Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Parkinsonism hyperpyraexia syndrome in Parkinson's disease patients undergoing deep brain stimulation: An indirect consequence of COVID-19 lockdowns

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Lockdowns due to the COVID-19 pandemic can affect patients with Parkinson's disease (PD), ranging from motor deterioration to severe akinetic crisis [1–3]. While current literature mainly focuses on the direct effects of COVID-19 infection, indirect effects, including psychological concerns, emotional stress, and lack of medical resources, should not be underestimated [2]. Here, we report two PD patients, the first patient with globus pallidus interna deep brain stimulation (GPi DBS) and the second patient with subthalamic nucleus DBS (STN DBS), both of whom were diagnosed with Parkinsonism-Hyperpyraexia Syndrome (PHS) due to battery depletion of the DBS device as an indirect effect of lockdown (Supplementary table 1). These cases highlight that, during lockdown situations, close monitoring of DBS patients with additional risks of PHS should be considered even before the usual notification point of an elective replacement indicator (ERI) [4].

Two male PD patients with bilateral dual-channel DBS (Patient 1: Fig. 1A; Patient 2: Fig. 1B) who were clinically stable reported sudden-onset fever (both $> 38^{o}$C) and severe parkinsonism, progressing rapidly within three days to respiratory insufficiency requiring intubation and care in an intensive care unit. The diagnosis of PHS in both patients was made based on markedly elevated serum creatine phosphokinase, high fever, and worsening parkinsonism as detailed in supplementary table 1. Six months before this acute worsening, their battery indicators were normal at 2.71 and 2.70 V with corresponding total electrical energy delivered (TEED = [(Voltage)^{2}x(frequency)x(pulse width)/impedance]) of 358.01 and 689.63 J per second respectively, therefore their usual three-monthly appointments were postponed during the COVID-19 lockdown. However, at the time of this emergency admission, where both patients tested negative for SARS-CoV-2 using real-time RT-PCR of a nasopharyngeal swab, "end-of-service" was reported on the battery indicator of both patients. Dopaminergic medications were resumed at high dosages, followed by emergency battery replacement in both patients. MDS-UPDRS scores returned to their baseline levels of 9 and 8 points in Patient 1 and 2 respectively within seven weeks after admission (Fig. 1 and Supplementary table 1).

PHS can be a life-threatening condition with reported predisposing factors including old age, STN target, long disease duration, and prolonged DBS usage with the latter two factors applying to both our patients [5,6]. As evident in our cases, PHS can also occur in a patient with GPi DBS and, though PHS is rarely reported in association with DBS battery depletion in PD patients, emergency battery replacement is required in these situations [7,8]. Therefore, assessment of risk factors can help clinicians determine which patients need to be most closely followed and treated most aggressively [6]. Individualistic care needs to be prioritised, with a patient's risk of acquiring COVID-19 balanced with the risk from delaying care for DBS [9]. This report aims to increase awareness of these serious complications and remind neurologists to consider battery depletion as a possible cause of sudden worsening of parkinsonism in DBS patients even when normal battery levels were recorded at their last follow-up. DBS patients with high energy consumption, reflected by high TEED, are more likely to have a shorter battery lifespan than those with low TEED, however, what should be considered a high TEED has not been established. Online resources are available to provide help with estimating the longevity of DBS batteries [10]. However, clinical judgement should also take into consideration the presence of other risk factors, clinical severity, rate of progression, and supporting laboratory findings, not solely be based on TEED alone.

These two cases have drawn attention to the need to be more vigilant in DBS patient care during pandemic situations. Therefore, we propose the following practical considerations are applied to the care of DBS patients during lockdown [9]: 1) Set up protocols to manage DBS patients and increase the use of patient programmers; 2) Teach patients how to handle patient programmers, with particular focus on warning signs or alert indicators such as ERI; 3) Remind patients to contact their neurologists immediately in the event of sudden system failures with oral levodopa always available in case high dosages need to be resumed; 4) Make available emergency consultations for DBS patients who may require emergency battery replacement, and 5) Set up telemedicine facilities to maintain regular contact with DBS patients to support patients if any concern arises, strengthen patient's ability to handle their DBS system and patient programmer, and monitor battery life [9]. Increasing awareness of potential DBS complications and managing concerns promptly are vital for the well-being of DBS patients, particularly during this most challenging time.

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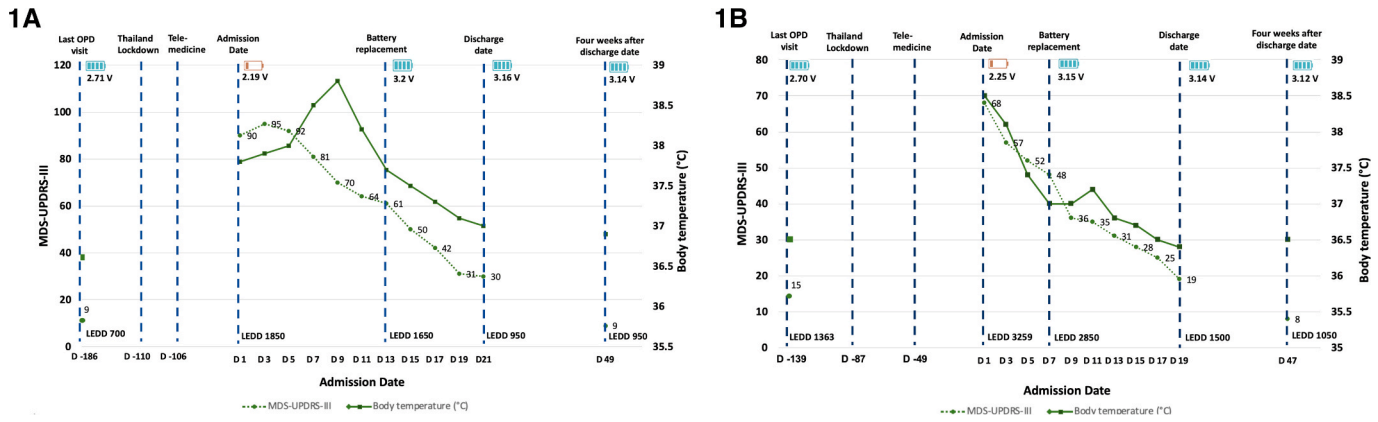

Fig. 1. The diagram illustrated the MDS-UPDRS score (dash line) and body temperature (bold line) of patient 1 (1A) and patient 2 (1B) along the time course of illness. MDS-UPDRS: Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS); OPD: Out-patient Department; LEDD: Levodopa Equivalent Daily Dose.

Authors' roles

Concept or design of the work, O.P. and R.B.; acquisition, analysis, and interpretation of data, O.P. and S.V.; drafting and revising the manuscript, O.P. and R.B. All authors have read and agreed to the published version of the manuscript.

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Onanong Phokaewvarangkul: receives salary from King Chulalongkorn Memorial Hospital, has received consultancy and/or honoraria/lecture fees from Boehringer-Ingelheim, Britannia, Ipsen, Medtronic, and Novartis.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2021.04.010.

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