The Management of Neurological Disease during the COVID-19 Pandemic

COVID-19 Pandemi Sürecinde Nörolojik Hastalıklara Yaklaşım

Melis Doğanay Ocalan, Alev Leventoğlu

Ufuk University, Faculty of Medicine, Department of Neurology, Ankara, Turkey

ABSTRACT

In this current pandemic period, neurological disorders are the most devastating disease group among all disease groups considered which created the highest health burden for patients, their relatives, and healthcare workers which keeps increasing with aging world population. COVID-19 directly invades lungs, it also involves the nervous system. However, it is too early to know whether COVID-19 will have long-term impacts on patients with neurologic disease. The COVID-19 pandemic has changed people’s daily routines, and it all happened in a short period. Neurologists are affected negatively by the COVID-19 pandemic in a few key ways, including: a reduced ability on admission or transfer of critically ill neurologic patients. During these exceptional times, a huge need arose for neurologists in the frontline and expected to be aware of and conscious for diagnosing neurological complications of COVID-19. In this process, the use of telemedicine (telenurology) in the field of neurology is a significant approach to evaluate patients. Telemedicine has been used as a platform for rehabilitation, neurological examinations, neuropsychology and other specialty services. Management of neurological diseases such as Parkinson disease, multiple sclerosis, intracranial infections, epilepsy, dementia, headache, neuromuscular diseases, and stroke had been affected in this process. In this review article, the main goal is to discuss how the diagnosis, proper management of people with existing neurological disease during pandemic period.

Key Words: COVID-19, pandemia, neurology, management, telemedicine

Received: 05.12.2020
Accepted: 05.18.2020

ÖZET

Nörolojik bozukluklar; pandemi döneminde hastalar, yakınları ve sağlık çalışanları için en yüksek sağlık yükünü yaratan hastalık grupları arasındadır ve bu durum yaşanan dünya nüfusu ile birlikte artmaktadır. COVID-19 hastalığı direkt olarak akciğer tutulumu yapmasının yanı sıra, sinir sistemini de etkilemektedir. Ancak, COVID-19’u nörolojik hastalığı olan hastalar üzerinde uzun vadeli etkileri olup olmazsağını bilmek için henüz çok erkendir. COVID-19 salgını, insanların günlük yaşamlarını değiştirdi ve bunların hepsi çok kısa bir sürede içinde geçerleştı. Nöroloji uzmanları, COVID-19 pandemi sürecinde önemli durumlar olan kritik nörolojik hastalıkların kabulü ve bu hastaların sevk edilmesi konularında, karar verme konusunda olumsuz yönde etkilendi. Bu olağanüstü dönemde, nörolojinin bastırılması ve yönetiminde ön safhada yer almalıdır ve COVID-19’un nörolojik komplikasyonlarını önlemek için dikkatli olmalıdır. Bu dönemde nöroloji alanında teleteş (telenöroloji) kullanımı, hastaların değerlendirilmesi için önemli bir yaklaşım olarak gündeme gelmektedir. Teleteş rehabilitasyon, nörolojik muayene, nöropsikoloji ve diğer uzmanlık hizmetleri için bir platform olarak kullanılacaktır. Parkinson hastalığı, multipl skleroz, intrakraniyal enfeksiyonlar, epilepsi, demans, baş ağrısı, nöromusküler hastalıklar ve inme gibi nörolojik hastalıkların yönetimi bu süreçte getirilmiştir. Bu makalede COVID-19 döneminde nörolojik hastalığı olan kişilerin tanısı, tedavisi ve yönetimi tartışılacaktır.

Anahtar Sözcükler: COVID-19, pandemi, nöroloji, yönetim, teletıp

Geçiş Tarihi: 12.05.2020
Kabul Tarihi: 18.05.2020
INTRODUCTION

While the viral pandemia starting from Wuhan city of China and spreading all over the world which caused by the virus named SARS-CoV-2 and the disease named coronavirus disease 2019 (COVID-19), World Health Organization (WHO) along with all ministries of health worldwide has also been informed about the symptoms of the disease, methods of diagnosis, and treatment approaches for the evaluation of patients with neurological disease or new neurological complaints (1).

The World Federation of Neurology (WFN) (2), the European Academy of Neurology (EAN) (3), The American Academy of Neurology (AAN) (4) and Turkish Neurological Society (5) has published several reports on the neurological findings along with COVID-19 prevention and treatment approaches in neurological diseases that may arise from COVID-19 itself. Older adults are at a significantly increased risk of developing severe disease following SARS-CoV-2 infection. We know that over 95% of these deaths occurred in those older than 60 years. More than 50% of all deaths were reported on people aged 80 years or older. Several papers also reported that 8 out of 10 deaths has occurred in individuals with at least one underlying co-morbidity, in particular those with cardiovascular diseases/hypertension and diabetes, but also with a range of other chronic underlying diseases (6). Especially for patients that the disease of patients with neurological disease is over 65 years old which generates most affected group by the pandemic, the event may be adversely affected not only in the pandemic period but also in the post-pandemic period. During this period, especially when restrictions on leaving home considered, problems arise in the regulation of the treatment of the patients who previously diagnosed neurological diseases, in the management of patients who wish to consult a doctor with new neurological complaints. How should neurologists manage these issues during a pandemic? In our country, very few number of patients over 60 years of age live in elderly nursing homes unlike other countries, often alone or with their families. The prevalence of neurological diseases is not fully known during the pandemic period, since patients do not go to health centers with the concern of COVID-19 transmission and neurological symptoms are not taken seriously by individuals. In this review article, we shared our experience on approach to the management of patients who already have neurological diseases or newly diagnosed during the pandemic process and present our recommendations on the management of patients with neurological symptoms originating from COVID-19 in the course of the COVID-19 pandemic, which is also important in our country.

Although neurological involvement is rare in patients with COVID-19, neurological manifestations such as acute cerebrovascular diseases, unconsciousness, and encephalopathy may occur in patients with advanced systemic effects of infection (7). The disease may begin with neurological symptoms or the patients may develop neurological complications during systemic treatment. Neurologists can examine patients infected with COVID-19 in the outpatient clinic, the emergency room, and in-patient ward. For this reason, the staff need to wear favourably disposable personal protection equipment such as work caps, surgical masks, work clothes such as scrubs, face shields/googles, gloves properly, and use hand sanitiser that contains ethanol, hydrogen peroxide or sodium hypochlorite. For patients with neurological symptoms which suspected COVID-19, it is recommended that the patient’s evaluation completed on COVID-19 designated clinic and then consult a neurologist. Infected patients may show neurological symptoms initially (8). Another concern for neurologists is the vulnerability of patients with neurological disease when combined with COVID-19. This is also the desire of (6) especially for patients receive the modifying therapies and immunosuppression. Many neurological patients are at risk due to diabetes, heart disease or COPD (chronic obstructive pulmonary disease) among with being old (9). There are no clear data on the outcomes or treatment of patients with pre-existing neurological diseases, and in particular, the effects of immunosuppression (10, 11).

The number of neurologists are not enough to serve the patients with critical illness or chronic disease due to the high number of patients due to COVID-19 pandemics; reduced routine follow-up; risk of individual exposure when neurological diseases are increasing with the aging world population considered. We know that corona viruses are not primarily neurotropic viruses. The primary targets of the virus are respiratory epithelium. The target receptor for cell binding and subsequent internalization is angiotensin converting enzyme-2 receptor (ACE2). ACE2 receptors are also found in glial cells in the brain and spinal neurons.

For this reason, it can adhere to neuronal tissue and cause damage. As another way, during the viremia stage of the disease, the virus can enter the brain with the breakdown of the blood brain barrier. Another estimated mechanism is the invasion of peripheral nerve terminals by the virus which then gains entry to the CNS through the synapse connected route. Neuropathological mechanism of CNS damage likely by hypoxic brain injury and an immune mediated damage to the CNS. Immune mediated damage is due to the cytokine storms with activation of T lymphocytes and macrophages and endothelial cells, and increased levels of inflammatory cytokines, more release of interleukins 6 causes vascular leakage, activation of complement and coagulation cascade, disseminated intravascular coagulation and finally end organ damage (12).

The important neurologic manifestations of SARS-CoV-1 associated disease, vary from fairly specific symptoms (eg, loss of sense of smell or taste, myopathy, and ischemic or hemorrhagic stroke, transverse myelitis, acute hemorrhagic necrotizing encephalopathy, ataxia, encephalitis, Guillain Barre syndrome, Miller-Fisher syndrome, neuralgia) to more non-specific symptoms (eg, headache, reduced level of consciousness, dizziness, or seizure, agitation, delirium, confusion, or executive dysfunction (7, 11-22). Neurologists should also keep in mind the potential risks for postinfectious disorders.

Management of neurological diseases such as Parkinson Disease (PD), multiple sclerosis (MS), intracranial infections, epilepsy, dementia, headache, neuromuscular diseases, and stroke is affected in this process. In this review article, it is discussed how the diagnosis, treatment and management of people with existing neurological disease should be during global COVID-19 pandemic period.

Neurological manifestations of COVID-19

The neurological manifestations and complications of COVID-19 can be divided into central and peripheral categories. Central nervous system manifestations including headache and encephalopathy, acute cerebrovascular disease related symptoms, intracranial infection related symptoms, peripheral nervous system symptoms and neuromuscular symptoms.

Stroke

COVID-19 pandemic has been so large and widespread. However, under such extreme situations, there has been no previous experience that can be used to develop plans for the emergency management of acute stroke treatment. Therefore, the control of the COVID-19 is very important, at the same time the management of stroke must not be neglected (23). Stroke remains a medical emergency even during a pandemic period. Management of the patients with stroke for hyper acute treatments such as thrombolysis and thrombectomy impacts have functional outcomes and mortality. These patients should avoid entering the neurological intensive care unit and be treated in a private room (24). Factors that affect outcomes in patients with stroke can include exposure to in-hospital pathogens; acute treatment, and post stroke care such as rehabilitation. During a pandemic period, stroke protection and provide a framework for key considerations including screening, personal equipment, and crisis resource management. Considerations and suggested algorithms can be utilized and adapted for local practice (25). If acute ischemic stroke patient with suspected or unverified diagnosis of COVID-19 is accepted, neurologists and infectious disease specialists are collectively urgent treatment. In this case, Chest CT shows very high sensitivity for new corona infection findings (> 95%) (26). Although specificity is also important to initiate the procedure, in case of doubt, the patient is treated as COVID-19 positive.

Prophylactic anticoagulated therapy is recommended for ischemic stroke patients with a high D-dimer level. These patients should be transferred for the isolation ward, and neurologists should assist in the management (8). In acute ischemic stroke, the team that will administer IV tPA must use full personal protective equipment and employ maximum compliance with contact safety rules (25, 27). The use of Telestroke must be maximized in the pandemic period because all aspects of acute stroke evaluation can be performed.

Intracranial Infection

Some patients infected with COVID-19 have had symptoms similar to those with intracranial infections such as headaches, seizures and impaired consciousness. In some patients, central nervous system symptoms can be observed before pulmonary symptoms are seen. Therefore, neurologists should be alert when viewing COVID-19 infected patients, and patients with suspected status should be performed head MRI with or without contrast should be seen.
It is recommended to search for SARS-CoV-2 nucleic acid using PCR by performing lumbar puncture. Treatment strategies such as reducing cerebral edema, treating and preventing seizures should be considered for these COVID-19 patients with intracranial infection, and guidelines should be followed (8).

Parkinson’s Disease and Movement Disorders

The risk of Parkinson’s patients catching COVID-19 is not different from other individuals. However, older adults are at the highest risk of developing a serious case of COVID-19, and since most patients with Parkinson’s disease (PD) are typically older, the disease may be severe if the virus is caught. Patients with parkinsonism hospitalized for pneumonia had a lower rate of in-hospital mortality, but the length of hospital stay (28). In addition, patients with PD have a higher risk of intra-hospital complications such as delirium, adverse drug reactions, syncope, aspiration pneumonia, falls and fractures (29). Therefore, strategies to prevent these complications are important.

Increased psychological stress and social isolation due to pandemic may temporarily worsen various motor symptoms in patients (e.g. tremors, freezing of walking or dyskinesia), reducing the effectiveness of dopaminergic drugs. In addition, increased stress can possibly unmask a hidden hypokinetic severe syndrome by consuming its compensatory mechanisms (30). In case of COVID-19 infection, neurologists should ensure that adequate doses of previous PD medications, especially L-dopa, are recommended for any pneumonia in Parkinson’s patients, as recommended to avoid stiffness and reduced vital respiratory failure (31).

Self-management strategies that reduce stress, increase coping or increase physical exercise will play an increasing role in PD treatment (30). However, this universal crisis can significantly change the care of patients with PD and other movement disorders towards better acceptance of telemedicine consultations and evaluations (32). In fact, apart from stiffness and postural reflex disorder, many basic features of the disease can be recorded or watched on video by video consultations (33). The International Parkinson’s and Movement Disorders Association has developed a step-by-step practical guide on how to apply telemedicine for a motion disorders clinic on its website (34).

Myasthenia Gravis/Lambert-Eaton Myasthenic Syndrome

Most of our patients with myasthenia gravis (MG) / Lambert-Eaton Myasthenic Syndrome (LEMS) constitute a greater potential risk group for COVID-19 related complications. Patients with myasthenia gravis must comply with hand washing, masking and social distance measures. First of all, patients should not abandon existing drugs without consulting their doctor. In addition, there is no evidence that symptomatic treatments such as pyridostigmine put the patient at any increased risk. Therefore, the treatments they use should not be interrupted unless there are other clinical reasons. Immunosuppressive therapy increases the risk of infections, exacerbation and treatment of the disease or stop the risk of worsening the transition only symptomatic treatment is important. If a patient is stable under immunotherapy, treatment should continue unchanged. There is no evidence that infusion therapies such as intravenous immunoglobulin or plasma exchange increase the risk of COVID-19. However, unless necessary to be seen as an emergency, telehealth visits are recommended to all of our patients. Some of neuromuscular patients use oral steroids (cortisone) or another immunosuppressant drug (e.g. azathioprine, methotrexate, etc.). Since these drugs suppress the immune system, our patients are considered to be at risk for infections. However, in case of discontinuation of the drugs used, the diseases may recur or worsen. There is no information that COVID-19 infection is more severe in patients taking these drugs yet. For this reason, we do not recommend discontinuing or reducing their medication. The decision on whether to initiate a B cell depletion therapy needs to be taken into account in particular, as the risk of viral disease complications is higher, and should be postponed to a later date. When changing or stopping an existing immunosuppressive therapy that carries a potential risk for increasing disease activity and/or MG exacerbation or crisis, people with MG and their MG healthcare providers should consider specific side effects and benefits (35).

Epilepsy

The effects of COVID-19 on epileptic patients and the prevalence of new epilepsy cases remain uncertain. There is no evidence that the use of seizure medications (also called antiepileptic drugs (AEDs) or antiseizure medications or drugs) increases the risk of coronavirus infection except ACTH, steroids, and immunotherapies.

People with seizures and epilepsy should make sure they take their medication regularly and always as prescribed. The problem is that going to emergency department owing to increased or uncontrollable seizures could expose the patient to coronavirus. Epilepsy foundation does not recommend going to emergency room unless there is a real emergency. It is very important to maintain the control of seizures, besides the prevention of COVID-19. Some societies do not recommend changing AEDs of patients with well-controlled seizures, as seizure exacerbations or status epilepticus may increase the risk of COVID-19 infections (36,37).

Migraine

Headaches can be a symptom of systemic viral infections and are no exception for COVID-19 (39). The presence of a headache is not helpful for the diagnosis or prognosis of COVID-19 infection, and 8% of patients may have headaches. Headache in COVID-19 infection is likely to be associated with fever and may be related to it (15). Patients with primary headaches, especially migraines, should follow the recommended treatment and pay attention to dietary triggers, especially alcohol consumption, which can be increased under isolation. Maintaining regular sleep and eating habits and managing stress is important because they are common migraine triggers. Under social isolation conditions, anxiety and depression disorder can worsen and adversely affect chronic headaches and excessive drug use. Medication intake for acute treatment for migraine should be limited to less than twice a week. According to treatment guidelines, NSAIDS, especially ibuprofen, naproxen, diclofenac, has proven efficacy and safety in clinical trials of the symptomatic treatment of migraine and is therefore recommended for acute treatment. In addition, indomethacin is the only treatment available for some Trigeminal autonomic cephalalgias (TACs). In general, NSAIDs have great therapeutic value in headaches. FDA has new recommendations for the use of NSAIDs (38,39).

Neurologists are working to keep individuals with migraine out of the emergency department and hospital, while also foregoing or at least minimizing face-to-face visits and procedural treatments. Moreover, telehealth provides an important opportunity to continue to care for vulnerable population and, help avoid urgent care visits that put patients at risk and burden the over-whelmed healthcare system (38).

Alzheimer’s disease and related dementias

Patients Alzheimer’s disease and related dementias (AD/ADRD) are among the patients with which this virus can be transmitted. These patients are at greater risk than the rest of the society because they have many additional diseases such as diabetes and high blood pressure and are mostly of advanced age. Due to the risk of Covid-19 contamination, patients should not apply to the hospital for check-up or report renewal and prescribing, except for new neurological complaints and urgent reasons (shortness of breath, high fever, chest and abdominal pain, and so on). Therefore, patients, except for complaints that may be, and bringing them to the hospital for reasons such as routine check-ups or renewing reports increase the risk of virus transmission. COVID-19 pandemic further exacerbates AD/ADRD patient’s vulnerability, due to both the morbidity and mortality from COVID-19. The indirect effects of the pandemic on the social supports and the health care system on which they depend. Initiating a new medication during the pandemic may be associated with higher risk, especially if components of routine screening are disrupted such as in-person clinical assessments, blood work, or electrocardiogram, or the ability to follow up on adverse events just in time (40).

Symptoms of dementia, such as motor agitation, wandering, or intrusiveness may undermine efforts to maintain isolation (41). Creative ideas to incorporate alternative social physical activities safely within the home are needed. The pandemic and its consequences may also be experienced as a trauma, followed by post-traumatic stress disorder (42). Stress and trauma can accelerate cognitive deterioration (43). Thereby people are turning to technology to stay socially connected and access areas including health care. Some individuals with AD/ADRD may have trouble using technology due to cognitive impairment. They may need instruction and support to use these tools.

The COVID-19 pandemic crisis may facilitate the development of non-pharmacological interventions that can be delivered at the home of the participants or that use small portable devices that can be easily used in private homes (44).
A Special Role of Telemedicine During the COVID-19 Pandemic

Recently, it has been aimed to avoid unnecessary hospital visits of patients by using telemedicine in the COVID-19 period. It is known that telemedicine has previously been validated as a tool for assessing disability in MS. It is preferable to make the visits of MS patients through telemedicine or telephone due to the risks during the pandemic period (48). Telemedicine within neurology (teleneurology) is growing as an approach for evaluating patients (e.g., stroke, Parkinson’s disease, MS, and epilepsy). It has been used as a platform for rehabilitation, neurological examinations, neuropsychology, and other specialty services. Telemedicine provides doctors’ consultation by keeping patients away from the crowd. Thus, prevents the spread of COVID-19 among patients (49).

As a result, COVID-19 is a highly contagious disease that has become a worldwide pandemic. Infected patients may show neurological symptoms in the early stages. Neurologists should pay close attention to these symptoms and have a high index of suspicion when evaluating patients in an endemic region. However, this global pandemic could deliver an advantage of screening and evaluating for remote learning and supporting processes including all health-care workers among with neurologists and promise a faster organization skill for national health-care services.

Conflict of interest

No conflict of interest was declared by the authors.

REFERENCES

1. WHO. International Health Regulations Emergency Committee on novel coronavirus in China 2019-nCoV, World Health Organization, Geneva, Switzerland (2020)
2. https://wfneurology.org/covid-19-and-world-neurology
3. https://www.ean.org/research/resources/neurology-updates
4. https://www.aan.com/tools-and-resources/covid-19-neurology-resource-center/
5. Öztürk Ş, Covid-19 and Neurology, Turk J Neurol, DOI:10.4274/tnrd.galenos.2020.
6. (http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/statements/statement-older-people-are-at-highest-risk-from-covid-19-but-all-must-act-to-prevent-community-spread).
7. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol. 2020.
8. Jin H, Hong C, Chen S, Zhou Y, Wang Y, Mao L, et al. Consensus for prevention and management of coronavirus disease 2019 (COVID-19) for neurologists. Stroke Vasc Neurol. 2020.
9. Onder G, Rezza G, Brusaferro S. Case-Fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA 2020.
10. Manji H, Carr AS, Brownlee JW, Lunn MP. Neurology in the time of covid-19. J Neurol Neurosurg Psychiatry. 2020.
11. D’Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. Liver Transplant 2020.
12. Ahmad I, Rathore FA. Neurological manifestations and complication of COVID-19: A Literature J Clin Neurosci. 2020.
13. Duong L, Xu P, Liu A. Meningoencephalitis without respiratory failure in a young female patient with COVID-19 infection in Downtown Los Angeles, early April 2020. Brain Behav Immun. 2020.
14. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020.
15. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395: 497-506.
16. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020.
17. Lee Y, Min P, Lee S, Kim SW. Prevalence and Duration of Acute Loss of Smell or Taste in COVID-19 Patients. J Korean Med Sci. 2020;35:174.
18. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features. Radiology. 2020;210:187.
19. Toscano G, Palmerrini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. N Engl J Med. 2020.
20. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 Infection: causality or coincidence? Lancet Neurol. 2020;19:383–4.
21. Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, San Pedro-Guerrero L, Gordo-Mañas R et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. Neurology. 2020.
22. Ye M, Ren Y, Tu L. Encephalitis as a clinical manifestation of COVID-19. Brain Behav Immun. 2020.
23. Li Y, Wang M, Zhou Y, Chang J, Xian Y, Mao L, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. 2020.
24. Zhao J, Rudd A, Liu R. Challenges and Potential Solutions of Stroke Care During the Coronavirus Disease 2019 (COVID-19) Outbreak. Stroke. 2020;51:1356–7.
25. Khosravani H, Rajendram P, Notario L, Chapman MG, Menon BK. Protected Code Stroke: Hyperacute Stroke Management During the Coronavirus Disease 2019(COVID-19) Pandemic. Stroke. 2020.
26. Caruso D, Zerunian M, Polici M, et al. Chest CT Features of COVID-19 in Rome, Italy. Radiology 2020.
27. Topcuoglu MA, Arsava EM, Ozdemir AO. Acute Ischemic Stroke Treatment In Covid-19 Pandemia: Expert Opinion. Turkish Journal of Cerebrovascular Diseases 2020; 26: 91–4.
28. Jo T, Yasunaga H, Michihata N, et al. Influence of Parkinsonism on outcomes of elderly pneumonia patients. Parkinsonism Relat Disord 2018; 54: 25–29.
29. Lubinski M, Rushworth RL, Tisch S. Hospitalisation and comorbidities in Parkinson’s disease: a large Australian retrospective study. J Neurol Neurosurg Psychiatry 2015; 86: 324–30.
30. Zach H, Dirkx MF, Pasman JW, Bloem BR, Helmich RC. Cognitive Stress Reduces the Effect of Levodopa on Parkinson’s Resting Tremor. CNS Neurosci Ther. 2017;23:209-15.

31. Monteiro L, Souza-Machado A, Valderramas S, Melo A. The effect of levodopa on pulmonary function in Parkinson’s disease: a systematic review and meta-analysis. Clin Ther. 2012;34:1049-55

32. Fasano A, Antonini A, Katschschlager R, Krack P, Odin P, Evans AH et al. Management of Advanced Therapies in Parkinson’s Disease Patients in Times of Humanitarian Crisis: The COVID-19 Experience. Mov Disord Clin Pract 2020;7:361-372.

33. Ben-Pazi H, Browne P, Chan P, Cubo E, Gutman M, Hassan A, et al. International Parkinson and Movement Disorder Society Telemedicine Task Force. The Promise of Telemedicine for Movement Disorders: an Interdisciplinary Approach. Curr Neurol Neurosci Rep. 2018;18:26.

34. Papa SM, Brundin P, Fung VSC, Kang UJ, Burn DJ, Colosimo C, et al. Impact of the COVID-19 Pandemic on Parkinson’s Disease and Movement Disorders. Mov Disord. 2020.

35. International MG/COVID-19 Working Group, Jacob S, Muppidi S, Guidon A, Guptill J, Hehir M, et al. Guidance for the management of myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) during the COVID-19 pandemic. J Neurol Sci. 2020;412.

36. Kuroda N. Epilepsy and COVID-19: Associations and important considerations. Epilepsy Behav. 2020;108,

37. Sun T, Guan J. Novel coronavirus and the central nervous system. Eur J Neurol. 2020

38. Szerperka CL, Alani J, Barmherzig R, Klein BC, Minen MT, Halker Singh RB, et al. Migraine Care in the Era of COVID-19: Clinical Pearls and Plea to Insurers. Headache. 2020;60:833-842.

39. https://www.ema.europa.eu/en/news/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19

40. Brown EE, Kumar S, Rajji TK, Pollock BG, Mulsant BH. Anticipating and Mitigating the Impact of the COVID-19 Pandemic on Alzheimer’s Disease and Related Dementias. Am J Geriatr Psychiatry. 2020.

41. McDermott MM, Newman AB. Preserving Clinical Trial Integrity During the Coronavirus Pandemic. JAMA. 2020.

42. Nicol GE, Piccirillo JF, Mulsant BH, Lenze EJ. Action at a Distance: Geriatric Research during a Pandemic. J Am Geriatr Soc. 2020.

43. Tsolaki M, Papaliagkas V, Kounti F, Messini C, Boziki M, Anogianakis G, et al. Severely stressful events and dementia: a study of an elderly Greek demented population. Psychiatry Res. 2010;176:51-4.

44. Gough N, Brkan L, Subramaniam P, Chiuccariello L, De Petrillo A, Mulsant BH, et al. Feasibility of remotely supervised transcranial direct current stimulation and cognitive remediation: A systematic review. PLoS One. 2020;15

45. Willis MD, Robertson NP. Multiple sclerosis and the risk of infection: considerations in the threat of the novel coronavirus, COVID-19/SARS-CoV-2. J Neurol. 2020; 267:1567-9

46. Giovannoni G, Hawkes C, Lechner-Scott J, Levy M, Waubant E, Gold J. The COVID-19 pandemic and the use of MS disease-modifying therapies. Mult Scler Relat Disord. 2020;39.

47. Brownlee W, Bourdette D, Broadley S, Killestein J, Ciccarelli O. Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. Neurology.2020.

48. Bove R, Bevan C, Crabtree E, Zhao C, Gomez R, Garcha P, et al. Toward a low-cost, in-home, telemedicine-enabled assessment of disability in multiple sclerosis. Mult Scler. 2019;25:1526-34

49. Yeroushalmi S, Maloni H, Costello K, Wallin MT. Telemedicine and Multiple Sclerosis: A Comprehensive Literature Review. J Telemed Telecare. 2019,