




# Impulse Control Disorders in Parkinson's Disease: Has COVID-19 Related Lockdown Been a Trigger?

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**ABSTRACT:** **Background:** Parkinson's disease (PD) patients, especially those on dopamine agonists (DA), are at risk of impulse control disorders (ICD). Little attention has been paid to the influence of environmental factors. **Cases:** Retrospective analysis of consecutive PD patients seen in our outpatient Movement Disorders Clinic during 2 months (September–November 2020) to explore the frequency of ICD during the preceding 2-month lockdown period, and comparison with an equivalent control group (September–November 2019). Among 114 patients assessed, 15 (13%) presented ICD during the lockdown, versus 6 (4.5%,  $P$  0.02) in the control group. When analyzing only patients on DA, ICD occurrence increased to 31% (vs. 9.6% pre-lockdown,  $P$  0.026). ICD during lockdown required drug regime adjustment in 80% (vs. 16.7% pre-lockdown,  $P$  0.014). **Conclusion:** During COVID-19 lockdown, the occurrence of ICD in PD patients taking DA was higher than expected, and with increased severity. Environmental stressors may play a role in ICD presentation in vulnerable patients.

Parkinson's disease (PD) patients, and especially those taking dopamine agonists (DA), are at risk of presenting impulse control disorders (ICD).<sup>1</sup> Patient and disease-related factors such as male sex, younger age at diagnosis, previous substance abuse, and previous affective disorders, such as depression, have all been demonstrated to increase the risk of ICD occurrence in PD.<sup>2</sup> However, little attention has been paid to the role of environmental factors in the development of ICD.

During 2020, the COVID-19 pandemic has made necessary restrictive measures worldwide to control viral expansion, such as transient lockdowns. Evidence from previous epidemics like SARS-CoV-1 has shown psychological consequences in the general population resulting from such stressful contexts.<sup>3</sup> Indeed, patients suffering from PD have experienced clinical worsening during these months, both in psychological and motor aspects.<sup>4</sup> On the other hand, it has been suggested that impulsive and addictive behaviors have increased in the general population during COVID-19 lockdown.<sup>5</sup> However, to the best of our knowledge, a specific assessment of the impact of these restraining measures in the presentation of PD-related ICD has

not been reported yet. In this retrospective analysis, we aimed to explore if the limiting measures applied in the current pandemic could have played a role in the occurrence of ICD in PD patients.

## Case Series

This study has been performed in Madrid, Spain, where the strictest lockdown was established from mid-March to mid-May 2020. Patients diagnosed with PD consecutively visited from September 7th to November 7th, 2020, in the Movement Disorders Unit of the Ramón y Cajal Hospital, Madrid, were included. For comparison, a pre-lockdown control group of consecutive PD patients with follow-up visits from September 2nd to November 19th, 2019, in the same Unit, was selected. Their electronic medical records were retrospectively reviewed. All patients had been seen by the same neurologist (AAC) who, as part of the routine clinical assessment, performed a systematic screening of ICD through clinical interrogation. Demographic

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**TABLE 1** Clinical and demographic characteristics of the lockdown and control group

	Lockdown group	Control group	Statistical significance
Patients (n)	114	135	—
Age, mean $\pm$ SD	72 $\pm$ 11 years	73 $\pm$ 10 years	$P > 0.05$
Male sex, n (%)	65 (57%)	70 (51.9%)	$P > 0.05$
Dopamine agonist	48 (52%)	52 (39%)	$P > 0.05$
Previous ICD	12 (10.5%)	10 (7.4%)	$P > 0.05$

and clinical features of the patients were registered and analyzed, with special attention to drug prescription during the lockdown. Patients with dementia were excluded from the analysis. Statistical significance was set at  $P < 0.05$ . Results are reported as percentages, mean and standard deviation unless otherwise specified.

In the lockdown group, a total of 114 PD patients were analyzed: 65 (57%) were males, with a mean age of 72 ( $\pm$ 11) years and a mean disease duration of 7 ( $\pm$ 5) years. Forty-eight (42%) patients were on DA. Demographic and clinical variables of the lockdown and control groups (135 patients, 51.9% male, 39% on DA) are detailed in Table 1. There were no statistically significant baseline differences between the two groups.

Fifteen patients of the lockdown group, all of them on DA, developed ICD during the lockdown period, with a frequency that was significantly higher than in the control group (13% vs. 4.5%  $P$  0.02). Also, when considering only patients on DA, ICD was significantly more frequent in the lockdown group than in the control sample (31% vs. 9.6%,  $P$  0.026). In this subgroup of patients on DA, adjustment of dosage was needed more frequently to control ICD manifestations during the lockdown, than in the control group (80% vs. 16.7%,  $P$  0.014). There were no significant differences in the baseline characteristics between the patients who developed ICD in the lockdown and the control period (Table 2). Characteristics of patients who developed ICD during lockdown are detailed in Table 3.

All patients presenting with ICD during lockdown had been on stable doses of DA before its occurrence. Remarkably, DA

doses, measured in levodopa equivalent daily dose (LEDD), were similar between those who developed ICD during the lockdown and those who did not (175  $\pm$  68 mg vs. 151  $\pm$  865 mg  $P > 0.05$ ). Compared to those who did not develop ICD during the lockdown, the patients who did were significantly younger (65  $\pm$  11 years vs. 73  $\pm$  11 years,  $P = 0.013$ ), and had a younger age at PD onset (57  $\pm$  11 years vs. 66  $\pm$  11 years,  $P = 0.004$ ). They also presented higher incidence of previous depression (53% vs. 27%,  $P = 0.041$ ) and previous ICD (33% vs. 7%,  $P = 0.006$ ).

## Discussion

During the 2-month lockdown period, we observed an incidence of 13% of ICD in PD patients and 31% among the subgroup of those who were taking DA. These frequencies were significantly higher than those in the pre-lockdown control group (4.5% overall,  $P$  0.02, and 9.6% of those taking DA,  $P$  0.026). A significantly higher number of patients required treatment adjustment, suggesting more severe ICD presentations in the lockdown group.

Clinical and demographic characteristics between the lockdown group and the control group were strictly comparable (Table 1), as were the characteristics of the patients who developed ICD during lockdown and pre-lockdown (Table 3). Patients who developed ICD during lockdown showed several of the well-known ICD risk factors, such as younger age,

**TABLE 2** Characteristics of the patients who developed ICD in the lockdown and control groups

	Lockdown group	Control group	Statistical significance
Patients total, n	114	135	—
Patients with ICD, n	15	6	—
ICD (% of the group)	13%	4.5%	—
ICD (% of those on DA)	31%	9.6%	—
Age, mean $\pm$ SD	64.9 $\pm$ 11 years	60.8 $\pm$ 9 years	$P > 0.05$
Male sex, n (%)	10 (66.7%)	4 (66.7%)	$P > 0.05$
Dopamine agonist, n (% of those presenting ICD)	15 (100%)	5 (83.3%)	$P > 0.05$
Previous ICD, n (% of those presenting ICD)	5 (33%)	0 (0%)	$P > 0.05$
Severity (change in treatment required, n, % of ICD)	12 (80%)	1 (16.7%)	$P$ 0.014

TABLE 3 ICD features in the lockdown group

Patient	Sex (M: Male, F: Female)	Age (yr)	Dopamine Agonist	DA Dose (mg)	ICD	Severity Required Change of Treatment	Previous ICD (on Remission Pre-Lockdown)
1	F	71	Ropirinol	8	Compulsive eating	Yes	Compulsive eating
2	F	52	Rotigotine	8	Compulsive eating	Yes	Compulsive eating
3	F	73	Rotigotine	8	Compulsive eating	Yes	No
4	M	53	Ropirinol	20	Compulsive eating	Yes	No
5	M	62	Ropirinol	8	Compulsive eating	Yes	No
6	M	86	Rotigotine	8	Compulsive eating	Yes	Compulsive eating
7	F	61	Pramipexol	1.57	Compulsive eating	Yes	No
8	M	68	Pramipexol	1.05	Hypersexual behavior	Yes	Hypersexual behavior
9	M	78	Ropirinol	8	Hypersexual behavior	Yes	No
10	M	54	Rotigotine	8	Hypersexual behavior	Yes	No
11	M	51	Ropirinol	8	Compulsive buying	Yes	Compulsive buying
12	M	54	Ropirinol	12	Punding	No	No
13	M	68	Rotigotine	6	Punding	No	No
14	F	77	Rotigotine	8	Punding	No	No
15	M	72	Ropirinol	8	Compulsive eating and buying	Yes	No

younger age at PD onset or more frequent history of depression and previous ICD<sup>6</sup> when compared to those who did not, suggesting a higher vulnerability for ICD occurrence. However, the main exogenous risk factor, which is DA intake, had remained unchanged during the lockdown period before ICD occurrence, and no significant differences in DA dose were observed among patients on DA treatment who did or did not develop ICD.

Yet, both groups were strictly comparable, the DA doses had been stable, and the frequency and severity of ICD during lockdown was strikingly higher, which points in the direction that there must be another factor involved.

The risk of ICD in PD patients, mainly among patients taking DA, has been largely studied. The prevalence of ICD in PD has been reported to be heterogeneous among studies and different countries, ranging from 4%<sup>6</sup> to 28%<sup>2</sup> of PD patients, and around 17% in those patients taking DA.<sup>7,8</sup>

Symptoms such as intrusion, avoidance, or hyperarousal, typical of posttraumatic stress disorder (PTSD),<sup>9</sup> have been reported in the general population in the previous epidemics.<sup>3</sup> Indeed, there is also evidence that the present scenario of the pandemic, and the recent lockdown, has increased the risk of other addictive and compulsive behaviors in the general population.<sup>5</sup>

Similarly, recent studies have shown that PD patients have been suffering a high burden of stress and psychological symptoms<sup>4</sup> during this pandemic. In this regard, it is of interest to

highlight that another entity associated with catastrophes, PTSD, has been suggested to be linked to a hyperdopaminergic state.<sup>10</sup> Our results suggest that a highly stressful environment, such as it could be the lockdown, may have played a role in facilitating the development of ICD in vulnerable PD patients, such as those with a previous history of depression or other well-known ICD risk factors. Thus, we claim that more attention should be given to environmental factors in ICD occurrence.

We acknowledge certain limitations of our study, mainly the retrospective and single-center design, and the relatively small sample size. No objective scales for depression or ICD symptoms were used either, yet most of them consider the items assessed in standard clinical interrogation. Although further research is warranted on this topic, this seemingly increased risk needs to be recognized by clinicians, considering the clinical relevance of ICD, and the importance of identifying, monitoring and managing this complication for both patients and their families.

In conclusion, we aim to raise awareness that environmental stressors such as COVID-19 related lockdown may prompt severe ICD, especially in susceptible PD patients taking DA. These complications add to the already reported complications of the COVID-19 pandemic for PD patients, such as sedentary behaviors, worsening in motor and non-motor symptoms and reduced access to healthcare resources.

## Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

P.R.S.: 1A, 1B, 1C, 2B, 2C, 3A, 3B

R.M.F.: 1B, 1C, 2C, 3A, 3B

E.N.V.: 1B, 3B

I.P.: 1B, 3B

J.C.M.C.: 1B, 3B

A.A.C.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

## Disclosures

**Ethical Compliance Statement:** Institutional review board or ethics committee approval was not necessary for this work. Informed patient consent was not necessary for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. Pablo Rábano-Suárez takes responsibility for the integrity of the data and the accuracy of the data analysis.

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## References

1. Corvol JC, Artaud F, Cormier-Dequaire F, et al. Longitudinal analysis of impulse control disorders in Parkinson disease. *Neurology* 2018;91(3): e189–e201.
2. 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(4):317–324.
3. Mak IW, Chu CM, Pan PC, Yiu MG, Chan VL. Long-term psychiatric morbidities among SARS survivors. *Gen Hosp Psychiatry* 2009;31(4): 318–326.
4. Shalash A, Roushdy T, Essam M, et al. Mental health, physical activity, and quality of life in Parkinson's disease during COVID-19 pandemic. *Mov Disord* 2020;35(7):1097–1099.
5. di Renzo L, Gualtieri P, Pivari F, et al. Eating habits and lifestyle changes during COVID-19 lockdown: an Italian survey. *J Transl Med* 2020;18(1):229.
6. Eisinger RS, Ramirez-Zamora A, Carbutaru S, et al. Medications, deep brain stimulation, and other factors influencing impulse control disorders in Parkinson's disease. *Front Neurol* 2019;10:86.
7. 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(5):589–595.
8. Vriend C. The neurobiology of impulse control disorders in Parkinson's disease: from neurotransmitters to neural networks. *Cell Tissue Res* 2018; 373(1):327–336.
9. van der Heide A, Meinders MJ, Bloem BR, Helmich RC. The impact of the COVID-19 pandemic on psychological distress, physical activity, and symptom severity in Parkinson's disease. *J Parkinsons Dis* 2020;10(4): 1355–1364.
10. Hoexter MQ, Fadel G, Felício AC, et al. Higher striatal dopamine transporter density in PTSD: an in vivo SPECT study with [(99m)Tc] TRODAT-1. *Psychopharmacology (Berl)* 2012;224(2):337–345.