

Higher perceived stress and exacerbated motor symptoms in Parkinson's disease during the COVID-19 lockdown in New Zealand

Rebekah L Blakemore, Maddie J Pascoe, Kyla-Louise Horne, Leslie Livingston, Bob N Young, Beth Elias, Marie Goulden, Sophie Grenfell, Daniel J Myall, Toni L Pitcher, John C Dalrymple-Alford, Campbell J Le Heron, Tim J Anderson, Michael R MacAskill

ABSTRACT

AIMS: Stress plays a key role in Parkinson's disease (PD) by acting on the dopaminergic system and worsening patients' motor function. The impact of New Zealand's strict lockdown measures to contain COVID-19 on perceived stress and PD motor symptoms remains unknown. Here we examined the relationship between perceived levels of stress, changes in physical activity levels and PD motor symptoms during lockdown.

METHODS: During lockdown, 134 participants with PD and 49 controls completed a survey assessing perceived stress, self-reported changes in PD motor symptoms and physical activity duration and intensity prior to and during lockdown.

RESULTS: Perceived stress was higher in PD than controls, and in those reporting a worsening of tremor, balance/gait, dyskinesia and bradykinesia compared to those indicating no change during the COVID-19 lockdown. These effects were not modulated by physical activity.

CONCLUSIONS: Reducing stressors may be an important adjunct treatment strategy to improve motor function in PD.

As the COVID-19 pandemic continues to grip the globe, there is concern for the increased vulnerability of those with chronic disease, including Parkinson's disease (PD).¹ New Zealand was placed under strict lockdown for 33 days. Residents were required to stay home except to exercise or access essential services. Although crucial to control the spread of the virus, these drastic measures had the potential to significantly impact on mental and physical wellbeing.

People with PD may have an impaired ability to cope with sudden changes to everyday life due to their cognitive and motor inflexibility,^{2,3} which stems from nigrostriatal dopamine depletion, a pathological hallmark of the disease. Stress also plays an important role in PD by acting on

the dopaminergic system and worsening motor symptoms.⁴⁻⁷ Heightened stress can reduce the efficacy of levodopa treatment, resulting in further worsening of motor symptoms.⁸ However, physical activity can counteract the detrimental effects of stress and might even exert neuroprotective effects.^{9,10} The COVID-19 lockdown period may have therefore placed this cohort, relative to those without PD, at greater risk of experiencing higher stress, which, together with potential changes in physical activity, could exacerbate interactions between stress and their already compromised motor system. Our objectives were to examine whether during New Zealand's stringent lockdown period (1) perceived stress was higher in PD than controls, (2) there was a direct relationship between

higher perceived stress and worsening of PD motor symptoms and (3) these effects were modulated by physical activity.

Material and methods

Participants

Participants were recruited from the established PD longitudinal study at the New Zealand Brain Research Institute (NZBRI). One hundred and forty-nine participants with PD and 51 healthy controls were invited to take part in a survey during the nationwide lockdown, either online or by phone. Of the 200 people invited, 134 PD (M=72 years, SD=7) and 49 controls (M=78 years, SD=7) completed the survey (a response rate of 92%). All PD participants had previously completed comprehensive neuropsychological¹¹ and MDS-UPDRS¹² assessments as part of their participation in the NZBRI longitudinal PD study (Table 1).

Data collection occurred between 17 April and 14 May 2020, during New Zealand's Alert Level 4 and Level 3 periods.¹⁴ At Alert Level 4 (commencing 25 March), New Zealanders were in strict lockdown unless providing an essential service. At Alert Level 3 (beginning 27 April and lasting 17 days), restrictions were slightly loosened, but vulnerable individuals (those over 70 years or immunocompromised) were advised to continue self-isolating where possible. At the commencement of data collection, Alert Level 4 had been in place for 22 days. As far as we are aware, none of our participants tested positive for COVID-19.

All participants gave informed consent. The study was conducted within an existing longitudinal PD study that was approved by the Health and Disability Ethics Committee of the New Zealand Ministry of Health.

Measures

Participants completed a suite of scales and questionnaires as part of the survey. Study data were collected and managed using REDCap electronic data capture tools¹⁵ hosted at NZBRI. We report findings from three scales: First, we created the PD motor symptom scale (PDMSS) to examine self-reported perceived changes in four motor symptoms since lockdown began: tremor, dyskinesia, balance/gait and bradykinesia. For each motor symptom, PD participants indicated whether they had noticed any changes in their symptom presentation during lockdown compared to before lockdown. If so, two further questions probed whether that symptom was 'better' or 'worse', and the magnitude of that change was measured on a four-point Likert scale (slight, mild, moderate, substantial).

Second, the perceived stress scale (PSS-10)^{16,17} assessed participants' (PD and controls) perceived stress levels during lockdown. Participants self-reported how frequently they had felt a certain way on a five-point Likert scale (from 0 ('Never') to 4 ('Very often')). For the present study, the wording of each question was intentionally altered from 'In the last month' to 'Since lockdown began'. One further question required participants to report

Table 1: Percentage distribution of self-reported changes (worsening) in PD motor symptoms during the COVID-19 lockdown. Clinical characteristics^a of our patient cohort (n=134): mean disease duration 11 years (SD=6); Hoehn-Yahr score¹³ 2.4 (SD=0.6); last pre-lockdown Part III MDS-UPDRS¹² 'ON' PD medication 34.0 (SD=13.2).

Motor Symptom (% reporting symptom)	No change	Slight	Mild	Moderate	Severe
Tremor (89%)	70%	12%	7%	7%	4%
Dyskinesia (88%)	74%	11%	8%	7%	0%
Bradykinesia (98%)	64%	14%	10%	8%	4%
Balance/gait (98%)	53%	15%	15%	13%	4%

^aThese scores were obtained during each participant's most recent assessment visit as part of the NZBRI longitudinal PD study, on average 12 months (SD=10) prior to the present data collection.

whether their stress levels were higher, lower or about the same compared to before lockdown began.

Third, we created the physical activity levels questionnaire (PALQ) to assess the frequency, duration and intensity of each participant's physical activity during the preceding seven days (during lockdown) and in the seven days prior to lockdown. This questionnaire was based on items included in the International Physical Activity Questionnaire.¹⁸ PD participants also indicated whether they had participated in an exercise group, class or programme specifically for people with PD before the lockdown, and if so, whether they had been able to continue this in some form during lockdown.

Statistical analyses

Perceived stress, physical activity levels and self-reported changes in motor symptoms during lockdown were examined using Bayesian multilevel modelling. The probabilistic language Stan was used along with the R packages rstan (v2.19.3) and brms (v2.13.0) to fit Bayesian models and generate estimates within the R statistical environment (v4.0.1¹⁹). First, group differences in perceived stress and physical activity levels (total hours active over the week and intensity) were analysed. In these models, group was included as a predictor and the intercept varied by participant. The total hours active and physical activity intensity models additionally included a group-by-timepoint interaction term (before versus during lockdown). Next, we examined whether there was a relationship between perceived stress, PD motor symptom changes and physical activity. For each symptom (tremor, dyskinesia, balance/gait, bradykinesia), scores of symptom worsening from the PDMSS were collapsed across 'slight' to 'substantial' levels to generate a summary score of 'Worsened' versus 'No change' in symptoms during lockdown. The resulting motor symptom change scores for each symptom were modelled with a primary predictor of PSS score. Results are reported as the means of the posterior distribution, together with 95% credible intervals (CI) and the probability of the parameter being greater than zero. Anonymised data that support the findings of this study will be shared by the corresponding author

upon reasonable request from any qualified investigator.

Results

Mean perceived stress levels in both groups were relatively low (PD, M=12.1, SD=6.4; controls, M=8.6, SD=6.0); however, perceived stress was higher in those with Parkinson's than controls (by 3.6 points, 95% CI [1.5, 5.7], probability of perceived stress being higher in Parkinson's P>99%; Figure 1A). The majority of PD participants (69%) reported their stress levels were about the same during lockdown compared to the period immediately prior to lockdown. Twenty-two percent felt their stress levels were higher and 9% felt they were lower. Similar results were found for controls (stress levels about the same 67%; higher, 20%; lower, 12%).

Despite being in lockdown, both PD and controls continued being physically active, with no evidence of a difference in the overall amount of time spent being active in the current week compared to the week prior to lockdown, and no evidence of a difference between groups (Figure 1B). Almost half the PD participants (49%) considered their physical activity levels during lockdown to be light in intensity, 42% moderate in intensity and 9% indicated their physical activity was vigorous, involving hard physical effort. Similar physical activity intensities were reported for controls (light, 51%; moderate, 42%; vigorous, 7%), as well as prior to lockdown. Twenty-three percent of PD participants indicated they were attending a PD-specific exercise group prior to lockdown, of which 37% said they were able to continue during lockdown via, for example, online classes. There was no evidence of a relationship between perceived stress and physical activity duration or intensity during lockdown for either group.

In those with PD, we examined any self-reported changes since lockdown in the motor symptoms of tremor, dyskinesia, bradykinesia and balance/gait. Of the 89% of PD participants who self-reported tremor, 70% indicated no changes in their tremor since lockdown began. The remaining 30% reported a worsening that ranged from slight to severe changes (Table 1). Dyskinesia and bradykinesia

also showed similar patterns of change. Of the 98% of participants who self-reported balance/gait problems, almost half indicated these symptoms were exacerbated during lockdown.

Next we examined whether subjective motor symptom changes were associated with perceived levels of stress. As shown in Figure 1C–F, scores on the perceived stress scale were higher in those reporting a worsening of tremor (by 2.4 points, 95% CI [0.7, 4.2], probability of perceived stress being higher in those reporting a worsening of tremor $P > 99\%$), dyskinesia (2.1 points, 95% CI [0.1, 4], $P = 98\%$), balance/gait (1.8 points, 95% CI [0.2, 3.4], $P = 99\%$) and bradykinesia (1.6 points, 95% CI [-0.01, 3.17], $P = 97\%$) compared to those indicating these symptoms did not change during lockdown. Including physical activity duration and intensity as predictors in these analyses did not improve the model fits.

Discussion

Consistent with previous literature showing stress plays a key role in PD and alters motor system functioning,^{4–8} perceived stress was higher in PD than healthy controls and, importantly, higher in PD participants reporting a worsening of motor symptoms during lockdown compared to those reporting no impact of lockdown on motor symptoms. Over a quarter of PD participants reported changes in one or more motor symptoms during lockdown. A worsening of PD motor symptoms since the onset of the COVID-19 pandemic has been reported by others.^{20–24} Consistent with van der Heide et al,²⁵ our results extend these findings to show a direct relationship between higher perceived stress and deterioration of motor function in PD; however, they cannot demonstrate causality (ie, whether increased symptom presentation increases stress or vice versa).

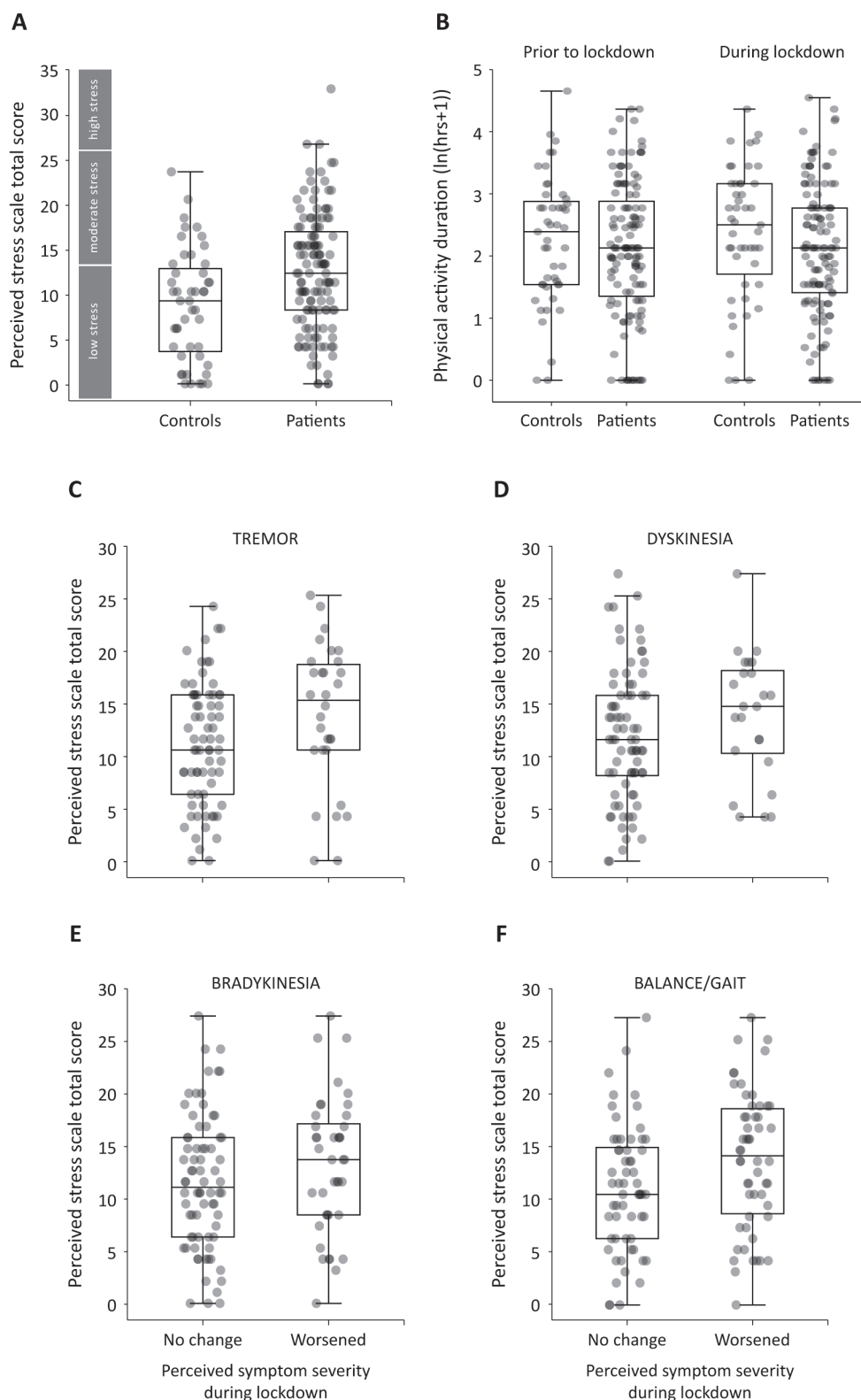
Interestingly, the levels of perceived stress reported here appear lower than that found in the general population across the globe

during the pandemic.^{26–28} The low levels of stress in this study are consistent with our findings of no change in depression or anxiety levels in the same PD and control cohort during lockdown compared to pre-lockdown (unpublished observations), possibly due to the effectiveness of the New Zealand government's policy and strategy to contain the virus.²⁹ The relative success of this swift and stringent response may have contributed to the mental and physical wellbeing of residents and thus influenced the results we report here. However, the low perceived stress levels could also reflect the older age of our participants and a larger percentage of male responders (58%), as perceived stress during the pandemic is reported to be higher in females and younger people.^{26,28}

New Zealand's strict lockdown did not appear to impact on participants' reported physical activity levels, perhaps in part because explicit provision for outdoor exercise was a feature of government guidelines. Moreover, the effects of stress on motor symptom presentation and the between-group differences in perceived stress during lockdown were not modulated by physical activity duration or intensity. These findings contrast with other reports that demonstrate reduced physical activity since the pandemic in PD,^{24,25} which was associated with worsening of symptoms (combining both motor and non-motor symptoms together).²⁵ The lack of support for previous research showing beneficial effects of physical activity on stress^{9,10,30} may be explained by the already low average stress levels of our groups.

Given New Zealand's unique pandemic response to COVID-19, our findings may not generalise to other PD and older-aged healthy control cohorts around the world. Nonetheless, monitoring and addressing stress levels, particularly as this pandemic continues, may be an important adjunct strategy to mitigate exacerbation of symptoms and improve motor function in PD.

Figure 1: (A) Total perceived stress scores (PSS) since lockdown began for PD patients and controls. (B) Duration of time spent being physically active over the week immediately prior to lockdown and one week during lockdown for patients and controls. Includes physical activity level intensities ranging from light to vigorous. Data for time (hours) were log transformed before analysis. (C–F) PSS scores for those participants reporting a worsening of their motor symptoms (Worsened) compared to those participants reporting no change in their symptom presentation (No Change), for (C) tremor, (D) dyskinesia, (E) bradykinesia and (F) balance/gait. Box plots illustrate the median and quartiles; individual patient and control data are also shown (grey circles).



Competing interests:

Nil.

Acknowledgements:

We acknowledge people who have collected earlier data for the existing New Zealand Brain Research Institute's longitudinal Parkinson's disease study, including Saskia van Stockum, Charlotte Graham, Krysta Callander, Megan Livingstone and Meisha Nicolson.

Author information:

Rebekah L Blakemore: PhD; New Zealand Brain Research Institute, Christchurch, New Zealand; School of Physical Education, Sport and Exercise Sciences, University of Otago, Dunedin, New Zealand; Brain Health Research Centre, University of Otago, Dunedin, New Zealand.

Maddie J Pascoe: BSc; New Zealand Brain Research Institute, Christchurch, New Zealand.
Kyla-Louise Horne: PhD; New Zealand Brain Research Institute, Christchurch, New Zealand; Department of Medicine, University of Otago, Christchurch, New Zealand; Brain Research New Zealand – Rangahau Roro Aotearoa Centre of Research Excellence.

Leslie Livingston: BA (Hons); New Zealand Brain Research Institute, Christchurch, New Zealand; Department of Medicine, University of Otago, Christchurch, New Zealand

Bob N Young: MSc; New Zealand Brain Research Institute, Christchurch, New Zealand.

Beth Elias: MA; New Zealand Brain Research Institute, Christchurch, New Zealand.

Marie Goulden: BN PGCert; New Zealand Brain Research Institute, Christchurch, New Zealand; Brain Research New Zealand – Rangahau Roro Aotearoa Centre of Research Excellence
Sophie Grenfell: MSc; New Zealand Brain Research Institute, Christchurch, New Zealand.

Daniel J Myall: PhD; New Zealand Brain Research Institute, Christchurch, New Zealand.

Toni L Pitcher: New Zealand Brain Research Institute, Christchurch, New Zealand; Department of Medicine, University of Otago, Christchurch, New Zealand; Brain Research New Zealand – Rangahau Roro Aotearoa Centre of Research Excellence.

John C Dalrymple-Alford: PhD; New Zealand Brain Research Institute, Christchurch, New Zealand; Brain Research New Zealand – Rangahau Roro Aotearoa Centre of Research Excellence; School of Psychology, University of Canterbury, New Zealand.

Campbell J Le Heron: FRACP, DPhil; Department of Medicine,

University of Otago, Christchurch, New Zealand; Department of Neurology, Christchurch Hospital, Christchurch, New Zealand.

Tim J Anderson: FRACP, MD; New Zealand Brain Research Institute, Christchurch, New Zealand.

Michael R MacAskill: PhD; Department of Medicine, University of Otago, Christchurch, New Zealand; Brain Research New Zealand – Rangahau Roro Aotearoa Centre of Research Excellence; Department of Neurology, Christchurch Hospital, Christchurch, New Zealand.

Corresponding author:

Dr Rebekah Blakemore, School of Physical Education, Sport and Exercise Sciences, University of Otago, 55 Union Street, Dunedin, 9016, New Zealand, +643 479 8387
rebekah.blakemore@otago.ac.nz

URL:

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