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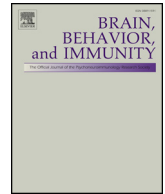
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The impact of nutrition on COVID-19 susceptibility and long-term consequences

Michael J. Butler^a, Ruth M. Barrientos^{a,b,c,d,*}^a Institute for Behavioral Medicine Research, Ohio State University, Columbus, OH, United States^b Department of Psychiatry and Behavioral Health, Ohio State University, Columbus, OH, United States^c Chronic Brain Injury Program, Discovery Themes Initiative, The Ohio State University, Columbus, OH, United States^d Department of Neuroscience, Ohio State University, Columbus, OH, United States

A B S T R A C T

While all groups are affected by the COVID-19 pandemic, the elderly, underrepresented minorities, and those with underlying medical conditions are at the greatest risk. The high rate of consumption of diets high in saturated fats, sugars, and refined carbohydrates (collectively called Western diet, WD) worldwide, contribute to the prevalence of obesity and type 2 diabetes, and could place these populations at an increased risk for severe COVID-19 pathology and mortality. WD consumption activates the innate immune system and impairs adaptive immunity, leading to chronic inflammation and impaired host defense against viruses. Furthermore, peripheral inflammation caused by COVID-19 may have long-term consequences in those that recover, leading to chronic medical conditions such as dementia and neurodegenerative disease, likely through neuroinflammatory mechanisms that can be compounded by an unhealthy diet. Thus, now more than ever, wider access to healthy foods should be a top priority and individuals should be mindful of healthy eating habits to reduce susceptibility to and long-term complications from COVID-19.

COVID-19 is a respiratory disease caused by the novel coronavirus, SARS-CoV-2, that has reached pandemic status. While COVID-19 affects all groups, severe pathology and mortality is disproportionately highest in the elderly, underrepresented minorities (blacks/African Americans and Latinos), and/or in those with underlying comorbidities. Obesity and type 2 diabetes, two prominent risk factors for severe COVID-19, may underlie the health disparity observed in these populations (Dietz and Santos-Burgoa, 2020; Dharmasena et al., 2016). The high prevalence of these risk factors, worldwide, but especially in the U.S. and other developed countries, is likely driven by increased consumption of the typical Western diet (WD) consisting of high amounts of saturated fat (HFD), refined carbohydrates and sugars, and low levels of fiber, unsaturated fats, and antioxidants (Cordain et al., 2005).

The WD, which is high in saturated fatty acids (SFAs), can lead to chronic activation of the innate immune system and an inhibition of the adaptive immune system. Briefly, excessive SFA consumption can induce a lipotoxic state and activate the innate immune system via activation of toll-like receptor 4 expressed on macrophages, dendritic cells, and neutrophils. This triggers activation of canonical inflammatory signaling pathways that produce proinflammatory mediators and other effectors of the innate immune system (Roger and Calder, 2018). Furthermore, consumption of a HFD in mice increased macrophage infiltration to lung tissue, specifically in the alveoli (Tashiro et al.,

2017). This is especially relevant to COVID-19 patients given the high rate of infection among lung alveolar epithelial cells and the involvement of lung tissue inflammation and alveolar damage in COVID-19 pathology (Xu et al., 2020).

In addition to innate immunity, WD or HFD consumption inhibits T and B lymphocyte function in the adaptive immune system, potentially via an increase in oxidative stress. Specifically, HFD-induced oxidative stress impairs T and B cell proliferation and maturation, and induces B cell apoptosis, which contributes to B cell immunodepression (Green and Beck, 2017). This has important implications in host defense against viruses. Previously, HFD-fed mice showed increased lung pathology due to influenza infection and a delayed adaptive immune response (Green and Beck, 2017). Moreover, HFD-fed mice have memory T cell deficits against influenza, exhibited by impaired response to antigen presentation and clearance of the virus (Green and Beck, 2017). Therefore, consumption of a WD significantly impairs adaptive immunity while ramping up innate immunity, leading to chronic inflammation and severely impairing host defense against viral pathogens. Given that the elderly and African American communities have a greater inherent sensitivity to inflammatory modulators, consumption of unhealthy diets by these groups could pose an amplified risk to severe COVID-19 pathology. Moreover, T and B cell counts were also significantly lower in patients with severe COVID-19 (Qin et al., 2020);

* Corresponding author at: Institute for Behavioral Medicine Research, and Department of Psychiatry and Behavioral Health, Ohio State University, 460 Medical Center Drive, Columbus, OH 43210, United States.

E-mail address: ruth.barrientos@osumc.edu (R.M. Barrientos).

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thus, there could be a potential interaction between WD consumption and COVID-19 on adaptive immunity impairment.

As mentioned earlier, the high rates of obesity and diabetes among minority populations may account, at least in part, for the health disparities observed in response to COVID-19 in these groups (Dharmasena et al., 2016). Data suggest that minorities have increased barriers to access healthy food choices and nutritional education, likely due to increased rates of poverty and decreased access to quality healthcare in the U.S. (Dharmasena et al., 2016). Thus, the access to healthy, fresh whole foods should be made more readily available to those who cannot normally afford it in order to relieve the chronic disease burden in these communities. Indeed, studies show that consuming healthy foods has a rapid anti-inflammatory effect, even in the presence of obesity pathology (Connaughton et al., 2016). A change in these policies could also have long-term benefits on disease prevention, including COVID-19, by increasing the efficacy of vaccines, given that vaccines have been shown to be less effective in obese individuals (Green and Beck, 2017).

Given that, even in the most at-risk populations, the vast majority of COVID-19 patients are expected to recover, there could be a number of indirect long-term consequences of the disease. In addition to potential long-term lung damage, the possible impacts on neurological function are not insignificant. This is because it is known that peripheral inflammatory events can evoke an exaggerated and persistent neuroinflammatory response in vulnerable individuals. Furthermore, there is a well-known association between pathological levels of neuroinflammation and neurodegenerative diseases such as Alzheimer's and other forms of dementia. Thus, profound challenges of the immune system like COVID-19 could potentiate the neuroinflammatory response and disease onset in these vulnerable groups. In support of this notion, there have been instances of dementia in the elderly following viral infection, including respiratory viruses such as influenza (Honjo et al., 2009).

In sum, it is critical to consider the impact of lifestyle habits, such as consumption of unhealthy diets, on the susceptibility to COVID-19 and recovery. Furthermore, the large number of people that will recover from COVID-19 may lead to a spike in chronic medical conditions that could be further exacerbated by unhealthy diets or in vulnerable

populations. Therefore, it is our recommendation that individuals refrain from eating foods high in saturated fats and sugar and instead consume high amounts of fiber, whole grains, unsaturated fats, and antioxidants to boost immune function (Connaughton et al., 2016).

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