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Neurological Sequelae of Post-COVID-19 Fatigue: A Narrative Review of Dipeptidyl Peptidase IV-Mediated Cerebrovascular Complications

(2024) *Current Issues in Molecular Biology*, 46 (12), pp. 13565-13582.

DOI: 10.3390/cimb46120811

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Abstract
Coronavirus disease 2019 (COVID-19) has been a global pandemic affecting millions of people's lives, which has led to 'post-COVID-19 fatigue'. Alarmingly, severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) not only infects the lungs but also influences the heart and brain. Endothelial cell dysfunction and hypercoagulation, which we know occur with this infection, lead to thrombo-inflammation that can manifest as many myriad cardio-cerebrovascular disorders, such as brain fog, fatigue, cognitive dysfunction, etc. Additionally, SARS-CoV-2 has been associated with oxidative stress, protein aggregation, cytokine storm, and mitochondrial dysfunction in neurodegenerative diseases. Accordingly, the identification of molecular targets involved in these actions could provide strategies for preventing and treating this disease. In particular, the very common enzyme dipeptidyl peptidase IV (DPPIV) has recently been identified as a candidate co-receptor for the cell entry of the SARS-CoV-2 virus with its involvement in infection. In addition, DPPIV has been reported as a co-receptor for some viruses such as Middle East respiratory syndrome-coronavirus (MERS-CoV). It mediates immunologic reactions and diseases such as type 2 diabetes mellitus, obesity, and hypertension, which have been considered the prime risk factors for stroke among other types of cardio-cerebrovascular diseases. Unlike angiotensin-converting enzyme 2 (ACE2), DPPIV has been implicated in aggravating the course of infection due to its disruptive effect on inflammatory signaling networks and the neuro–glia–vascular unit. Regarding the neurological, physiological, and molecular grounds governing post-COVID-19 fatigue, this review focuses on DPPIV as one of such reasons that progressively establishes cerebrovascular grievances following SARS-CoV infection. © 2024 by the authors.

Author Keywords
cerebrovascular; dipeptidyl peptidase IV; neurodegenerative diseases; post-COVID-19 fatigue; SARS-CoV-2

Index Keywords
angiotensin converting enzyme 2, D dimer, dipeptidyl peptidase IV, ferritin, glial fibrillary acidic protein, glucagon like peptide 1, granulocyte colony stimulating factor, immunoglobulin enhancer binding protein, interleukin 17, interleukin 1beta, interleukin 2, interleukin 6, interleukin 7, interleukin 8, tumor necrosis factor, vascular cell adhesion molecule 1, vasculotropin; ageusia, anosmia, anxiety, cardiovascular disease, cerebrovascular accident, cerebrovascular disease, cognitive defect, coughing, cytokine storm, degenerative disease, depression, dizziness, dyspnea, endothelial dysfunction, fatigue, genetic variability, Guillain Barre syndrome, headache, heart palpitation, human, hyperglycemia, inflammatory bowel disease, long COVID, memory disorder, molecular docking, myocarditis, nausea and vomiting, neurologic disease, non insulin dependent diabetes mellitus, oxidative stress, pandemic, protein aggregation, Review, thorax pain, thromboembolism, thromboinflammation

Chemicals/CAS
dipeptidyl peptidase IV, 54249-88-6; ferritin, 9007-73-2; glucagon like peptide 1, 89750-14-1; interleukin 2, 85898-30-2; interleukin 8, 114308-91-7; vasculotropin, 127464-60-2

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Publisher: Multidisciplinary Digital Publishing Institute (MDPI)

ISSN: 14673037
CODEN: CMBIF
Language of Original Document: English
Abbreviated Source Title: Curr. Issues Mol. Biol.
2-s2.0-85213435472
Document Type: Review
Publication Stage: Final
Source: Scopus