RESEARCH PAPER

Impulse control disorder in patients with Parkinson's disease under dopamine agonist therapy: a multicentre study

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ABSTRACT

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Background Impulse control disorders (ICDs) encompass a wide spectrum of abnormal behaviour frequently found in cases of Parkinson's disease (PD) treated with dopamine agonists (DAs). The main aim of this study was to analyse ICD prevalence with different DAs.

Methods We carried out a multicentre transversal study to evaluate the presence of ICDs in patients with PD chronically treated (>6 months) with a single nonergolinic DA (pramipexole, ropinirole, or rotigotine). Clinical assessment of ICD was performed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's disease.

Results Thirty-nine per cent of patients (91/233) fulfilled the clinical criteria for ICD. The group of patients with ICD symptoms (ICD+) differed from those without ICD symptoms (ICD-) in younger age and type of DA intake. Oral DA treatment (pramipexole and ropinirole) was associated with higher risk of ICDs compared with transdermal DA (rotigotine): 84/197 (42%) patients treated with oral DA developed ICD, versus 7/36 (19%) patients treated with transdermal DA (Fisher's exact text <0.01). In univariate analysis, a younger age (p<0.01), treatment with rasagiline (p < 0.05), and especially treatment with an oral DA (pramipexole or ropinirole) (p<0.01) were significantly associated with ICD. Multivariate analysis confirmed that oral DA remained significantly associated with ICD (p: 0.014, OR: 3.14; 1.26-7.83).

Conclusions ICD was significantly associated with the use of the non-ergolinic oral DA (pramipexole and ropinirole) when compared with transdermal non-ergolinic DA (rotigotine). Since pramipexole, ropinirole and rotigotine are non-ergolinic DAs with very similar pharmacodynamic profiles, it is likely that other factors including route of administration (transdermal vs oral) explain the difference in risk of ICD development.

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To cite: Garcia-Ruiz PJ, Martinez Castrillo JC, Alonso-Canovas A, et al. J Neurol Neurosurg Psychiatry 2014;85: 841–845. Impulse control disorders (ICDs) encompass a wide spectrum of abnormal behaviours including compulsive gambling, compulsive buying and abnormal sexual and eating behaviours.¹

ICDs were found to occur frequently in patients with Parkinson's disease (PD) receiving treatment with dopaminergic medication.^{1–9} In addition, other compulsive behaviours were also detected in treated PD including compulsive dopaminergic medication usage, punding, compulsive shopping, hobbyism, and aimless wandering⁵ ⁷ ^{10–17}; hence, the broader term 'impulsive-compulsive disorders' was also suggested for this medication-related condition.⁷ ¹⁸

Dopamine agonists (DAs) have been consistently correlated with ICD,^{1 3 4-8 14} although younger age, gender, a previous personality profile and the use of other antiparkinsonian medications including levodopa (LD) and monoaminooxidase-B inhibitors are also considered risk factors.^{2 8-10 19} At present, it is not known whether there is similar risk of ICD with different DAs; a recent survey from Perez-Lloret *et al* showed that all DAs were related to an increased risk of ICD, thus further supporting a class effect.⁸

As Weintraub et al pointed out,¹⁸ studies intended to analyse ICD in the context of antiparkinsonian medication are particularly difficult for several reasons. First, many patients do not report even serious side effects to their neurologist²⁰; this may be particularly true regarding ICD, either due to embarrassment or because they do not suspect an association with PD treatment.¹⁸ Second, several aspects of ICD such as compulsive shopping and extreme hobbysm are not considered abnormal behaviour for many patients; partly for these reasons, ICD are usually under-recognised.¹⁸ A further problem arises: with the passage of time, many patients with PD are switched from one medication to another, including different DAs,²¹ and in some cases a combination of DAs may be used,²² making the link between individual medications (especially individual DA) and ICD difficult to establish.

We carried out a multicentre transversal study to evaluate the presence of ICD in patients with PD chronically treated with a single non-ergolinic DA. The main aim of this study was to analyse ICD prevalence with different DAs (pramipexole, ropinirole and rotigotine).

PATIENTS AND METHODS

We studied patients with PD recruited from Movement Disorders Clinics of five different centres in Spain from July 2012 to April 2013. All patients had PD according to clinical criteria.²³

Inclusion criteria were current treatment with a single oral or transdermal DA (pramipexole, ropinirole or rotigotine) for at least 6 months.

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Exclusion criteria were previous or concomitant treatment with different DAs (including apomorphine) and dementia.

A transversal assessment was conducted, including demographic and clinical features: Age, gender, duration of disease, duration of DA exposure and concomitant non-DA antiparkinsonian medication (LD, monoaminooxidase-B inhibitor), presence of fluctuations, total Unified Parkinson's disease Rating Scale (UPDRS)²⁴ and motor subscale (UPDRS-III) on medication (if fluctuation were present) after their morning dose of medication. Total LD equivalent daily dose was calculated according to previously suggested conversion formulae.²⁵ All patients were assessed using self-administered long version of the Impulsive-Compulsive Disorders for Questionnaire in Parkinson's Disease (QUIP) according to previously recommended optimal cut-off points for maximum sensitivity and specificity.¹⁸ Patients with scores in the range of ICD were classified as ICD+; in addition, ICD subtypes and scores were registered.

Univariate analysis was performed to compare baseline clinical features and presence of ICD among the three DA subgroups (pramipexole, ropinirole and rotigotine), as well as between oral DA (pramipexole or ropinirole) and transdermal DA (rotigotine) subgroups. A multivariate logistic regression analysis of the variables reaching or approaching statistical significance in univariate analysis was designed to rule out for potential confounders.

Statistical study methods included descriptive statistics, Kruskal-Wallis test and Fisher's test when appropriate, as well as multivariate logistic regression analysis (G-Stat statistical program). Level of significance was set at p < 0.05.

The study received approval from the local ethics committees.

RESULTS

Two hundred and thirty-three patients were included in the study (mean age 66 ± 9.7 years). Relevant clinical features of the study population are detailed in table 1. All patients were treated with DA (mean exposure: 5.9 years±4.1 years). One hundred and ninety-seven patients were taking an oral DA

Table 1 Clinical features of the study population
n: 233
Gender: male 145 (62.2%); female 88 (37.7%)
Age: 66±9.7 years
UPDRS (TOTAL): 29.9±13
UPDRS III: 20.2±9.18
Exposure time: 5.9±4.1 years
Motor fluctuations: 96 (41.2%)
DA type:
Oral 197 (84.5%)
Pramipexole: 116 (49.8%)
Ropinirole: 81 (34.8%)
Transdermal
Rotigotine: 36 (15.5%)
DA-LEDD: 202±93.3
MAOI: 154 (66.1%): Rasagiline 148 (63.5%); Selegiline: 6 (2.6%)
Amantadine: 15 (6.4%)
Levodopa: 175 (75.1%); LD-LEDD: 600.4±317.5
Total LEDD: 723.8±422.2
Data are shown as number and percentage for gualitative variables

and mean±SD for quantitative variables. DA-LEDD, dopamine agonist levodopa equivalent daily dose; MAOI, monoaminooxidase-B inhibitor; UPDRS, unified Parkinson's disease rating scale. including pramipexole (116) and ropinirole (81) while 36 were treated with transdermal rotigotine. Most patients (81.2%) were taking extended release forms of pramipexole and ropinirole (pramipexole retard or requip prolib), although 57.9% were initially treated with immediate release forms of oral DA and over time, switched to an extended release form of the same DA. Table 2 displays clinical variables regarding DA subtypes (pramipexole, ropinirole or rotigotine). Patients taking an oral DA had significantly higher total UPDRS and UPDRS-III scores and had significantly longer exposure time than patients treated with transdermal rotigotine (p<0.05), while total LD equivalent daily dose was higher in the latter group (p<0.01).

Ninety-one patients (39.1%) had ICD as detected by QUIP-scale, but only 28 (12%) spontaneously referred ICD symptoms in clinical interview. Clinical features of ICD are detailed in table 3 and figure 1. Table 4 shows the association between ICD and clinical variables. In univariate analysis, a younger age (p<0.01), treatment with rasagiline (p<0.05) and especially treatment with an oral DA (pramipexole or ropinirole) (p<0.01) were significantly associated with ICD (table 3). There was no significant difference in ICD for those patients treated with immediate release forms of oral DA compared with those treated with extended release forms (Fisher's test p>0.05). No centre effect was observed either.

In multivariate analysis, treatment with an oral DA remained significantly associated with ICD (p: 0.014) with an OR of 3.14 (95% CI 1.26 to 7.83). Rasagiline (p=0.032, OR 2.12, 95% CI 1.07 to 4.21) and younger age (p=0.028, OR 0.96, 95% CI 0.93 to 0.99) were also significantly associated with ICD, while no significant association was found between ICD and total and motor subscales of UPDRS or time of DA exposure.

DISCUSSION

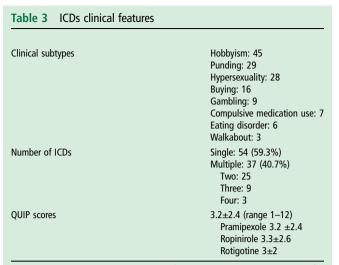
Frequency of ICD is increased in patients with PD¹⁻¹⁹ Since PD itself does not seem to carry an increased risk for development

Table 2	Clinical features of patients treated with oral DA and	
transderm	al DA	

	Pramipexole (n:116)	Ropinirole (n:81)	Rotigotine (n:36)	p Value
Male	73 (62.9)	47 (58)	25 (69.4)	0.4890 (NS)
Age (years)	66.8±8.7	64.8±10.4	66.3±11.3	0.3617 (NS)
Total UPDRS	30.5±12.1	31.4±13.9	24.6±12.9	0.0259*
UPDRS III	21±9	20.8 ±9.1	16.6±9.4	0.0336*
Fluctuations	47 (40.5)	37 (45.7)	12 (33.3)	0.4465 (NS)
Exposure time (years)	6.4±4.2	6±4.3	4.3±2.6	0.0213*
DA-LEDD (mg)	188.3±81.3	196.67±99.05	258.33±98.14	0.0003†
LD-LEDD (mg)	554.5±279.7	665.4±343.9	596.5±355.1	0.1067 (NS)
MAOI:				0.2943 (NS)
Rasagiline	69 (59.5)	52 (64.2)	27 (75)	
Selegiline	5 (4.3)	1 (1.2)	0 (0)	
Amantadine	4 (3.5)	7 (8.6)	4 (11.1)	0.1588 (NS)
Total LEDD	668.4±372.8	787.7±450.7	758.7±490	0.1288 (NS)
Scale-ICD	50 (43.1)	34 (42)	7 (19.4)	0.0317*

Data are shown as number and percentage for qualitative variables and mean $\pm \text{SD}$ for quantitative variables.

DA-LEDD, dopamine agonist levodopa equivalent daily dose; LD-LEDD, levodopa equivalent daily dose; ICD, impulse control disorder; MAOI, monoaminooxidase-B inhibitor; UPDRS, Unified Parkinson's Disease Rating Scale. * Oral DAs versus rotigotine. †Rotigotine versus oral DAs.



Data are shown as number and percentage for qualitative variables and mean $\pm \text{SD}$ for quantitative variables.

ICD, impulse control disorder; QUIP, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease.

of ICD,²⁶ it is clear that medication plays a main role, and DA intake is consistently reported as a major risk factor.^{1 3 4–8 14} At present, ICD is generally considered a DA class effect and not specific for any DA,^{8 9} however most DA- related behavioural problems were observed with oral DA (including pramipexole or ropinirole) ^{5 6 8} and rarely with transdermal DA (rotigotine).^{27 28}

The main goal of this study was to assess the presence of ICD in patients with PD treated with DA. All the patients included in this study had been taking a single DA for at least 6 months and we excluded patients who had been taking two different DAs at the same time, either in combination or consecutively; for the sake of making the potential relationship between ICD and individual DA clearer.

The frequency of ICD in this particular population was very high: 39% of patients fulfilled the criteria for ICD according to the QUIP questionnaire. This test has been previously validated,¹⁸ with a sensitivity of 100% for patient-completed and informant-completed instruments²⁹; although other tests for ICD detection have been proposed.³⁰ Despite this high prevalence of ICD in patients treated with DA, most patients (and caregivers) did not consider their ICD a serious problem, and only 28/91 patients complained or spontaneously commented on this type of side effect. In this regard, the majority of ICD + patients (63/91) might experience what Papay defined as subsyndromal ICD symptoms.²⁹ In any case, it is well known that patients with PD are reluctant to report side effects⁸ ²⁰ and most medication-related side effects are under-reported.⁸ ⁹ ²⁰

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The group of patients with ICD symptoms (ICD+) differed from those without ICD symptoms (ICD-) in several aspects, including younger age, rasagiline use and especially type of DA intake. Treatment with an oral DA (pramipexole and ropinirole) was strongly associated with a higher risk of ICD compared with transdermal DA (rotigotine), with an OR of 3.14. Forty-two per cent of patients treated with oral DA developed ICD versus 19% taking transdermal DA: this difference appears to be clear enough despite the relatively small number of patients taking rotigotine. Certainly, the number of patients treated with oral DA (pramipexole: 116; ropinirole: 81) was much higher than those treated with transdermal DA (rotigotine: 36 patients). This difference may be explained by the fact that rotigotine was more recently introduced than the other DA; which also explains the longer exposure time in the group of patients treated with pramipexole and ropinirole compared with those treated with rotigotine (see table).

We also studied whether the treatment with a standard or extended release form of oral DA (ropinirole or pramipexole) could be a significant factor for the presence of ICD; we did not find significant differences between standard versus extended release oral DA.

Pramipexole, ropinirole and rotigotine are non-ergolinic DAs with a similar pharmacodynamic profile.²⁹⁻³⁶ The binding profile of pramipexole and ropinirole is rather similar: they mainly interact with dopamine receptors D2, D3 and D4. However, rotigotine also interacts with D2, D3 and D4, as well as with D1 and D5 receptors. The significance of these differences is not well understood, and it would be speculative to use them to explain the differences in our study. Other factors that may explain the different risk of ICD could be the more constant plasmatic levels on rotigotine or perhaps the route of administration (transdermal vs oral route). Transdermal delivery bypasses erratic gastric emptying and may avoid other changes in gastrointestinal motility associated with PD with an impact on plasmatic levels of the drug.³² This greater stability of plasma levels might explain, at least in part, the relatively low risk of ICD associated with transdermal rotigotine we observed.

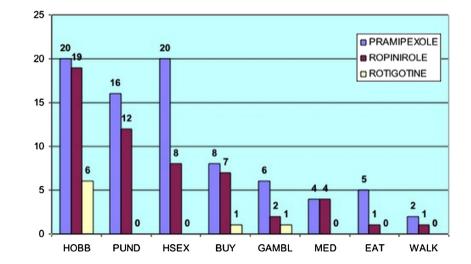


Figure 1 ICD clinical subtypes in the three dopamine agonist subgroups. HOBB: hobby-ism; PUND: punding; HSEX: hypersexuality; BUY: compulsive buying; GAMBL: gambling, MED: compulsive medication use; EAT: compulsive eating disorder; WALK: walkabout.

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Table 4 Association of clinical features and ICD

	ICD + (n: 91)	ICD — (n: 142)	p (univariant)	p (multivariant regression analysis)
Male	62 (68.1)	83 (58.5)	0.1370 (NS)	-
Age (years)	63.9±9.3	67.3±9.7	0.0084	p=0.028, OR 0.96, 95% CI 0.93 to 0.99
Total UPDRS	30.2±13.4	29.6±12.9	0.7293 (NS)	NS
UPDRS III	20.2±9.2	20.3±9.2	0.9423 (NS)	NS
Fluctuations	39 (42.9)	57 (40.1)	0.6811 (NS)	-
Exposure time (years)	6.1±4.4	5.8±3.9	0.6024 (NS)	NS
Oral DA	84 (92.3)	113 (79.6)	0.0087	p=0.014, OR 3.14
Transdermal DA	7 (7.7)	29 (20.4)		(95% CI 1.26 to 7.83)
DA-LEDD (mg)	207.5 ±89.2	198.55±96	0.4770 (NS)	-
LD-LEDD (mg)	617.1±337	591.3±307.	0.6078 (NS)	-
MAOI:	67 (76.6)	87 (61.3)	0.0519 (NS)	-
Rasagiline	66 (72.5)	82 (57.8)	0.0222	p=0.032, OR 2.12,
Selegiline	1 (1.1)	5 (3.7)	0.2548 (NS)	95% CI 1.07–4.21
Amantadine	7 (7.7)	8 (5.6)	0.5322 (NS)	-
TOTAL LEDD (mg)	707.6±433	734.2 ±416.4	0.6401 (NS)	-

Data are shown as number and percentage for qualitative variables and mean±SD for quantitative variables.

DA-LEDD, dopamine agonist levodopa equivalent daily dose; ICD, impulse control disorder; MAOI, monoaminooxidase-B inhibitor; UPDRS, Unified Parkinson's Disease Rating Scale.

Finally, we observed an association between ICD and concomitant treatment with rasagiline, with an OR of 2.2. Rasagiline treatment had been previously suggested to be a risk factor for ICD in previous works,⁸ although our sample differs from other studies in the fact that all our patients were treated with DA. This observation might indicate that rasagiline may potentiate the already high risk of developing ICD in patients taking DA, although further studies are warranted to confirm this impression.

We must acknowledge some limitations to our study. First, the number of patients treated with rotigotine is smaller and the exposure time shorter that the oral DA groups. Second, a switch from immediate release to prolonged release formulations of oral DAs was permitted in the inclusion criteria. We cannot thus analyse the impact of the different formulations in the development of ICD. Finally, the retrospective cross-sectional nature of our study limits the generalisation of our results, and prospective studies are warranted to confirm if the risk of developing ICD on rotigotine treatment is lower than that of oral DAs as our study suggests.

CONCLUSION

In summary, chronic oral DA (ropinirole and pramipexole) treatment appeared to be associated with a higher risk of developing ICD (detected by QUIP) compared with transcutaneous DA (rotigotine) treatment in our cohort. Rasagiline might have potentiated this increased risk. Further prospective studies are warranted to confirm these findings. Patients with PD on treatment with DA, especially the oral formulations, require a close follow-up for an early detection and management of this potentially serious adverse event.

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Contributors PJG-R, JCMC and AA-C contributed to conception, design, acquisition of data, analysis and interpretation of data, and wrote the first draft version. AHB, LV, MM, PSA and NOG contributed to acquisition of data. IMF analysed the data. All authors critically revised the manuscript and approved the final version.

Competing interests PJG-R has received research support from Allergan, UCB, Boehringer-Ingelheim, and speaking honoraria from Italfarmaco, UCB, GSK, Allergan, Novartis and Merz. JCMC has received research support from Allergan, Novartis and Abbott, and speaking honoraria from Abbott, Italfarmaco, UCB, GSK, Boehringer-Ingelheim, Allergan, Ipsen, Novartis and Merz.

Patient consent Obtained.

Ethics approval Local ethics committee of each hospital.

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REFERENCES

- Weintraub D, Siderowf AD, Potenza MN, et al. Association of dopamine agonist use with impulse control disorders in Parkinson disease. Arch Neurol 2006;63:969–73.
- 2 Molina JA, Sáinz-Artiga MJ, Fraile A, et al. Pathologic gambling in Parkinson's disease: a behavioral manifestation of pharmacologic treatment? *Mov Disord* 2000;15:869–72.
- 3 Ondo WG, Lai D. Predictors of impulsivity and reward seeking behavior with dopamine agonists. *Parkinsonism Relat Disord* 2008;14:28–32.
- 4 Voon V, Fernagut PO, Wickens J, et al. Chronic dopaminergic stimulation in Parkinson's disease: from dyskinesias to impulse control disorders. *Lancet Neurol* 2009;8:1140–9.
- 5 Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. Arch Neurol 2010;67:589–95.
- 6 Bastiaens J, Dorfman BJ, Christos PJ, *et al.* Prospective cohort study of impulse control disorders in Parkinson's disease. *Mov Disord* 2013;28:327–30.
- 7 Djamshidian A, Averbeck BB, Lees AJ, et al. Clinical aspects of impulsive compulsive behaviours in Parkinson's disease. J Neurol Sci 2011;310:183–8.
- 8 Perez-Lloret S, Rey MV, Fabre N, et al. Prevalence and pharmacological factors associated with impulse-control disorder symptoms in patients with Parkinson disease. Clin Neuropharmacol 2012;35:261–5.
- 9 Santangelo G, Barone P, Trojano L, et al. Pathological gambling in Parkinson's disease. A comprehensive review. Parkinsonism Relat Disord 2013;19:645–53.
- 10 Fernandez HH, Friedman JH. Punding on L-dopa. Mov Disord 1999;14:836-8.
- 11 Giovannoni G, O'Sullivan JD, Turner K, et al. Hedonistic homeostatic dysregulation in patients with Parkinson's disease on dopamine replacement therapies. J Neurol Neurosurg Psychiatry 2000;68:423–8.
- 12 Voon V. Repetition, repetition, and repetition: compulsive and punding behaviors in Parkinson's disease. *Mov Disord* 2004;19:367–70.
- 13 Miwa H, Kondo T. Increased writing activity in Parkinson's disease: a punding-like behavior? Parkinsonism Relat Disord 2005;11:323–5.
- 14 Nirenberg MJ, Waters C. Compulsive eating and weight gain related to dopamine agonist use. *Mov Disord* 2006;21:524–9.
- 15 Fasano A, Elia AE, Soleti F, et al. Punding and computer addiction in Parkinson's disease. Mov Disord 2006;21:1217–18.
- 16 Katzenschlager R. Dopaminergic dysregulation syndrome in Parkinson's disease. J Neurol Sci 2011;310:271–5.
- 17 Kim J, Kim M, Kwon do Y, et al. Clinical characteristics of impulse control and repetitive behavior disorders in Parkinson's disease. J Neurol 2013;260:429–37.
- 18 Weintraub D, Hoops S, Shea JA, et al. Validation of the questionnaire for impulsive-compulsive disorders in Parkinson's disease. Mov Disord 2009;24:1461–7.
- 19 Vitale C, Santangelo G, Erro R, et al. Impulse control disorders induced by rasagiline as adjunctive therapy for Parkinson's disease: report of 2 cases. Parkinsonism Relat Disord 2013;19:483–4.
- 20 Perez-Lloret S, Rey MV, Fabre N, et al. Do Parkinson's disease patients disclose their adverse events spontaneously? Eur J Clin Pharmacol 2001;68:857–65.
- 21 Grosset K, Needleman F, Macphee G, et al. Switching from ergot to nonergot dopamine agonists in Parkinson's disease: a clinical series and five-drug dose conversion table. *Mov Disord* 2004;19:1370–4.
- 22 Stocchi F, Vacca L, Berardelli A, et al. S. Dual dopamine agonist treatment in Parkinson's disease. J Neurol 2003;250:822–6.
- 23 Hughes AJ, Daniel SE, Kilford L, et al. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–4.

- 24 Lang AE, Fahn S. Assessment of Parkinson's disease. In: Munsat TL, ed. *Quantification of Neurological deficit*. Boston, Mass: Butterworth-Heinemann, 1989: 285–09.
- 25 Tomlinson CL, Stowe R, Patel S, *et al.* Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Mov Disord* 2010;25: 2649–53.
- 26 Weintraub D, Papay K, Siderowf A. Parkinson's Progression Markers Initiative. Screening for impulse control symptoms in patients with de novo Parkinson disease: a case-control study. *Neurology* 2013;80:176–80.
- 27 Wingo TS, Evatt M, Scott B, et al. Impulse control disorders arising in 3 patients treated with rotigotine. *Clin Neuropharmacol* 2009;32:59–62.
- 28 Sprenger FS, Seppi K, Poewe W. Drug safety evaluation of rotigotine. Expert Opin Drug Saf 2012;11:503–12.
- 29 Papay K, Mamikonyan E, Siderowf AD, et al. Patient versus informant reporting of ICD symptoms in Parkinson's disease using the QUIP: validity and variability. Parkinsonism Relat Disord 2011;17:153–5.

- 30 Djamshidian A, O'Sullivan SS, Sanotsky Y, et al. Decision making, impulsivity, and addictions: do Parkinson's disease patients jump to conclusions? *Mov Disord* 2012;27:1137–45.
- 31 Reichmann H, Bilsing A, Ehret R, *et al.* Ergoline and non-ergoline derivatives in the treatment of Parkinson's disease. *J Neurol* 2006;253(Suppl 4):36–8.
- 32 Giladi N, Boroojerdi B, Korczyn AD, et al. AH. Rotigotine transdermal patch in early Parkinson's disease: a randomized, double-blind, controlled study versus placebo and ropinirole. *Mov Disord* 2007;22:2398–404.
- 33 Antonini A, Tolosa E, Mizuno Y, et al. A reassessment of risks and benefits of dopamine agonists in Parkinson's disease. *Lancet Neurol* 2009;8:929–37.
- 34 Perez-Lloret S, Rascol O. Dopamine receptor agonists for the treatment of early or advanced Parkinson's disease. CNS Drugs 2010;24:941–68.
- 35 Rascol O, Perez-Lloret S. Rotigotine transdermal delivery for the treatment of Parkinson's disease. *Expert Opin Pharmacother* 2009;10:677–91.
- 36 Löber S, Hübner H, Tschammer N, et al. Recent advances in the search for D3- and D4-selective drugs: probes, models and candidates. *Trends Pharmacol Sci* 2011;32:148–57.



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