parkinson's disease.** *Brain J Neurol* 2014, **137**:1145–1155.

115. Kehagia AA, Housden CR, Regenthal R, Barker RA, Müller U, Rowe J, Sahakian BJ, Robbins TW: **Targeting impulsivity in Parkinson's disease using atomoxetine.** *Brain J Neurol* 2014, **137**:1986–1997.
116. Ye Z, Altena E, Nombela C, Housden CR, Maxwell H, Rittman T, Huddleston C, Rae CL, Regenthal R, Sahakian BJ, et al.: **Improving Response Inhibition in Parkinson's Disease with Atomoxetine.** *Biol Psychiatry* 2015, **77**:740–748.
117. Okai D, Askey-Jones S, Samuel M, O'Sullivan SS, Chaudhuri KR, Martin A, Mack J, Brown RG, David AS: **Trial of CBT for impulse control behaviors affecting Parkinson patients and their caregivers.** *Neurology* 2013, **80**:792–799.
118. Okai D, Askey-Jones S, Samuel M, David AS, Brown RG: **Predictors of response to a cognitive behavioral intervention for impulse control behaviors in Parkinson's disease.** *Mov Disord Off J Mov Disord Soc* 2015, **30**:736–739.
119. Kasemsuk C, Oyama G, Hattori N: **Management of impulse control disorders with deep brain stimulation: A double-edged sword.** *J Neurol Sci* 2017, **374**:63–68.
120. Kim A, Kim YE, Kim H-J, Yun JY, Yang H-J, Lee W-W, Shin CW, Park H, Jung YJ, Kim A, et al.: **A 7-year observation of the effect of subthalamic deep brain stimulation on impulse control disorder in patients with Parkinson's disease.** *Parkinsonism Relat Disord* 2018, **56**:3–8.
121. Abbes M, Lhommée E, Thobois S, Klinger H, Schmitt E, Bichon A, Castrioto A, Xie J, Fraix V, Kistner A, et al.: **Subthalamic stimulation and neuropsychiatric symptoms in Parkinson's disease: results from a long-term follow-up cohort study.** *J Neurol Neurosurg Psychiatry* 2018, **89**:836–843.
122. Santin M des N, Voulleminot P, Vrillon A, Hainque E, Béreau M, Lagha-Boukbiza O, Wirth T, Montaut S, Bardinet E, Kyheng M, et al.: **Impact of Subthalamic Deep Brain Stimulation on Impulse Control Disorders in Parkinson's Disease: A Prospective Study.** *Mov Disord Off J Mov Disord Soc* 2020, doi:10.1002/mds.28320.

* Study on the impact of deep brain stimulation of the subthalamic nucleus, confirming the resolution of impulse control disorders in most cases afterward (but an increased risk of developing apathy) and the increased risk of developing impulse control disorders for subjects with preoperative apathy.

Figure



Table

Table 1. Different types of impulse control disorders and related behaviors in Parkinson's disease, their frequency and the relevant screening and evaluation tools.

Class	Type	Description	Frequency % [range]	Relevant screening tools in PD
Impulse control disorders	Pathological gambling	Addiction to casino games and slot machines, scratch card games, online gambling, with potentially devastating financial repercussions	3.8% [0% - 14.0%]	ABSPD, MDS-UPDRS 1.6, MIDI, QUIP, QUIP-RS, SCOPA, SOGS
	Binge eating	Recurrent episodes characterized by eating, in a small span of time, an excessive amount of food	4.9% [0.3% - 34.8%]	ABSPD, MDS-UPDRS 1.6, QUIP, QUIP-RS
	Compulsive shopping	Excessive shopping and buying behavior that leads to distress or impairment, with devotion of excessive time or money to these behaviors	4.7% [0% - 20%]	ABSPD, MDS-UPDRS 1.6, MIDI, QUIP, QUIP-RS, SCOPA
	Hypersexuality	Persistent or recurrent sexual or erotic thoughts or fantasies and desire for sexual activity	5.4% [0.7% - 23.8%]	ABSPD, MDS-UPDRS 1.6, MIDI, QUIP, QUIP-RS, SCOPA
Other behavioral addictions	Hobbyism	Recurrent and repetitive excessive activities such as physical exercise, gardening, handiwork, taking a stroll on		ABSPD, QUIP, QUIP-RS

		the Internet, painting, sewing, etc.		
	Punding	Intense fascination with repetitive manipulations of technical equipment, and continual handling, examining, sorting common objects	4.9% [0.3% - 14%]	ABSPD, MDS-UPDRS 1.6, QUIP, QUIP-RS
	Dopamine dysregulation syndrome	Intake of large doses of dopamine drugs in excess of that required to control motor symptoms, repetitive requests to physicians for larger doses of dopamine replacement therapy or self-escalation of these doses without medical approval	2.3%	ABSPD, MDS-UPDRS 1.6, QUIP, QUIP-RS
	Walkabouts	Excessive strolling and difficulties to sit still		
	Compulsive hoarding	Procurement of an excessive number of worthless objects that may lead to unsafe living conditions	12.2%	

Abbreviations:

ASBPD, Ardouin Scale of Behavior in Parkinson's Disease; MDS-UPDRS, Movement Disorders Society Revision of the Unified Parkinson's Disease Rating Scale; MIDI, Minnesota Impulsive Disorders Interview; PD, Parkinson's disease; QUIP, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease; QUIP-RS, Questionnaire for Impulsive-

Compulsive Disorders in Parkinson's Disease – Rating Scale; SCOPA, Scales for Outcomes in Parkinson's Disease; SOGS, South Oaks Gambling Screen.