COVID-19 and its impact on human motor control

PAULO H. S. PELICIONI1 | AURELIO D. SANTOS2 | KARINE V. TAKO3 | PAULO C. R. SANTOS4,5

1 Falls, Balance and Injury research Centre - Neuroscience Research Australia, Sydney, NSW, Australia.
2 Centro Universitário Leão Sampaio, Juazeiro do Norte, CE, Brazil.
3 Universidade Federal de Sergipe, Lagarto, SE, Brazil.
4 University of Groningen, University Medical Center Groningen, Department of Human Movement Sciences, Groningen, The Netherlands.
5 São Paulo State University (UNESP), Graduate Program in Movement Sciences, Institute of Biosciences, Posture and Gait Studies Laboratory (LEPLO), Rio Claro, SP, Brazil.

Correspondence to: Paulo Henrique Silva Pelicioni - Neuroscience Research Australia - 139 Barker Street - Randwick 2031 NSW Australia.
email: p.pelicioni@neura.edu.au
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ABBREVIATIONS
CNS Central Nervous System
COVID-19 Coronavirus disease 2019
LoS Length of stay
SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2
WHO World Health Organization

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ABSTRACT: COVID-19 is affecting people differently worldwide with its impact ranging from pneumonia, acute respiratory distress syndrome to death. The direct and indirect effects of COVID-19 on a person’s motor control including on the execution of balance and gait tasks varies. This paper outlines why this may occur and explores neurological complications, mental health, cardiorespiratory complications, hospitalization and reduced physical activity level from COVID-19, and how these issues might affect human motor control. This paper also suggests how these issues may be minimised through strategies such as telehealth and physical exercise programs.

KEYWORDS: COVID-19 | Motor control | Gait | Balance

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, also known as coronavirus disease 2019 (COVID-19), can lead to acute respiratory distress syndrome, pneumonia, and, other health problems, which can lead to poor prognoses, including death.1 Consequently, in March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. There have been approximately 1.33 Million deaths worldwide, at the time of writing in mid-November 2020. Despite not being infected, the lockdown measures may impact people’s health with an increase in health issues such as mental health, reduced physical activity levels and social disconnection.2,3 Unfortunately, this scenario may be worsened for individuals who have been affected by COVID-19, especially human motor control. By affecting neurological features COVID-19 may impair the central mechanisms involved in the planning, execution and adaptation of motor tasks.

The objectives of this paper are to outline the neurological, mental health, and cardiorespiratory issues caused by the COVID-19 infection on motor control and more specifically to human gait and balance control. In addition, we highlight how the hospitalization and mandatory isolation (to contain the spread of the infection) might also affect human gait and balance control. This paper discusses how the neurological, mental health, cardiorespiratory, hospitalization and mandatory isolation issues combined are perhaps affecting human balance and gait. In addition, we briefly discuss the importance of physical activity strategies to further reduce the disadvantages caused by COVID-19 infection and its negative impact on human health, such as the promotion of physical exercise regimes.
1. Neurological complications

Recent growing evidence showed that several impairments on the Central Nervous System (CNS) were caused by COVID-19 infection.\cite{4,5,6} Such evidence also suggested that over one-third of COVID-19 patients manifest neurological complications,\cite{7} such as headaches, impaired consciousness, anosmia, paresthesia, and myalgias.\cite{5} As well as the typical neurological manifestations, abnormalities in CNS may be present in postmortem brains due to SARS-CoV-2. For instance, regarding coronaviruses, Ding and colleagues\cite{8} indicated the presence of SARS-CoV viral RNA within brain tissues of infected patients. SARS-CoV infection can easily spread through brain areas, such as thalamus and brainstem and related pathways.\cite{9} Furthermore, like many other coronaviruses infections, patients infected with COVID-19 are more susceptible to present with additional CNS damage, such as toxic encephalopathy and severe acute demyelinating lesions.\cite{10}

Physiological aspects related to COVID-19 infection presumably explain the neurological damage in patients. Brain hypoxic is normally evident in COVID-19 patients and can lead to toxic encephalopathy,\cite{4} which increases the risk of ischemic brain injury and cerebral haemorrhage. Previous evidence also indicated that SARS-CoV can directly affect the CNS via the cerebral spinal fluid,\cite{11} causing nerve damage, and consequently, lead to the neurological symptoms mentioned above.\cite{4}

2. Mental Health issues

Psychological distress and mental illness can be directly and indirectly related to COVID-19 outbreaks.\cite{12} Directly, theoretical models and physiological aspects related to the infection also explain the increase in psychological symptoms. In particular, COVID-19-related infections on cerebral spinal fluid and CNS may result in changes in neurotransmitter pathways such as serotoninergic dorsal raphe system.\cite{9} Deficits on neurotransmitters are closely related to an increase in the prevalence of depression, anxiety, and fatigue symptoms.\cite{13,14,15} Furthermore, the serotoninergic dorsal raphe system (system related with non-motor symptoms – anxiety, depression, fatigue) are connected with several other brain regions (cortex, striatum, amygdala, substantia nigra, hippocampus, and locus coeruleus).\cite{16}

Among the recommendations to mitigate the spread of the virus, the WHO is strongly advising measures of mandatory isolation and quarantine. Mathematical models and databases reliably suggest that quarantine measures are important to reduce incidence and mortality resulting from COVID-19.\cite{17,18} However, consequences of mandatory isolation and quarantine involve drastic changes in human behaviour and lifestyle, exacerbating the risk of mental illness in these individuals. For example, people in quarantine are more susceptible to develop anxiety, fatigue, insomnia, irritability, and indecisiveness.\cite{19} Specifically considering anxiety and depression, Tang and colleagues\cite{20} verified a high trait of both anxiety and depression among quarantined vs. not quarantined people and, perhaps, the most worrying of the results is that approximately 80% of 1160 responders indicated an anxiety trait. Therefore, the direct and indirect effects of COVID-19 on mental health indicators are a huge concern to health systems worldwide.
3. Cardiorespiratory complications

COVID-19 infection is associated with several cardiovascular complications, such as myocarditis, arrhythmias, and venous thromboembolism. Cardiovascular comorbidities are frequent in people infected with COVID-19, maybe as a consequence of myocarditis. Patients who present with severe complications from COVID-19 are identified only one week after the onset of symptoms of respiratory distress and/or hypoxemia and may progress rapidly to acute respiratory distress syndrome. Such complications can hinder the cardiovascular rehabilitation process.

4. Hospitalization

Patients with COVID-19 infection present with different levels of severity. Those individuals presenting with moderate to severe complications are more likely to be hospitalized. Hospital care can vary from general ward-based care to high dependency units with oxygen support and intensive care, where patients may be intubated for mechanical ventilation. The patients' length of stay (LoS) depends on the level of care required, as well as on the geographic setting the patients are hospitalized in since there is a heterogeneity of COVID-19 care guidelines within countries.

A recent systematic review reported LoS of patients infected with COVID-19 in hospital and intensive care units (ICU) worldwide. The median hospital LoS ranged from 3 to 19 days and the median of intensive care patients LoS ranged from 4 to 19 days. This study also revealed that patients who survived had longer LoS than those who died. In a different study, Mishra and colleagues reported that the median length of hospital stay in India was 17 days. In all these studies, the mean age of people hospitalized due to COVID-19 was approximately 59 years. Since scientific evidence suggests that hospitalization causes several negative impacts on motor function, long hospitalization as a result of COVID-19 infection can exacerbate these negative effects, consequently affecting individuals' mobility and quality of life, especially older and vulnerable people.

5. Physical inactivity

The COVID-19 pandemic is an unprecedented, global, public health crisis. Entire populations have been under strict lockdown measures, and, for those infected with COVID-19, they have had to follow strict, mandatory, self-isolation measures. Mandatory isolation, in addition to the decline in the health status described in sections 1-4 (above), is increasing individuals' sedentary behavior. In addition, immobilization and bed rest due to hospitalization and physical inactivity can decrease the ability of organ systems to resist viral infection and increase the risk of damage to the immune, respiratory, cardiovascular, musculoskeletal and CNS.

Confinement and a sedentary lifestyle can cause a rapid deterioration of cardiovascular health and premature deaths among populations of increased cardiovascular risk. Reduced physical activity levels lead to an impaired aerobic capacity at all levels of the oxygen cascade, from the cardiovascular system, including peripheral circulation, to the oxidative function of skeletal muscle. Even a short period of physical inactivity (1-4 weeks) can lead to deficits in cardiovascular function and structure and increased cardiovascular risk factors.

Physical inactivity due to COVID-19 infection can lead to changes in the musculoskeletal system. For example, muscle mass loss occurs quickly, being detectable...
within two days of a period of inactivity. This loss of muscle mass is associated with denervation of muscle fiber. Damage to neuromuscular junctions is mainly explained by the suppression of muscle protein synthesis.\textsuperscript{30,31,33} A simple short-term reduction in physical activity levels significantly impacts skeletal muscle protein and carbohydrate metabolism, causing anabolic resistance and peripheral insulin resistance. Peripheral insulin resistance induced by short-term inactivity in skeletal muscle and adipose tissue, with consequent accumulation of triglycerides in the liver, can lead to hepatic insulin resistance and dyslipidemia. With regard to the endocrine system, physical inactivity affects glucose homeostasis and reduces insulin sensitivity. Physical inactivity is associated with fat deposition, associated with systemic inflammation and activation of antioxidant defenses, exacerbating muscle loss.\textsuperscript{31}

Due to COVID-19, hospitalization is more prevalent in older adults and vulnerable people. These individuals may be more likely to have cardiometabolic diseases, as well as frailty.\textsuperscript{2,3,33} A transition from active-to-sedentary and sedentary behaviour leads to slower gait speed and deficits in the mobility of healthy older adults and people with neurological disorders.\textsuperscript{34,35,36,37,38}

**DISCUSSION**

We have discussed, with some evidence how health and cardiorespiratory issues, hospitalization and physical inactivity due to COVID-19 may affect human gait and balance control. Although there is no direct evidence showing that COVID-19 would affect human motor control, brain damage resulting from COVID-19 infection is plausible affecting the planning and organization of movement outputs. As stated in section 1, some neurological impairments were caused by the COVID-19 infection. Thus, impairments in brain structure and function, such as thalamus and brainstem, directly affect human movement.\textsuperscript{39} The thalamus and brainstem are essential for controlling motor tasks, such as posture and gait. The brainstem is involved in the automatic process of the regulation of postural muscle tone and postural reflexes, and CNS structures seem to be involved in the cognitive process of postural maintenance when humans are learning new motor skills or need to adapt their posture.\textsuperscript{40,41} Such assumptions are supported by data from neurological populations, such as Parkinson’s disease and thalamic disease, where these patients show deficits in postural and gait control when these areas are affected.\textsuperscript{42,43,44,45}

Similarly, neurological COVID-19-related symptoms might also affect motor control. Myalgias may acutely impair the movement execution. Previous data indicates that pain is related to gait disturbances.\textsuperscript{46,47} Myalgias is therefore presumably affected by peripheral and central features also involved in motor control. Also, COVID-19 sensorial-related impairments (e.g. anosmia, paresthesia) could affect motor control. Sensorial information is essential to cognitive control of human movement, as well as movement planning, organization, and execution.\textsuperscript{48} Therefore, if the quality and processing of sensorial information is impaired, the motor performance (e.g., gait) is also affected.\textsuperscript{40}

Mental health issues are also associated with a decline in motor control. Experimental data indicated that anxiety affects the efficiency of tasks that require relatively high levels of attention.\textsuperscript{49} The interference of anxiety and depression on gait control is also observed in the literature.\textsuperscript{50,51} The most common changes in gait control exhibited by people who have anxiety include slower walking speed, shorter step length, reduced cadence, and dysfunction in balance and mobility.\textsuperscript{52} Similarly to anxiety,
depression also affects the gait and posture control, as well as spatial-temporal characteristics of human gait. Depression and falls have a bidirectional relationship. Older adults who experienced falls are twice as likely to be depressed. The interplay relationship between depression and gait/postural impairments, which can result in falls, is explained by the underlying mechanism of depression and motor impairments. Both depression and impairments in gait/posture control are mediated through cognitive, sensory, and motor pathways. Therefore, impairments caused by COVID-19 on CNS may result in serious consequences to mental health, such as the development of anxiety and depression, by affecting brain areas and pathways also involved in motor control.

As mentioned in section 3, cardiorespiratory complications caused by COVID-19 may also affect balance and gait control. Individuals with acute cardiovascular diseases caused by the COVID-19 infection may be more prone to periods of prolonged inactivity: bed rest, reduced number of steps and sitting for long periods of time. This prolonged period of physical inactivity contributes to the reduction of muscle mass and strength, as well as a decline in cardiorespiratory fitness. It is possible that physical inactivity is associated with limitations of static balance, causing a decline in gait speed, as well as walking speed, which corresponds to a robust indicator of health status. This in turn is a strong predictor of morbidity and mortality, mainly in older adults.

It is well-known that the impact of hospitalization can negatively affect mobility among older adults. A study of 959 hospitalized patients aged over 65 years showed that younger patients and longer LoS (among other factors) were associated with mobility decline. This mobility decline is more accentuated in older adults, coinciding with the average age of hospitalized patients due to COVID-19.

In summary, the numerous neurological complications associated with COVID-19 are likely to be associated with impairments in motor control, resulting in poor motor behaviour. Drastic consequences of COVID-19 might occur in the functionality and independence of patients, mainly when accompanied by other factors, such as aging and/or the presence of comorbidities. However, the interpretation regarding the COVID-19 effect on motor control should be treated cautiously since it is still early to have a consistent overview of the long-term neurological, mental health and cardiorespiratory issues caused by COVID-19.

 Although the consequences of COVID-19 extend to different age groups, presumably, such consequences may manifest more often in older and vulnerable populations. Even healthy ageing is associated with typical declines in neurological and cardiorespiratory functions, which are reflected in mental health issues, decreased physical activity levels and increased risk of falling. These age-related characteristics are examples of why WHO have recognized older adults as a “vulnerable” population with regards to COVID-19. In combination with the latter, there is a relatively higher number of hospitalization, readmission and deaths related to this population. Reasonably, the potential direct and indirect effects of COVID-19 on motor control may be more prominent in older people than in young adults. Since the declines on multi-systems are even more pronounced in vulnerable populations, the consequences of COVID-19 might drastically affect their use of internal resources, as well as their capacity to effectively allocate such resources during a motor task.

A multidisciplinary approach should be encouraged (including psychologists, neurologists, physiotherapists and exercise physiologists) for patients who were
hospitalised as soon as they are discharged from the hospital settings. Regarding the serious impact on the cardiorespiratory system caused by COVID-19, a program focusing on improving the symptoms of dyspnea, reducing possible complications, minimizing disabilities and preserving physical function should be encouraged. Allied-health professionals should focus on gradual recovery models in order to promote patients’ return to their activities in society as soon as possible. Considering the average age of patients hospitalized due to COVID-19 (59 years) and the average length of hospital stay, early mobilization should be considered to minimize the negative impacts on mobility and motor control.

CONCLUSION

Respecting individuals’ limitations and regardless of individuals’ ages, a physical activity program should be encouraged and prescribed. Jimenez-Pavon and colleagues presented a special commentary giving details about how physical exercise can work as a therapy against mental and physical consequences of COVID-19. These exercises should be adjusted for older and vulnerable people to reduce the deficits caused by COVID-19. Either regular face-to-face protocols (for countries which do not have any more lockdown restrictions, or if these restrictions were eased) and/or via telehealth (for countries which are still dealing with lockdown measures, for example, Brazil and the United States) are to be encouraged in order to manage the deficits caused by neurological, mental, cardiorespiratory issues, hospitalization, and physical inactivity.

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REFERENCES


