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Original

Prolonged Neurocognitive Consequences of COVID-19 in Workers from the Escuela Politécnica del Litoral of Ecuador

Consecuencias neurocognitivas del COVID-19 prolongado en trabajadores de la Escuela Politécnica del Litoral del Ecuador

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Abstract

Background: Post-SARS-CoV-2 recovery, individuals often experience anxiety, depression, insomnia, and cognitive disorders such as attention and memory deficits, persisting for weeks.

Objective: evaluate cognitive performance, through memory and executive functions in young adults, 12 weeks after recovering from COVID-19 infection.

Method: A retrospective case-control observational study was conducted with 40 COVID-19 recovered subjects and 13 non-infected individuals. The study evaluated executive functions, memory, and attention 12 weeks post-recovery.

Results: The findings reveal that recovered COVID-19 patients exhibit decreased processing speed, increased omission of stimuli, slower reaction times, and impaired ability to recall visuospatial stimuli compared to uninfected individuals. These cognitive deficits were noted weeks following recovery from COVID-19's acute phase.

Conclusions: Recovered individuals show significant cognitive function alterations, particularly in attention and executive functions, 12 weeks post-acute phase. Early detection of these impairments is crucial for timely intervention, essential to prevent further cognitive decline. The study highlights the necessity of prospective research to understand the long-term effects of COVID-19 on previously infected adults. Such insights are vital for developing strategies to maintain the mental health of this population.

Resumen

Introducción: Después de la recuperación del SARS-CoV-2, las personas a menudo experimentan ansiedad, depresión, insomnio y trastornos cognitivos, como déficits de atención y memoria, que persisten durante semanas.

Objetivo: evaluar el rendimiento cognitivo, a través de la memoria y las funciones ejecutivas en adultos jóvenes, 12 semanas después de recuperarse de la infección por COVID-19.

Método: Se realizó un estudio observacional retrospectivo de casos y controles con 40 sujetos recuperados de COVID-19 y 13 individuos no infectados. El estudio evaluó las funciones ejecutivas, la memoria y la atención 12 semanas después de la recuperación.

Resultados: Los hallazgos revelan que los pacientes recuperados de COVID-19 exhiben una menor velocidad de procesamiento, una mayor omisión de estímulos, tiempos de reacción más lentos y una menor capacidad para recordar estímulos visuoespaciales en comparación con los individuos no infectados. Estos déficits cognitivos se observaron semanas después de la recuperación de la fase aguda de COVID-19.

Conclusiones: Los individuos recuperados presentan alteraciones significativas de las funciones cognitivas, particularmente en atención y funciones ejecutivas, 12 semanas post-fase aguda. La detección temprana de estos deterioros es crucial para una intervención oportuna, esencial para prevenir un mayor deterioro cognitivo. El estudio destaca la necesidad de realizar investigaciones prospectivas para comprender los efectos a largo plazo de la COVID-19 en adultos previamente infectados. Estos conocimientos son vitales para desarrollar estrategias para mantener la salud mental de esta población.

Palabras clave: síndrome post-agudo COVID-19, deterioro, funciones ejecutivas.

Introduction

The SARS-CoV-2 pandemic has brought to light a broad array of persistent sequelae, particularly impacting neurocognitive functions. Preliminary studies have noted various neuropsychiatric symptoms in individuals recovering from COVID-19, such as enduring cognitive disturbances weeks beyond the acute phase of the disease.[1] These manifestations, including altered mental status and memory.[2] disorders, underscore the critical role of thorough neuropsychological evaluations for this demographic The precise pathophysiological mechanisms contributing to these cognitive and neuropsychiatric conditions—believed to be associated with elevated inflammatory cytokine levels and central nervous system alterations—are yet to be fully elucidated.[3,4] Symptoms such as fatigue, muscle weakness, and headaches emerge as recurrent among those suffering from long COVID syndrome.[5,6]

Within this framework, the present study aims to explore the neurocognitive repercussions in individuals who have recuperated from a COVID-19 infection, with a special focus on memory and executive functions. This research is pivotal for enhancing our understanding of COVID-19's long-term sequelae and for the development of targeted interventions to mitigate these neuropsychological impacts.[7] The goal is to assess cognitive performance in young adults 12 weeks post-recovery, aiming to shed light on the extent and nature of these impairments, thereby informing future therapeutic approaches.

This investigation primarily targets the cognitive aftereffects observed in young adults post-COVID-19 recovery, concentrating on memory and executive function assessments 12 weeks after recuperation. While it provides valuable insights into the persistence of cognitive dysfunctions, the study's findings are contingent upon the specific population sample and timeline, potentially limiting broader applicability. Additionally, the research focuses on a relatively narrow window post-recovery, necessitating further studies to explore the longevity and full spectrum of these cognitive sequelae.

The outcomes of this study have significant implications for clinical practice and public health strategies, particularly in tailoring rehabilitation programs aimed at cognitive recovery among COVID-19 survivors. Insights gained may also contribute to the formulation of guidelines for the neuropsychological assessment and management of individuals with long COVID. While the immediate applicability is to a young adult population, the findings could pave the way for future research that explores similar interventions across different age groups and demographic settings, enhancing the generalization of results.

By delineating the neurocognitive impacts of COVID-19 and exploring the effectiveness of specific interventions, this study not only fills a critical gap in our current understanding but also serves as a cornerstone for subsequent research efforts aimed at addressing the pandemic's enduring consequences on mental and cognitive health. For this reason, this research aims to evaluate cognitive performance, through memory and executive functions, in young adults 12 weeks after recovering from COVID-19 infection.

Method

Study design, participants and procedures

This retrospective observational case-control study was conducted in Guayaquil at the Universidad Politécnica del Litoral's Department of Student. The sample was obtained through simple sampling. It reviewed 171 PCR tests performed on ESPOL workers between March 16, 2021, and August 8, 2021, focusing on 142 positive COVID-19 cases. The study included 40 positive cases and a control group of 13 healthy individuals with recent negative PCR tests. The participants' age ranged from 25 to 36 years, with an average age of 30.08 years and an average schooling of 19.77 years. All participants had no history of physical or mental health issues before the study. The study adhered to biosafety regulations and received ethical approval (Code: ESPOL-GBP-GTE-016-2023). Workers who survived COVID-19 infection who were working at the time of the investigation and who had an evolution of 12 weeks, or more were included. Surviving subjects who were not working were excluded.

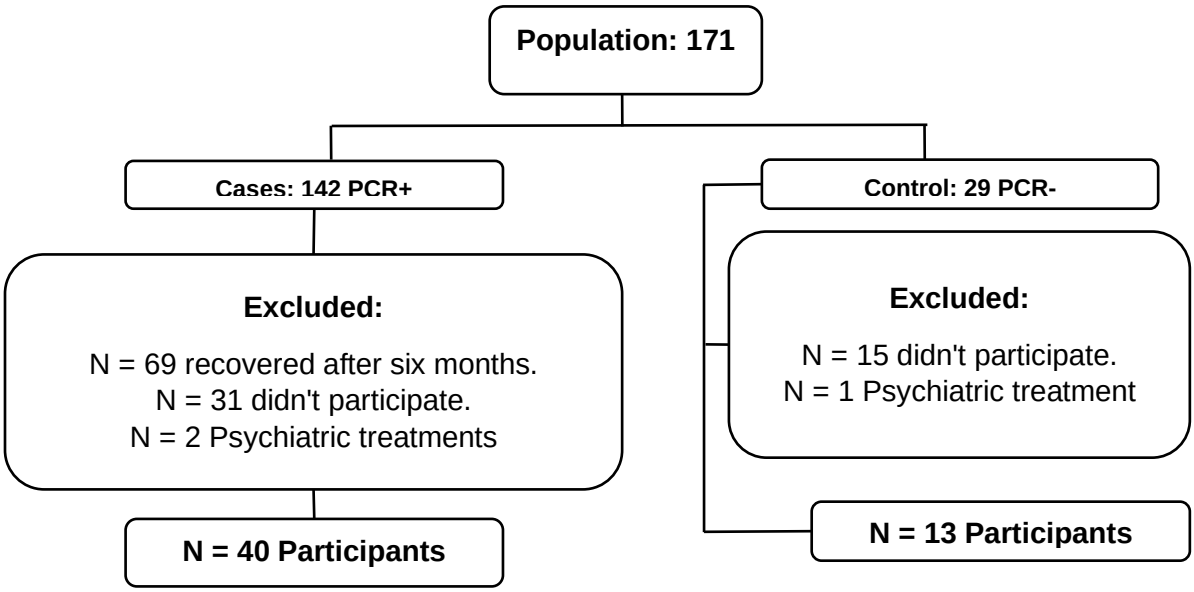

Fig. 1. Study design and sample selection

Note. *Flow diagram describing the recruitment, evaluation, and application of psychological tests.*

Variables and Instruments

An ad hoc form were applied to collect demographic data (age, sex, years of schooling). Selective attention and mental concentration were evaluated using the Six-finger Attention Test N. D2 through a scale of correctness, concentration, commission, and omission.[8] Encoding and evocation of auditory information

through tasks such as encoding, spontaneous recall, learning curve, and cued recognition were measured using the Spontaneous Memory Curve/Tulving Word List (TWL).[9] The Rey-Osterrieth Complex Figure (ROCF) was used to evaluate visuospatial ability, agnosias, apraxias and visual memory problems,[10] consisting of hand-copying a complex geometric drawing in a variable time, to evaluate the level of precision, location, accuracy and organization of the elements that make up the figure. The quantitative model was used through an independent analysis of each of the 18 elements of the image that composes it.

The Neuropsi Motor Functions Test: Attention and Memory was used to assess motor coordination. This test uses 5 measurement components: 1.- Follow object; 2.- Opposite reactions; 3.- Choice reaction; 4.- Change of hand position; 5.- Sequential drawings. The scores of all the tests are added and a total motor coordination score is obtained.[11]

To evaluate the ability to inhibit cognitive interference, which occurs when the processing of a characteristic of the stimulus affects the simultaneous processing of another attribute of the same stimulus, the Stroop Test (SCWT) was used, which has also been used to measure other cognitive functions such as attention, processing speed, cognitive flexibility and working memory.[12]

Procedures

Electronic medical records and lab results of confirmed COVID-19 cases were reviewed. Both case and control groups underwent neuropsychological evaluations, including tests for coding, memory, motor functions, and cognitive interference, conducted in individual sessions.

Statistical analysis

Data were analyzed using SPSS version 28. The Shapiro-Wilk test checked data normality, and descriptive analyses were performed on various cognitive and motor function variables. The Mann-Whitney U test and Spearman correlations assessed differences and relationships between groups, with a significance value of < 0.05.

This study was approved by the research ethics committee of the Escuela Politécnica del Litoral (Approval code: ESPOL-GBP-GTE-016-2023). Approval date: 07/03/2023, in accordance with the Declaration of Helsinki for research on human beings. Informed consent was obtained from all subjects involved in the study.

Results

The final sample included 40 subjects recovered from COVID-19 infection (cases) composed of 22 women (55%) and 18 men (45%) with a mean age of 41.12 years (range 25 and 63), and a mean of 17.41 years of schooling, and a control group composed of 13 subjects of both sexes with an average age of 30.08 years (range 26 and 35), and an average of 19.77 years of schooling (Table 1).

Table 1. Descriptive analysis of the sociodemographic variables and the results of cognitive functions

	Case (n = 40)				Control (n = 13)			
Variables	**Min.**	**Max.**	**M**	**SD**	**Min.**	**Max.**	**M**	**SD**
Demographic								
Age	25	63	41,12	10,457	26	35	30,08	2,629
Years of education	7	23	17,42	4,338	18	22	19,77	1,301
Attention								
Concentration	57	229	145,85	44,226	145	222	187,38	24,459
Hits	74	231	155,90	41,946	148	222	189,15	23,888
Mistakes	0	108	11,23	27,727	0	4	1,23	1,235
Omission	0	146	32,25	36,920	2	16	7,46	4,313
Visual spatial memory								
Hits Coding	24,00	36,00	34,675	2,46397	35,00	36,00	35,923	0,27735
Time Coding	1,25	5,00	2,6736	1,04159	2,12	3,31	2,5008	,43057
Hits evocation	4,00	34,00	19,750	7,21732	23,00	34,00	29,000	3,78594
Time evocation	1,38	5,00	2,7710	0,74874	2,43	3,47	2,7315	,35482
Semantic memory								
Spontaneous coding	4,70	10,00	6,7800	1,25804	7,00	9,00	7,7385	,58386
Intrusion coding	,00	4,00	,6750	1,16327	,00	2,00	,5385	,77625
Spontaneous evocation	3,00	10,00	7,0250	1,74661	6,00	9,00	7,6923	,85485
Intrusion evocation	0,00	3,00	,2750	,71567	0,00	0,00	0,0000	0,00000
Key recognition	6,00	14,00	11,225	1,31046	8,00	12,00	10,307	1,18213
False positive	0	4	0,90	1,057	0	2	0,31	0,630
Total recognition	6	12	10,33	1,760	8	12	10,00	1,291
Executive functions								
Inhibitory time	0,25	1,23	,4410	,19134	0,27	0,38	0,3054	0,03643
Inhibitory control	24,00	36,00	34,450	2,46982	35,00	36,00	35,846	0,37553
Motor coordination	15,00	20,00	18,825	1,35661	17,00	20,00	19,538	1,12660

Note: *Descriptive analysis of Case (n = 40) and Control (n = 13) of Minimum (Min), Maximum (Max), Mean (M) and standard deviation (SD).*

The Mann-Whitney U analysis with a 95% confidence index in the attention variables suggests that there is a significant difference in the concentration of 0.003 p value, in correct answers with 0.017 p value and in omission with 0.002 p value (Table 2). The results suggest that subjects recovered from COVID-19 have lower concentration, lower correct rate and greater omission of stimuli than the control group.

Regarding semantic memory, a significant difference was found in spontaneous coding of 0.050 p value, suggesting that people recovered from COVID-19 encode less semantic auditory information than those who did not get sick, and, in cue recognition tasks, subjects recovered from COVID-19 presented greater correctness than subjects in the control group.

Comparative analysis of visuospatial encoding resulted in a significant difference of 0.025 p value in the encoding of visuospatial information and a p value of 0.001 in the evocation of visuospatial information, suggesting that individuals recovered from COVID-19 encode and evoke less visual-spatial information than individuals who did not get sick.

In relation to executive functions, the analysis showed a significant difference in the Stroop task of 0.003 p-value in correct answers and a p-value of 0.001 in reaction time, which suggests that those who recovered from COVID-19 present fewer hits and longer reaction time to visual stimuli. In the case of motor functions, the comparative analysis suggests a significant difference in the motor coordination task with a p-value of 0.023, indicating that subjects recovered from COVID-19 present less motor coordination of their hands than people who did not become ill.

Table 2. Comparison of independent samples

	Case (n = 40)	Control (n = 13)	U-Man Whitney
	$\bar{x}$	$\bar{x}$	*P< 0.05*
Attention			
Concentration	23,41	38,04	,003*
Hits	24,11	35,88	,017*
Mistakes	28,25	23,15	,289
Omissions	30,78	15,38	,002*
Semantic Memory			
Spontaneous coding	23,66	37,27	0,050*
Intrusions coding	26,89	27,35	9,12
Spontaneous evocation	25,38	32,00	1,71
Intrusions evocation	28,14	23,50	1,10
Key recognition	30,00	17,77	0,009*
False positive	29,10	20,54	0,055
Total recognition	28,51	22,35	1,98
Visual spatial memory			
Hits coding	24,76	33,88	,025*
Time coding	27,06	23,91	,959
Hits evocation	22,39	41,19	0,001*
Time evocation	26,80	27,62	,869
Executive functions			
Inhibitory control	23,69	37,19	0,003*
Inhibitory time	31,30	13,77	0,001*
Motor coordination	24,45	34,85	0,023*

Note: *Non-parametric comparative analysis of independent samples using Mann-Whitney U with one-sided significance P < 0.05.*

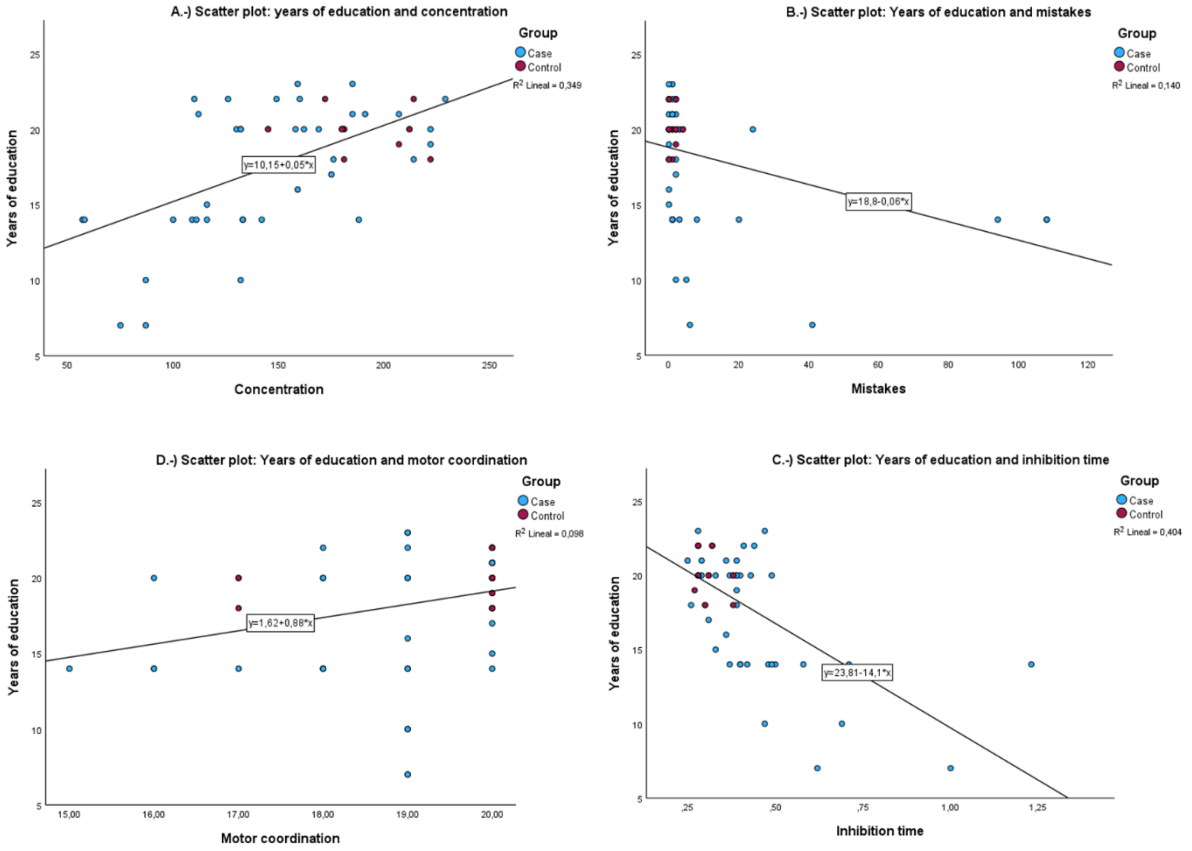

Fig. 2. Scatter plot of year of education and mistakes, concentration, motor coordination and inhibition time.

Note: ***non-parametric correlational analysis with significance of 0.001 and a Sperman Coefficient A) p= 0.50 in case group concentration, B.) p= –0.48 in case group mistakes, C.) p= –0.59 in case group inhibition time and D.-) p= 0.34 in case group motor coordination.***

The results of the evaluation of executive functions suggest a moderate negative relationship with p value = -0.59** between "years of education" and "inhibition time". In contraposition, the relationship between "motor coordination" and "years of education" shows a weak positive result with p value = 0.34*, which indicates the low educational level corresponds to a longer response inhibition time and, on the contrary, high educational level is related to a higher level of motor coordination.

The result of a weak positive improvement between "years of education" and "motor coordination" (p = 0.34) indicates that a higher educational level may be related to better motor coordination, probably due to the relationship that exists between educational level and the adoption of healthy lifestyles, including more active participation in physical exercises, which in turn can improve the performance of cognitive functions.

Individuals with more education have access to better health care resources, facilitating more efficient recovery and, therefore, better motor coordination, which can determine the level of post-COVID recovery and the healthy development of cognitive and motor skills.

Discussion

The analysis of demographic factors revealed statistically weak results with no notable differences by gender and age. In the case group (n = 40), there were 22 women (55%) and 18 men (45%), with a mean age of 41.12 years (range 25 to 63), and an average of 17.41 years of education. In the control group (n = 13), there were subjects of both genders with a mean age of 30.08 years (range 26 to 35) and an average of 19.77 years of education. A meta-analysis with 5515 records revealed the presence of cognitive decline in executive functions, processing speed, attention, and memory in COVID-19-recovered individuals, without differentiation by severity, cognitive domains, age, or gender.[13,14] In the Ecuadorian population (n = 50) that experienced COVID-19 symptoms, no significant relationship was found between cognitive decline and factors such as gender (p = 0.647), age (p = 0.302), and educational level (p = 0.515), using the MoCA in subjects between 18 and 65 years old.

Clinical observations suggest that the severity of infection, hospitalization, and the use of multiple medications can significantly influence the level of cognitive decline.[1] Some memory, language, and executive function tests have been used in subjects with self-reported cognitive symptoms to objectively determine these manifestations. Researchers found a consistent pattern of memory deficits in those subjects who had experienced COVID-19 infection, with an increase in deficits related to the severity of self-reported symptoms in outpatient subjects. Studies in hospitalized subjects show a marked difference in the assessment results of cognitive decline compared to outpatient subjects.[15]

Significant differences were found in the Stroop task (p = 0.003) in correct responses and reaction time (p = 0.001), indicating a decrease in reaction time to visual stimuli in COVID-19-recovered subjects, as previously demonstrated in earlier studies. In subjects evaluated with the Stroop test and the MoCA, 6 months after COVID-19 diagnosis, a significant impact was found on attention skills, executive functions, as well as learning and long-term memory.[16] The results suggest that hospitalized individuals are more likely to have deficiencies in attention, executive functioning, and verbal memory, or slower processing speed.[16-17]

The Nautilus project evaluated 428 subjects in the first year post-COVID-19 (319 survivors and 109 healthy controls) aged between 18 and 65, applying a comprehensive battery of neurocognitive tests. In this study, learning and long-term memory, processing speed, language, and executive functions were significantly worse in the post-COVID group compared to healthy controls.[18] A study of young adult COVID-19 survivors (mean age 49.12 years; SD: 7.84) assessed the impact on cognition and neurological manifestations of COVID-19 in subjects exposed to different health conditions (non-hospitalized n = 21; hospitalized without ICU or oxygen therapy n = 42; hospitalized with ICU and oxygen therapy n = 107;

and ICU patients, n = 31), where no significant differences were found in any of the tests performed based on the severity of the disease ($p > 0.05$), and only 55 patients reported subjective cognitive complaints. Additionally, subjects with neurological symptoms scored lower on the tests conducted (Trail Making Test B, reverse digits, letters and numbers, digit and symbol modalities test, and Stroop color tests).[1]

The persistence of symptoms 12 weeks after COVID-19 infection with neurocognitive manifestations that negatively impact an individual's functioning and quality of life has been defined as post-COVID syndrome,[6] with increasing evidence of its existence. Some individuals experience decreased memory and attention, as well as sleep disturbances, which persist over time and suggest a long-term negative effect. Decreased working memory, language expression, and executive function are the most described manifestations.[18-20] The study from Escuela Politécnica del Litoral in Ecuador highlights significant cognitive impairments in individuals recovered from COVID-19. Compared to a control group, these individuals show reduced attention, concentration, and correct answer rates. They also exhibit deficits in semantic memory, specifically in encoding and recognizing auditory information, and in visuospatial encoding and recall. Furthermore, the study finds impairments in executive functions, such as reaction time and accuracy in the Stroop task.

Interestingly, a correlation between education level and certain cognitive abilities is noted. Higher education correlates moderately negatively with inhibition time and weakly positively with motor coordination. This suggests that education may influence cognitive and motor function recovery after COVID-19.

Conclusions

These findings are crucial in understanding COVID-19's comprehensive impact, especially in terms of the 'pandemic disconnection syndrome', which refers to widespread neuropsychological impairments. The study emphasizes the importance of considering pre-infection cognitive performance as a determinant of post-infection performance and calls for more research to fully understand the extent and persistence of these cognitive deficits. This knowledge is vital for healthcare strategies and supporting individuals with long-term COVID-19 effects as the world transitions to the post-pandemic phase.

Recommendations

Considering the significant cognitive and executive deficits observed in individuals recovered from COVID-19, it is imperative to incorporate regular and comprehensive neuropsychological assessments as part of post-recovery follow-up. These assessments should particularly focus on memory, attention, and executive functions to identify any persistent impairments early on. The implementation of personalized cognitive rehabilitation programs, including training in memory skills, attention, and executive functions, is crucial for facilitating the recovery of these individuals. Additionally, ongoing research should be promoted to explore innovative therapeutic strategies addressing these deficits.

Given the observed link between educational level and the recovery of cognitive and motor functions, there is also a suggestion to focus on education to improve post-COVID-19 outcomes. This can include promoting brain-stimulating activities such as reading, strategy games, and exercises that encourage coordination and planning. Furthermore, it is vital to raise awareness about the importance of a healthy lifestyle, including balanced nutrition, regular exercise, and adequate rest, as an integral part of the recovery process. These recommendations aim not only to improve the quality of life for those affected but also to minimize the long-term impact of COVID-19 on the cognitive and physical health of the population.

Scientific contribution

This study conducted at the Escuela Politécnica del Litoral in Ecuador contributes to science by providing a deep understanding of the prolonged neurocognitive consequences following recovery from COVID-19. By comparing recovered individuals with an uninfected control group, significant deficits in executive functions, attention, semantic memory, and visuospatial skills were observed up to 12 weeks after the acute phase of the disease. Moreover, it highlights the relationship between education level and certain cognitive abilities, suggesting that higher education might positively influence the recovery of cognitive and motor functions after COVID-19. These findings are crucial for the development of healthcare strategies and support for individuals with long-term effects of COVID-19, thereby contributing to the global understanding of the neuropsychiatric sequelae of the pandemic and the importance of early detection and intervention.

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Conflicts of Interest

The authors declare no conflict of interest.

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Author Contributions

- Conceptualization: JAVF, BJR, SECJ contributed to the conceptualization of the study.
- Curation: BJR, SECJ were in charge of data curation.
- Formal Analysis: JAVF, BJR, SECJ, RVS, IDCP, ARC, LPBV carried out the formal analysis. Research: JAVF, BJR, SECJ participated in the research.
- Methodology: JAVF, BJR, SECJ, ARC developed the methodology.
- Resources: RVS, IDCP, LPBV provided the necessary resources.
- Supervision: JAVF, BJR, SECJ, IDCP supervised the project.
- Visualization: JAVF, BJR, SECJ, RVS, MGMD, IDCP, ARC, LPBV were responsible for the visualization.
- Writing–original draft: JAVF, BJR, SECJ wrote the original draft of the manuscript.

- Writing–Review & Editing: JAVF, BJR, SECJ, RVS, IDCP, ARC, MGMD, LPBV participated in the manuscript review and editing.

Data availability

The data rests in a repository. If a reader or reviewer requires it, they can be shared with the authors' permission.