CORRESPONDENCE

Predominance of visuoconstructive impairment after mild COVID-19?

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TO THE EDITOR:

We have read with great interest the study by de Paula et al., about selective visuoconstructional impairment following mild COVID-19 with inflammatory and neuroimaging findings [1]. The article contributes to the evidence suggesting cognitive and structural brain consequences of SARS-CoV-2 infection at 4.35 ± 2.45 months after the RT-PCR confirmation.

We congratulate the authors on performing this study involving a large cohort of patients with COVID-19 that were evaluated multimodally, including neuroimaging (structural MRI and FDG-PET), blood biomarkers and cognitive assessments after the acute onset of the infection. Research on the neuropsychological performance after SARS-CoV-2 infection is needed to better understand the consequences of COVID-19. Growing body of evidence confirms the presence of cognitive, neuroimaging and pathological implications of SARS-CoV-2 infection [2–5], and this study adds scientific contributions to the field. However, we would like to highlight some results from the present study that captured our attention.

The authors reported a frequent impairment in the Rey-Osterrieth Complex Figure (ROCF) copy. These findings contrast with other studies in the literature on patients after COVID-19. For instance, in our experience, in patients after 9 months from the acute phase, we found no impairment in ROCF copy compared with the normative data, while other cognitive domains such as attention, executive functions and memory showed dysfunction [5]. According to the other case series reported up to date using comprehensive neuropsychological assessment and normative data or healthy controls as reference, cognitive profile in patients after COVID-19 (especially in those reporting cognitive complaints) is usually characterized by a predominant attention/processing speed dysfunction, executive and episodic memory deficits [2, 5, 6]. Conversely, tests such as the copy of a complex figure are largely preserved or only impaired in patients with impairment in several cognitive domains [5, 7]. On the contrary, patients from the present study revealed impairment of ROCF copy in 24% of the sample (shown in Table 1), which is curious in post-COVID patients, especially in the absence of cognitive deficits in other cognitive domains.

Furthermore, using a cutoff of $z < -1.5$ SD, the authors found 24% of impairment in ROCF copy, 5% of impairment in ROCF immediate recall and 7% of impairment in ROCF delayed recall in these post-COVID patients. Following previous studies, the performance in ROCF copy influences ROCF immediate and delayed recall results [8, 9]. When the patient shows impairment in ROCF copy performance, the patient will usually drag the same errors in the subsequent ROCF immediate and delayed recall scores, added to the possible memory errors that may arise. This would generally result in a similar or worse score in these following subtests [10]. It is unexpected to obtain a much better performance in ROCF immediate and delayed recall when ROCF copy is highly impaired (as shown in Table 1 and Supplementary Fig. 1).

Additionally, we observed in Table 1 that the mean score of ROCF (copy) was 34.14 ± 2.95 for the COVID-19 patients and 29.22 ± 4.41 for the control group. Similarly, scores in the ROCF immediate recall and ROCF delayed recall were also higher in the COVID-19 group than in the healthy control group.

It would be of great interest for the readers to share the reference of the Brazilian normative data and the details of the normative study in comparison with the sample enrolled in the study. It would help in the better understanding of the scores of these tests in the population and especially, in the results of the present study. In addition, the details of the neuropsychological test scores in Table 1 should be specified (i.e., whether the scores are raw scores, number of items, seconds, percentiles, etc. is important for the interpretation), as there are some tests with unexpected scores (e.g., Digit Span Forward with a mean score of 51.16).

Finally, the authors conducted a voxel-based brain mapping analysis for T1-MRI and FDG-PET imaging, investigating the correlation between the ROCF score and brain volumes and metabolism. This is a well-known and validated method in research, and results are very valuable to disentangle the mechanisms underlying cognitive deficits in post-COVID patients. However, one of the main issues of this approach is the risk of type I errors due to multiple comparisons because the general linear model is applied to each voxel in the image [11]. Because the authors report some large clusters, especially in white matter volume, we wondered whether these clusters survived an FWE or FDR correction [12].

The study of the neurological consequences of COVID-19 is a rapidly growing research area, and many studies are in progress. For this reason, we believe it is essential to advance in discussing methodological aspects and potential biases of each work to improve the comparability between studies. Thus, our letter aims to raise some methodological aspects to enhance our knowledge on this important issue with great health and social impact.

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AUTHOR CONTRIBUTIONS

JAMG and MDC wrote the original draft. JMG and MY critically reviewed the manuscript for important intellectual content.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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