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## **The clinical impact of COVID-19 infection on people with Parkinson's**

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### Abstract

The impact of COVID-19 has been, and continues to be, felt across the world. For some people the risks associated with contracting this virus are greater than others due to underlying health conditions. This article explores the impact of COVID-19 for people with Parkinson's and how specialist health services are having to change to continue to support this group of patients.

Over the last few weeks, our world has changed beyond recognition due to the COVID-19 pandemic. Many specialist nurses have been redeployed to different clinical areas to support front line staff, while those left managing specialist services have had to rapidly redesign and adjust ways of working. This article explores the impact that COVID-19 is currently having on people with Parkinson's Disease (PD) (Figure 1) and how services they rely on to manage their complex long-term neurological condition have changed.

**The risk of Covid-19 for people with Parkinson's** COVID-19 is a newly discovered coronavirus (coronavirus 2 (SARS-CoV-2)) and is a highly infectious viral disease that was first reported in Wuhan, China at the end of December 2019. Due to the alarming level of spread and severity the World Health Organisation (WHO) characterised COVID-19 as a global pandemic on 11 March 2020. For many, COVID-19 has a clinical presentation similar

to influenza, typically with fatigue, fever, hyposmia, loss of taste and non-productive cough (Chen et al, 2020; Guan and Zhong, 2020). Diarrhoea has been a reported symptom, which could indicate initial infection through the gastrointestinal tract. Neurological symptoms, such as headache and nausea, can also occur for some people contracting the virus (Carod-Artal, 2020). Coronaviruses, including COVID-19, are likely to be neurotropic with spread via the lingual or olfactory nerves, as anosmia/hyposmia and ageusia is reported in many infected patients, a symptomatology that closely resembles one of the most prominent pre-motor symptoms of PD (Schaeffer et al, 2020). Most infected patients (approximately 80%) experience a mild clinical form and recover without complications (Huang et al, 2020) Wang et al, 2020). For some, particularly those considered to be most at risk, symptoms of COVID-19 can be much more severe, resulting in severe respiratory difficulties, pneumonia and end-stage intravascular coagulation (Chaudhuri, 2020).

By 15 April 2020, the Department of Health and Social Care (DHSC) in England stated that all people should 'Stay at home, protect the NHS, save lives'. Further recommendations were given to people aged 70 or over, or those with an underlying health condition, to stay at home at all times, avoiding leaving to even buy food, collect medicine or exercise until at least the end of June 2020. People at high risk, and described as clinically extremely vulnerable, were contacted via the NHS and provided with extra support to ensure they were able to remain at home. Although people with PD have not been classified as 'extremely vulnerable', they are classified as 'moderately vulnerable', which means they should only leave their home to buy food or medicine or exercise once daily. There is reasonable evidence stemming from basic science and immunological science that people with PD are at greater risk of developing COVID-19, and there is evidence to suggest they may have more severe symptoms if they do contract the virus. A potential relationship of coronavirus and clinical consequences with relevance to PD was reported almost 20 years previously (Fazzini et al, 1992). People who are older with more advanced PD may represent a particularly vulnerable population due to respiratory muscle rigidity, as well as possibly brain

stem involvement related impairment of cough reflex alongside pre-existing dyspnoea, may lead to increased severity of COVID-19 infection (van Wamelen et al, 2020a). These features of PD increase the chance of developing aspiration pneumonia, which is cited as a well-known cause of mortality in PD (Kalf et al, 2012). A recent paper by Antonini et al, (2020) reported the first series of ten cases of people with PD and COVID-19-positive and found that those of older age (mean 78.3 years) with longer disease duration (mean 12.7 years) were particularly susceptible to COVID-19, with a substantially high mortality rate (40%). Those on advanced therapies, such as deep brain stimulation or levodopa infusion therapy, seem especially vulnerable; with a mortality rate of 50% among the four such cases, this is a cause for concern (Antonini et al, 2020).

For those people with PD who are severely affected with pneumonia, possibly needing ventilation, or for those at end of life, a strategy for the use of non-oral dopaminergic drugs needs to be implemented (Antonini et al, 2020; Chaudhuri, 2020). Non-oral dopaminergic therapies will also need to be considered if swallowing becomes unsafe and nil by mouth is recommended or if diarrhoea is present, as oral PD medication may not be efficacious. This may mean liquid levodopa via a PEG or nasogastric tube, use of transdermal rotigotine patches, or apomorphine injection or infusion (with careful monitoring of potential side effects), so that dopamine agonist or levodopa withdrawal syndrome can be avoided and worsening motor and nonmotor symptoms of PD are avoided (Chaudhuri, 2020). An additional aspect is the possible need for increased levodopa equivalent dose (LED), as is evident in the case series by Antonini et al (2020). Non-oral dopaminergic therapies will also need to be considered if swallowing becomes unsafe and nil by mouth is recommended. For mild upper respiratory tract infections, over-the-counter cough and cold remedies are often used. However, in some cases such drugs may interact with monoamine A oxidase inhibitors (Rasagiline, Selegiline, Safinamide) so a discussion with the pharmacist or phone consultation with their PD specialist service may be required to ensure that there are no adverse events. In view of the high rate of resistance – although no longer recommended for

treatment of influenza – the antiviral drug Amantadine, used to treat dyskinesia in PD, has been cited as a drug of potential interest, among other adamantanes (Torres et al, 2007). At this time, there is no data on the safety and efficacy of Amantadine and it has not been tested to determine if it is a potentially useful treatment in people with PD infected with COVID-19, and should be used with caution due its side effect profile (Cimolai, 2020).

### **The hidden impact of Covid-19 on people with Parkinson's**

Staying at home, and isolating from others, has meant dramatic changes to daily routines and lifestyles for everyone. Activities previously taken for granted – such as shopping, social gatherings, collecting medications, providing childcare or attending a day centre (to name but a few) – have all had to stop. Such drastic changes to lifestyles and routines require a flexible adaptation to new circumstances, which is a cognitive operation that depends on normal dopaminergic functioning (Helmich and Bloem, 2020). A very insightful paper by Helmich and Bloem (2020) discussed the large body of literature that demonstrates many people with PD experience cognitive and motor inflexibility, as a result of nigrostriatal dopamine depletion that forms the pathophysiological substrate of PD (Helmich et al, 2009). Furthermore, it has been hypothesized that dopamine-dependent adaptation is a requirement for successful coping that, when deficient, leads to a sense of loss of control and increased psychological stress (Douma and de Kloet, 2020). On top of this, there is also the clearly reported indirect possible effects, such as the impact of stress, self-isolation and anxiety, as well as the consequences of prolonged immobility due to the lockdown (Helmich and Bloem, 2020; Prasad et al, 2020). Helmich and Bloem (2020), also identified that increased levels of stress during the COVID-19 pandemic may have several short-term (as well as long-term) adverse consequences for people with PD. It is already understood that increased psychological stress can temporarily worsen various motor symptoms of PD, such as tremor, freezing of gait or dyskinesias (Macht et al, 2007; Prasad et al, 2020; Zach et al,

2017), while it reduces the efficacy of dopaminergic medication (Zach et al, 2017). Helmich and Bloem (2020) hypothesised there is also the possibility that there will be an increase in the number of newly diagnosed people with PD during, or shortly after, the pandemic, as increased stress may unmask a latent hypokinetic rigid syndrome, possibly by depleting compensatory mechanisms (Djamshidian and Lees, 2014; Snyder et al, 1985; van Wamelen et al, 2020b) .

At present, the guidance from the DHSC for healthcare professionals is to avoid all face-to-face contact, unless there is a clear and urgent need to do so. This means that outpatient clinics have been cancelled and the ability to provide standard PD care is being compromised by the strain on healthcare systems brought about by this pandemic (Papa et al, 2020). Many PD specialist services are using telehealth and telephone-based services to continue to monitor and support people with PD, with positive feedback from users. The benefits of telehealth are becoming apparent, providing a means to see people with PD within their own home, at a time of day that is more suitable and in a more relaxed and convenient way than a outpatients clinic appointment would be. For some PD services, telehealth is also proving to be more responsive to the needs of people with PD, as they can be seen much more quickly if an issue arises, rather than having a long wait to be seen in outpatients. In 2019, NHS England published their Long-Term Plan, which committed to reducing face-to-face outpatient appointments by a third; with greater use of telehealth and telephone-based services, this target may become a reality.

## **Conclusion**

At present, it is too early to know what the long-term impacts of COVID-19 will be for people with PD and PD specialist services. Until we have additional clinical data available from large-scale, register-based observational studies, it seems that 'young' people with PD at early motor stage without any significant comorbidities may not have high risk for adverse

outcomes in case of COVID-19 infection. However, frail elderly older people with PD , with advanced motor disease, comorbidities or undertaking advanced therapies may, indeed, be a 'high-risk' group. It is, therefore, important that we use this unique opportunity to monitor and then understand how the pandemic influences the course of PD. Technologies such as wearable sensors or biological biomarkers could provide important data (Helmich and Bloem, 2020). It is also a time for PD services to examine and reflect on any new ways of working in determining how best to support people with PD, and their families, in the future.

#### Key learning....

- All people with PD fall into the vulnerable group, with potential for severe illness if they contract COVID-19; older people with multiple comorbidities may be particularly at risk
- In acutely ill patients, non-oral dopaminergic treatment strategies need to be implemented
- Rigidity of respiratory muscles as well as impaired cough reflex increases the risk of developing pneumonia or potentially fatal respiratory failure
- Recently acquired, unexplained hyposmia may be a sign of COVID-19 infection

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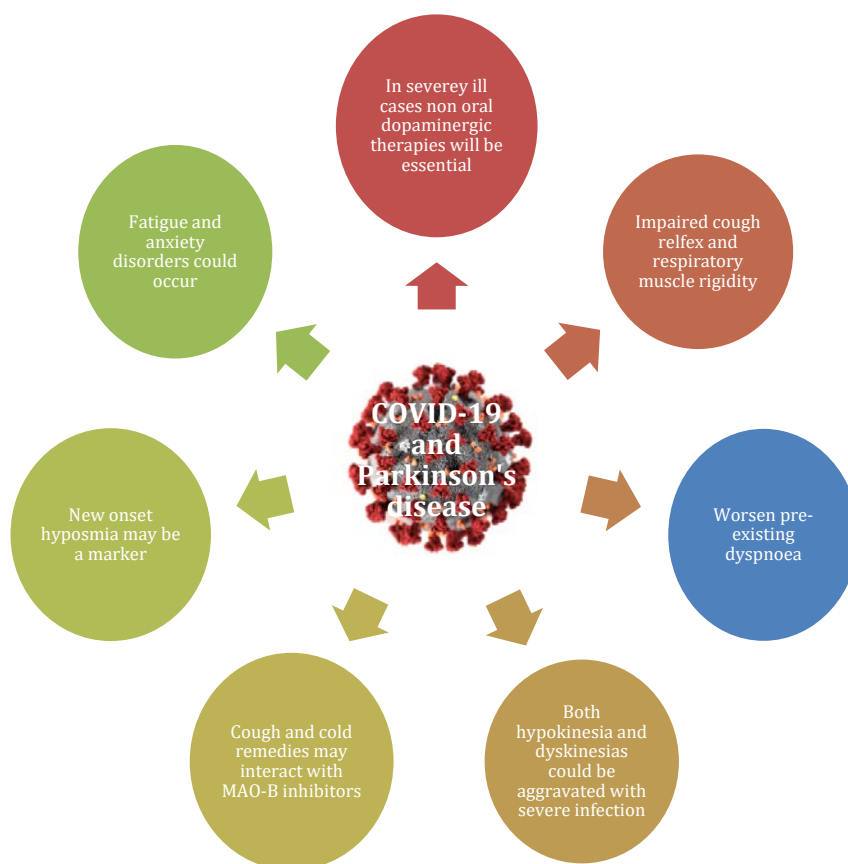


Figure 1