



Untreated if unrecognized: A cognitive profile of sustained subjective executive dysfunctions in COVID-19

Bob O. de Groot, Chiara Biserni, Anselm B. M. Fuermaier & Stefanie Enriquez-Geppert

To cite this article: Bob O. de Groot, Chiara Biserni, Anselm B. M. Fuermaier & Stefanie Enriquez-Geppert (2023): Untreated if unrecognized: A cognitive profile of sustained subjective executive dysfunctions in COVID-19, Applied Neuropsychology: Adult, DOI: 10.1080/23279095.2023.2223329

To link to this article: <https://doi.org/10.1080/23279095.2023.2223329>



© 2023 The Author(s). Published with license by Taylor & Francis Group, LLC



Published online: 19 Jun 2023.



Submit your article to this journal [↗](#)



Article views: 676





View related articles [↗](#)



View Crossmark data [↗](#)

Untreated if unrecognized: A cognitive profile of sustained subjective executive dysfunctions in COVID-19

Bob O. de Groot^a, Chiara Biserni^a, Anselm B. M. Fuermaier^a , and Stefanie Enriquez-Geppert^{a,b} 

^aDepartment of Clinical and Developmental Neuropsychology, University of Groningen, The Netherlands; ^bDepartment of Biomedical Sciences of Cells and Systems, University Medical Center Groningen, Groningen, The Netherlands

ABSTRACT & STATEMENT OF IMPACT

SARS-COV-2 infection can result in acute and long-lasting cognitive complaints, causing ongoing impairments in daily life which poses a challenge to society. Consequently, the evaluation and characterization of cognitive complaints, specifically in the domain of executive functions (EFs) affecting daily life, is imperative in formulating an effective neuropsychological response.

In total 442 participants aged 18–65+ years from the Netherlands, Germany, Mexico, and Spain were included in an online questionnaire. Among others, the questionnaire consisted of demographics, the Behavior Rating Inventory of Executive Functioning for Adults (BRIEF-A), measures of subjective disease progression severity and experienced subjective impairment in daily activities. To assess whether daily life activities are affected by EF impairments, the main BRIEF-A composite score (GEC) was analyzed. To determine whether disease-related COVID-19 factors predict EFs complaints in daily life, a stepwise regression analysis was performed with i) experienced disease severity, ii) time since disease, and iii) health risk factor as predictors.

The study revealed noteworthy differences in the occurrence of EFs problems in daily life between both groups, as indicated by the GEC, which exhibited a medium effect size even 6 months post-COVID-19 diagnosis even in mild disease progression. The scores of the BRIEF-A subscales follow a domain-specific profile, and includes clinically relevant impairments in: Working memory, Plan/Organize, Task Monitor, Shift, which are affected by the experienced severity of the disease. This cognitive profile has important implications for targeted cognitive training in rehabilitation and has the potential for an applicability to other viruses as well.

KEYWORDS

Executive dysfunctions; mild cognitive impairment; post-COVID-19 syndrome; prolonged subjective cognitive impairment



Introduction

COVID-19, which is caused by the SARS-CoV-2 virus, manifests itself in most cases as a mild to moderate respiratory illness. However, neurological manifestations such as dizziness, headaches, and moreover neurocognitive problems can occur and may persist beyond the initial illness (Aghagoli et al., 2021; Asadi-Pooya & Simani, 2020; Liguori et al., 2021). “Long COVID,” “brain fog” or “post-COVID 19 syndrome” are in the media spotlight, and these symptoms have also been officially defined by the World Health Organization (WHO) as post-COVID-19 syndrome.

Although the main focus has been on acute medical treatment, the shift to long-term consequences such as fatigue, muscle weakness and neuropsychological sequelae are becoming increasingly important in the current research (Huang et al., 2021). Little is known however, about which cognitive problems are experienced, and how these persist over time in formerly infected individuals. Nor is it known to what extent they affect occupational, psychological and daily life (e.g., Burdick et al., 2021). This knowledge is,

however, urgently needed to prepare and test an appropriate neuropsychological response, evaluation and treatment, and inform newly arising post-COVID-19 clinics (e.g., the University of Michigan Health Post Covid-19 Clinic). The present study fills current research gaps by examining specific cognitive complaints from the affected person’s perspective, which manifest themselves in everyday life and are experienced as resulting in impairments in functioning. We aim to present a cognitive profile associated with individuals reporting a post-COVID-19-syndrome, specifically focused on the role of executive functioning.

Executive functions (EFs) are a particularly important cognitive domain, as they play a crucial role in everyday functioning, as well as in academic and occupational success (Ramos-Galarza et al., 2019). EFs are essential for controlling thoughts and behavior and are described as higher cognitive functions that control lower processes such as attention or memory (Karr et al., 2018; Miyake et al., 2000; Stuss, 2011). EFs enable people to deal with new situations and problems that arise in everyday life (Brugges & Simons, 2005), and thus contribute to a controlled behavioral

CONTACT Stefanie Enriquez-Geppert  s.enriquez.geppert@rug.nl  Department of Clinical and Developmental Neuropsychology, Faculty of Behavioural and Social Sciences, University of Groningen, Grote Kruisstraat 2/1, 9712 TS Groningen, The Netherlands.

© 2023 The Author(s). Published with license by Taylor & Francis Group, LLC

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

response when automatic routine behavior is not effective. In turn, disruptions in EFs have a major negative impact on functioning in everyday life.

Disease mechanisms

To understand the effects on cognition, COVID-19 specific factors such as neurotropic and neurotoxic effects are examined, and potential mechanisms of action underlying both acute and long-lasting effects are explored (Islam et al., 2020; Mehandru and Merad 2022). Neurotropic and neurotoxic effects of SARS-CoV-2 are reported as direct or indirect infiltration pathways to the brain (Asadi-Pooya & Simani, 2020; Butler & Barrientos, 2020; Chen et al., 2020). Severe COVID-19 infection can trigger a complex inflammatory response that can lead to a cytokine storm, releasing pro-inflammatory cytokines that seem to act as key mediators in cognitive impairment (Alnefeesi et al., 2020; Cothran et al., 2020). In contrast, it has been proposed that the underlying pathophysiology of long-COVID is a persistent state of low-grade infection (Islam et al., 2020; Mehandru and Merad, 2022). As a more severe infection has been associated with cognitive impairment and specifically in domains such as working memory (Alnefeesi et al., 2020; Cothran et al., 2020); it can be expected that this association also exists for executive functioning as we have conceptualized it in the current study.

The role of disease severity and executive functioning

Neuropsychological complaints have previously been documented in severe cases of respiratory failure, such as acute respiratory distress syndrome (ARDS) resulting from infection by coronaviruses. For example, chronic memory impairment was observed in a review of ARDS reports (Riordan et al., 2020). Regarding COVID-19, it is estimated that ARDS occurs in 42% of COVID-19 patients with pneumonia (Gibson, Qin & Puah, 2020). Neuropsychological effects on EFs are also reported in connection with the previous coronaviruses such as SARS and MERS in a meta-analysis of 72 studies (Rogers et al., 2020). In another observational series of 58 COVID-19 patients with ARDS admitted to the ICU, 70% experienced neurological symptoms such as agitation and confusion, and a further 33% developed dysexecutive syndrome on discharge from hospital (Helms et al., 2020). Burdick et al. (2021) investigated the frequency, severity and profile of cognitive impairment in patients recovering from prolonged COVID-19 hospitalization ($n = 57$) who required intubation and mechanical ventilation. The majority were found to have mild forms of cognitive impairment, mainly in the areas of attention and executive functions. Similar findings were reported in a large-scale study by Hampshire et al. (2020), which included more than 84,000 hospitalized participants who were ventilated, non-hospitalized individuals who received help due to breathing problems, and patients without breathing problems. In this study, cognitive deficits were observed even when age, gender, education level, preexisting medical disorders, fatigue, depression and anxiety were controlled for. Regarding persistence, Miskowiak et al. (2021) reported cognitive impairment in daily life functioning for at least 3 or 4 months after hospital discharge for 80% of their

sample ($N = 29$), with EFs and verbal learning being the most impaired. In all these severe cases and courses, it must be emphasized that hypoxia and hypoxemia seem to play an important role in the development of cognitive dysfunction (Riordan et al., 2020).

In general, the reported outcomes for long-lasting cognitive dysfunction, including executive deficits, are also consistent with the outcomes for cognitive deficits in survivors of other critical illnesses (Norman et al., 2016; Rothenhäusler et al., 2001). Critical illness is thereby characterized by factors such as calculated risk of death, duration of ventilatory support and length of stay in the intensive care unit. Persistent cognitive deficits and slow recovery are observed, for example, in major surgery, after carotid and cardiac surgery for ARDS, and in general intensive care (Heyer et al., 2002; Hopkins et al., 1999; Jackson et al., 2003; Moller et al., 1998; Newman et al., 2001; Rothenhäusler et al., 2001; Sukantarat et al., 2005). It seems therefore likely that the risk of long-lasting cognitive dysfunction increases with the severity of the disease.

A crucial question in post-COVID-syndrome is whether persistent cognitive impairments can occur even in mild courses that negatively affect daily functioning over a significantly long period of time (Del Brutto et al., 2021; Ferruci et al., 2021). Initial studies and anecdotal reports from rehabilitation clinics confirm this assumption. For example, non-hospitalized COVID-19 patients showed mild impairments in sustained attention (Zhou et al., 2020), similarly, subclinical cognitive impairment in memory and attention was found in mild-to-moderate COVID-19 ($N = 18$) (Woo et al., 2020). Furthermore, there is evidence that even asymptomatic COVID-19 patients show cognitive deficits in tasks such as perception, naming and fluency (Amalakanti et al., 2021). Among these cognitive domains, problems and disruptions in EF are frequently mentioned. For instance, executive dysfunction in particular has been found to persist for at least 98 days after acute COVID-19 symptoms in non-hospitalized patients (Hellmuth et al., 2021).

The above-mentioned findings on the effects of COVID-19 on cognition even in milder cases underline the need for further research to investigate whether and what limitations are experienced in everyday life due to cognitive impairments. A focus on EFs is warranted, given its relevance for tasks in everyday life.

The current study

To capture the actual behavioral manifestations of executive functioning complaints experienced in daily life, the current study utilizes subjective measures in individuals indicated previously being infected with COVID-19. The current study focuses on the subjective assessment of cognitive complaints in daily life. Regularly used clinical screening instruments (e.g., MMSE) are likely not sensitive enough to capture the subclinical yet debilitating cognitive deficits that are at the focus of this study. In order to recognize, identify and appropriately develop treatment of cognitive impairments in everyday life, the subjective assessment of EFs is informative and relevant.

Methods

Participants and recruitment

In this online study, a total of 530 participants were recruited. Data collection took place between February and July 2021. This original sample consisted of 429 female and 100 male participants, with one participant falling into the “other” category. Within this sample, 350 participants declared having had COVID-19, and a healthy control group of 180 participants declared never having had COVID-19. Recruitment of all groups was done using convenience sampling, by posting on social media (Instagram, LinkedIn, a Facebook Group with $\pm 21,000$ members), and by distributing the questionnaire via acquaintances. The survey was further distributed through a Dutch group of individuals who had recovered from COVID-19. In addition, flyers were disseminated among general practitioners, medical staff in a hospital and via other healthcare professionals that handed out the flyers among individuals with COVID-19. The study was spread via general practitioners and acquaintances, most notably in The Netherlands, Germany, Mexico, and Spain, and was translated into the corresponding languages. Informed consent was obtained from all participants of the study before the questionnaire was presented. Participants who did not give their consent or who did not enter a response, were excluded from the analyses. Participants were not (financially or otherwise) compensated for their participation. The study has been approved by the Ethics Committee of the Department of Psychology and is conducted in accordance with the Declaration of Helsinki.

Assessment battery

A set of already established and adapted (neuro)psychological self-report instruments were compiled and named “Groninger Neuropsychological COVID-19 Test battery Cognitive Complaints (CoCo-19)” using Qualtrics. Five domains were used for in the test battery: demographics, functional outcome, neuropsychological, personality and psychological (the General Anxiety Disorder-7 questionnaire (GAD-7, Spitzer et al., 2006) for anxiety, the Beck’s Depression Inventory (BDI: Beck et al., 1996) for the assessment of depressive symptoms). Taking the total length of the test battery into account, an effect of fatigue and difficulty with concentration was considered. In fact, the most relevant neuropsychological questionnaires were located in the first half of the questionnaire to avoid such effects. The questionnaire was available in five different languages, using available official translations if possible. If these were not available, items were translated by native speakers of the corresponding language.

Inclusion and exclusion criteria

Entries in the dataset were excluded from the analyses if informed consent was not answered or not given, if they were hospitalized and if their completion time was unreasonably low (e.g., only logging in for a few seconds, then closing the questionnaire). We excluded hospitalized

patients from our study due to the limited sample size, which did not allow for statistical analysis. In addition, participants who showed invalid responses on the BRIEF-A were excluded from the analysis: a negativity score ≥ 4 , infrequency score ≥ 3 or an inconsistency score ≥ 8 (Roth et al., 2005).

Importantly, participants who did not fully complete the questionnaire were not automatically excluded from the analysis. Given the nature of the subject being studied (i.e., cognitive dysfunction; lack of concentration; fatigue), and the length of the questionnaire (>60 min), it cannot be expected of all participants to complete the questionnaire entirely. To avoid a bias toward less severely ill patients, not all incomplete responses were deleted per se, but were included in the analyses after manually and individually assessing them for validity (i.e. screening the response patterns for reporting bias such as unreasonably extreme scores). All participants who gave informed consent and at least completed the questionnaire until the final BRIEF-A questionnaire were included into the main analysis.

Procedure

Upon accessing the Qualtrics link, a choice between five languages was presented. After selecting their preferred language, the objective of the study was presented followed by the informed consent. Once informed consent was completed, demographics were assessed. Besides age, gender, living situation, preexisting conditions and medication intake, participants were asked whether they had been diagnosed with COVID-19. If participants indicated having been diagnosed with COVID-19, further questions were asked about date of diagnosis, inpatient stay, experienced disease severity of the disease and related medication intake. Medication intake was not further specified.

Measures of experienced COVID-19 disease severity

Of the participants who indicated having been infected with SARS-CoV-2 in our sample, 329 (62.1%) indicated experiencing symptoms that they perceived as typical for COVID-19. Moreover, 26 (4.9%) participants reported being hospitalized following their COVID-19 diagnosis. Notably, 164 (30.9%) participants reported making use of medications for their COVID-19 symptoms. Our reliance on self-report of this information, provides the risk that participants are unaware that they have been infected with SARS-CoV-2 due to an asymptomatic disease course.

As a measure of severity in our analyses, subjective disease progression severity and experienced subjective impairment of daily activities were measured. Participants assessed their disease progression severity on a slider from 1 to 100 (i.e., “Please rate the severity of your disease course.”).

Self-reports on executive functions

The standardized measures Behavior Rating Inventory of Executive Functioning for Adults (BRIEF-A) was used to assess subjective EFs in daily life (Roth et al., 2005). The BRIEF-A consists of 75 items, which are subdivided into

nine non-overlapping theoretically and empirically derived clinical subscales: Inhibit, Self-Monitor, Plan/Organize, Shift, Initiate, Task Monitor, Emotional Control, Working Memory, and Organization of Materials. Additionally, three validity scales are included. In the items of the BRIEF-A, participants subjectively rate their perceived complaints in situations where EFs are used. Based on these clinical subscales, three composite measures can be derived: Global Executive Composite (GEC); Metacognition Index (MI); Behavioral Regulation Index (BRI). The GEC is a grand summary score of all items, and reflects general executive functioning. A higher score indicates more difficulty in general EFs (for further information see the BRIEF-A interpretive report or manual). A summary of Cronbach's Alpha of the BRIEF-A scales in this study are found in Table 1. To compute the T-scores, the healthy control group of the study was used as a reference ($t = 50$). Doing so, we make use of a comparison group which was recruited within the same (unstandardized) context to allow for valid comparison. The use and comparison of T-scores allows for an indication of the clinical relevance of these effects in daily life functioning, with higher scores indicating more complaints. In the current context, we conceptualize a substantially lower score compared to our comparison group as subjectively reported mild cognitive impairment. The BRIEF-A includes a proxy version, which was not administered in the current study.

Statistical analysis

The raw dataset was imported from Qualtrics, and was imported into SPSS. Each language provided a separate dataset, which were merged into our main dataset. IBM SPSS Statistics version 27 (IBM SPSS Statistics, New York, NY, United States) was used for performing statistical analyses.

Group differences between the COVID-19 group and control group in BRIEF-A scores

To test in our main analysis whether daily life activities are affected due to problems in executive functioning in individuals who suffered from COVID-19 compared to subjected reporting never having had COVID-19, the main composite score (GEC) was analyzed with an independent t-test assessing the GEC comparing the two groups (COVID and Non-COVID). In all the mentioned analyses, p -values below 0.05 were judged significant. In addition, raw test scores of all nine clinical subscales were

transformed into T-scores for visualization of the clinical relevance for each participant. Higher scores on (subscales of) the BRIEF-A represent more reported complaints.

Predicting executive dysfunction in daily life with disease-related factors

To test whether disease-related COVID-19 factors contribute as predictors for EF complaints in everyday life, as an exploratory analysis a stepwise regression analysis was performed with the three predictors (i) experienced disease severity, (ii) time since disease, and (iii) risk factors for exactly those subscales that showed the largest group differences. Assumptions for regression were assessed for violations (e.g., linearity, normality, homogeneity, independence of observations), using Q-Q plots and tests (Casewise diagnostics and Durbin-Watson test); no violations were found. A correlational analysis was used to assess multicollinearity, multicollinearity requirements were regarded with bivariate correlations below 0.7 (Mukaka, 2012). All statistical analyses were carried out using SPSS version 27.

Results

Final participant sample

The actual sample consisted of $N = 442$ participants ($n = 84$ male, $n = 358$ female). Within this sample, 296 participants reported having had COVID-19 and a healthy control group of 146 participants reported never having had COVID-19 before. Both groups differed significantly ($F = 14.85$, $p < .001$) regarding their mean BDI-scores (COVID-19: $M = 12.91$, $SD = 7.29$; Control: $M = 8.54$, $SD = 10.97$) which both are considered as minimal depression. Figure 1 shows the relation between the two groups and scores on BDI scores. The sample included 255 Dutch, 154 German, 22 Spanish, and eleven English speaking participants. The largest age groups within this sample were ages between 18 and 29 ($n = 121$; 27.4%), and ages between 50 and 64 years ($n = 129$; 29.2%). Some participants suffered comorbid health problems as is reported in Table 2, of which heart attack, diabetes, obesity, hypertension, stroke were considered as health risk factors for COVID-19. Participants reporting at least one of these health problems were identified as having a health risk (Table 3).

Table 1. Summary and description of the BRIEF-A subscales in the current study.

Scales	Description	Cronbach's alpha
Global Executive Composite (GEC)	Overarching summary score of all scales	.967
Metacognition Index (MI)	Reflecting ability to initiate, problem-solve, sustain	.921
Initiate	WM, plan and organize problem solving ideas,	
Working memory	monitor success or failure and organizing	
Plan/Organize	materials and environment	
Task monitor	Capturing ability to maintain regulatory control of	
Organization of materials	behavioral and emotional responses	
Behavioral Regulation Index (BRI)		.957
Inhibit		
Shift		
Emotional control		
Self-monitor		

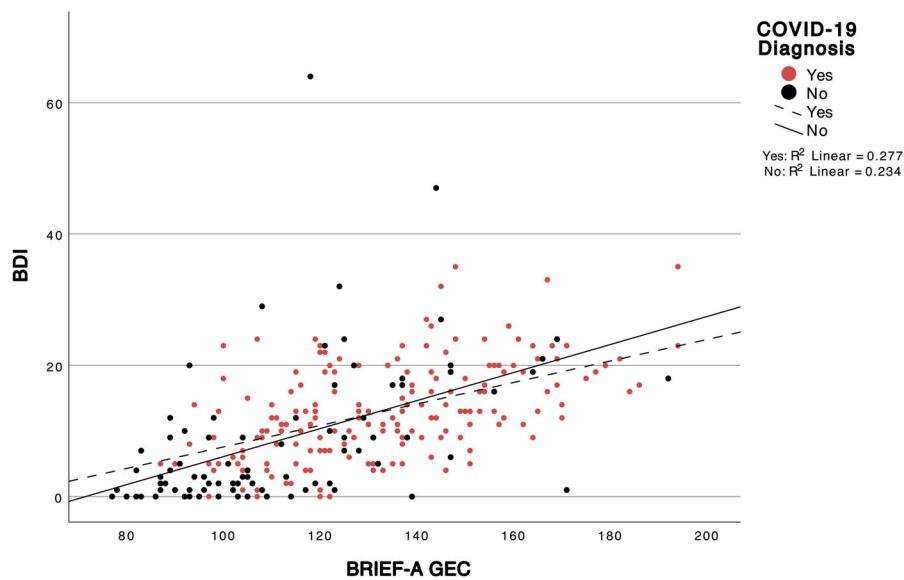


Figure 1. Scatterplot visualizing distribution of BDI scores and BRIEF-A GEC scores.

Table 2. Sample characteristics.

Characteristics	COVID-19 group		Control group		Full sample		
	n	%	n	%	n	%	
Gender							
	Female	258	87.2	100	68.5	358	81.0
	Male	38	12.8	46	31.5	84	19.0
Age ranges (in years)							
	18–29	52	17.6	69	57.3	121	27.4
	30–39	64	21.6	18	12.3	82	18.6
	40–49	76	25.7	15	10.3	91	20.6
	50–64	96	32.4	33	22.6	129	29.2
	65 or older	8	2.7	11	7.5	19	4.3
Highest educational qualification							
	Less than highschool degree	1	.3	7	4.8	8	1.8
	Highschool diploma	11	3.7	6	4.1	17	3.8
	Education/Apprenticeship	95	32.1	27	13.7	115	26.0
	Study without degree	26	8.8	27	18.5	69	12.0
	Bachelor’s degree	76	25.7	40	27.4	116	26.2
	Master’s degree	50	16.9	19	13.0	69	15.6
	Doctorate	37	12.5	27	18.5	64	14.5
Employment status							
	Employed, working 1–39 h per week	165	55.7	44	30.1	209	47.3
	Employed, working 40 or more hours per week	45	15.2	22	15.1	67	15.2
	Self-employed	16	5.4	9	6.2	25	5.7
	Full-time student	18	6.2	40	27.4	58	13.1
	Part-time student	0	0	0	0	0	0
	Househusband/housewife	3	1.0	7	4.8	10	2.3
	Not employed, looking for work	4	1.4	7	2.7	8	1.8
	Not employed, not looking for work	2	.7	14	2.7	6	1.4
	Retired	11	3.7	14	9.6	25	5.7
	Not able to work	32	10.8	2	1.4	34	7.7
Previous psychological or neurological disorder	Yes	43	14.5	13	14.5	56	12.7
Intake medication for (psychological) disorder	Yes	54	18.2	13	8.9	72	16.3
Health issues							
	Diabetes	8	2.7	4	2.2	12	2.7
	Obesity	36	13.1	10	6.1	46	10.4
	High blood pressure	27	8.3	8	5.6	35	7.9
	None	225	75.7	123	84.2	348	78.7

Table 3. Characteristics of the COVID-19 group.

	n	%
Diagnosed with SARS-CoV-2	296	67.0
Loss of taste and/or smell and/or fatigue	279	94.3
Medication against COVID-19 conditions	136	45.9
	M	SD
Severity of disease course ^a	59.46	24.23
Days since COVID-19 diagnosis	175.68	126.96

COVID-19 severity and executive functions

In our main analysis, we assessed the relationship between subjective COVID-19 disease severity and EFs for the main summary score. First, as expected the independent samples T-test on the GEC scale scores of the BRIEF-A between the COVID-19 group ($M = 130.89, SD = 26.80$) and the control group ($M = 113.05, SD = 26.65$) showed a

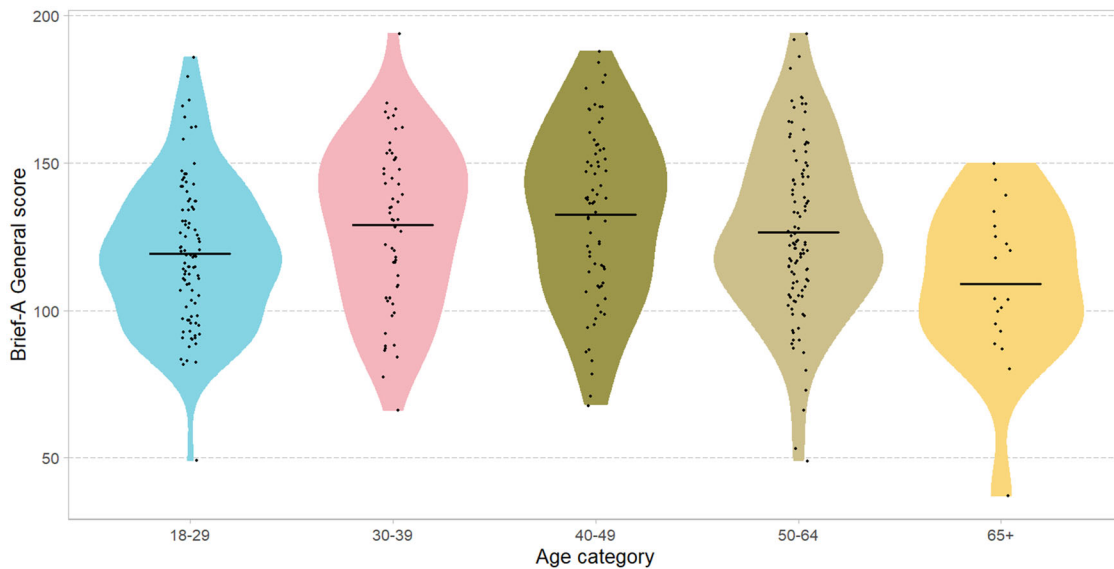


Figure 2. Violin plots of the composite score GEC per age decade. Shown is the mean as well.



Figure 3. Radar chart showing T-scores of BRIEF-A domains according to disease severity and relative to the healthy control group of the study. The radar shows the distribution of scores on the BRIEF-A according to the disease severity for all nine clinical subscales: Inhibit, Self-Monitor, plan/organize, Shift, Initiate, Task Monitor, Emotional Control, Working Memory, and Organization of Materials. Scores are transformed into T-scores, using the non-COVID group (yellow) as the reference. A T-score of 50 indicates the average of the healthy control group, T-scores below 50 indicate poorer performance than controls. The severity of the disease is subdivided into benign (blue), mild (orange) and severe (gray).

significant difference with a medium effect size $t(345) = 5.779$, $p < .001$, $d = .667$). Participants who have been infected with COVID-19 scored significantly higher on the GEC than healthy control participants (Figure 2).

To visualize the statistical effect on the composite score GEC, disease severity is subdivided into the increasing degrees of severity: benign, mild and severe according to the cutoff scores of the severity percentage slider: <24%,

25–74% and 75%>, respectively. These three severity groups were then plotted against the T-scores of each of the nine subscales of the BRIEF-A, see Figure 3. From this radar chart it can be observed that (1) the scores of the BRIEF-A subscales follow a domain-specific profile, (2) and seem to be affected by the experienced severity of the disease. Clinically relevant impairments are observed in four subscales: (1) Working Memory, with differences

of 1–1.5 SD compared to Controls, (2) Plan/Organize, (3) Task Monitoring for which only the severe group scores 1 SD higher than Controls and (4) Shifting for which the severe group scores almost 1 SD higher than the controls.

Predicting functional outcomes in post-COVID participants

To allow for prediction of the most affected subscales of the BRIEF-A (Working Memory, Plan/Organize, Task Monitor, and Shift see Figure 1), four stepwise linear regressions were conducted only for the COVID-19 group with each subscale as an outcome variable. The factors included into the models were (1) disease severity, (2) days since diagnosis (3), and general risk factors (i.e. heart attack, diabetes, obesity, hypertension, stroke as mentioned above). In all four stepwise regressions (Working Memory, Plan/Organize, Task Monitor, and Shift as outcome variables), severity was a significant predictor. In the following, we report the regression models to predict the most affected subscales.

In the first regression analysis, disease severity significantly predicted scores on the Shift scale of the BRIEF-A ($\beta = .234, p < .001$). Risk factors and days since diagnosis variables were excluded from the model due to their marginal predictive value. However statistically significant ($F(1, 226) = 13.095, R = .234, p < .0001$), the fitted regression model had a small effect size ($R^2_{adj} = .051$), meaning severity explained 5% of the variance in the Shift subscale scores.

In the second regression analysis using the Plan/Organize subscale, disease severity significantly predicted scores on the Plan/Organize scale ($\beta = .212, p < .0001$), with a small effect size significant fitted regression model ($F(1, 226) = 10.596, R = .212, R^2_{adj} = .041, p = .001$). Again, risk factors and time since diagnosis were excluded from the model. Severity predicted 4% of the variance in the Planning/Organization scale.

In the third regression, Task Monitor was predicted by disease severity as the only significant factor ($\beta = .205, p < .001, F(1, 226) = 9.883, R = .205, p = .002$). Severity predicted around 4% of the variance in the Task Monitor scale ($R^2_{adj} = .038$).

Discussion

The present study investigated subjectively reported cognitive impairment in everyday life in people with previous COVID-19, focusing on EFs in a representative large sample of 529 predominantly female participants of a wide range of ages (18–65+ years), education level and employment status. The findings indicate that individuals reporting an infection with COVID-19 continue to experience notable and clinically significant subjectively reported mild cognitive impairment in daily life functioning even after 6 months post-diagnosis, as compared to their healthy counterparts. Closer inspection reveals a specific cognitive profile for EF complaints, with clinically relevant subjectively reported mild cognitive impairments in working memory, planning

and organization, shifting and task monitoring, which are related to the experienced severity of COVID-19 symptoms. An exploratory analysis assessing predictors for the subjectively reported mild cognitive impairments focused on disease-related variables such as (1) disease severity, (2) time since diagnosis and (3) risk factors for a severe disease course, found that only disease severity explained approximately 5% of the variance. This provides a small but statistically significant contribution toward predicting subjectively reported mild cognitive impairments. In the following, the clinically relevant cognitive profiles of EFs are discussed, followed by a detailed discussion of disease-related predictors of subjectively reported mild cognitive impairment. This section concludes with a discussion of limitations and implications for further studies and applications.

Persistent and specific cognitive impairments Post-COVID

The cognitive effects on everyday life revealed a specific profile, with the greatest effects on the domains of working memory, planning and organizing, task monitoring and shifting abilities. Quantification of this cognitive profile shows that individuals diagnosed with COVID-19 report one standard deviation more EF-complaints compared to the control group. People with a previous COVID-19 report clinically relevant subjectively reported mild cognitive impairment in terms of switching between activities, shifting attention, retaining information in daily life tasks, evaluating one's performance, and tracking one's behavior or that of others. These symptoms were moreover reported an average of 6 months after diagnosis, suggesting that cognitive symptoms appear to persist over a longer period of time and do not return to a previous state once the infection has cleared, as also suggested by Nalbandian et al. (2021) and Yong (2021).

The results of the study also show that severity and duration of acute symptoms, as disease-specific factors, predicted EF complaints to only a small extent. As the pattern of long COVID mechanisms may differ from that of the severity of acute SARS Cov-2 infection (Islam et al., 2020; Mehandru and Merad, 2022), it is interesting for further studies to include other medical objective factors for the prediction of cognitive problems in everyday life. Monitoring of structural measures or enzyme markers may play a role, as alterations in brain structure (Douaud et al. 2022) and dysfunctional inflammatory processes in cerebrospinal fluid (John et al., 2020) have been reported in individuals with post-COVID-19 and impaired cognition. Additionally, an already infected immune system or an altered immune response to (respiratory) viruses in general could present as predispositions to consider in long COVID.

The reasons for a specific cognitive profile of subjectively reported mild cognitive impairment may on the one hand reflect a specific impact of the virus on specific brain networks underlying specific cognitive functions. Previous research already indicated cognitive complaints after

COVID-19 to exhibit an executive pattern (Becker et al., 2021). On the other hand, a specific cognitive profile of impairments may be due to a pattern of subjective reporting in our sample. Possibly, cognitive problems are not perceived at all or are simply classified as less relevant for the functioning of daily life. We therefore suggest interpreting the identified profile as a pattern of most relevant affected domains of disturbed EFs in tasks of daily life, rather than as an objective cognitive profile following COVID-19.

Is the cognitive profile specific for COVID-19?

The introduction of the clinical case definition by WHO (ICD-10 codes (U09) and ICD-11 codes (RA02)), is an important step to better understand the condition after COVID-19, and to take appropriate action. Similarly to post infection fatigue described after Ebola virus, Epstein-Barr virus and cytomegalovirus (Moldofsky & Patcai 2011; Hickey et al., 2006), the question arises whether cognitive complaints are specific to COVID-19 or could be the consequence of a preexisting immune response due to another (viral) infection (Crook et al., 2021). An alternative explanation for the effects that were observed in our study, could be more general long-term effects after a (respiratory) viral infection of different viruses, too, and represent rather a long-influenza than long-COVID syndrome. There is some evidence that (for example) the Influenza-A virus can cause alterations in cognition (Beraki et al., 2005). In order to form projections for COVID-19, a recent review listed several viral agents that have shown to affect cognition (Damiano et al., 2022). Although discussing how different viruses may affect cognition and relate to our results is beyond the scope of this study, its effects could be taken into account in future research. Nonetheless, the official recognition of post-COVID-19-syndrome offers the opportunity to scientifically understand possible neglected cases as well as more obvious and severe ones.

Limitations

It is important to consider certain limitations. Firstly, the disease severity scale used in this study is subject to potential rating discrepancies, since participants self-rated the severity of their disease using a scale from 0 to 100. As a result, reported individual differences in severity scores may not accurately reflect the actual objective severity of disease symptoms, and could be largely independent of them. This means, for example, that two people suffering from the same disease symptom will give different severity ratings. Furthermore, people can be completely unaware of their asymptomatic disease course, which could unjustly have placed them in the comparison group. Future research should aim to combine objective disease data with these subjective measures to discover and understand possible associations.

It is important to recognize that this survey study, which utilizes preexisting groups, is primarily observational in nature and thus does not enable making any

causal conclusions regarding the effects of COVID-19 on EFs. In this respect, groups may differ in many more variables, here for instance regarding age and depression congruent with the commonly assumed multifactorial model of post-COVID health complaints. Thus we explicitly do not control for differences in aspects of health and functioning (e.g., depression), because this may distort the true nature of the groups and thus invalidate group comparisons. Future studies on larger and well-defined samples are needed that allows a thorough investigation of the role of comorbid health complaints preexistent to the COVID-19 infection (Ng et al., 2022).

Finally, as our sample clearly shows a bias toward women, our findings need to be interpreted against this background and possible conclusions for, e.g., disease management between men and women need to be considered (Regitz-Zagrosek, 2012). Another point to consider in this regard is that several studies have shown that a severe COVID-19 course is more common in men (Jin et al., 2020; Vahidy et al., 2021). Effects for sex were lost in our analyses, since there was not accounted for the bias toward women in our sample. Further research should take into account effects for sex on COVID-19 outcomes (Gebhard et al., 2020; Meng et al., 2020; Vahidy et al., 2021).

Implications and future directions

Long-lasting subjectively reported mild cognitive impairment following COVID-19 infection appears to be linked with a decline in daily functioning in a significant proportion of the population. It is important to emphasize that the observed subjectively reported mild cognitive impairment in daily life functioning does not only occur in the most severely ill patients, but that even individuals with relatively mild symptoms can experience persistent cognitive impairments that affect their daily lives.

The herewith identified profile of subjectively reported mild cognitive impairment has the potential to provide insights leading to the development of a cognitive training program in rehabilitation settings. Utilizing cognitive training programs may aid individuals in recovering from COVID-19 related mild cognitive impairments and allow them to return to their work or education, thereby facilitating the restoration to their daily life functioning. The cognitive profile as proposed in the current study provides insight that can help the development of a targeted cognitive training, which takes into account an individual's specific cognitive strengths and weaknesses (Vanderlind et al., 2021). Furthermore, the identification of individual profiles together with possible objective data can give the practitioner a comprehensive diagnostic report of which functions are intact, which have declined and which are covered by compensatory mechanisms. Importantly, even the least severe disease group also showed a mild cognitive impairment, which corresponds with previous literature that *not only* the most severe COVID-19 cases experience long-term cognitive decline. This is important to consider for policy makers in order to ensure adequate access to services for all

affected people. A next step also includes the identification of predictors of these post-acute disease problems.

The concept of a cognitive profile of persistent mild cognitive impairment found in COVID-19 could also be another test case for persistent cognitive impairment following other viruses, e.g., influenza, which have been less in focus so far. Pending further replication of such cognitive profiles in COVID-19 and other viruses, long-lasting complaints in these groups of people should be further explored to allow for development of personalized treatment.

Acknowledgements

We would like to thank our participants who contributed to this study with their time and interest. Another thank you also goes to our creative students who wrote their theses in this field or completed their research internships with us: Christina, Kim, Joost. Lino, a joy to the family; born in the time of COVID spree; bringing happiness and glee; with singing and sport talents, so free. A future so bright and bold; with talents to unfold; by your dreams always be told; and your heart always holds gold.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

ORCID

Anselm B. M. Fuermaier  <http://orcid.org/0000-0002-2331-0840>
Stefanie Enriquez-Geppert  <http://orcid.org/0000-0001-7305-0111>

Data availability statement

Data are available upon request.

References

- Aghagoli, G., Gallo Marin, B., Katchur, N. J., Chaves-Sell, F., Asaad, W. F., & Murphy, S. A. (2021). Neurological involvement in COVID-19 and potential mechanisms: A review. *Neurocritical Care*, 34(3), 1062–1071. <https://doi.org/10.1007/s12028-020-01049-4>
- Alnefeesi, Y., Siegel, A., Lui, L. M. W., Teopiz, K. M., Ho, R. C. M., Lee, Y., Nasri, F., Gill, H., Lin, K., Cao, B., Rosenblat, J. D., & McIntyre, R. S. (2020). Impact of SARS-CoV-2 infection on cognitive function: A systematic review. *Frontiers in Psychiatry*, 11, 621773. <https://doi.org/10.3389/fpsy.2020.621773>
- Amalakanti, S., Arepalli, K. V. R., & Jillella, J. P. (2021). Cognitive assessment in asymptomatic COVID-19 subjects. *Virusdisease*, 32(1), 146–149. <https://doi.org/10.1007/s13337-021-00663-w>
- Asadi-Pooya, A. A., & Simani, L. (2020). Central nervous system manifestations of COVID-19: A systematic review. *Journal of the Neurological Sciences*, 413, 116832. <https://doi.org/10.1016/j.jns.2020.116832>
- Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. (1996). Comparison of Beck Depression Inventories-IA and-II in psychiatric outpatients. *Journal of Personality Assessment*, 67(3), 588–597. https://doi.org/10.1207/s15327752jpa6703_13
- Becker, J. H., Lin, J. J., Doernberg, M., Stone, K., Navis, A., Festa, J. R., & Wisnivesky, J. P. (2021). Assessment of cognitive function in patients after COVID-19 infection. *JAMA Network Open*, 4(10), e2130645. <https://doi.org/10.1001/jamanetworkopen.2021.30645>
- Beraki, S., Aronsson, F., Karlsson, H., Ögren, S. O., & Kristensson, K. (2005). Influenza A virus infection causes alterations in expression of synaptic regulatory genes combined with changes in cognitive and emotional behaviors in mice. *Molecular Psychiatry*, 10(3), 299–308. <https://doi.org/10.1038/sj.mp.4001545>
- Burdick, K. E. (2021). The impact of COVID-19 on cognition in severe cases highlights the need for comprehensive neuropsychological evaluations in all survivors. *Neuropsychopharmacology*, 46, 2225.
- Burgess, P. W., & Simons, J. S. (2005). Theories of frontal lobe executive function: Clinical applications. In P. W. Halligan, & D. T. Wade (Eds), *The Effectiveness of Rehabilitation for Cognitive Deficits* (pp. 211–231). Oxford Academic.
- Butler, M. J., & Barrientos, R. M. (2020). The impact of nutrition on COVID-19 susceptibility and long-term consequences. *Brain, Behavior, and Immunity*, 87, 53–54. <https://doi.org/10.1016/j.bbi.2020.04.040>
- Chen, G., Wu, D., Guo, W., Cao, Y., Huang, D., Wang, H., Wang, T., Zhang, X., Chen, H., Yu, H., Zhang, X., Zhang, M., Wu, S., Song, J., Chen, T., Han, M., Li, S., Luo, X., Zhao, J., & Ning, Q. (2020). Clinical and immunological features of severe and moderate coronavirus disease 2019. *The Journal of Clinical Investigation*, 130(5), 2620–2629. <https://doi.org/10.1172/JCI137244>
- Cohen, J. (1992). A power primer. *Psychological Bulletin*, 112(1), 155–159. <https://doi.org/10.1037/0033-2909.112.1.155>
- Cothran, T. P., Kellman, S., Singh, S., Beck, J. S., Powell, K. J., Bolton, C. J., & Tam, J. W. (2020). A brewing storm: The neuropsychological sequelae of hyperinflammation due to COVID-19. *Brain, Behavior, and Immunity*, 88, 957–958. <https://doi.org/10.1016/j.bbi.2020.06.008>
- Crook, H., Raza, S., Nowell, J., Young, M., & Edison, P. (2021). Long Covid—Mechanisms, risk factors, and management. *BMJ*, 374, n1648. <https://doi.org/10.1136/bmj.n1648>
- Damiano, R. F., Guedes, B. F., de Rocca, C. C., de Pádua Serafim, A., Castro, L. H. M., Munhoz, C. D., Nitri, R., Filho, G. B., Miguel, E. C., Lucchetti, G., & Forlenza, O. (2022). Cognitive decline following acute viral infections: Literature review and projections for post-COVID-19. *European Archives of Psychiatry and Clinical Neuroscience*, 272(1), 139–154. <https://doi.org/10.1007/s00406-021-01286-4>
- Del Brutto, O. H., Wu, S., Mera, R. M., Costa, A. F., Recalde, B. Y., & Issa, N. P. (2021). Cognitive decline among individuals with history of mild symptomatic SARS-CoV-2 infection: A longitudinal prospective study nested to a population cohort. *European Journal of Neurology*, 28(10), 3245–3253. <https://doi.org/10.1111/ene.14775>
- Douaud, G., Lee, S., Alfaro-Almagro, F., Arthofer, C., Wang, C., McCarthy, P., Lange, F., Andersson, J. L. R., Griffanti, L., Duff, E., Jbabdi, S., Taschler, B., Keating, P., Winkler, A. M., Collins, R., Matthews, P. M., Allen, N., Miller, K. L., Nichols, T. E., & Smith, S. M. (2022). SARS-CoV-2 is associated with changes in brain structure in UK Biobank. *Nature*, 604(7907), 697–707. <https://doi.org/10.1038/s41586-022-04569-5>
- Ferrucci, R., Dini, M., Groppo, E., Rosci, C., Reitano, M. R., Bai, F., Poletti, B., Brugnera, A., Silani, V., D'Arminio Monforte, A., & Priori, A. (2021). Long-lasting cognitive abnormalities after COVID-19. *Brain Sciences*, 11(2), 235. <https://doi.org/10.3390/brainsci11020235>
- Gebhard, C., Regitz-Zagrosek, V., Neuhauser, H. K., Morgan, R., & Klein, S. L. (2020). Impact of sex and gender on COVID-19 outcomes in Europe. *Biology of Sex Differences*, 11(1), 29. <https://doi.org/10.1186/s13293-020-00304-9>
- Gibson, P. G., Qin, L., & Puah, S. H. (2020). COVID-19 acute respiratory distress syndrome (ARDS): Clinical features and differences from typical pre-COVID-19 ARDS. *The Medical Journal of Australia*, 213(2), 54–56.e1. <https://doi.org/10.5694/mja2.50674>
- Hampshire, A., Trender, W., Chamberlain, S. R., Jolly, A., Grant, J. E., Patrick, F., Mazibuko, N., Williams, S., Barnby, J. M., Hellyer, P., & Mehta, M. A. (2020). Cognitive deficits in people who have

- recovered from COVID-19 relative to controls: An N = 84,285 online study. *Psychiatry and Clinical Psychology*. <https://doi.org/10.1101/2020.10.20.20215863>
- Hellmuth, J., Barnett, T. A., Asken, B. M., Kelly, J. D., Torres, L., Stephens, M. L., Greenhouse, B., Martin, J. N., Chow, F. C., Deeks, S. G., Greene, M., Miller, B. L., Annan, W., Henrich, T. J., & Peluso, M. J. (2021). Persistent COVID-19-associated neurocognitive symptoms in non-hospitalized patients. *Journal of Neurovirology*, 27(1), 191–195. <https://doi.org/10.1007/s13365-021-00954-4>
- Helms, J., Kremer, S., Merdji, H., Clere-Jehl, R., Schenck, M., Kummerlen, C., Collange, O., Boulay, C., Fafi-Kremer, S., Ohana, M., Anheim, M., & Meziani, F. (2020). Neurologic features in severe SARS-CoV-2 infection. *The New England Journal of Medicine*, 382(23), 2268–2270. <https://doi.org/10.1056/NEJMc2008597>
- Heyer, E. J., Sharma, R., Rampersad, A., Winfree, C. J., Mack, W. J., Solomon, R. A., Todd, G. J., McCormick, P. C., McMurtry, J. G., Quest, D. O., Stern, Y., Lazar, R. M., & Connolly, E. S. (2002). A controlled prospective study of neuropsychological dysfunction following carotid endarterectomy. *Archives of Neurology*, 59(2), 217–222. <https://doi.org/10.1001/archneur.59.2.217>
- Hickie, I., Davenport, T., Wakefield, D., Vollmer-Conna, U., Cameron, B., Vernon, S. D., Reeves, W. C., & Lloyd, A. (2006). Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: Prospective cohort study. *BMJ (Clinical Research ed.)*, 333(7568), 575. <https://doi.org/10.1136/bmj.38933.585764.AE>
- Hopkins, R. O., Weaver, L. K., Pope, D., Orme, J. F., Bigler, E. D., & Larson-Lohr, V. (1999). Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*, 160(1), 50–56. <https://doi.org/10.1164/ajrccm.160.1.9708059>
- Hu, Z., Song, C., Xu, C., Jin, G., Chen, Y., Xu, X., Ma, H., Chen, W., Lin, Y., Zheng, Y., Wang, J., Hu, Z., Yi, Y., & Shen, H. (2020). Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Science China. Life Sciences*, 63(5), 706–711. <https://doi.org/10.1007/s11427-020-1661-4>
- Huang, C., Huang, L., Wang, Y., Li, X., Ren, L., Gu, X., Kang, L., Guo, L., Liu, M., Zhou, X., Luo, J., Huang, Z., Tu, S., Zhao, Y., Chen, L., Xu, D., Li, Y., Li, C., Peng, L., ... Cao, B. (2021). 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. *Lancet (London, England)*, 397(10270), 220–232. [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8)
- Islam, N., Sharp, S. J., Chowell, G., Shabnam, S., Kawachi, I., Lacey, B., Massaro, J. M., D'Agostino, R. B., & White, M. (2020). Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries. *BMJ (Clinical Research Ed.)*, 370, m2743. <https://doi.org/10.1136/bmj.m2743>
- Jackson, J. C., Hart, R. P., Gordon, S. M., Shintani, A., Truman, B., May, L., & Ely, E. W. (2003). Six-month neuropsychological outcome of medical intensive care unit patients. *Critical Care Medicine*, 31(4), 1226–1234. <https://doi.org/10.1097/01.CCM.0000059996.30263.94>
- Jin, J.-M., Bai, P., He, W., Wu, F., Liu, X.-F., Han, D.-M., Liu, S., & Yang, J.-K. (2020). Gender differences in patients with COVID-19: Focus on severity and mortality. *Frontiers in Public Health*, 8, 152. <https://doi.org/10.3389/fpubh.2020.00152>
- John, S., Hussain, S. I., Piechowski-Jozwiak, B., Dibu, J., Kesav, P., Bayrlee, A., Elkambergy, H., John, T. L. S., Roser, F., & Mifsud, V. A. (2020). Clinical characteristics and admission patterns of stroke patients during the COVID 19 pandemic: A single center retrospective, observational study from the Abu Dhabi, United Arab Emirates. *Clinical Neurology and Neurosurgery*, 199, 106227. <https://doi.org/10.1016/j.clineuro.2020.106227>
- Karr, J. E., Areshenkoff, C. N., Rast, P., Hofer, S. M., Iverson, G. L., & Garcia-Barrera, M. A. (2018). The unity and diversity of executive functions: A systematic review and re-analysis of latent variable studies. *Psychological Bulletin*, 144(11), 1147–1185. <https://doi.org/10.1037/bul0000160>
- Liguori, C., Pierantozzi, M., Spanetta, M., Sarmati, L., Cesta, N., Iannetta, M., Ora, J., Mina, G. G., Puxeddu, E., Balbi, O., Pezzuto, G., Magrini, A., Rogliani, P., Andreoni, M., & Mercuri, N. B. (2021). Depressive and anxiety symptoms in patients with SARS-CoV2 infection. *Journal of Affective Disorders*, 278, 339–340. <https://doi.org/10.1016/j.jad.2020.09.042>
- Mazza, M. G., Palladini, M., De Lorenzo, R., Magnaghi, C., Poletti, S., Furlan, R., Ciceri, F., Rovere-Querini, P., & Benedetti, F. (2021). Persistent psychopathology and neurocognitive impairment in COVID-19 survivors: Effect of inflammatory biomarkers at three-month follow-up. *Brain, Behavior, and Immunity*, 94, 138–147. <https://doi.org/10.1016/j.bbi.2021.02.021>
- Mehandrou, S., & Merad, M. (2022). Pathological sequelae of long-haul COVID. *Nature Immunology*, 23(2), 194–202. <https://doi.org/10.1038/s41590-021-01104-y>
- Meng, Y., Wu, P., Lu, W., Liu, K., Ma, K., Huang, L., Cai, J., Zhang, H., Qin, Y., Sun, H., Ding, W., Gui, L., & Wu, P. (2020). Sex-specific clinical characteristics and prognosis of coronavirus disease-19 infection in Wuhan, China: A retrospective study of 168 severe patients. *PLoS Pathogens*, 16(4), e1008520. <https://doi.org/10.1371/journal.ppat.1008520>
- Miskowiak, K., Johnsen, S., Sattler, S., Nielsen, S., Kunalan, K., Rungby, J., Lapperre, T., & Porsberg, C. (2021). Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. *European Neuropsychopharmacology*, 46, 39–48. <https://doi.org/10.1016/j.euroneuro.2021.03.019>
- Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “frontal lobe” tasks: A latent variable analysis. *Cognitive Psychology*, 41(1), 49–100. <https://doi.org/10.1006/cogp.1999.0734>
- Moldofsky, H., & Patcai, J. (2011). Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC Neurology*, 11(1), 37. <https://doi.org/10.1186/1471-2377-11-37>
- Moller, J., Cluitmans, P., Rasmussen, L., Houx, P., Rasmussen, H., Canet, J., Rabbitt, P., Jolles, J., Larsen, K., Hanning, C., Langeron, O., Johnson, T., Lauven, P., Kristensen, P., Biedler, A., van Beem, H., Fraidakis, O., Silverstein, J., Beneken, J., & Gravenstein, J. (1998). Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study. *Lancet*, 351(9106), 857–861. [https://doi.org/10.1016/S0140-6736\(97\)07382-0](https://doi.org/10.1016/S0140-6736(97)07382-0)
- Mukaka, M. M. (2012). Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi Medical Journal : The Journal of Medical Association of Malawi*, 24(3), 69–71. 23638278
- Nalbandian, A., Sehgal, K., Gupta, A., Madhavan, M. V., McGroder, C., Stevens, J. S., Cook, J. R., Nordvig, A. S., Shalev, D., Sehrawat, T. S., Ahluwalia, N., Bikdeli, B., Dietz, D., Der-Nigoghossian, C., Liyanage-Don, N., Rosner, G. F., Bernstein, E. J., Mohan, S., Beckley, A. A., Seres, D. S., ... Wan, E. Y. (2021). Post-acute COVID-19 syndrome. *Nature Medicine*, 27(4), 601–615. <https://doi.org/10.1038/s41591-021-01283>
- Newman, M. F., Kirchner, J. L., Phillips-Bute, B., Gaver, V., Grocott, H., Jones, R. H., Mark, D. B., Reves, J. G., & Blumenthal, J. A. (2001). Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *The New England Journal of Medicine*, 344(6), 395–402. <https://doi.org/10.1056/NEJM200102083440601>
- Ng, R., Vargas, G., Jashar, D. T., Morrow, A., & Malone, L. A. (2022). Neurocognitive and psychosocial characteristics of pediatric patients with Post-Acute/Long-COVID: A retrospective clinical case series. *Archives of Clinical Neuropsychology*, 37(8), 1633–1643. <https://doi.org/10.1093/arclin/acac056>
- Norman, B. C., Jackson, J. C., Graves, J. A., Girard, T. D., Pandharipande, P. P., Brummel, N. E., Wang, L., Thompson, J. L., Chandrasekhar, R., & Ely, E. W. (2016). Employment outcomes after critical illness: An analysis of the bringing to light the risk factors and incidence of neuropsychological dysfunction in ICU Survivors Cohort. *Critical Care Medicine*, 44(11), 2003–2009. <https://doi.org/10.1097/CCM.0000000000001849>

- Ntaios, G., Michel, P., Georgiopoulos, G., Guo, Y., Li, W., Xiong, J., Calleja, P., Ostos, F., González-Ortega, G., Fuentes, B., Alonso de Leciñana, M., Díez-Tejedor, E., García-Madrona, S., Masjuan, J., DeFelipe, A., Turc, G., Gonçalves, B., Domigo, V., Dan, G.-A., ... Lip, G. Y. (2020). Characteristics and outcomes in patients with COVID-19 and acute ischemic stroke: The global COVID-19 stroke registry. *Stroke*, *51*(9), e254–e258. <https://doi.org/10.1161/STROKEAHA.120.031208>
- Pilotto, A., Cristillo, V., Piccinelli, S. C., Zoppi, N., Bonzi, G., Sattin, D., Schiavolin, S., Raggi, A., Canale, A., Gipponi, S., Libri, I., Frigerio, M., Bezzi, M., Leonardi, M., & Padovani, A. (2021). Long-term neurological manifestations of COVID-19: Prevalence and predictive factors. *Neurology*. <https://doi.org/10.1101/2020.12.27.20248903>
- Poletti, S., Palladini, M., Mazza, M. G., De Lorenzo, R., Irene, B., Sara, B., Beatrice, B., Ceciclio, B., Stefania, C., Valentina, C., Elisa, C., Jacopo, C., Marta, C., Elena, C., Federica, C., Sarah, D., Greta, D., Camilla, D. P., ... Benedetti, F. (2022). Long-term consequences of COVID-19 on cognitive functioning up to 6 months after discharge: Role of depression and impact on quality of life. *European Archives of Psychiatry and Clinical Neuroscience*, *272*(5), 773–782. <https://doi.org/10.1007/s00406-021-01346-9>
- Ramos-Galarza, C., Acosta-Rodas, P., Bolaños-Pasquel, M., & Lepe-Martínez, N. (2019). The role of executive functions in academic performance and behaviour of university students. *Journal of Applied Research in Higher Education*, *12*(3), 444–455. <https://doi.org/10.1108/JARHE-10-2018-0221>
- Regitz-Zagrosek, V. (2012). Sex and gender differences in health: Science & society series on sex and science. *EMBO Reports*, *13*(7), 596–603. <https://doi.org/10.1038/embor.2012.87>
- Riordan, P., Stika, M., Goldberg, J., & Drzewiecki, M. (2020). COVID-19 and clinical neuropsychology: A review of neuropsychological literature on acute and chronic pulmonary disease. *The Clinical Neuropsychologist*, *34*(7-8), 1480–1497. <https://doi.org/10.1080/13854046.2020.1810325>
- Rogers, J. P., Chesney, E., Oliver, D., Pollak, T. A., McGuire, P., Fusar-Poli, P., Zandi, M. S., Lewis, G., & David, A. S. (2020). Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. *The Lancet. Psychiatry*, *7*(7), 611–627. [https://doi.org/10.1016/S2215-0366\(20\)30203-0](https://doi.org/10.1016/S2215-0366(20)30203-0)
- Roth, R. M., Isquith, P. K., & Gioia, G. A. (2005). BRIEF-A: Behavior rating inventory of executive function—Adult version. *Psychological Assessment Resources*.
- Rothenhäusler, H.-B., Ehrentraut, S., Stoll, C., Schelling, G., & Kapfhammer, H.-P. (2001). The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: Results of an exploratory study. *General Hospital Psychiatry*, *23*(2), 90–96. [https://doi.org/10.1016/S0163-8343\(01\)00123-2](https://doi.org/10.1016/S0163-8343(01)00123-2)
- Smit, D., Koerts, J., Bangma, D. F., Fuermaier, A. B. M., Tucha, L., & Tucha, O. (2021). Look who is complaining: Psychological factors predicting subjective cognitive complaints in a large community sample of older adults. *Applied Neuropsychology: Adult*. <https://doi.org/10.1080/23279095.2021.2007387>
- Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine*, *166*(10), 1092–1097. <https://doi.org/10.1001/archinte.166.10.1092> 16717171
- Stuss, D. T. (2011). Functions of the frontal lobes: Relation to executive functions. *Journal of the International Neuropsychological Society*, *17*(05), 759–765. <https://doi.org/10.1017/S1355617711000695>
- Sukantarat, K. T., Burgess, P. W., Williamson, R. C. N., & Brett, S. J. (2005). Prolonged cognitive dysfunction in survivors of critical illness. *Anaesthesia*, *60*(9), 847–853. <https://doi.org/10.1111/j.1365-2044.2005.04148.x>
- Vahidy, F. S., Pan, A. P., Ahnstedt, H., Munshi, Y., Choi, H. A., Tiruneh, Y., Nasir, K., Kash, B. A., Andrieni, J. D., & McCullough, L. D. (2021). Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area. *PLoS One*, *16*(1), e0245556. <https://doi.org/10.1371/journal.pone.0245556>
- Vanderlind, W. M., Rabinovitz, B. B., Miao, I. Y., Oberlin, L. E., Bueno-Castellano, C., Fridman, C., Jaywant, A., & Kanellopoulos, D. (2021). A systematic review of neuropsychological and psychiatric sequelae of COVID-19: Implications for treatment. *Current Opinion in Psychiatry*, *34*(4), 420–433. <https://doi.org/10.1097/YCO.0000000000000713>
- Woo, M. S., Malsy, J., Pöttgen, J., Seddiq Zai, S., Ufer, F., Hadjilaou, A., Schmiedel, S., Addo, M. M., Gerloff, C., Heesen, C., Schulze Zur Wiesch, J., & Friese, M. A. (2020). Frequent neurocognitive deficits after recovery from mild COVID-19. *Brain Communications*, *2*(2), fcaa205. <https://doi.org/10.1093/braincomms/fcaa205>
- Yong, S. J. (2021). Long COVID or post-COVID-19 syndrome: Putative pathophysiology, risk factors, and treatments. *Infectious Diseases (London, England)*, *53*(10), 737–754. <https://doi.org/10.1080/23744235.2021.1924397>
- Zhou, H., Lu, S., Chen, J., Wei, N., Wang, D., Lyu, H., Shi, C., & Hu, S. (2020). The landscape of cognitive function in recovered COVID-19 patients. *Journal of Psychiatric Research*, *129*, 98–102. <https://doi.org/10.1016/j.jpsychires.2020.06.022>