RESEARCH

WHAT BOTHERED PATIENTS WITH PARKINSON DISEASE DURING THE COVID-19 LOCKDOWN?
AN ANALYSIS OF TELEPHONE RECORDS

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Abstract

Introduction: It has been suggested that patients with Parkinson's disease are more susceptible to the negative consequences of restrictions for Coronavirus pandemic regulations. We evaluated whether the lockdown caused a change in the subjective complaints of the Parkinson's disease patients.

Material and Methods: Telephone records of the Parkinson's disease patients in the 2.5 months of the lockdown in 2020 were categorized and compared to the records of the same period of 2018 and 2019.

Results: In total, 666 complaints/questions were categorized from 625 telephone calls of 391 patients. The percentage of motor-related complaints did not differ significantly across the years. In 2020, calls about administrative issues increased significantly compared to 2018 (OR= 3.7 95% CI:1.5-9.3; p= 0.004) and 2019 (OR= 2.1, 95% CI:1.0-4.5; p= 0.044). Moreover in 2020, the odds of calling due to behavioral/psychotic symptoms increased by at least 3 times compared to 2018 (OR=3.7, 95% CI:1.3-10.8 p= 0.014) and 2019 (OR=3.0, 95% CI:1.2-7.4 p= 0.018). Anxiety was also more frequent but only compared to 2019.

Conclusions: The results highlight the necessity of taking urgent action to improve the organizational and psychosocial needs of Parkinson's disease patients in times of humanitarian crises.

Keywords: Parkinson Disease; COVID-19; SARS-CoV-2; Telemedicine; Pandemic.

INTRODUCTION

Starting from December 31th 2019, the world has been introduced to the COVID-19 which has rapidly spread across the world causing a pandemic (1). The exponential increase in infection and mortality rates across the world created a global crisis and forced many countries to take immediate actions, including closing the borders, schools, and shopping malls, restricting gatherings, or even imposing a curfew (2,3). These drastic measures have profoundly changed the daily life of almost everyone; however, the elderly with chronic diseases or disabilities may be the ones who have most suffered from these regulations, if not from the infection itself (4-6).

Most individuals with Parkinson's disease (PD) belong to this affected group. Since the beginning of the pandemic, the impact of the COVID-19 and the associated restrictions on the daily lives of patients with PD have been recognized and discussed (4,7). Concerning the difficulties that PD patients may encounter during this period, several negative physical and psychosocial outcomes such as increased anxiety, loneliness, depression, sleep problems, or reduced physical activity were highlighted (4,6-8). Indeed, studies reporting patient interviews showed an increase in anxiety and stress (9–11). Therefore, in this study, we aimed to contribute to the understanding of the impact of the lockdown on the lives of PD patients by comparing the telephone records of the same time-interval of the last three years.

METHODS

Review of the telephone records

In this retrospective study, the documentation of the telephone records of PD patients diagnosed according to the UK Brain Bank Criteria was evaluated. In Turkey, the pandemic started a couple of weeks following Europe, with the first case of COVID-19 reported on March 10, 2020. To limit the spread of the virus, authorities implemented immediate restrictions for the rest of March, April, and May. Thus, the telephone calls and the patients' subjective complaints/questions noted covering the following 2.5 months of the strict lockdown, between March 15 and June 1, 2020, were subsequently reviewed. To compare the call reasons during the pandemic, telephone records of the same period of 2018 and 2019 were also evaluated (March 15, 2018/19 – June 1, 2018/19). The reason(s) of telephone calls were extracted and categorized as "motor symptom", "non-motor symptom" or "other reasons". The motor symptoms mainly consisted of slowness or tremor, and therefore were taken as a whole. Categories of "non-motor symptom" and "other reasons" were further divided into detailed sub-categories. The classification of the recorded complaints (or questions) was performed by a movement disorders specialist blinded to the year of call to avoid observer bias. The study was approved by the ethical committee of the University of Ankara School of Medicine, and all procedures were in accordance with the Declaration of Helsinki.

Statistical analysis

In this study, telephone records from the last three years were compared regarding the subjective complaints of the patients. It should be mentioned that the analysis of the records revealed an overlap of 14.6% regarding the patients between the groups of years (same patient calling in different years). Such a situation is relatively rarely encountered in statistics that the groups of comparison are neither independent nor paired but partially overlapped. Although the overlap rate was modest in this case, it could potentially endanger the accuracy of the analysis by violating the assumption of independence of the conducted tests for the comparison of the categorized problems. Therefore, before the analysis, a reliability test using Fleiss Kappa was performed for this group of patients to detect any "agreement" or pattern between the years for the reason of calling (κ <0.50 was considered showing

independence). Having seen no agreement (see the results), further analyses were then performed.

Age, sex, disease duration, and the Hoehn and Yahr (H&Y) stage at the latest examination in the year of call were compared across the years after removing the overlaps using one-way ANOVA, Kruskal-Wallis, or Pearson's Chi-square (χ^2) as appropriate. The frequency of the classified complaints reported in the same interval of the last three years was compared with the Pearson's Chi-square or Fisher's exact test. For the comparison of the complaints/questions, the significance threshold was adjusted to $p<0.016$ (0.05/3) according to Bonferroni for multiple comparisons. Then, logistic regression models were created for the complaints/questions that showed significant differences between years to determine whether these effects are independent of potential confounders, given the possible effect of increased age, disease duration, or severity in three consecutive years.

The data that supports the findings of this study are available in the supplementary material of this article.

RESULTS

Descriptive data regarding the patients and the telephone calls are given in Table-1. A Tukey post hoc test of one-way ANOVA ($F(2,327)= 3.21$, $p= 0.042$) revealed a significantly higher mean age in 2019 compared to 2018 ($p= 0.033$). Years did not differ significantly with regard to sex (Pearson's χ^2, $p=0.51$) and disease duration ($F(2,326)= 0.357$, $p= 0.700$). Disease severity (H&Y) compared by Kruskal-Wallis H test ($\chi^2(2)= 6.615$, $p= 0.037$) showed higher values in 2018 ($p=0.015$) and 2020 ($p=0.049$) opposed to 2019.

Overall, 666 complaints or questions were categorized from 625 telephone calls of 391 patients. Nine call-reasons could not be categorized and ex-

Table 1. Patient information and documentation of the telephone records.

	2018 (n=129)	2019 (n=148)	2020 (n=114)
Patient information			
Age, mean (SD)	62.8 (11.3)	66.9 (10.7) ǂ	65.1 (10.8)
Male sex, n (%)	69 (53.5)	76 (51.4)	56 (49.1)
Disease duration, mean (SD)	7.6 (5.4)	7.9 (5.4)	8.1 (5.9)
Hoehn & Yahr, median (IQR)	2.0 (1) *	2.0 (0)	2.0 (1) *
Telephone records, n			
Number of patients	129	148	114
Frequency of calls for patients	1-4	1-7	1-14ᵗ
Total number of calls	208	211	206
Average number of calls per patient (SD)	1.61 (0.78)	1.42 (0.87)	1.81 (1.5)
Total number of complaints	232	230	204
Average number of complaints per patient (SD)	1.80 (0.52)	1.55 (1.20)	1.79 (0.61)

SD, standard deviation
t In 2020 only one patient called more than 5 times
ǂ Significant compared to 2018 (Tukey post hoc test of one-way ANOVA, p=0.033)
* Significant compared to 2019 (Kruskal-Wallis H test, 2018 vs. 2019 p=0.015; 2020 vs. 2019 p=0.049)

cluded. The analysis of patient information yielded a modest overlap (n=57, 14.6% of all patients) between the years. Twenty-five (19.4%) and 11 (8.5%) of the patients called in 2018, also called in 2019 and 2020, respectively. Fifteen (10.1%) patients that called in 2019 also called in 2020. Six patients made a call in three years consecutively. The Fleiss Kappa for these patients showed poor reliability between the years (κ=0.18 for 2018-2019, κ=0.04 for 2018-2020, and κ=0.06 for 2019-2020), indicating that the groups are independent of each other concerning the reason of calling.

Table-2 shows the comparison of the categorized complaints (motor symptoms, non-motor symptoms, and other reasons) and the further categorizations. No significant difference was detected between years regarding the percentage of motor symptoms. An increase was found in 2020 for non-motor symptoms (29.9%), but that was significant only compared to 2019 (18.7%, p=0.005) (Figure 1). The detailed classification of the non-motor symptoms showed no significant difference between 2020 and previous years for pain, depression, orthostatic hypotension, urinary dysfunction, sleep-related problems, memory loss, or other non-motor symptoms (comprised of constipation, erectile dysfunction, and sweating). Telephone calls due to anxiety were significantly increased in 2020 (19.7%) and 2018 (14.6%), in contrast to 2019 (0%, p<0.010 for both). With regard to the psychotic or behavioral symptoms, year of 2020 peaked (31.1%) compared to 2018 (10.9%, p=0.008) and 2019 (16.3%, p=0.085) (Table-2, Figure 2).

Table 2. Categorization of the reported complaints/questions.

	2018 (n=232)	2019 (n=230)	2020 (n=204)
Motor symptoms, n (%)	113 (48.7)	92 (40.0)	102 (50)
Non-motor symptoms, n (%)	55 (23.7)	43 (18.7)	61 (29.9) *
Anxiety	8 (14.6) *	0	12 (19.7) *
Depression	2 (3.6)	0	2 (3.3)
Behavioral symptoms/psychosis[1]	6 (10.9)	7 (16.3)	19 (31.1) ǂ
Sleep problems	4 (7.3)	7 (16.3)	9 (14.8)
Memory problems	6 (10.9)	2 (4.7)	4 (6.6)
Orthostatic hypotension	1 (1.8)	3 (7.0)	2 (3.3)
Urinary problems	2 (3.6)	4 (9.3)	1 (1.6)
Pain	14 (25.5)	12 (27.9)	7 (11.5)
Other non-motor symptoms	12 (21.8)	8 (18.6)	5 (8.2)
Other reasons, n (%)	61 (26.3) *	93 (40.4)	37 (18.1) *
Administrative/logistics issues	7 (11.5)	14 (15.1)	17 (45.9) *ǂ
Medication adverse effect	28 (45.9) *	20 (21.5)	11 (29.7)
Questions about PD	7 (11.5)	15 (16.1)	1 (2.7)
Non-PD problems[2]	19 (31.1)	44 (47.3)	8 (21.6) *
Unclassified, n (%)	3 (1.3)	2 (0.9)	4 (2.0)

* Significant compared to 2019 in Pearson's Chi-square or Fisher's exact test (p< 0.016).

ǂ Significant compared to 2018 in Pearson's Chi-square or Fisher's exact test (p< 0.016).

1 This item includes behavioral and psychotic symptoms including, but not limited to irritability, agitation, hallucinations, delusions, disorganized speech and behaviors.

2 This item includes questions about issues including, but not limited to non-PD medication, non-neurological symptoms or diseases.

In 2020, calls unrelated with motor or non-motor symptoms (other reasons, 18.1%) were significantly fewer than 2019 (40.4%, p< 0.001) but not 2018 (26.3%, p=0.045) (Table-2, Figure 1). The details of these calls revealed a significant boost in questions (45.9%) related to administrative or logistics issues such as clinic appointments or obtaining medication as opposed to 2018 and 2019 (11.5%, 15.1%; p< 0.001). Questions regarding medical problems other than PD (such as the interaction of a newly prescribed drug on PD medication or DBS management before an operation.) were significantly fewer in 2020 (21.6%) compared to 2019 (47.3%, p=0.007) but not in 2018 (31.1%, p=0.306) (Table-2, Figure 3).

For the variables that showed significant differences in 2020, we performed logistic regressions to

Figure 1. Categorization of the reported complaints/ questions

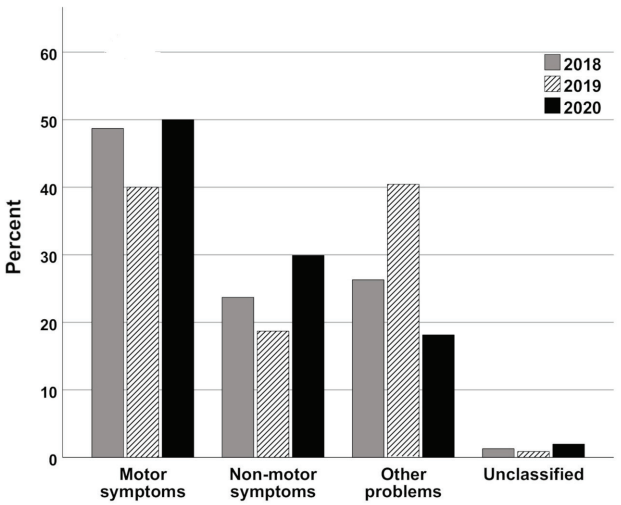


Figure 2. Categorization of the reported complaints/ questions (other reasons)

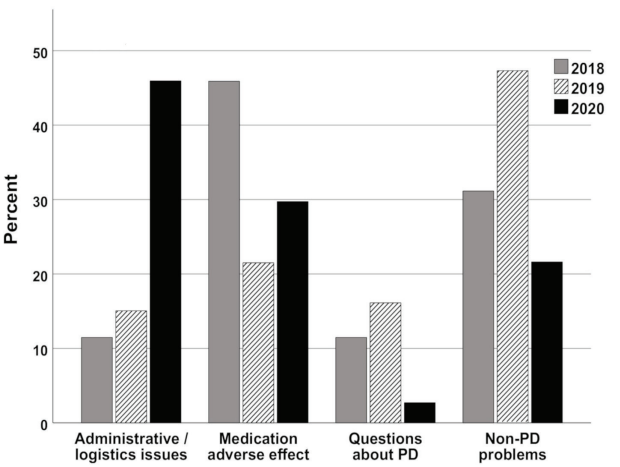
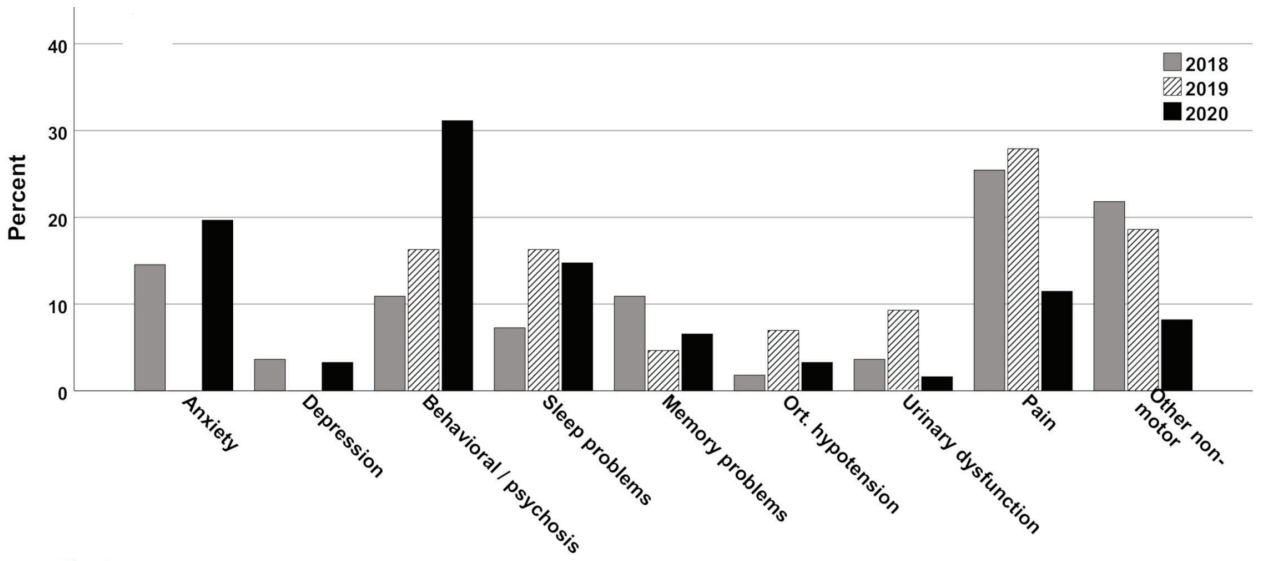


Figure 3. Medical problems other than Parkinson's disease



ascertain whether these are independent of potential confounding effects of age, sex, disease duration, or severity. For anxiety, the regression model (Nagelkerke R2= 19% $\chi^2(6)= 20.703$, p= 0.002) showed no significant difference in 2020 against 2018 (OR= 1.3, 95% CI: 0.4-3.8, p=0.638). The regression model for the presence of behavioral/psychotic symptoms also showed a good fit (Nagelkerke R2= 11%, $\chi^2(6)= 17.702$, p= 0.007) and correctly classified 92% of the cases. In 2020, the odds of calling because of such symptoms was 3.7 and 3.0 times greater in comparison to 2018 (95% CI: 1.3-10.8 p= 0.014) and 2019 (95% CI: 1.2-7.4 p= 0.018), respectively. For administrative/logistics issues as the dependent variable, the regression model explained 6% (Nagelkerke R2) of the variance in group membership and correctly classified 89% of cases ($\chi^2(5)= 11.473$, p< 0.075). The year of 2020 was significantly associated with an increase in administrative/logistics questions compared to 2018 (OR= 3.7, 95% CI: 1.5-9.3; p= 0.004) and 2019 (OR= 2.1, 95% CI: 1.0-4.5; p= 0.044), independent of the effects of the confounders. And finally, for the non-PD-related questions, the regression model showed a good fit with a significant relationship (Nagelkerke R2 = 9%; $\chi^2(5)= 21.070$, p= 0.002) between the predictors and the grouping. The model showed that in 2020, the odds of calling to ask about non-PD issues decreased by 77% compared to 2019 (95% CI: 0.10-0.52; p <0.001). Against 2018, the odds decreased by %55, but showed no significant effect (95% CI: 0.19-1.1; p= 0.077)(Table-3).

DISCUSSION

In this study, we analyzed the telephone records of the PD patients within the 2.5-month-period of lockdown and compared them with the same interval of the two previous years. Our results showed an increase in calls related to administrative/logistics inquiries in 2020. Also, behavioral/psychotic symptoms were more frequently reported in 2020 compared to 2018 and 2019. Apart from these in 2020, a decline in questions regarding non-PD-related issues and increased anxiety were also detected, but these were not decisive because a significant contrast was found only compared to 2019.

Starting from the first weeks of 2020, all the intense regulations against the pandemic limited everyone's routine lives significantly. Regulations during the pandemic compelled patients with PD to reduced physical activity, increased loneliness, depression, and stress. It has also been argued that PD patients constitute a more vulnerable group given the already existing impairment in physical, psychiatric, and cognitive domains in most patients (4). Besides, news in the media about the rapid spread of the virus and susceptibility of the elderly for COVID-19 (especially ones with chronic diseases) probably escalated the anxiety of the patients further, not to mention the concerns and uncertainties for reaching to medication or medical assistance when needed throughout the lockdown(12).

For complaints/questions other than motor or non-motor symptoms, administrative/logistic issues were significantly higher in 2020 than in previous years. This category included questions about appointments for the outpatient clinic or difficulties in obtaining PD medication. In March, the expiration date of all repeat prescriptions (for chronic diseases) was extended for three months in Turkey; however, some of the patients were not aware of this. It should also be mentioned that in the first months of 2020, there was a shortage of entacapone-containing drugs in the market due to an administrative issue, possibly unrelated to the pandemic, which may contribute to our finding regarding the increase in calls of administrative/logistic issues in 2020. Nevertheless, our findings agree with a recent large-scale survey performed by the Michael J. Fox Foundation, which showed that 62% of the 7200+ survey responses pointed out administrative problems such as canceled appointments and reduced home-care facilities or issues for obtaining medications (13).

Another expected problem under lockdown cir-

Table 3. Details of the logistic regression analyses.

	B (SE)	OR	95% CI	P value
Anxiety*				
Constant	-3.96 (1.6)	0.02	-	0.02
Age	-0.01 (0.02)	0.99	0.94 - 1.03	0.62
Sex	1.05 (0.61)	2.85	0.86 - 9.40	0.09
Disease duration	-0.03 (0.05)	0.97	0.87 - 1.08	0.62
Disease severity	-0.03	1.79	0.90 - 3.50	0.09
Year (2019 vs. 2018)	-	-	-	-
Year (2020 vs. 2018)	0.26 (0.55)	1.29	0.44 - 3.85	0.64
Year (2020 vs. 2019)	-	-	-	-
Behavioral/psychotic issues*				
Constant	-6.13(1.4)	0.00	-	0.00
Age	0.03(0.02)	1.03	0.99 - 1.07	0.20
Sex	0.68(0.42)	1.97	0.87 - 4.47	0.10
Disease duration	-0.001(0.04)	1.00	0.93 - 1.07	0.98
Disease severity	0.37(0.24)	1.45	0.90 - 2.32	0.12
Year (2019 vs. 2018)	0.23(0.59)	1.25	0.39 - 4.03	0.70
Year (2020 vs. 2018)	1.32(0.54)	3.75	1.31 - 10.77	0.01
Year (2020 vs 2019)	1.19(0.46)	3.01	1.22 - 7.42	0.02
Administrative/logistics issues*				
Constant	-2.15	0.12	-	0.06
Age	0.003(0.02)	1.00	0.97 - 1.03	0.85
Sex	0.01(0.34)	1.01	0.52 - 1.95	0.98
Disease duration	0.03(0.03)	1.03	0.97 - 1.20	0.37
Disease severity	-0.31(0.26)	0.73	0.44 - 1.23	0.24
Year (2019 vs. 2018)	0.56(0.49)	1.77	0.68 - 4.56	0.25
Year (2020 vs. 2018)	1.32(0.46)	3.76	1.51 - 9.32	0.004
Year (2020 vs. 2019)	0.76(1.17)	2.14	1.02 – 4.49	0.04
non-PD related questions*				
Constant	-1.32(0.97)	0.27	-	0.17
Age	0.006(0.01)	1.01	0.98 - 1.03	0.63
Sex	-0.19(0.28)	0.83	0.48 - 1.44	0.51
Disease duration	0.02(0.03)	1.02	0.96 - 1.07	0.52
Disease severity	-.40(0.24)	0.67	0.42 - 1.06	0.09
Year (2019 vs. 2018)	0.67 (0.32)	1.95	1.03 – 3.69	0.04
Year (2020 vs. 2018)	-0.79(0.45)	0.45	0.45 - 1.09	0.08
Year (2020 vs. 2019)	-1.46(0.42)	0.23	0.10 - 0.52	<0.001

*predicted probability for each dependent variable is the presence of the given title compared to its absence used as reference. OR, odds ratio; CI, confidence interval

cumstances was increased anxiety in PD patients. This could not be confirmed in our study convincingly. Anxiety constituted around 20% of the non-motor complaints that were reported during the pandemic. This percentage is higher than 2019, in which no anxiety was mentioned in calls but was close to 2018 (14.5%). Previously, three studies implicated high prevalence (59-82%) for anxiety during the lockdown (8-10). These rates may be explained by the study design, i.e., these studies conducted telephone interviews or web-based questionnaires and addressed anxiety directly, which probably led to an elevated positive response. Indeed, in studies that the patients vocalized their complaints without being explicitly asked, reported anxiety rates were lower, analogous to our data (14-15) regular clinical services for Parkinson's disease (PD. Thus, it can be argued that while anxiety is probably boosted in the lockdown and may be confirmed when asked, it is severe enough only in a particular group of patients to prompt contact with the physician. Besides, mood problems are ambiguous and may present as diverse symptomatology such as fatigue, sleep problems, motor or behavioral symptoms, or be overshadowed by cognitive impairment (16). This overlap between the somatic and neuropsychiatric features may also partly explain the lack of expected peak in 2020. Therefore, our findings suggest that emotional problems such as depression, stress, or anxiety may not be revealed spontaneously and should be questioned actively for recognition.

Concerning other non-motor reasons of calling, disturbances such as constipation, sweating, and erectile dysfunction (grouped as other non-motor symptoms) as well as pain were disclosed half as much as the previous years in 2020, but the difference did not reach statistical significance. Additionally, an increase in sleep-related problems due to physical inactivity and stress may also be expected in 2020 (4), but no such difference was detected in our data. Again, this finding does not exclude the likely increase of sleep-related disturbances but instead suggests that sleep problems were not the primary complaint of the patients or caregivers during the lockdown period. In one study, 79.6% of the 113 patients described a new symptom or worsening of slowness or stiffness (60.2% each) during the lockdown period than post-lockdown, during which Covid-19 infection continued contrary to our study that found no significant differences between the years. A worsening of non-motor symptoms like anxiety, depression, sleep disorders, aches, and pain was also found in this study similar to ours (17). In another study, a questionnaire was conducted on 100 patients revealing an equal number of patients suffering from motor and non-motor symptoms. However, the UPDRS-III scores did not differ significantly before and after the restriction, which may indicate underlying anxiety in worsening of motor symptoms without objective confirmation (18).

In our study, a notable distinction was in the high rate of behavioral symptoms/psychosis in 2020. These complaints doubled compared to 2019 and tripled compared to 2018 suggesting apparent distress over PD patients over the lockdown period. Of course, as mentioned, these symptoms are probably not isolated from other PD-related manifestations and may present as a consequence of a combination of motor, neuropsychiatric, and cognitive disturbances (6,16). For instance, it may well be that some of the behavioral symptoms have manifested themselves out of increased irritability due to an underlying unreported anxiety/stress. Therefore, it may be plausible to argue that among all non-motor symptoms, the increase in behavioral or psychotic symptoms in 2020 does not signify one distinct non-motor symptom but rather point to a negative overall neuropsychological effect of the lockdown on the lives of PD patients.

One limitation of the present study may be its design, i.e., evaluating the patients' self-reported complaints may cause some symptoms to get unnoticed. It is possible that despite experiencing a PD-related disturbance, the patient or the caregiver

might not have sought medical assistance thinking that they cannot be helped, or they might not have depicted the complete picture of the problem on the phone. This would imply that the rates we found could be underestimated, especially for less distressing symptoms. On the other hand, relying on patient-reported complaints may be superior to, e.g., telephone interviews in illustrating the patients' subjective perception under the lockdown. For instance, when asked, one can affirm increased anxiety, but this may not be her/his most important concern. Another strength of the current study is including the records of the previous two years, which enabled us to control the rates of 2020 against periods from "normal daily life" as previously suggested (4). Having the records of two "normal" previous years also allowed us to visualize the random fluctuations in patients' complaints as seen in anxiety or sleep problems (Figure 2). Blinded evaluation of the telephone records is also a strong point ruling out the observer bias towards the year of the telephone call. To our knowledge, this is the first study that compared telephone records of PD patients between ordinary life and a period from a global crisis.

In conclusion, within the lockdown period of 2.5 months in 2020, we have found an increase in complaints/questions about administrative issues and behavioral/psychotic symptoms in patients with PD. These disturbances, notable as they may be, are influenced by several factors such as the length of the lockdown, access to medical care, or contact abilities of the PD patients with the caregiver or family members, all of which are more or less modifiable. On that account, our results provide evidence for the probable predicaments of the PD patients during the ongoing and future large-scale crises and suggest that taking preventive measures against organizational problems, providing rapid and sustainable health care and medication supply are crucial in such circumstances. Moreover, efforts should be directed towards finding ways to monitor and alleviate behavioral symptoms of PD patients that would help to maintain the quality of life in crisis periods.

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