



Commentary

COVID-19: A pandemic that threatens physical and mental health by promoting physical inactivity



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ABSTRACT

Ever since the outbreak of Coronavirus disease 2019 (COVID-19) in late 2019, it has killed millions of people worldwide. Even people not stricken by this disease are not spared from its negative economic, social, and health-related drawbacks. This commentary provides insight into the potential mechanisms involved in the development of depression and emotional negativity escalating during the current pandemic. In particular, preventive measures of COVID-19, such as staying at home, are sedentarism measures that decrease physical activity. Physical inactivity alters gut microbiome structure in a fashion that promotes gut dysbiosis and flaring of systemic inflammation, leading to the buildup of body fat. Obesity, which contributes to a trail of health-depleting disorders, furthers gut microbial disintegration while fat tissue stimulates the release of cytokines, promotes metabolic resistance, and alters signaling involved in the production of antioxidants. As a result, the body gets flooded by toxic molecules such as pro-inflammatory mediators, free radicals, and advanced glycation end products. These toxic molecules alter cellular function in all body tissues, including those of the brain. Neuroinflammation is associated with progressive declines in cognitive and motor functions along with dysregulation in emotions. Counteracting the sedentarism enforced by the COVID-19 pandemic through the participation in suitable indoors activities and the intake of healthy food is likely to protect against or revert physiological impairments that may affect people retreating to their homes during the current crisis, eventually restoring physical and mental health.

Coronavirus disease 2019 (COVID-19) is a highly contagious viral infection.¹ It is transmitted among humans through droplet and physical contact, which allow severe acute respiratory syndrome-coronavirus-2 (SARS-Cov-2) to bind Angiotensin-Converting Enzyme (ACE) II receptors and enter the respiratory tract to evoke pneumonia and systemic organ failure leading to premature death in around 15% of patients.^{1,2} Research reports the expression of ACE-II receptors in gastrointestinal enterocytes, presence of SARS-Cov-2 RNA in the feces of affected patients, and increased COVID-19-related mortality in people with gut microbiome alterations²—mostly because of immune failure induced by toxic metabolites of endobacteria.^{3,4} Imbalance of gut microbial structure is associated with intestinal injury allowing bacterial endotoxins to get access to the blood stream and remotely affect several organs including the brain resulting in psychological and cognitive alterations.^{5,6}

The lethality associated with the evolving COVID-19 crisis has forced most governments to enforce strict social distancing measures in order to minimize the chances of infection transmission.^{4,7} These lockdown measures largely require citizens to stay at home and avoid going out except for buying foods and medicines or performing very vital work activities.⁸ Staying at home entails a remarkable decrease in the level of physical activity among a large sector of the population in most communities due to a significant increase in sedentary behaviors,⁹ which pertain to stopping work temporarily or working online; having lower chances for walking and exercising e.g., on the streets or in public parks; and allocating more time for social media and television (TV) watching, which are commonly accompanied by eating not related to hunger.^{10,11} In fact, longitudinal data from China indicate that the COVID-19

outbreak is associated with prolonged sleeping time and decreased physical activity among young groups (< 35 years).¹²

Depression, anxiety, distress, and fear constitute most COVID-19-related emotional responses, which may result in emotional dysregulation and negative social behaviors.^{4,13} Dysfunctional emotions are associated with maladaptive behaviors (e.g., illicit drug use) and poor quality of life.¹⁴ A recent systematic review shows that fear of contracting viral infections and social isolation associated with the tight social distancing measures heighten emotional negativity and feelings of loneliness, eventually increasing the risk for suicide among people witnessing great pandemics such as SARS-CoV 2002.¹³ In addition to economic recession, lack of resources (e.g., food supply), lack of emotional support associated with distancing measures,⁴ we believe that lack of physical activity associated with staying at home during the current pandemic may considerably, in part, heighten emotional negativity in a manner that may alter body immunity and increase the risk for contracting COVID-19 infection. In this light, the current commentary raises the emerging concern as to whether skeletal muscle disuse linked to the global COVID-19-related lockdown measures enforced by most countries would be associated with physical and mental drawbacks (Fig. 1).

Physical inactivity may contribute to negative moods via several facets. On one hand, sedentary life-style may affect mental health by reshaping the structure of resident gut microflora,^{4,15} which drastically shifts to obesogenic colonization patterns resulting in increased production of inflammation markers and free radicals,⁷ which play a major role in the development of mental disorders (e.g., depression) as well as physical disorders (e.g., insulin resistance and obesity). These physical

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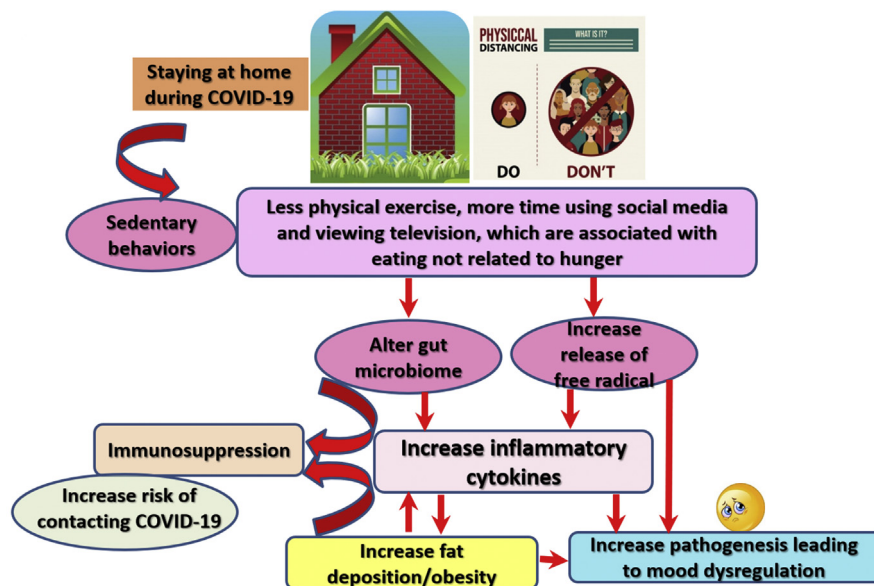


Fig. 1. Schematic illustration of the association between staying at home during the COVID-19 pandemic as a sedentary behavior and gut microbiome alteration resulting in heightened inflammation, weight gain/obesity, and the development of depression and negative emotions.

disorders are further associated with negative mood states.^{6,16–18} Results of high-throughput sequencing of 16s rRNA gene uncover significant differences in 11 gut genera between sedentary and active women. The latter express higher abundance of bacterial species that promote healthy functioning of the host such as *Faecalibacterium prausnitzii*, *Roseburia hominis* and *Akkermansia muciniphila*, which correlate with key indices of body composition such as body fat percentage and muscle mass.⁴ Alterations in the adipokine profile prompt adipose tissue dysfunctions to activate macrophages and increase the release of cytokines resulting in a chronic state of inflammation.^{4,19} Among physiological processes affected by this scenario, glucose and lipid metabolism gets strongly impaired as a result of decreased sensitivity of tissues involved in glucose uptake (e.g., skeletal muscle) to insulin as a result of the blocking effects of cytokines.⁴ Glycemic dysregulation induces the production of advanced glycation end products (AGEs) through non-enzymatic binding of reducing sugars to cellular protein and lipid structures. AGEs accelerate inflammatory reactions and oxidative stress through their binding to several cell-surface receptors.^{6,7}

Cumulative knowledge denotes a major effect of inflammation—induced by physical inactivity as well as by pathologies embroiled in various physical health conditions (including COVID-19)—in the development of depressive disorders. In this respect, research reports a higher prevalence of depression and anxiety in people with high fat mass.^{18,19}

From another perspective, physical exercise promotes cellular regenerative capacity through activation of adenosine monophosphate-activated protein kinase (AMPK) and nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathways. AMPK and Nrf2 regulate cellular activities involved in the cleavage of free radicals, production of internal antioxidants, activation of autophagy, regulation of metabolism, and DNA repair resulting in better tolerance to constant changes and higher resilience to environmental aggressions such as virulent infections.⁷ Hence, lack of physical activity deprives the body of the resilience granted by the detoxifying effects of AMPK and Nrf2, which entails an increased likelihood for developing pathologies that underlie various diseases such as immunosuppression^{4,7}—essential for the development of COVID-19.³ In this regard, a meta-analytic review comprising 193,166 participants from 13 cross-sectional and 11 longitudinal studies reports a higher occurrence of depressive disorders among sedentary participants (RR = 1.25; CI: 1.16–1.35). Subgroup analysis based on the type of

sedentary behaviors resulted in (RR = 1.13; CI: 1.06–1.21) and (RR = 1.22; CI 1.10–1.34) for TV viewing and computers/internet use for a long time, respectively.¹¹ On the other side, physical exercise is increasingly used as an effective nonpharmacologic treatment for depression with a recorded efficacy both as a monotherapy and in combination with antidepressant drugs.¹⁸

Staying at home during the COVID-19 crisis is associated with a considerable rise in domestic violence as indicated by 20%, 25% and 30% increase of calls to the Domestic Violence Helplines during the first week following announcement of the confinement in one region of Spain, the United Kingdom, and Cyprus, respectively.⁸ This might be a read out for negative emotions that develop secondary to social isolation, the uncertainty associated with life during the pandemic,⁴ and physical inactivity.¹¹ On the other hand, engaging in organized physical activity is documented to reduce anxiety, restlessness, irritability, and aggression in people with dementia, who express age-related reduction in the levels of physical activity.¹⁰

Based on the aforementioned background, physical inactivity may alter body composition (increasing fat mass) in a fashion that promotes the development of emotional negativity. Therefore, efforts directed toward the enhancement of mental health during the current pandemic should discourage physical inactivity, especially in highly distressed individuals. Participating in a regular, structured physical activity indoors may be a multidimensional strategy to revert alterations in gut microbiota, body composition, and mood that result from prolonged home stay imposed by the COVID-19 crisis.⁴ Dietary modifications that involve less intake of high-caloric food and increased consumption of low glycemic-index foods or going on dietary restriction may complement the effect of exercise both on body composition, physical health, and on mental status.⁴

Submission statement

This manuscript has not been published and is not under consideration for publication elsewhere.

Authors’ contributions

A.M.A and H.K wrote and edited the manuscript.

Conflict of interest

The authors have no conflicts of interest to declare.

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