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Letter to the Editor

## **Prospective Studies are needed to Assess Whether Sars-Cov-2 Vaccinations Change Serum/CSF Biomarkers in Neurologic Disease**

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We read with interest the article by Jacono *et al.* on a study of 110 vaccinees with neurological disease, such as multiple sclerosis (MS), Alzheimer's disease, Parkinson's disease, frontotemporal dementia, and vascular dementia, regarding the question whether SARS-CoV-2 vaccinations induce a response in the serum or cerebrospinal fluid (CSF), as assessed by various inflammatory and non-inflammatory parameters [1]. No signs of neuro-inflammation, axonal loss, systemic inflammation were found in these patients after SARS-CoV-2 vaccinations [1]. The study is compelling, but has limitations that are cause of concerns and should be discussed.

The main limitation of the study is that only a limited number of CSF parameters was evaluated. The study only included the parameters CSF protein, glucose, number of cells, and level of neurofilament light chains [1]. The study did not include cytokines, chemokines, intrathecal immunoglobulins, neopterin, tau, A $\beta$ 1-42, glial factors, and 14-3-3 [2]. Thus, the methods applied are not appropriate to approach the aims of the study to evaluate whether SARS-CoV-2 vaccinations induce serum or CSF changes in patients with neurological disorders.

A second limitation of the study is that it was not mentioned how many of the included patients had a previous SARS-CoV-2 infection and how many had previous central nervous system (CNS) disease other than those included. From various CNS disorders (e.g., meningitis, encephalitis, ADEM, NMO) it is known that they may change CSF composition, even over a long period of time. These include infectious, toxic, immunologic, and neoplastic CNS diseases.

Since the results strongly depend on the latency between last vaccination and onset of clinical presentation, it is crucial to know how long after vaccination symptoms developed.

We also should know how pre-existing CSF or serum abnormalities, prior to the vaccination were ruled out. Disregarding whether a patient had neuro-inflammatory or neuro-degenerative disease, it should be ruled out that particularly CSF parameters were already abnormal before the vaccination. It is not comprehensible in this regard why MS patients were included since they often present with abnormal CSF composition without having received a SARS-CoV-2 vaccination.

Overall, the interesting study has limitations that put the results and their interpretation into perspective. Addressing these issues would strengthen the conclusions and could improve the status of the study. Study results are only reliable if it can be guaranteed that pre-morbidities that lead to serum or CSF changes have been sufficiently ruled out.

### **Acknowledgements**

#### **Statement of Ethics:**

- The study was approved by the institutional review board (responsible: Finsterer J.) at the 4<sup>th</sup> November 2022.
- Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

**Data Availability Statement:** Data that support the findings of the study are available from the corresponding author.

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**Author Contribution:** JF: design, literature search, discussion, first draft, critical comments, final approval.

**Disclosures:** The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Compliance with Ethics Guidelines:** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

**Keywords:** SARS-CoV-2, Vaccination, CNS, Biomarker, CSF

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### References

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