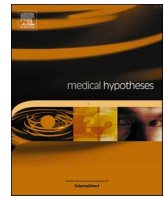




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## Correspondence

## Calcitonin gene-related peptide: A biomarker for stroke in SARS-CoV-2 infection?



## ARTICLE INFO

## Keywords

COVID-19  
CGRP  
Ischemic stroke  
CBF

## ABSTRACT

COVID-19 infection was mainly associated with respiratory symptoms, but lately, ischemic stroke (IS) has been reported in several cases. The incidence of IS in SARS-CoV-2 infection is increasing, and its mechanism is still not fully understood. Calcitonin gene-related peptide (CGRP) -the abundantly expressed protein in the peripheral and central nervous system- showed low expression in SARS-CoV-2 patients. This peptide is strongly implicated in regulating cerebral blood flow (CBF) and improving neurological deficits after cerebral arterial occlusion. We assume that a possible interplay between the low circulating levels of CGRP may affect CBF, thus worsening the symptoms of IS in SARS-CoV-2 patients.

## Introduction

The association of Ischemic stroke (IS) and SARS-CoV-2 infection was reported with an occurrence of up to 4.9% during initial hospitalization [1]. However, the exact mechanism underlying these lesions remains unclear.

Calcitonin gene-related peptide (CGRP) is a vasoactive peptide released from sensory nerves and involved in attenuating cerebral ischemia, CGRP regulates the subfamilies of mitogen-activated protein kinase [2] and promote cell proliferation through the Wnt/ $\beta$ -catenin pathway as seen in the figure [3]. Therefore, CGPR can improve motor and sensitive functions after middle cerebral artery occlusion, as reported in an *in vivo* study [3]. Furthermore, besides its neuroprotective effects, CGRP has an anti-inflammatory role by reducing interleukin-2 production [4].

Recently a published case report by Aradi et al. 2019 indicated an association between CGRP antagonists and IS in young women; therefore, the decreased levels of CGRP might suppress its protective vasodilatory effect in cerebral arteries [5].

Interestingly, autopsies of SARS-CoV-2 infection cases revealed that nerve tissues are damaged [6]. In addition, Ochoa-Callejero et al. 2021 [4] observed that serum CGRP levels were significantly lower in 57 SARS-CoV-2 patients. Consequently, low CGRP levels might be correlated with cerebral vasospasm and ischemic lung lesions.

All the presented data herein were relevant to the conclusion that the low CGRP levels in SARS-CoV-2 infections might be a culprit in the ischemic process and worsening the brain arterial occlusion, thus leading to IS.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

The authors are thankful for biorender.com for creating the figures and graphical abstract with license number (YJ23EWE1KS).

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Abbreviations: CGRP, Calcitonin gene-related peptide; CBF, Cerebral blood flow.

<https://doi.org/10.1016/j.mehy.2022.110807>

Received 29 November 2021; Received in revised form 11 January 2022; Accepted 10 February 2022

Available online 23 February 2022

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