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Response to Letter to the Editor from Josef Finsterer: “Explaining Long COVID: A Pioneer Cross-Sectional Study Supporting the Endocrine Hypothesis”

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Dear J. Finsterer,

We have read your letter with great interest [1]. We appreciate the insightful commentary provided by the reader regarding our recent article investigating the endocrine implications in long COVID patients [2].

The author highlighted the importance of considering chronic stress and its potential impact on the hypothalamic-pituitary-adrenal (HPA) axis in long-COVID patients. In a recent meta-analysis, the pooled prevalence of depression and anxiety among patients with long-COVID syndrome was estimated to be 23% [3]. In this context, it is recognized that chronic stress would exacerbate the cortisol response, potentially leading to a pseudo-Cushing state [4]. However, it's crucial to emphasize that our study primarily focused on evaluating corticotrophic insufficiency. Consequently, the inclusion of stress assessments might have resulted in a diminished number of patients diagnosed with corticotrophic insufficiency due to the masking effect of stress-induced cortisol elevation, instead of a higher prevalence of corticotrophic insufficiency.

The concern regarding the potential central nervous system (CNS) involvement in causing pituitary insufficiency in the acute stage of SARS-CoV-2 infection (SC2I) is indeed valid. Determining the actual occurrence rate of hypophysitis following COVID-19 proves to be challenging [4]. There are only some cases that were reported, with one case of infundibuloneuro-hypophysitis [5]. However, our study focused on evaluating endocrine function during the post-infection period. Pituitary hormone determination and MRI scans in the acute stage of SC2I were not within the scope of our study.
The author also highlighted a discrepancy in the exclusion criteria. All patients included in the study underwent thyroid assessment, with results values within normal limits. Regarding diabetes, patients were evaluated before the Insulin Tolerance Test, and they exhibited normal glycemic parameters in order to achieve hypoglycemia. While some patients had a history of certain conditions, these were well-controlled and did not present significant deviations from normal values.

For the final point, the alternative hypotheses proposed to explain long-COVID are indeed critical considerations in understanding the multifaceted nature of this syndrome [6]. While our study primarily focused on exploring the endocrine hypothesis, we acknowledge the importance of addressing these alternative mechanisms comprehensively.

The multifaceted nature of the virus, with its ability to affect multiple tissues and organs through various mechanisms, underscores the complexity of long-COVID [7]. While endocrine involvement may play a role in some aspects of long COVID, it is evident that the syndrome encompasses a wide array of manifestations that cannot be solely attributed to endocrine dysfunction. Therefore, understanding long COVID requires a comprehensive exploration of the interplay between viral pathophysiology, immune dysregulation, inflammatory processes, and other potential mechanisms, reflecting the intricate nature of this condition [8].

In summary, we appreciate the author’s insightful comments on our study. Various hypotheses exploring these symptoms were raised, however a closer examination of the residual symptoms experienced by these patients reveals that some closely resemble the symptoms associated with anterior pituitary deficiencies, particularly corticotroph or somatotroph. Consequently, the endocrine hypothesis involving anterior pituitary insufficiency was considered to explain long-COVID syndrome.
Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

Dr ACH Taieb drafted the manuscript. All authors read and approved the final manuscript.

Data availability statement

No data were used for this manuscript.

References:


