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José María Trejo-Gabriel-Galán

*Servicio de Neurología, Hospital Universitario de Burgos, Avda. Islas Baleares, 3, 09006 Burgos, Spain*

*E-mail address: jtrejojy@gmail.com*

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## Neuropsychological rehabilitation program for patients with post-COVID-19 syndrome: a clinical experience<sup>☆</sup>



### Programa de rehabilitación neuropsicológica en pacientes con síndrome post-COVID-19: una experiencia clínica

Dear Editor:

Most patients with SARS-CoV-2 infection recover within days or weeks. However, symptoms persist in some 10% of patients.<sup>1</sup> Post-COVID-19 syndrome, as it has been called, is a series of symptoms that appear during or after SARS-CoV-2 infection, persist for longer than 12 weeks, and cannot be explained by other causes. It usually presents as a combination of symptoms that frequently overlap and may fluctuate and change over time, affecting multiple systems.<sup>2</sup>

Patients with post-COVID-19 syndrome may present memory and concentration problems, brain fog, anxiety, and mood disorders.<sup>3</sup> These alterations have a negative impact on the patient's performance in family, social, or work settings. Neuropsychological rehabilitation may help these patients to recover brain function, improve functional capacity, and increase emotional well-being.

In June 2020, Institut Guttmann started an 8-week outpatient neurorehabilitation programme for patients with post-COVID-19 syndrome. The programme includes respiratory therapy, physical therapy, and neuropsychological rehabilitation (mood intervention, compensatory strategies,

and cognitive therapy). Patients received cognitive therapy at home, using the Guttmann NeuroPersonalTrainer® platform (5 sessions/week of one-hour duration). The programme's planning assistant designed the intervention based on pre-treatment assessment results,<sup>4</sup> selecting the tasks to be completed during each session and adjusting the difficulty through a combination of parameters (number of stimuli, type of stimulus, speed of presentation, task duration, etc). The platform's task plan addresses several cognitive domains (attention, memory, executive function, and language, among others).

We present the results from 50 patients with no history of neurological disease who completed our neuropsychological rehabilitation programme between June 2020 and January 2021.

Mean age (SD) was 53.3 (12.78) years (range, 26-76). Women accounted for 54% (n = 27) of the total. Level of education was low ( $\leq 8$  years of formal schooling) in 9 patients, average (9-12 years) in 14, and high ( $\geq 13$  years) in 27. The mean time elapsed between the first positive PCR test and inclusion in the neurorehabilitation programme was 24.18 weeks (SD: 7.91; range, 12-37). A total of 31 patients (62%) were admitted to hospital (either to the intensive care unit or to other wards). Significant differences were observed between hospitalised and non-hospitalised patients in sex ( $P < .001$ ) and age ( $P = .001$ ). Men accounted for 67.7% of hospitalised patients (n = 21), whereas 89.5% (n = 17) of non-hospitalised patients were women. Non-hospitalised patients were younger (mean [SD] of 45.6 years [10.2], vs 58 [11.9] years in hospitalised patients).

Patients were administered a short assessment test battery before and after completion of the neuropsychological rehabilitation programme, including the following tests: forward and backward digit span, Rey Auditory Verbal Learning Test (RAVLT; learning, recall, and recognition), a formal phonemic fluency task (PMR), and the Hospital Anxiety and Depression Scale (HADS). Pre- and post-treatment results were compared with the Wilcoxon test for related samples ( $\alpha < .05$ ). Effect size was calculated with the Pearson correlation coefficient. Effect size was considered small for  $r \approx 0.10$ , median for  $r \approx 0.30$ , and large for  $r \approx 0.50$ .<sup>5</sup>

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In neuropsychological rehabilitation, and in neurorehabilitation in general, observing psychometric changes after an intervention inevitably leads us to question whether these differences reflect a true change (recovery) or rather constitute a consequence of the practice effect (change or improvement resulting from practice or repeated exposure to an assessment test). We attempted to minimise the impact of the practice effect on post-treatment results by correcting raw scores according to the procedure used by Lubrini et al.,<sup>6</sup> which is in turn based on a study by Calamia et al.<sup>7</sup>

In the group of non-hospitalised patients, significant differences were observed between pre- and (corrected) post-treatment scores in the backward digit span ( $P = .048$ ;  $r = 0.32$ ), RAVLT-learning ( $P = .004$ ;  $r = 0.47$ ), RAVLT-recall ( $P = .002$ ;  $r = 0.5$ ), RAVLT-recognition ( $P = .004$ ;  $r = 0.46$ ), HADS-anxiety ( $P = .021$ ;  $r = 0.39$ ), and HADS-depression ( $P = .046$ ;  $r = 0.34$ ). In the group of hospitalised patients, significant differences were observed in RAVLT-learning ( $P = .005$ ;  $r = 0.36$ ), RAVLT-recall ( $P < .001$ ;  $r = 0.5$ ), RAVLT-recognition ( $P = .033$ ;  $r = 0.27$ ), PMR ( $P = .042$ ;  $r = 0.25$ ), HADS-anxiety ( $P = .002$ ;  $r = 0.42$ ), and HADS-depression ( $P = .001$ ;  $r = 0.46$ ).

All patients included in the neuropsychological rehabilitation programme performed better on memory tasks after treatment. Hospitalised patients also performed better on the phonemic fluency task after the intervention (this test is sensitive to alterations in executive control, particularly response initiation and maintenance, inhibition, organisation, cognitive flexibility, and monitoring). Pre-treatment HADS scores revealed symptoms of anxiety and depression in both hospitalised and non-hospitalised patients. After the intervention, the likelihood of presenting symptoms of anxiety or depression decreased significantly.

Our study did not include a control group due to its practical nature and the circumstances surrounding the implementation of the rehabilitation programme. We are aware that this limits the possibility of extrapolating our results on the effectiveness of this intervention. However, our experience suggests that neuropsychological rehabilitation is useful in the treatment of cognitive and mood disorders in patients with post-COVID-19 syndrome. Studies with longer follow-up periods are needed to determine whether improvements persist in the medium and long term.

## Conflicts of interest

Guttmann NeuroPersonalTrainer<sup>®</sup> is in part property of Institut Guttmann. García-Molina, Rodríguez-Rajo, and

Sánchez-Carrión participated in the theoretical and conceptual development of the platform.

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A. García-Molina<sup>a,b,c,\*</sup>, M. Espiña-Bou<sup>a,b,c</sup>,  
P. Rodríguez-Rajo<sup>a,b,c</sup>, R. Sánchez-Carrión<sup>a,b,c</sup>,  
A. Enseñat-Cantallos<sup>a,b,c</sup>

<sup>a</sup> Institut Guttmann, Institut Universitari de Neurorehabilitació adscrit a la UAB, Badalona, Barcelona, Spain

<sup>b</sup> Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Barcelona, Spain

<sup>c</sup> Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain

\* Corresponding author.

E-mail address: [agarciam@guttmann.com](mailto:agarciam@guttmann.com)  
(A. García-Molina).

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