

This study is supported by the National Parkinson Foundation.

BACKGROUND

- ❖ ICD in PD patients has been linked to DA use but may occur in patients without DA exposure.
- ❖ The ICD spectrum includes craving for sweets, gambling, shopping, computer use, binge eating, and sexual activities.¹
- ❖ The role of dopaminergic medication dosages on the whole spectrum has not been described, although pramipexole is most often incriminated.
- ❖ The objective of this study is to describe the relationship between exposure to levodopa and dopamine agonists (DA) and the presence of various ICD in a group of patients with PD.

METHODS

Patients with idiopathic PD and unaffected controls completed self-administered questionnaires regarding various ICD:

- ❖ South Oaks Gambling Screen⁴ (SOGS)
- ❖ Yale-Brown Obsessive Compulsive Screen – Shopping Version⁵ (YBOCS-SV)
- ❖ YBOCS – Computer Use Version (YBOCS-CUV; modified from the YBOCS-SV)
- ❖ Sexual Compulsivity Scale⁶ (SCS)
- ❖ YBOCS – Binge Eating⁷ (YBOCS-BE)
- ❖ Craving Questionnaire (modified from Alcohol Craving Questionnaire⁸)

Inclusion criteria

- ❖ Idiopathic Parkinson's disease (PD patients only)
- ❖ Able and willing to complete rating scales
- ❖ Written informed consent

Exclusion criteria

- ❖ Current participation in another clinical study
- ❖ History of unstable psychiatric disease (as determined by the investigator)

All subjects completed all questionnaires. Scales were scored according to published guidelines.

Patients were grouped according to active DA use, and the prevalence of ICD in each were compared.

Mean total levodopa equivalent doses and DA equivalent doses were compared.

Total levodopa equivalent dose =

$$\begin{aligned} & \text{regular levodopa dose} \times 1 \\ & + \text{levodopa CR dose} \times 0.75 \\ & + \text{pramipexole dose} \times 67 \\ & + \text{ropinirole dose} \times 16.67 \\ & + \text{pergolide dose} \times 100 \\ & + \text{bromocriptine dose} \times 10 \\ & + [\text{reg. levodopa dose} + (\text{CR levodopa dose} \times 0.75)] \times 0.25 \\ & \text{if taking COMT-1} \end{aligned}$$

RESULTS

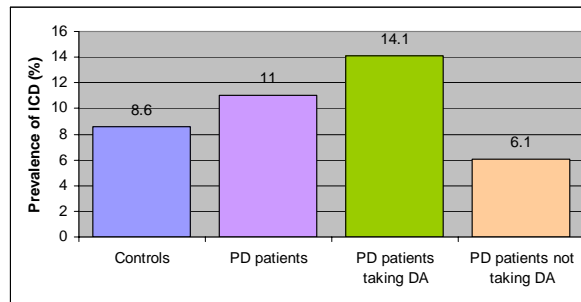
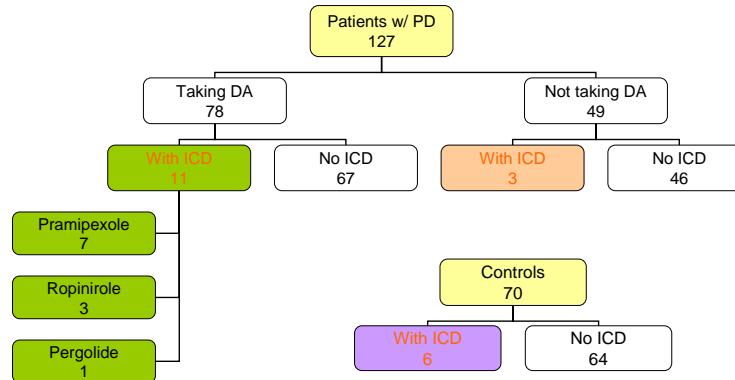


Table 1. Levodopa equivalent doses of PD patients with and without ICD

	With ICD	No ICD	p value
Total levodopa equivalent dosage	836±575 n=14	636±444 n=113	0.13
DA equivalent dosage	326±138 n=11	233±144 n=67	0.19

Table 3. Odds ratio for ICD with dopaminergic medications

Pramipexole	1.4
Ropinirole	1.27
Levodopa	0.09

Table 2. Equivalent doses of dopaminergic medications in patients with ICD

	N (# as monotherapy)	DA equivalent dosage	p value	Total levodopa equivalent dosage
Pramipexole	7 (2)	322±147	0.85	831±692
Ropinirole	3 (0)	343±172		826±134
Pergolide	1 (0)	300	--	1800
Levodopa only	3	0	--	533±306

CONCLUSIONS

- ❖ ICD amongst PD patients occur more often in those taking DA
 - These differences were not statistically significant, but this could be due to small sample size
- ❖ The dopaminergic medication exposure was higher (but not statistically significant) in those with ICD, but there was no difference between individual DA equivalent dosages.
 - Patients with and without ICD were exposed to similar dosages of dopaminergic medication.
 - This suggests the possibility that underlying factors (other than medications) that vary between individuals with PD may contribute to the development of ICD.
 - Such factors may include past or family history of psychiatric disorders or substance use/abuse, duration of PD, or age at onset of PD¹⁷.
- ❖ In this small study, the odds ratio for ICD in PD patients taking either pramipexole or ropinirole was similar.
 - The odds ratio was lowest with levodopa alone.
 - Pramipexole and ropinirole both stimulate D2/D3 receptors, but pramipexole has much greater D3 affinity.
 - Levodopa has much greater D1 receptor affinity than either DA.
- ❖ Functional neuroimaging studies suggest differential (reduced) activation in the ventromedial prefrontal cortex and the ventral striatum in the brains of patients with ICD who do not have PD.^{8,9}
 - D1-like receptors are predominant in frontal areas.
 - D-1 and D2-like receptors are present in the striatum and nucleus accumbens.
 - Dopaminergic deficit in PD may predispose patients to development of ICD after treatment with D2-like and/or D1-like receptor agonists through stimulation (or over-stimulation) of reward pathways including nucleus accumbens.
- ❖ This study suggests that exposure to non-ergot DA in general (and in one case, an ergot DA), rather than individual drugs, predispose to ICD.
- ❖ Larger studies are needed for confirmation.

REFERENCES

1. Jimenez-Shahed J, Davidson T, Calhoun K, Jankovic J. Craving for sweets and other compulsive behaviors in patients with Parkinson's disease. AAN 2008.
2. Lesieur HR, Blume SB. The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. Am J Psychiatry. 1987;144:1184-8.
3. Koran LM, Chuong HW, Bullock KD, Smith SC. Citalopram for compulsive shopping disorder: an open-label study followed by double-blind discontinuation. J Clin Psychiatry. 2003;64:793-8.
4. Kalichman SC, Rompa D. The Sexual Compulsivity Scale: further development and use with HIV-positive persons. J Pers Assess. 2001; 76:379-95.
5. McElroy SL, Arnold LM, Shapira NA, Keck PE Jr, Rosenthal NR, Karim MR, Kamin M, Hudson JL. Topiramate in the treatment of binge eating disorder associated with obesity: a randomized, placebo-controlled trial. Am J Psychiatry. 2003;160:255-61.
6. Singleton, E. G., Tiffany, S. T., & Henningfield, J. E. (2003). The Alcohol Craving Questionnaire (ACQ-Now). In J. P. Allen & V. B. Wilson (Eds.), Assessing Alcohol Problems: A Guide for Clinicians and Researchers (2nd ed., pp. 271-281). NIH Publication No. 03-3745. Bethesda, MD: NIAAA
7. Potenza MN, Voon V, Weintraub D. Drug Insight: impulse control disorders and dopamine therapies in Parkinson's disease. Nat Clin Pract Neurol. 2007;3:664-72.
8. Potenza MN, Steinberg MA, Skudlarski P, et al. Gambling urges in pathological gambling: a functional magnetic resonance imaging study. Arch Gen Psychiatry. 2003;60:828-36.
9. Reuter J, Raedler T, Rose M, Hand I, Gläscher J, Büchel C. Pathological gambling is linked to reduced activation of the mesolimbic reward system. Nat Neurosci. 2005;8:147-8.