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ORIGINAL ARTICLE

Post-acute sequelae of COVID-19 in young adults: Mental fatigue and decreased cognitive flexibility

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Background and purpose – Post-acute sequelae of COVID-19 (PASC) describes the occurrence of persistent symptoms following COVID-19 infection. Neurological and psychiatric symptoms may include fatigue, post-exertional malaise, cognitive complaints, sensorimotor symptoms, headache, insomnia, depression, and post-traumatic stress disorder. The aim of this study was to evaluate the long-term effects of COVID-19 infection on mental fatigue and cognitive flexibility in young adults.
Methods – Simple random sampling method was used to enroll university students into the study between December 25 and 31, 2022. The time since active infection, central neurological findings (such as headache, dizziness, and loss of smell or taste), and the presence of lung involvement were recorded. The Mental Fatigue Scale (MFS) and the Cognitive Flexibility Inventory (CFI) were administered to all participants.
Results – The study included 102 cases and 111 controls. The case group had a significantly higher total MFS score (12.95; 9.69 respectively) ($p<0.001$) and significantly lower total CFI score (100.01; 109.84 respectively) ($p<0.001$) than the control group. The case group experienced more frequent mental fatigue than the control group ($p<0.001$). Among all participants, a history of COVID-19 infection was identified as a risk factor for developing mental fatigue (odds ratio/OR: 2.74). In the case group, female sex (OR: 0.38) and lung involvement (OR: 10.74) were risk factors for developing mental fatigue.

A Covid-19 posztakut következményei fiatal felnőtteknél: mentális fáradtság és csökkent kognitív rugalmasság
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Háttér és cél – A Covid-19 posztakut következményei (PASC) megnevezés a Covid-19-fertőzést követő tartós tünetek előfordulását írja le. A neurológiai és pszichiátriai PASC-tünetek közé tartozhat a fáradtság, az erőkifejtés utáni rossz közérzet, a kognitív panaszok, a szenzomotoros tünetek, a fejfájás, az álmatlanság, a depresszió és a poszttraumás stresszbetegség. A jelen vizsgálat célja az volt, hogy fiatal felnőtteknél felmérje a Covid-19-fertőzés hosszú távú hatásait a mentális fáradtságra és a kognitív rugalmasságra.
Módszerek – Egyszerű véletlen mintavételi módszerrel vontunk be egyetemi hallgatókat a vizsgálatba 2022. december 25. és 31. között. Rögzítettük az aktív fertőzés óta eltelt időt, a központi idegrendszeri neurológiai tüneteket (például fejfájás, szédülés, szaglás- vagy ízlelésvesztés) és a tüdőérintettség jelenlétét. Minden résztvevővel elvégeztük a Kognitív/Mentális Fáradtság Skálát (MFS) és a Kognitív Rugalmassági Leltárt (CFI).
Eredmények – A vizsgálatba 102 esetet és 111 kontrollt vontunk be. A kontrollcsoporttal összehasonlítva, az esetcsoportban szignifikánsan magasabb volt az MFS-összpontszám (12,95; 9,69) ($p < 0,001$) és szignifikánsan alacsonyabb volt a CFI-összpontszám (100,01; 109,84) ($p < 0,001$). Az esetcsoportban gyakoribb volt a mentális fáradtság, mint a kontrollcsoportban ($p < 0,001$). Az összes résztvevő között a kórtörténetben szereplő Covid-19-fertőzést a mentális fáradtság kialakulásának kockázati tényezőjeként azonosítottuk (esélyhányados/OR: 2,74). Az esetcsoportban a női nem (OR: 0,38) és a tüdő

Conclusion – This study demonstrates that COVID-19 infection might have long-term negative effects on cognitive health, likely due to a combination of organic and psychogenic mechanisms.

Keywords: brain fog, COVID-19, mental fatigue, cognitive flexibility, neuropsychiatric disorders

érintettsége (OR: 10,74) volt a mentális fáradtság kialakulásának kockázati tényezője. **Következtetés** – A tanulmány azt mutatja, hogy a Covid-19-fertőzésnek hosszú távú negatív hatásai lehetnek a kognitív egészségre, valószínűleg organikus és pszichogén mechanizmusok kombinációja következtében.

Kulcsszavak: ködös agy, Covid-19, mentális fáradtság, kognitív rugalmasság, neuropszichiátriai rendellenességek

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus responsible for coronavirus disease 2019 (COVID-19), can lead to the development of both lung disorders and multiorgan syndromes[1]. The devastating health consequences of COVID-19 infection have been extensively described, and concerns have been increasing regarding the potential long-term effects of this disease. Many survivors develop persistent chronic and debilitating symptoms long after their initial recovery from COVID-19, even in cases of mild disease severity[2]. Symptoms that persist ≥ 2 months after COVID-19 recovery are referred to as long COVID or post-acute sequelae of COVID-19 (PASC). The National Institute for Health and Clinical Excellence, the Scottish Intercollegiate Guidelines Network, and the Royal College of General Practitioners have collectively defined PASC as signs and symptoms that develop during or after an infection consistent with COVID-19, persist for more than 3 months (or from date of positive test for asymptomatic), and cannot be explained by any alternative diagnosis[3]. The most commonly reported PASC symptoms are extreme fatigue, muscle weakness, shortness of breath, sleep difficulties, anxiety, depression, decreased lung capacity, memory/cognitive impairment, hyposmia/anosmia, and exercise intolerance[4]. Neurological and psychiatric PASC symptoms include fatigue, post-exertional weakness, cognitive complaints, sensorimotor symptoms, headache, insomnia, depression, and post-traumatic stress disorder (PTSD)[5].

Scientific and medical communities consider PASC to be a pressing matter that urgently needs to be addressed. However, most studies examining PASC have focused primarily on pulmonary complications[6]. It is known that PASC does not only consist of pulmonary symptoms, it can also be seen in both hospitalized patients and outpatients with a mild course. Among hospitalized patients, the reported prevalence of persistent symptoms following COVID-19 infection ranges from 32.6% to 87%[7]. In a cohort of outpatients, 37% of participants reported persistent fatigue, and 30% reported persistent cognitive impairment following COVID-19 infection[8].

The colloquial term 'brain fog' has become one of the top three symptoms reported by millions of individuals with PASC. Although this term is widely used by patients and the healthcare community, no consensus definition of brain fog has been established. In general, brain fog describes symptoms that affect executive function, such as attention deficits, short-term memory loss, reduced concentration, and decreased mental acuity[9]. Mental fatigue is defined as cognitive decline characterized by increased time required to regenerate mental energy, irritability, impaired memory, decreased concentration, and hypersensitivity to stress. Mental fatigue is frequently observed following traumatic brain injury, stroke, and inflammatory diseases that affect the central nervous system, but the pathogenesis and neurocognitive processes underlying mental fatigue are poorly understood[10]. Cognitive flexibility refers to mental processes in which individuals reconstruct their mental resources in a different order. It is defined as an individual's ability to adapt to constantly changing situations, reflecting executive functions such as attention and inhibition, and has a critical role in strategic decision making[11]. Brain fog may be a reflection of mental fatigue and decreased cognitive flexibility. The current study used the Mental Fatigue Scale (MFS) and the Cognitive Flexibility Inventory (CFI) to evaluate the long-term effects of COVID-19 infection on mental fatigue and cognitive flexibility in young adults.

Material and methods

Between December 25 and 31, 2022, Gaziantep University students aged 18-25 who agreed to participate in the study were included using face-to-face interview tech-

nique and simple random sampling method. In the power analysis, the number of samples to be taken in each group was determined as 88 according to 95% confidence, 95% test power and 0.5 effect size. Sociodemographic data questionnaires and scales were delivered to qualifying participants. Students who did not consent to participate in the study, those who consented to participate but failed to respond to some of the items, and those who selected multiple responses for the same item were excluded from the final analysis. In addition, individuals with any history of neurological or psychiatric diseases or who received medical treatment for neurological or psychiatric diseases (such as antidepressants, antipsychotics, and anticonvulsants) were excluded. Exclusion criteria also included any history of traumatic brain injury; systemic and endocrine diseases, such as chronic kidney failure, chronic liver disease, diabetes mellitus, and thyroid dysfunction; and primary sleep disorders (such as insomnia and parasomnia). Inclusion and exclusion criteria, based on self-report, were later verified from medical records.

The sociodemographic questionnaire was used to collect data on age, sex, history of COVID-19 infection (based on confirmation by polymerase chain reaction test), and exclusion criteria. Participants with a history of COVID-19 infection were asked to respond to additional questions regarding the time elapsed since active infection; neurologic symptoms, such as headache, dizziness, loss of smell or taste, experienced during or after acute infection; and the presence of lung involvement (as confirmed by computed tomography or anterior-posterior chest X-ray). The case group was divided into 3 subgroups, 3–6 months, 7–12 months, and >12 months, according to the time elapsed after acute infection.

After completing the sociodemographic form, participants were asked to complete the MFS and CFI. The study was conducted in accordance with the principles of the Declaration of Helsinki, and approval was obtained from the local ethics committee (approval number and date 2022/465, 21.12.2022). Informed consent was obtained from all patients that they agreed to have their medical records checked and their data stored.

Mental Fatigue Scale

The MFS consists of 15 items related to general fatigue, mental fatigue, memory problems, lack of initiative, slowness of thinking, mental recovery, concentration difficulties, sensitivity to stress, increased tendency to become emotional, irritability, sensitivity to light, sensitivity to noise, decreased nighttime sleep, increased overall sleep, and 24-hour variations. The response to each item is scored from 0 to 3, where 0 indicates normal function and 3 indicates maximum severity. The participants were able to record scores in 0.5-point increments. The total MFS score was obtained as the sum of the scores for the first 14 items. Item 15 was only for clinical use and evaluated variations in stated problems over a 24-hour period. A total MFS score of 10.5 or greater indicates the presence of mental fatigue[10].

Cognitive Flexibility Inventory

The CFI was developed by *Dennis* et al. to assess cognitive flexibility. The CFI is a 7-point, Likert-type scale consisting of 20 questions. The responses are coded as follows: strongly disagree (1), disagree (2), somewhat disagree (3), neutral (4), somewhat agree (5), agree (6), and strongly agree (7). Items 2, 4, 7, 9, 11, and 17 are scored in a reverse-coding manner. The final score is obtained by summing the scores from all items. A high CFI total score indicates high cognitive flexibility. The scale does not have a cut-off value[11].

Statistical analysis

Continuous variables are presented as the mean ± standard deviation, and categorical variables are presented as number (percentage). Data normality was verified using kurtosis and skewness analyses. Because all quantitative data in the study showed a normal distribution, parametric tests were used to compare differences between groups. Differences in continuous variables between groups were assessed with the independent-sample T-test, whereas differences in categorical variables were assessed with the Chi-square test. One-way analysis of variance was used to test variance. The effects of variables on mental fatigue were tested with logistic regression analysis. Logistic regression results are presented as the odds ratios (OR) and 95% confidence interval (CI). Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 22 for Windows. A p-value less than 0.05 was considered significant.

Results

A total of 298 university students were recruited and consented to study participation. After applying all inclusion and exclusion criteria, 102 students with a history of COVID-19 infection were enrolled in the case group, and 111 participants with no history of COVID-19 infection were enrolled in the control group. A flowchart showing the steps used to recruit the study cohort is shown in **Figure 1**. None of the cases reported hospitalization during the acute COVID-19 infection phase. The mean age of the study cohort was 22.6 years, including 120 (56.3%) women and 93 (43.7%) men. The case and control groups had similar mean ages and sex distributions. The mean total MFS and CFI scores for all participants

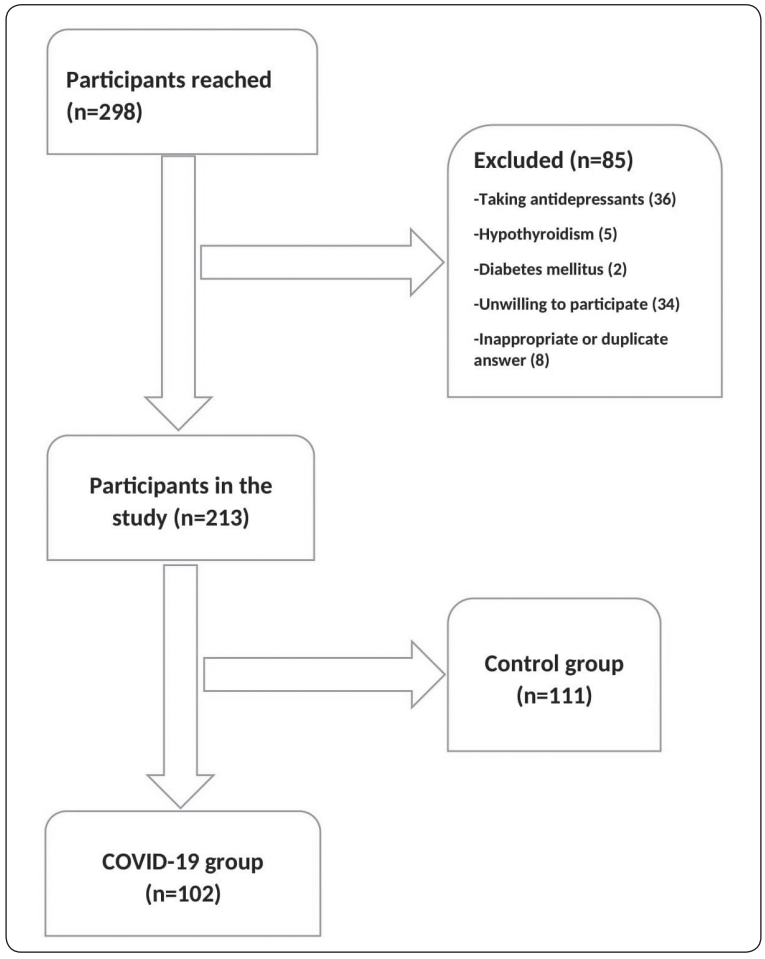

Figure 1. *Flowchart showing the steps used to recruit participants*

Table 1. *Descriptive characteristics of the participants*

Descriptive characteristics	Mean ± SD
Age, years	22.62 ± 2.12
Total MFS score	11.25 ± 5.88
Total CFI score	105.14 ± 16.92
	n (%)
Gender	
Female	120 (56.3)
Male	93 (43.7)
COVID-19 history	
Present	102 (47.9)
Absent	111 (52.1)
Mental fatigue	
Present	98 (46.0)
Absent	115 (54.0)

MFS: Mental Fatigue Scale, CFI: Cognitive Flexibility Inventory, SD: standard deviation

were 11.25 and 105.14, respectively. The MFS was above 10.5, indicating the presence of mental fatigue, in 98 (46%) individuals, whereas the MFS score was below 10.5, indicating no mental fatigue, in 115 (54%) individuals. The descriptive and sociodemographic characteristics of the participants are summarized in **Table 1**. The case group had a significantly higher mean total MFS score ($p < 0.001$) and a significantly lower mean CFI score ($p < 0.001$) than the control group. The frequency of mental fatigue was significantly higher in the case group than in the control group ($p < 0.001$). The comparisons of the case and control groups in terms of age, gender characteristics and scale scores are presented in **Table 2**.

During acute COVID-19 infection, 23 (22.5%) participants in the case group experienced headache and dizziness, 68 (66.7%) experienced loss of smell or taste, and 13 (12.7%) reported radiologically detected lung pathologies. No significant difference was identified in mean total MFS scores between cases with and without a history of headache and dizziness symptoms ($p = 0.880$). The mean total CFI score for cases who experienced headache and dizziness was significantly lower than the score for cases without these symptoms ($p = 0.006$). No significant differences in mean total MFS or CFI scores were identified between cases with and without a history of loss of smell or taste ($p = 0.987$ and $p = 0.149$, respectively). No significant differences were identified between the mean total MFS or CFI scores between cases with and without radiologically detected lung involvement ($p = 0.791$ and $p = 0.344$, respectively). The mean time elapsed since acute infection was 13.87 months. The cases were divided into three subgroups based on the time elapsed since acute infection. In the analysis of variance, no significant differences were observed in the mean total MFS or CFI scores among these subgroups ($p = 0.063$ and $p = 0.755$, respectively). Detailed data regarding the clinical characteristics and scale scores of the three case subgroups are shown in **Table 3**.

In the univariate logistic regression analysis that included all participants, a history of COVID-19 infection was significantly associated with the development of mental fatigue ($p<0.001$, OR: 2.74). The univariate logistic regression analysis that included only the case group revealed that female sex and the presence of radiologically detected lung involvement during acute in-

Table 2. *Descriptive characteristics of the patients with a history of COVID-19 and controls*

	COVID-19 group (n = 111)	Control group (n = 102)	p
Age (year)	22.80 ± 1.79	22.46 ± 2.38	0.251
Total MFS score	12.95 ± 6.20	9.69 ± 5.12	*<0.001*
Total CFI score	100.01 ± 17.24	109.84 ± 15.23	*<0.001*
Gender			
Female	62 (60.8%)	58 (52.3%)	0.210
Male	40 (39.2%)	53 (47.7%)	
Mental fatigue			
Present	60 (58.8%)	38 (34.2%)	*<0.001*
Absent	42 (41.2%)	73 (65.8%)	

MFS: Mental Fatigue Scale, CFI: Cognitive Flexibility Inventory

fection were associated with the development of mental fatigue. In a logistic regression model that included age; sex; the time elapsed since acute infection; radiologically detected lung involvement during acute infection; and symptoms of headache, dizziness, and loss of smell or taste during acute infection, factors identified as significantly associated with the development of mental fatigue were female sex ($p < 0.037$, OR: 0.38) and radiologically detected lung involvement during active infection ($p < 0.014$, OR: 10.74). The results of the multivariate logistic regression analysis are shown in **Table 4**.

Discussion

PASC encompasses a wide variety of organ disorders, and its exact cause is unknown, resulting in challenges during diagnosis, treatment, and prognostic determination[12]. However, PASC occurs frequently and may be reversible; therefore, identifying cases presenting with PASC is important in the clinical setting. Although PASC has a remarkable clinical presentation, studies on this subject remain limited. In this study, we obtained evidence that acute COVID-19 infections might lead to the long-term deterioration of cognitive function.

The most commonly proposed theory for PASC is that COVID-19 infection triggers an autoimmune process, resulting in an exaggerated innate immune response accompanied by cytokine activation[13]. Other factors associated with an active COVID-19 infection that have been proposed to contribute to post-infection neurological symptoms include micro-embolisms in brain tissue, small vessel disease, blood–brain barrier dysfunction, hypoxic-ischemic changes, tissue damage secondary to oxidative stress, neuro-inflammation, and factors related to hospitalization (mechanical ventilation and sedative medications)[14]. In addition, several key risk factors for PASC development have been identified, including severe COVID-19 disease presentation, experiencing more than five symptoms in the first week of the disease, female sex, old age, and the presence of comorbidities such as hypertension, type 2 diabetes mellitus[4]. The majority of patients who are hospitalized for treatment during the acute COVID-19 disease phase exhibit poor performance in memory and cognitive tests during clinical screening[15].

In our study, lung involvement was identified as a significant factor associated with mental fatigue. By contrast, *Townsend* et al. reported that long-term COVID-19 symptoms of COVID-19 were unrelated to disease severity during the acute phase[16]. In addition, long-term symptoms have been reported in various patients, regardless of the initial disease severity, including those with mild acute disease[17]. Similar long-term symptoms have also been reported for pediatric and adolescent individuals, who most commonly experience asymptomatic or mild COVID-19 infection[18]. None of the participants in our study reported any history of hospitalization due to COVID-19. The observation of long-term cognitive symptoms in asymptomatic patients and those with mild disease suggests that factors other than disease severity during the acute phase contribute to the development of long-term symptoms. Inflammatory markers can remain at high levels for long periods, even after asymptomatic and mild COVID-19 disease, which may indicate the development of a chronic inflammatory state[19]. Prolonged immune responses to the virus and prolonged neuroinflammation may play roles in PASC pathogenesis.

The increased frequency of PASC development among hospitalized patients and those with severe disease may be due to the older age of these patients. Older individuals are more susceptible to the development of cognitive deterioration and have a generally poor prognosis following COVID-19 infection, and many studies evaluating long-term cognitive changes after COVID-19 have included older patients in their samples. By contrast, all participants in our study were university students aged under 25 years. The young age of our study cohort eliminated the potentially confounding effect of the age-dependent decreases in cognitive functions from our results.

Regardless of the symptoms experienced or disease severity, patients with COVID-19 infection pre-

Table 3. *Data on the clinical characteristics and scale scores of the COVID-19 group*

COVID-19 group (n = 111)			
Gender		Total MFS score	
Female	62 (60.8%)	13.44 ± 6.26	0.326
Male	40 (39.2%)	12.20 ± 6.11	
		Total CFI score	
Female	62 (60.8%)	99.93 ± 17.06	0.951
Male	40 (39.2%)	100.15 ± 17.73	
Headache and dizziness during active infection		Total MFS score	
Present	23 (22.5%)	12.78 ± 5.12	0.880
Absent	79 (77.4%)	13.00 ± 6.51	
		Total CFI score	
Present	23 (22.5%)	91.47 ± 20.55	*0.006*
Absent	79 (77.4%)	102.50 ± 15.41	
Loss of smell and taste during active infection		Total MFS score	
Present	68 (66.6%)	12.96 ± 6.39	0.987
Absent	34 (33.3%)	12.94 ± 5.91	
		Total CFI score	
Present	68 (66.6%)	101.76 ± 15.71	0.149
Absent	34 (33.3%)	96.52 ± 19.75	
Pulmonary involvement during active infection		Total MFS score	
Present	13 (12.7%)	13.38 ± 4.00	0.710
Absent	89 (87.2%)	12.89 ± 6.48	
		Total CFI score	
Present	13 (12.7%)	95.76 ± 19.21	0.344
Absent	89 (87.2%)	100.64 ± 16.96	
Time since acute infection (months)		Total MFS score	
3-6	25	11.30 ± 5.33	
7-12	31	11.96 ± 6.06	0.063
>12	46	14.52 ± 6.49	
		Total CFI score	
3–6	25	101.88 ± 19.47	
7–12	31	100.45 ± 17.11	0.755
>12	46	98.71 ± 16.31	

MFS: Mental Fatigue Scale, CFI: Cognitive Flexibility Inventory

sent with $CD4^+$ and $CD8^+$ T cell dysfunction lasting up to 400 days after acute infection, similar to the T cell dysfunction observed in autoimmune diseases, and T cell dysfunction appears even more pronounced in patients with PASC[20]. Several COVID-19 characteristics resemble autoimmune disease, including clinical symptoms, the immune response, and pathogenic mechanisms. Autoimmune diseases, such as Guillain-Barré syndrome and systemic lupus erythematosus, have been reported to develop following COVID-19 infection[21, 22]. *Seessle* et al. observed several neurocognitive symptoms associated with antinuclear antibody titer elevation during the post–COVID-19 period[23]. In another study, long-term symptoms were found to occur more frequently in the female sex[24]. Together, these findings support the hypothesis that autoimmunity may be a mechanism underlying long-term COVID-19 symptoms. Autoimmune disorders develop more frequently in women, and in our study, the female sex was identified as a significant risk factor for the development of mental fatigue.

Impaired immune reactions secondary to COVID-19 infection may also contribute to cognitive decline by affecting the central nervous system. Neurological symptoms, such as headache and loss of smell or taste, that present during acute COVID-19 infection have been strongly associated with impaired performance in several subtests related to attention, memory, and executive function[25]. In our study, we found that the participants with neurological symptoms, including headache and dizziness, during acute infection had lower total CFI scores, suggesting that the virus, which has neurotropic properties, may migrate to the central nervous system during acute infection, causing chronic effects during the late period. However, we detected no correlation between neurological symptoms and mental fatigue scores. The decline of cognitive performance of patients who experience neurological symptoms during acute infection may resolve over time.

SARS-CoV-2 can enter the central nervous system through hematogenous routes or by retrograde trafficking between neurons. SARS-CoV-2 RNA may remain in the brain tissue for a long time, resulting in increasingly worsening neuronal loss over time[26]. Studies have suggested that the frontal circuits are preferentially targeted by SARS-CoV-2, contributing to executive dysfunction.

Table 4. *Results of the multivariate logistic regression analysis of mental fatigue*

	Mental fatigue				
Variables	β	SE	OR	p	95% CI
Age	–0.037	0.124	0.964	0.766	0.755–1.230
Gender					
Male/Female	–0.969	0.465	*0.379*	*0.037*	0.152–0.945
Headache and dizziness during active infection					
Present	–1.045	0.721	0.352	0.147	0.086–1.446
Loss of smell and taste during active infection					
Present	–0.689	0.599	0.502	0.250	0.155–1.623
Pulmonary involvement during active infection					
Present	2.374	0.970	*10.742*	*0.014*	1.605–71.905
Time since acute infection (month)					
3–6					
7–12	0.925	0.627	2.523	0.140	0.738–8.627
>12	0.704	0.562	2.022	0.210	0.673–6.077

β: standardized regression coefficient, SE: standard error, OR: odds ratio, CI: confidence interval

Although no direct link between frontal lobe abnormalities and post–COVID-19 cognitive impairment has yet been established, positron emission tomography (PET) studies suggest frontal hypometabolism in severe cases[15, 27]. Hypometabolism was detected in the cingulate cortex during fluorodeoxyglucose-PET examinations in two patients with long-term cognitive complaints (brain fog) following COVID-19 infection, despite a lack of pathological findings on conventional magnetic resonance imaging for either patient[28]. The cingulate cortex is involved in many cognitive functions. Previous experimental and clinical studies have shown that the anterior and posterior cingulate cortices play roles in emotion, memory, depression, and action-related decisions[29]. These brain regions may experience alterations secondary to both direct viral invasion and the enhanced inflammatory response during acute infection, leading to cognitive and mental changes in these patients.

Other mechanisms underlying cognitive impairment may include sleep disturbances, physical inactivity, altered eating habits, and emotional changes experienced by patients after COVID-19 infection. Social isolation, confinement, hysteria, and anxiety about losing loved ones during acute infection may contribute to the development of post-infection neuropsychiatric symptoms and sleep disorders[30]. Low cognitive flexibility levels have been associated with rumination, depression, and anxiety[11]. Increased stress and poor sleep quality during the pandemic period have also been proposed as contributors to reduced cognitive flexibility[31]. In addition, emotional disorders, such as depression, anxiety, and PTSD, which are commonly observed after COVID-19 infection, can increase cognitive complaints. Quarantine and isolation measures implemented during the pandemic period have also affected eating and physical activity habits, and an increased intake of foods high in simple carbohydrates, trans fat, and additives and low in nutrient density has been associated with increased systemic and neuroinflammation[32], which may also contribute to the development of PASC symptoms. *Rebello* et al. suggested that physical exercise could counteract PASC by enhancing the anti-inflammatory response, supporting brain homeostasis, and increasing insulin sensitivity[33]. Decreased physical exercise levels may predispose patients to long-term cognitive impairment following COVID-19 infection. The development of strategies that include increased physical exercise, dietary interventions, and stress response management may be beneficial by counteracting the effects of chronic inflammation, contributing to the retention of cognitive function[34].

Our study has some limitations. First, since all participants of this study were university students, the results of the study cannot be generalized to the whole population in terms of variables such as age, sociodemographic characteristics, and years of education. Second, due to the cross-sectional study design, no cause-and-effect relationships can be established between dependent and independent variables. Third, we did not have access to any pre–COVID-19 mental or cognitive assessments; therefore, we were unable to make any objective comparisons between pre- and post-infection cognitive functions. Fourth, data obtained through self-administered online surveys may be affected by biases, such as the inability to recall information or the unwillingness to disclose private data. And finally, the lack of vaccination status, the number of COVID-19 infections, infections with variants, lack of physical examination

findings of the patients, and the lack of knowledge of cognitive performance after acute illness are other limitations of our study.

Conclusions

This study demonstrated that SARS-CoV-2 infection might have long-term negative effects on cognitive health. These long-term effects are likely due to a combination of organic and psychogenic mechanisms. The data obtained from our study can help raise awareness regarding the emergence of long-term cognitive symptoms in patients with COVID-19, regardless of initial disease severity. Multicenter studies conducted with large population cohorts remain necessary to further clarify the long-term cognitive effects of COVID-19 infection.

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