



## UKE Paper of the Month Juni 2023

### Brain imaging and neuropsychological assessment of individuals recovered from a mild to moderate SARS-CoV-2 infection

Marvin Petersen, Felix Leonard Nägele, Carola Mayer, Maximilian Schell, Elina Petersen, Simone Kühn, Jürgen Gallinat, Jens Fiehler, Ofer Pasternak, Jakob Matschke, Markus Glatzel, Raphael Twerenbold, Christian Gerloff, Götz Thomalla, Bastian Cheng

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#### ABSTRACT:

As severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infections have been shown to affect the central nervous system, the investigation of associated alterations of brain structure and neuropsychological sequelae is crucial to help address future health care needs. Therefore, we performed a comprehensive neuroimaging and neuropsychological assessment of 223 nonvaccinated individuals recovered from a mild to moderate SARS-CoV-2 infection (100 female/123 male, age [years], mean  $\pm$  SD,  $55.54 \pm 7.07$ ; median 9.7 mo after infection) in comparison with 223 matched controls (93 female/130 male,  $55.74 \pm 6.60$ ) within the framework of the Hamburg City Health Study. Primary study outcomes were advanced diffusion MRI measures of white matter microstructure, cortical thickness, white matter hyperintensity load, and neuropsychological test scores. Among all 11 MRI markers tested, significant differences were found in global measures of mean diffusivity (MD) and extracellular free water which were elevated in the white matter of post-SARS-CoV-2 individuals compared to matched controls (free water:  $0.148 \pm 0.018$  vs.  $0.142 \pm 0.017$ ,  $P < 0.001$ ; MD [10–3 mm<sup>2</sup>/s]:  $0.747 \pm 0.021$  vs.  $0.740 \pm 0.020$ ,  $P < 0.001$ ). Group classification accuracy based on diffusion imaging markers was up to 80%. Neuropsychological test scores did not significantly differ between groups. Collectively, our findings suggest that subtle changes in white matter extracellular water content last beyond the acute infection with SARS-CoV-2. However, in our sample, a mild to moderate SARS-CoV-2 infection was not associated with neuropsychological deficits, significant changes in cortical structure, or vascular lesions several months after recovery. External validation of our findings and longitudinal follow-up investigations are needed.

#### STATEMENT:

Our research reveals vital insights into the enduring impacts of SARS-CoV-2 on the brain, using a large dataset with high-quality neuroimaging and in-depth clinical phenotyping. We were able to precisely characterize a post-infection imaging signature which is coherent with an ongoing neuroinflammatory response. Despite this, we found no substantial cognitive deficits in recovered patients. These findings call for further studies linking brain changes and potential neuropsychiatric effects of COVID-19, shedding light on the intricate links between disease and symptoms. This work is a prime example of cross-disciplinary collaboration at the University Medical Center Hamburg-Eppendorf, integrating expertise from the Departments of Neurology, Cardiology, Pathology, Psychiatry, and Neuroradiology. Moreover, we incorporated vital data from Hamburg citizens via the Hamburg City Health Study, highlighting both our institution's strength and the broader community's commitment to tackling COVID-19. The paper's high Altmetric score of 1331, as well as the significant social media attention it has drawn on Twitter (over 3200 tweets and 1 million views), reflect its impact and relevance. It ranks among the top 1% of all research outputs of the same age tracked by Altmetric and PNAS papers, proving its worth as a strong contender for the UKE Paper of the Month.

#### BACKGROUND:

This paper resulted from the cooperation of several UKE departments, the Departments of Psychiatry and Radiology Brigham and Women's Hospital in Boston as well as the Hamburg City Health Study. The effort was led by the Clinical Stroke and Imaging working group of Prof. Dr. Götz Thomalla and PD Dr. Bastian Cheng. The project was part of the PhD thesis of Marvin Petersen. Marvin Petersen and Felix L. Nägele share the first authorship. The project was part of the Sonderforschungsbereich 936 as well as the Schwerpunktprogramm 2041 funded by the DFG.