

Short Communication

Worsened Parkinson's Disease Progression: Impact of the COVID-19 Pandemic

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Abstract. Whilst some studies investigated the impact of viral infection or reduced access to medication during the COVID-19 pandemic in patients with Parkinson's disease (PD), data on the effects of pandemic restrictions are still scarce. We retrospectively analyzed motor symptoms of longitudinally followed PD patients ($n=264$) and compared motor disease progression before and during the COVID-19 pandemic. Additionally, we performed a trend analysis of the yearly evolution of motor symptoms in 755 patients from 2016 until 2021. We observed a worsening of motor symptoms and a significantly increased motor disease progression during pandemic-related restrictions as compared to before the COVID-19 outbreak.

Keywords: Parkinson's disease, COVID-19, confinement, motor disease progression, MDS-UPDRS part III

INTRODUCTION

Parkinson's disease (PD) represents a multisystem disorder with clinical key features pertaining to motor dysfunction. There is strong evidence that physiotherapy and physical activity with dedicated training improve not only levodopa-responsive but also axial motor symptoms [1]. For instance, a 2013 Cochrane review analyzed randomized controlled trials of physiotherapy versus no such intervention in patients with PD [2]. In this study comprising 39 trials with 1,827 patients, benefit for physiotherapy over up to 3 months was significant for clinician-rated Parkinson core motor symptoms, but also for gait velocity, freezing of gait, and postural stability. These are relevant symptoms related to ambulation of patients and quality of life. Additionally, data shows that

COVID-19-dependent restrictions have negative effects on mental health [3] besides correlative evidence showing a worsening of non-motor features and potentially exacerbated motor symptoms in PD [4]. Further, a recent pilot study including mobile assessments to collect self-report data showed that it was physical activity that led to highest self-satisfaction in PD-patients during COVID-19 restrictions [5].

Therefore, it seems likely that the COVID-19 pandemic with all consecutive confinement strategies such as quarantine—leading to reduction of physical activity and physiotherapy, but also psychosocial challenges that may lead to psychiatric deterioration—negatively impacts progression of PD. In fact, during the first two waves of the COVID-19 pandemic in Switzerland, pharmacotherapy was always fully available, but many PD patients were partially or totally deprived of physiotherapy, and confinement further reduced their daily physical and social activities. In addition, fitness centers, dancing classes, and many other team sports that are popular

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among PD patients but also socio-cultural institutions (e.g., restaurants, art galleries) were closed over many months. This challenge has been discussed already early during the pandemic [6, 7] and has ever since been corroborated by the literature [3, 8–11]. For instance, a Dutch group found that the pandemic evokes psychological distress and lifestyle changes including reduced physical activity [12]. This is because most countries markedly reduced not only public life, but also canceled healthcare services including physiotherapy, with detrimental effects on chronically ill patients [8].

However, most of the present literature on COVID-19 and PD focuses on the impact of the infection itself and reduced access to PD medication on mortality, motor as well as non-motor symptoms [13–19]. For instance, one study found that patients with COVID-19 experienced new or worsening motor and non-motor symptoms [18]. It also found that PD patients without COVID-19 infection reported disrupted medical care, exercise, and social activities, and worsened motor and non-motor symptoms. Only few other studies focused on the impact of the pandemic restrictions on the course of PD. A questionnaire-based study from India found that home confinement worsened motor symptoms and quality of life in 38.5% of 832 PD patients [20]. In 100 PD patients from South Korea, another study found reduced exercise related to subjective worsening of PD symptoms [21]. Similarly, an Italian group observed that 60% of 74 PD patients reported a significant worsening of their general conditions during lockdown, the reduction of physical activity being the main risk factor for such change [22].

As the previous studies on the impact of pandemic restrictions on motor symptom progression were questionnaire-based and subjective, we aimed to retrospectively examine motor symptom severity and progression in PD patients during the pandemic and in the years before. We hypothesized that lack of physiotherapy and other physical training opportunities but also a social isolation-dependent increase of psychological stress during the pandemic crisis was mirrored by exacerbated motor disease severity and progression in PD patients.

MATERIALS AND METHODS

This is a retrospective analysis of data ascertained from the movement disorders outpatient unit in the Department of Neurology, University

Hospital Zurich, Switzerland. All longitudinally followed patients with available scores of the third (motor) part of the Unified Parkinson Disease Rating Scale (UPDRS) of the International Parkinson and Movement Disorders Society (MDS) and with available entries regarding their levodopa equivalent dose (LED) during medication ON condition were included. The study was approved by the local ethics committee (“Kantonale Ethikkommission Zurich”). First, we aimed to conduct a descriptive analysis of the temporal trend of motor symptom severity: the data was resampled and represented as mean motor symptom scores per year from 2016 until 2021 (i.e., data was split into yearly time bins and the mean per time bin was calculated). The same procedure was applied to total LED. Next, motor disease progression was assessed by calculating the slope of a linearly fitted regression line through all data points per patient and timespan (i.e., slope of motor disease progression during 2018/2019 vs 2020/2021). To check whether a simple regression model was appropriate for the dataset, the residual values for each observation were plotted and inspected. For the analysis of disease progression, we included all PD patients who have had regular follow-up examinations in the years 2018/2019 and 2020/2021, and in whom a minimal observation time of at least two months in each timespan from September 2018 until December 2019 (16 months) and from January 2020 until April 2021 (16 months) was available.

Statistical testing was conducted using the built-in statistical libraries of Python (5.6.0, Python.org). To test whether there was a significant difference in motor symptom progression before as compared to during the pandemic crisis, the Wilcoxon signed-rank test was used. Significance was accepted at a $p \leq 0.05$ -level.

RESULTS

Inspection of the yearly trend between 2016 and 2021 in 755 patients revealed exacerbated motor symptom severity during the pandemic crisis compared to before: whilst the mean MDS-UPDRS part III scores progressed only slowly from 2016 until the onset of the pandemic crisis (beginning of 2020), there is a steep, pharmacotherapy-independent increase from 2020 onwards (i.e., during the crisis) as the mean LED remained unchanged between 2016 and 2021 (Fig. 1A).

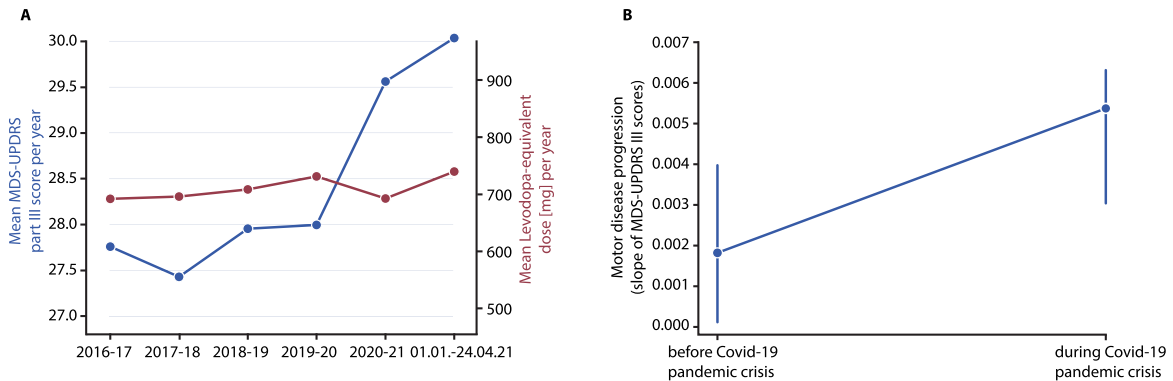


Fig. 1. A) Temporal trend analysis: Mean MDS-UPDRS part III scores of all PD patients ($n = 755$) resampled using a yearly time binning and comparing a time frame ranging from 2016–2021. B) Median (\pm SEM) motor disease progression as assessed by the slope (linearly fitted regression line through all data points per patient and timespan) of the MDS-UPDRS part-III score in each of 16 months before the crisis (until end of 2019) and 16 months during the crisis (until end of April 2021) of all PD patients who have had regular follow-up examinations during each timespan ($n = 264$).

Table 1
Characteristics of the study population

	PD patients ($n = 264$)
Age (y; mean \pm SD)	69.1 \pm 10.6
Females (%)	38.3
Disease duration (y; mean \pm SD)	14.5 \pm 7.5
Axial UPDRS (mean \pm SD)	6.1 \pm 4.3
Number of patients with documented COVID-19 diagnosis	4

To investigate motor disease progression, we analyzed data from 264 PD-patients (Table 1). The sample consisted of 101 females and the mean disease duration was 14.5 years. Only 4 patients were diagnosed with a COVID-19 infection and in all of them, symptoms were benign, flu-like, and transient. Comparing motor disease progression before (September 2018 - December 2019, median (\pm SEM) observation time: 350 ± 5.6 days, number of visits per period: 2–11) and during (January 2020 - April 2021, median (\pm SEM) observation time: 353 ± 5.8 days, number of visits per period: 2–15) the pandemic crisis revealed a worsened progression during the crisis. This is reflected by the significantly increased slope of UPDRS part-III motor score progression during as compared to before the crisis ($Z = -1.986$, $p = 0.047$; Fig. 1B). This pertains to a median disease progression of 0.73 MDS-UPDRS part III points/year before the crisis as compared to a median increase of 1.82 points per year during the crisis. The axial-UPDRS-III score [23], indicating progression of axial motor symptoms, did not differ ($p > 0.38$).

DISCUSSION

This retrospective study reveals that motor symptom progression in PD patients in Switzerland as measured using the MDS-UPDRS III is worse during the months with pandemic restrictions comprising reduced physical activity and social isolation, compared to the same time period before the COVID-19 pandemic. This view of an increase in motor symptom progression is further reinforced when inspecting the temporal trend of yearly mean MDS-UPDRS III scores providing further evidence for a worsening of motor function during the time of confinement. Importantly, the increase in symptom progression is not due to a potential reduction in medication. These findings corroborate the assumption that discontinuity in exercise-based therapy and social contacts exerts detrimental effects on motor symptoms. Conversely, confinement-specific protective effects through mask-wearing and reduced social interactions led to substantially diminished influenza infections [24–26] with possibly overall improved health in the elderly. This is not reflected in the present data, which further suggests strong effects that seem to occur under conditions of containment leading to a worsened functional outcome. The fact that confinement and reduced medical services affect psychiatric health [3] but may also worsen progression of chronic diseases such as PD has consequences for the decision-making process of lawmakers and governmental bodies. Further, whilst treatments for improving functional outcomes through telemedicine offer opportunities to treat patients at home

[8, 27–31], insurance bodies in many countries including Switzerland incomprehensibly require personal consultations for coverage of costs. More studies are needed to investigate whether telemedicine approaches can supplement traditional patient care [27, 32] and personal training.

This study has significant limitations, namely the retrospective setting and the assessment of MDS-UPDRS III in medication ON rather than OFF conditions. As physical daily activities and other contributing factors have not been measured in these patients, the study does not prove a causal link between confinement-dependent factors such as psychiatric status, activity level and worsened progression in PD. There is, however, evidence from qualitative studies suggesting an interrelation between physical activity and disease progression [14, 17, 19] and quantitative evidence that physical activity was significantly decreased during the stay-at-home mandate in PD-patients [5].

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CONFLICT OF INTEREST

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