rijksuniversiteit groningen

The effect of Long-COVID on memory, working memory, and attentiveness and its predicting power on quality of life and functional activity, tested in an online study

Karlotta von Bormann

Master Thesis – Applied cognitive neuroscience

S5177022

February 2024

Department of Psychology

University of Groningen

Examiner/Daily supervisor:

Jaroslav Krc

A thesis is an aptitude test for students. The approval of the thesis is proof that the student has sufficient research and reporting skills to graduate but does not guarantee the quality of the research and the results of the research as such, and the thesis is therefore not necessarily suitable to be used as an academic source to refer to. If you would like to know more about the research discussed in this thesis and any publications based on it, to which you could refer, please contact the supervisor mentioned.

Abstract

COVID-19 remains an important topic as research on Long-COVID continues to improve/expand and the severity and impact on people's health becomes clearer. This study was conducted to further study the neurocognitive impairments of Long-COVID patients and the effect on the quality of life and daily functional activity. 530 people took part in the study, 271 of whom were included in the data analysis. The participants took part in an online study consisting of 17 questionnaires covering demographics, functional outcomes, neuropsychological, personality, and psychological domains. The participants were divided into two groups: A group of participants who had been infected with SARS-CoV-2 at least once (n = 185) and a control group (n = 86). To assess the impact of Long-COVID on cognition, the composite scores of the Working Memory Questionnaire (WMQ) and the forgetfulness and distractibility scale of the Cognitive Failure Questionnaire (CFQ) were used for analysis. In addition, two regression analyses were performed to assess the impact of cognitive deficits on quality of life and functional activity using the WHO-Quality of Life Questionnaire (WHOQoL) and the Functional Activity Questionnaire (FAQ). The results show that Long-COVID participants have significantly worse scores on the WMQ, CFQ forgetfulness and CFQ distractibility scales than the control group. The severity of disease progression influences the severity of cognitive impairment, as more severely affected participants showed more severe impairment. Furthermore, WMQ, CFQ forgetfulness and CFQ distractibility scores significantly predicted WHOQoL and FAQ scores, with WMQ being the strongest predictor. These results emphasize the extent of symptoms suffered by long-term COVID patients.

Keywords: Long-COVID, working memory, quality of life, functional activity, cognitive function

Table of content

Cognitive functions 5
Executive functions, memory, and attention 5
The testing of cognitive functions 6
Disturbance of cognitive functions in different patient groups 6
Cognitive functions and the role of the brain 7
SARS-CoV-2 8
How SARS-CoV-2 infects the brain: Direct ways 8
How SARS-CoV-2 infects the brain: Indirect ways 9
The effect of SARS-CoV-2 on cognitive functions 9
Methods: 12
Participants and Recruitment 12
Assessment battery 13
In- and exclusion and final sample 15
Procedure 18
Statistical design 19
Results 20
Comparison of the COVID-group and Control group in working memory, memory, and attentiveness 21
Comparison of the severity groups 22
Predicting the quality of life in COVID-participants 25
Predicting the functional activity in COVID-participants 27
Discussion 29
Performance in memory, working memory, and attentiveness and COVID-19 29
Influence of severity on cognitive impairments 31
Predicting Quality of Life and functional activity 32
Limitations and implications 33
Conclusion 34
References 35
Appendix 64

Cognitive functions

Executive functions, memory, and attention

To live an organized and structured life, people need the ability to manage time and behavior, make decisions, solve problems, inhibit impulses. These so called “executive functions” (EF) are top-down cognitive processes that are responsible for planning, organizing, coordinating, and controlling our behavior (Diamond, 2013).

Executive functions can be divided into hot and cool functions. Hot EF imply the skills to regulate and manage the behavior and cognitive processes in an emotional setting - crucial for social interactions (Salehinejad et al., 2021). Cool EF refer to all executive functions that are not specifically important in an emotional situation. Examples would be working memory, shifting, focusing, planning, inhibition, and so on. (Salehinejad et al., 2021). Working memory (WM) describes the ability to store information in the short-term memory while completing other tasks (Baddeley, 1992). WM is important for following a task with multiple steps, staying focused, doing two tasks at the same time, solving problems, and simply memorizing or recalling things (Bergman-Nutley & Klingberg, 2014; Colom et al., 2010; Ding et al., 2019; Gathercole et al., 2008).

Executive functioning relies on more simple processes like motor control or attention and more difficult attention processes rely on good executive functioning. Attention, which describes the process to focus and concentrate on specific elements while ignoring others, is fundamental for some executive processes, like WM: In order to store information while completing other tasks, one has to focus on task-relevant stimuli and ignore distractors (Awh et al., 2006; Fougnie, 2008). WM capacities on the other hand influence distractibility and mind wondering (Kane et al., 2007).

Attention is also important for memory, as attention abilities decide over memory encoding and retrieval (Chun & Turk-Browne, 2007; Moen et al., 2017). Memory describes the process of acquiring, storing, retaining, and retrieving information.

This paper will focus on working memory, memory, and attention/attentiveness.

The testing of cognitive functions

There are various ways to test the individual's strengths and weaknesses of cognitive functions. Standardized tests or test batteries are commonly used. The Wisconsin Card Sorting Test, Stroop Test, N-back test, Go/No-Go tasks, and Trail Making Test measure different domains of executive functioning.

For testing attention capacity, the Attention Network Test as well as the Stroop Test or Trail Making Test are suitable. The Stroop test for example measures selective attention, cognitive control, and processing speed (Scarpina & Tagini, 2017), which points out the interaction between the various cognitive processes. To test memory functions, memory span or recall tasks are recommended. The Wechsler Memory Scale or Digit Span Test are examples of objective tests.

Depending on which aspect of EF, attention, and memory one wants to measure, different tests are used. To really get a complete understanding of the executive functioning of an individual, you need to measure multiple aspects of EF, select the tests carefully and assess the same aspect with multiple tests. Otherwise, the score on an EF task will be polluted by non-systematic and systematic non-EF variance. This problem is called the impurity problem (Snyder et al., 2015).

Apart from standardized tests or test batteries, subjective assessment strategies like questionnaires, interviews or reports from patients or their relatives are commonly used. Subjective assessments also gain of importance, since objective tests cannot capture the individual suffering (Hess et al., 2020). The Behavior Rating Inventory of Executive Function®–Adult Version (BRIEF-A) for example is a self-report questionnaire to measure EF. Nine domains of EFs are queried: Inhibit, Shift, Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials. Another way of subjectively testing EFs is with the working memory questionnaire (WMQ).

Disturbance of cognitive functions in different patient groups

Impairments of cognitive functions, like impulsive behavior, focusing problems, poor planning and organizing, poor memory, and so on, have been found in various patient groups. Patients with neurological disorders like traumatic brain injuries (Azouvi et al., 2016; Mathias & Mansfield, 2005)

and Parkinson's disease (Campos-Sousa et al., 2010; Poliakoff & Smith-Spark, 2008; Zgaljardic et al., 2006) exhibit problems with executive functions, memory, and attention, as well as neurodevelopmental disorders like ADHD (Fuermaier et al., 2015; Xie et al., 2020). ADHD patients for instance encounter problems with inhibition, impulsivity, planning, and working memory (Doyle, 2006; Kofler et al., 2018; Schoechlin & Engel, 2005).

Psychiatric disorders like Schizophrenia (Thai et al., 2019; Zalla et al., 2004), substance use disorder (Clark et al., 2017; Smith et al., 2014), or PTSD (Lagarde et al., 2010; Moradi et al., 1999) also show impairments in the domain of cognitive functions.

Physical damage to the brain, neurodegenerative processes and neurotransmitter imbalances can be responsible for the symptoms in these patient groups. Research has shown that impaired executive functions are associated with damage or alterations in the frontal regions (Picton et al., 2007; Rubia et al., 2001; Salehinejad et al., 2021), which will be discussed in more detail in the next chapter.

Cognitive functions and the role of the brain

The main area of the brain that is associated with EFs is concentrated in the frontal regions, especially the prefrontal cortex (PFC) (Bechara et al., 2000; Mazzola-Pomietto et al., 2009; Panikratova et al., 2020; Picton et al., 2007; Stern et al., 2000). Executive functions root from frontal lobe activity and maturation (Durston et al., 2006; Moriguchi & Hiraki, 2009), meaning that with the development of the frontal lobe, cognitive and executive abilities develop and strengthen.

The prefrontal regions interact with other regions to perform EFs, including the thalamus relaying sensory information within a thalamocortical network (Hwang et al., 2017; Hwang et al., 2020; Sherman & Guillery, 2002). Within this network especially the mediodorsal thalamus is associated with working memory and further EF (Hwang et al., 2020; Mitchell et al., 2015; Peräkylä, et al., 2017).

Another brain region involved in forming and maintaining EFs is the Hippocampus. While the Hippocampus is generally known for its role in memory (Barker & Warburton, 2011; Bird & Burgess,

2008), it has been found to play a role in working memory and processing speed (O'Shea et al., 2016; Toepper et al., 2010).

Attention has been associated with the PFC (Paneri & Gregoriou, 2017), the parietal lobe (Yin et al., 2012), thalamus (Ivanov et al., 2010), and so on. Furthermore, it has been found that executive functioning and attention processes work together in the PFC (Johnson et al., 2007).

Damage to the brain can lead to impairments in executive functions. Injuries, viruses, or illnesses can harm the central nervous system and therefore harm the cognitive abilities. The 2019 discovered respiratory coronavirus SARS-CoV-2 is one of many viruses that can affect the CNS (Proust et al., 2023). SARS-CoV-2 is responsible for over 6.9 million deaths since the beginning of the pandemic (World Health Organization, n.d.) and is still an ongoing topic in our society. Since the literature on the effect of SARS-CoV-2 on executive functions is still sparse, this paper will provide more and new information about the effect of COVID-19 on cognitive functions.

SARS-CoV-2

How SARS-CoV-2 infects the brain: Direct ways

Even though SARS-CoV-2 mostly affects the respiratory system, some COVID-19 patients complain about neurocognitive symptoms such as headaches, dizziness, impaired consciousness, fatigue, and so on (Mao et al., 2020; Wang et al., 2020), indicating neurological manifestations. This means that the virus can infiltrate the brain and disrupt the central nervous system. There are various ways for the virus to invade the brain directly: It can enter through the olfactory pathway via the olfactory bulb, where it gets transported via the olfactory nerve (Burks et al., 2021). It can enter through the blood-brain-barrier (BBB), in two different ways: The virus can lead to endothelial cell dysfunction which alters the blood-brain-barrier integrity (Alquisiras-Burgos et al., 2021; Reynolds & Mahajan, 2021; Zhang et al., 2021) or the virus can infect immune cells (Pontelli et al., 2020), “without production of the infectious virus but preserving infectivity” (Percivalle et al., 2021, p. 15). Therefore, the cell can cross the BBB without getting recognized as a virus (Trojan horse mechanism) (Zubair et al., 2020).

How SARS-CoV-2 infects the brain: Indirect ways

SARS-CoV-2 can also influence the brain in an indirect way. Inflammation, hypoxia, and demyelination are indirect ways of influencing and damaging the brain. The virus can cause an inflammatory response, that leads to a release of pro-inflammatory cytokines (Huang et al., 2020), which in turn can alter and disrupt the BBB permeability and make the entry of the virus into the brain possible (Alexopoulos et al., 2020; Erickson et al., 2021; Perrin et al., 2021). Neuroinflammation (Pilotto et al., 2021), such as Encephalitis (Benameur et al., 2020; Perrin et al., 2021), is the result.

Another indirect way for the virus to invade the brain is through hypoxia. Hypoxia describes low levels of oxygen in tissues and is found in COVID-19 patients (Alhusain et al., 2021; Yao et al., 2020). A hypoxic state in the brain can facilitate cell death (Feng et al., 2012; Oh et al., 2017) and break down the BBB permeability (Halder & Milner, 2020; Yang & Rosenberg, 2011). Furthermore, hypoxia is pro-inflammatory which can cause a hypoxia-induced neuroinflammation (Mukandala et al., 2016; Sapin et al., 2015).

Furthermore, invasion of the SARS-CoV-2 in the brain can cause demyelination (Ismail & Salama, 2022) and changes in the brain structure (Douaud et al., 2022): Douaud studied the brains of 401 participants, before and after their infection with COVID-19. Changes such as a reduction of grey matter thickness in the orbitofrontal cortex and parahippicampal gyrus or reduction in brain size were groundbreaking findings of the study. Cognitive decline was found to be a consequence.

The effect of SARS-CoV-2 on cognitive functions

Some patients that have recovered from COVID-19 continue to show symptoms, including cognitive deficits and impairments of executive functions (Beaud et al., 2021; Ghosh et al., 2020; Helms et al., 2020). This so called “post-acute COVID-19 syndrome" describes clinical symptoms that last for more than four weeks after the onset of the illness (Nalbandian et al., 2021). The “Post-acute COVID-19 syndrome” can fade out or manifest in a “Post-COVID-19 condition” also known as “Long-COVID”. The “Post-COVID-19 condition”, is defined as “the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2

months with no other explanation" (World Health Organization, 2022). It has been found that 10 to 20 % of COVID-patients develop long-COVID (World Health Organization, 2022).

The symptoms of Long-COVID are multifaceted: Fatigue, shortness of breath, (chest) pain, and loss of smell and taste are some of the main symptoms Long-COVID patients are facing (Kayaaslan et al. 2021; Peter et al., 2022; Petersen et al., 2021). But neurocognitive impairments, anxiety, depression, and sleep problems are burdening the patients as well (Kayaaslan et al., 2021). Neurocognitive complaints like "brain fog", attention, concentration, memory and especially working memory problems are common (Asadi-Pooya et al., 2022; Cui et al., 2023; Espinar-Herranz et al., 2023; Peter et al., 2022). De Groot et al (2023) found that long-COVID patients had the most severe impairments in working memory, across different levels of severity of disease progression. Tested cognitive impairments in COVID-19 hospitalized patients correlated with subjective complaints and quality of life (Delgado-Alonso et al., 2022; Miskowiak et al., 2021).

These neurocognitive symptoms affect the people's ability to work (Davis et al., 2021; Miskowiak et al., 2023), do their daily routine and overall quality of life (Miskowiak et al., 2023; Tabacof et al., 2022). Certain individuals even have to quit their job or cannot go back to work due to the presence of impairments (Davis et al., 2021). Additionally, it has been shown that risk for cognitive deficits remained elevated for COVID-19 patients two years after acute infection (Taquet et al., 2022), which demonstrates the magnitude of Long-COVID. Fatigue also has a big influence on the quality of life (Vélez-Santamaría et al., 2023) and on the daily life (Nielsen et al., 2022) in long-COVID patients.

The reason behind these impairments might be the invasion of the SARS-CoV-2 into the central nervous system: The entry of the virus through the olfactory bulb (olfactory pathway) can lead to hypometabolism of nearby brain regions (Donegani et al., 2021), that are responsible for cognitive functions like working memory (Luck et al., 2010) or attention switching (Varjačić et al., 2018). Studies also link hypometabolism in limbic/paralimbic regions in COVID-19 patients with cognitive deficits (Guedj et al., 2021).

Once the virus has invaded the brain, multiple regions are affected from it. It has been found that SARS-Cov-2 can infect the amygdala, cerebral cortex, brainstem, temporal and frontal cortex, and other brain regions (Gagliardi et al., 2021; Lukiw et al., 2022; Serrano et al., 2021). Especially the frontal cortex is found to be invaded (Toniolo et al., 2021): Studies showing frontal hypometabolism in COVID-19 patients that experience new cognitive disruptions (Delorme et al., 2020) and white matter lesions in frontal regions being linked to cognitive deficits in post-acute patients (Andriuta et al., 2022).

Another way of influencing cognitive functions could be through neuroinflammation (Lyra E Silva et al., 2022; Zhou et al., 2020). It has been shown that neuroinflammation in COVID-19 patients can lead to cognitive deficits, like attention, information processing, verbal fluency, and working memory deficits (Mazza et al., 2021). Hypoxia and hypoxemia (low levels of oxygen in the blood) is associated with executive, memory, and attentional impairments in post-COVID patients (Dondaine et al., 2022; García-Grimshaw et al., 2022).

Since the pandemic was a challenge for the whole world, factors like psychological stress can also lead to cognitive impairments (Ali Awan et al., 2021). The stressful environment that the pandemic created, was associated with cognitive complaints, and increase in depression and anxiety (Fiorenzato et al., 2021). The illness itself led to an increase in psychological complaints (Mazza et al., 2020) and to an increased suicide risk. A meta-analysis found that suicidality can be a symptom of Long-COVID, with a prevalence of 2% (Patel et al., 2022). Anhedonia, stress, anxiety, and depression are increased (Frontera et al., 2021; Lamontagne et al., 2021) and linked to cognitive impairments in COVID-19 patients (Brown et al., 2022; Delgado-Alonso et al., 2022).

Moreover, it has been observed that the severity of the course of the illness correlates with the severity of cognitive complaints (Ariza et al., 2023; Ollila et al., 2022; Vannorsdall et al., 2022). An online study of de Groot et al. (2023) examined how COVID-19 influences executive functions and impairments in the daily life by comparing a healthy control group with participants that were infected with COVID-19. Executive functions were assessed using the BRIEF-A inventory, among

others. Results show that there is a significant difference in the self-reported cognitive impairments between the control and the COVID-19 group, even after six months of the acute illness. The COVID-19 group significantly exhibited more executive dysfunctions than the control group in the domains of working memory, planning, and organization, shifting and task monitoring. Furthermore, these impairments correlate with the disease severity. Shockingly, even participants that experienced a mild disease severity exhibited cognitive impairments.

This paper uses the same data set as de Groot's et al. (2023) and analyses new hypotheses. To confirm the findings of the executive and cognitive impairments of long-term COVID patients, working memory, memory, and attention performance and the associated quality of life and functional activity are analyzed. Three hypotheses will be tested and discussed in this paper:

1. The Long-COVID group differs significantly in working memory, memory, and attentiveness from the healthy control group, tested with the Working Memory Questionnaire, Cognitive Failure Questionnaire forgetfulness scale, and Cognitive Failure Questionnaire distractibility scale.
2. There is a significant difference between the three severity groups within the Long-COVID group in working memory, memory, and attentiveness, with the severe group showing the worst scores. This hypothesis is tested with the same three questionnaires.
3. Working memory, memory, and attentiveness abilities predict quality of life and functional activity for the Long-COVID group, tested with the WHO-Quality of Life questionnaire and Functional Activity Questionnaire.

Methods:

Participants and Recruitment

530 participants between the age of 18 and 65+ took part in this study. 429 participants of the sample were female, 100 were male and one participant stated to be in the category “other”. The experimental group consisted of 350 participants that have been infected with the SARS-CoV-2 virus

(Long-COVID group) and the control group consisted of 180 participants that reported never been infected with the virus (Control group).

Ethics approval was obtained from the Ethics Committee of the Department of Psychology before recruitment began.

Participants were recruited through advertisement in social media (Instagram, LinkedIn, Facebook), word of mouth advertisement, and flyers in hospitals and other health care facilities. Furthermore, groups of people that have recovered from the SARS-CoV-2 drew attention to the study. General practitioners and acquaintances recruited participants in the Netherlands, Germany, Mexico, and Spain. The language of the questionnaire was adopted to the language of the participants.

Assessment battery

In this study an online questionnaire called the "Groninger Neuropsychological COVID-19 Test battery Cognitive Complaints (CoCo-19)" was used which was developed by de Groot et al. (2023). It consisted of demographics, functional outcome, neuropsychological, personality and psychological domains. The questionnaire was published on the website Qualtrics. In total, 17 questionnaires were included in the CoCo-19, but only 10 were used for the statistical analysis in this paper. For an overview of the questionnaires used in the analysis and their Cronbach's alpha, see table 1.

For the main analysis the WHO Quality of Life questionnaire (WHOQoL), the Functional Activity Questionnaire (FAQ), the Working Memory Questionnaire (WMQ) and the Cognitive Failure Questionnaire (CFQ) were used. These questionnaires assess life outcome and neuropsychological domains.

- The WHOQoL-bref is a 26-item questionnaire (a short form of the original WHOQoL), created by the World Health Organization to assess the quality of life in the domains of physical health, psychological, social relationships, and environment. It has good to excellent validity and reliability scores (Skevington et al., 2004; The WHOQOL group, 1998). Higher scores equal more quality of life. In this paper it is referred to as WHOQoL.

- The FAQ is a 10-item questionnaire assessing performance of daily tasks and activities, with good validity and reliability (González et al., 2022). Lower scores equal to more independence in daily tasks and activities and higher scores equal to impaired function and possible cognitive impairment.
- To test working memory the WMQ was utilized, which assess the domains short-term storage, attention, and executive control of working memory. Studies found good internal consistency, excellent test-retest reliability, and acceptable construct validity (Aksoy et al., 2022; Vallat-Azouvi et al., 2012). Lower scores indicate less working memory impairments.
- Finally, the CFQ, designed by Broadbent et al. (1982) assesses absent-mindedness. Three domains are tested in the questionnaire: forgetfulness, distractibility, and false triggering, which could be summarized under the domains of memory, attention, and "control of thought or action" (Bridger et al., 2013; Broadbent et al., 1982, p. 1). It is found to have a good test-retest reliability (Bridger et al., 2013). Lower scores predict better attentiveness, memory, and control of thought or action.

As shown in table 1, each questionnaire used in the analysis has at least an acceptable up to excellent reliability.

Table 1

Description of the questionnaires of the "CoCo-19" and their Cronbach's alpha level

Domain	Category	Questionnaire	Abbreviation	Cronbach's alpha
Life Outcome	Quality of Life	Quality of Life	WHOQoL	.924
	Functional Activity	Functional Activity questionnaire	FAQ	.925
Neuropsychological	General Cognition	Cognitive Failure Questionnaire	CFQ	.946
	Working memory	Working memory questionnaire	WMQ	.969
Psychological	General Health	Positive and Negative Affect Schedule	PANAS	Positive: .863 Negative: .867
	Sleep	Pittsburgh Sleep Quality Index	PSQI	.834
	Distress	Kessler Psychological Distress Scale	K-10	.859
	Depression	Beck's Depression Inventory	BDI	.848
	Anxiety	Generalized Anxiety	GAD-7	.851
	Fatigue	Fatigue Severity Scale	FSS	.954

Note. For calculating the Cronbach's alpha of the PSQI, only the questionnaire items five until eighteen were used.

In- and exclusion and final sample

Out of the 530 participants, 259 participants were excluded from statistical analyses for not filling out completely the WMQ, WHOQoL, FAQ, CFQ, PANAS, BDI, GAD-7, FSS, and the K-10. Next, participants with an unreasonably short questionnaire completion time were checked for reporting

bias with the BRIEF-A validity scale. No more participants were excluded. Hospitalized participants were left in the sample since they completed the questionnaire.

The remaining 271 participants were divided into two groups: The experimental group that consisted of Long-COVID participants (n = 185) and the control group that consisted of healthy participants (n = 86). Table 2 illustrates the distribution and frequencies of the main demographic data of the COVID and the non-COVID group. Participants had to give their informed consent, before starting with the questionnaire.

Table 2

Characteristics and demographics of the 271 participants

Characteristic	Long-COVID		Healthy		Full	
	n	*%*	*n*	*%*	*n*	*%*
Gender						
Female	160	86,5	50	58,1	210	77,5
Male	25	13,5	36	41,9	61	22,5
Age ranges (in years)						
18 – 29	38	20,5	36	41,9	74	27,3
30 – 39	33	17,8	8	9,3	41	15,1
40 – 49	44	23,8	7	8,1	51	18,8
50 – 64	64	34,6	25	29,1	89	32,8
65 or older	6	3,2	10	11,6	16	5,9
COVID-diagnosis	185	100	.	.	185	68,3
Typical COVID symptoms	175	94,6	.	.	175	64,6
Severity group “benign”	18	9,7	.	.	18	6,6
Severity group “mild”	108	58,4	.	.	108	39,9
Severity group “severe”	58	31,4	.	.	58	21,4
Highest completed education						
Less than high school diploma	.	.	1	1,2	1	,4
High school diploma	4	2,2	.	.	4	1,5
Education/ Apprenticeship	52	28,1	7	8,1	59	21,8
Study without degree	23	12,4	22	25,6	45	16,6
Bachelor’s degree	49	26,5	27	31,4	76	28,0
Master’s degree	29	15,7	9	10,5	38	14,0
Doctorate	28	15,1	20	23,3	48	17,7
Employment status						
Employed, working 1–39 h per week	97	52,4	23	26,7	120	44,3
Employed, working 40	29	15,7	13	15,1	42	15,5

or more hours per week						
Self-employed	14	7,6	6	7,0	20	7,4
Full-time student	14	7,6	20	23,3	34	12,5
Househusband/ housewife	3	1,6	3	3,5	6	2,2
Not employed, looking for work	2	1,1	2	2,3	4	1,5
Not employed, not looking for work	2	1,1	4	4,7	6	2,2
Retired	6	3,2	14	16,3	20	7,4
Not able to work	18	9,7	1	1,2	19	7,0

Procedure

The CoCo-19 was available in Dutch, German, Spanish, English, and French. The questionnaire was available online on Qualtrics and the data collection took part from the end of January 2021 until beginning of January 2022.

The questionnaire started with an informed consent, where the participants learned about the procedure and aim of the study. They were then asked about their age, gender, living situation, previous illnesses, medication, and previous COVID-19 infection. In case of a previous infection with SARS-CoV-2, participants were questioned about date of diagnosis, disease severity, related hospitalization, and related medication intake.

The first domain tested was life outcome. Life outcome was assessed using the FAQ, followed by the WHOQoL. Next, neuropsychological strengths were then measured using the ASCDQ, followed by the BRIEF-A, CFQ, FEDA, FLEI and the WMQ. Personality scores were determined using the NEO-FFI. Psychological domains were assessed with the BDI, followed by the FSS, GAD-7, K-10, PANAS, PSQI, SF-12 and finally UCLA. To finish the questionnaire, it took around 30 minutes.

Statistical design

The 271 participants were divided into two groups: The experimental group that consisted of Long-COVID participants (n = 185) and the control group that consisted of healthy participants (n = 86). Furthermore, the Covid group was divided in three severity groups. In the questionnaire, the participants could indicate how severe their course of the disease was on a scale from one to hundred. Participants that picked a number between one and 24 were arranged in the “benign” severity group, participants selecting numbers between 25 and 74 were arranged in the “mild” group and participants selecting numbers between 75 and 100 were arranged in the “severe” group. For the data analysis SPSS software (Version 29.0.1.1 (244)) was used.

Three hypotheses will be tested and discussed in this paper. The first hypothesis states that the long-COVID group differs significantly in working memory, memory, and attentiveness from the healthy control group. Working memory will be tested with the working memory questionnaire, memory will be tested with the CFQ forgetfulness scale, and attentiveness will be tested with the CFQ distractibility scale. The composite scores of each participant for each questionnaire will be calculated and the means will be compared with each other in a t-test of independent samples. To assess the normality assumption, the Kolmogorov-Smirnov test will be applied.

For second hypothesis the composite scores of the same questionnaires will be compared between the three severity groups of the Long-COVID group in a one-way ANOVA. A Holm-correction for multiple comparison correction will be conducted.

The third hypothesis states that working memory, memory, and attentiveness predict the quality of life and the functional activity for the long-COVID group. For that analysis two separate forward stepwise linear regression analysis will be conducted. The composite scores of the quality of life questionnaire (WHOQoL) and the functional activity questionnaire (FAQ) will serve as dependent variables and the composite scores of the WMQ, CFQ forgetfulness, and CFQ distractibility will be used as predictors. The aim is to identify the most relevant predictors and understand their contributions to the quality of life and functional activity for Long-COVID participants.

Apart from the hypotheses, basic descriptive statistics will be conducted. Since seven mean scores of seven questionnaires will be tested, a Holm-correction of alpha will be conducted due to multiple testing. For every analysis, significance was attributed to p-values below 0.05.

Results

Assumption for normality for the data of the QoL, WMQ, CFQ, FSS, BDI, GAD-7, PANAS-positive, PANAS-negative, PSQI, K-10, and the FAQ was checked using the Kolmogorov-Smirnov-test. The file was split into Long-COVID participants and healthy participants. Only the data of the CFQ for the COVID and the Control group, the PANAS positive for the Control group and the PSQI for the COVID group were normally distributed. Since most of the data was not normally distributed, non-parametric tests will be used for further analysis.

Firstly, the median and the interquartile range for the psychological tests were evaluated and compared between the COVID-group and the healthy group. The statistical comparison was executed by the Mann-Whitney-U test since the data is not normally distributed. Assumptions for the Mann-Whitney-U test were met. The experimental group differs significantly from the control group in every psychological questionnaire, see table 3.

Table 3

Comparison of the psychological questionnaires between the Long-COVID and the control group, carried out using the Mann-Whitney U test

Questionnaire	Long-COVID		Control group		*p*
	Mdn	*IQR*	*Mdn*	*IQR*	
FSS	53.00	20.50	21.00	21.00	<.001
BDI	33.00	11.00	24.50	11.00	<.001
GAD-7	11.00	5.00	10.00	6.00	.003
K-10	21.00	8.00	14.00	9.00	<.001
PANAS positive	26.00	12.00	32.50	10.25	<.001
PANAS negative	15.00	8.00	11.50	8.00	.001
PSQI	31.00	12.00	23.00	8.25	<.001

Note. In the PANAS positive two times the word “excited” appeared by accident.

Note. For the PSQI only questions five until 18 were used for analysis.

Comparison of the COVID-group and Control group in working memory, memory, and attentiveness

To test the first hypothesis, that the long-COVID group differs significantly in working memory, memory, and attentiveness from the healthy control group, three Mann-Whitney-u tests were conducted. To test if the two groups differ significantly in working memory, the composite scores of the WMQ were used. Results showed that the Long-COVID group exhibited significantly higher scores in the WMQ (*Mdn* = 83.00, *IQR* = 43.00) than the control group (*Mdn* = 45.50, *IQR* = 23.00) with a p-value of <.001, *U* = 2913.00 and a large effect size (r_{rb} = 0.51).

For comparing the performance in attentiveness and memory, the composite scores of the forgetfulness and the distractibility CFQ domain were used. Results showed that the Long-COVID group exhibited significantly higher scores in the CFQ forgetfulness (*Mdn* = 24.00, *IQR* = 11.00) than the control group (*Mdn* = 18.00, *IQR* = 6.00) with a p-value of <.001, *U* = 4039.50 and a medium effect

size (r_{rb} = 0.39). Regarding the distractibility domain, the COVID-group exhibited significantly higher scores (*Mdn* = 20.00, *IQR* = 8.00) than the control group (*Mdn* = 16.00, *IQR* = 7.00) with a p-value of <.001, *U* = 4646.00 and a medium effect size (r_{rb} = 0.33).

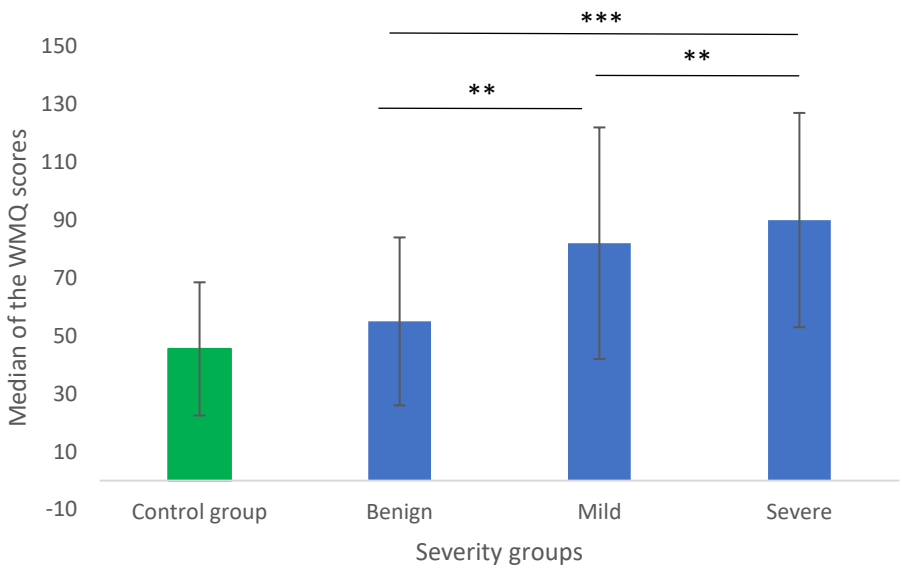
Comparison of the severity groups

To test the second hypothesis, which states that there is a significant difference between the means of the three severity groups of the Long-COVID group in the WMQ, CFQ-forgetfulness and CFQ-distractibility, a Kruskal-Wallis test and a Dunn test (1964) for pairwise comparison were conducted. The severity groups were divided in benign, mild, and severe.

For the Working memory questionnaire, the distribution of scores differed significantly in the three severity groups, $H(2) = 21.93$, $p = <.001$. The effect size, eta squared (η^2), was 0.11, indicating a moderate effect. When taking a closer look at pairwise comparisons, severity group “benign” differs significantly from severity group “mild” ($p = .007$), severity group “benign” differs significantly from severity group “severe” ($p = <.001$) and severity group "mild” differs from severity group “severe” ($p = .004$). For an illustration, see figure 1.

Figure 1

Comparison of the WMQ composite scores medians between the severity groups

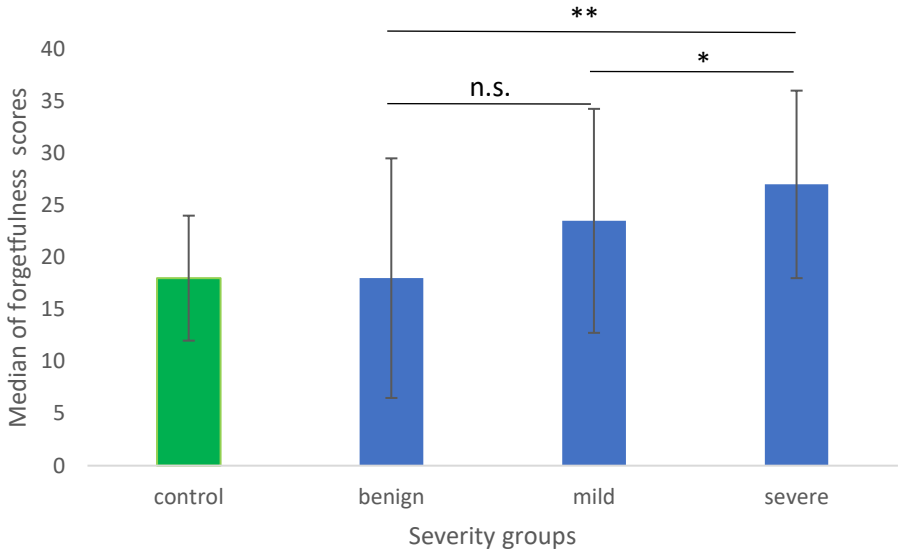


Note: Control group was added as a reference. The stars sympolizes the significance value. The interquatile range was used as error indicators.

For the forgetfulness domain of the Cognitive Failure Questionnaire, the distribution of scores differed significantly in the three severity groups, $H(2) = 12.00$, $p = .002$. The effect size, eta squared (η^2), was 0.05, indicating a small effect. Pairwise comparisons showed that severity group “benign” did not differ significantly from severity group “mild” ($p = .077$), severity group “benign” differed significantly from severity “severe” ($p = .004$), and severity group "mild” differed significantly from severity group “severe” ($p = .024$). For an illustration, see figure 2.

Figure 2

Comparison of the CFQ forgetfulness composite scores medians between the severity groups

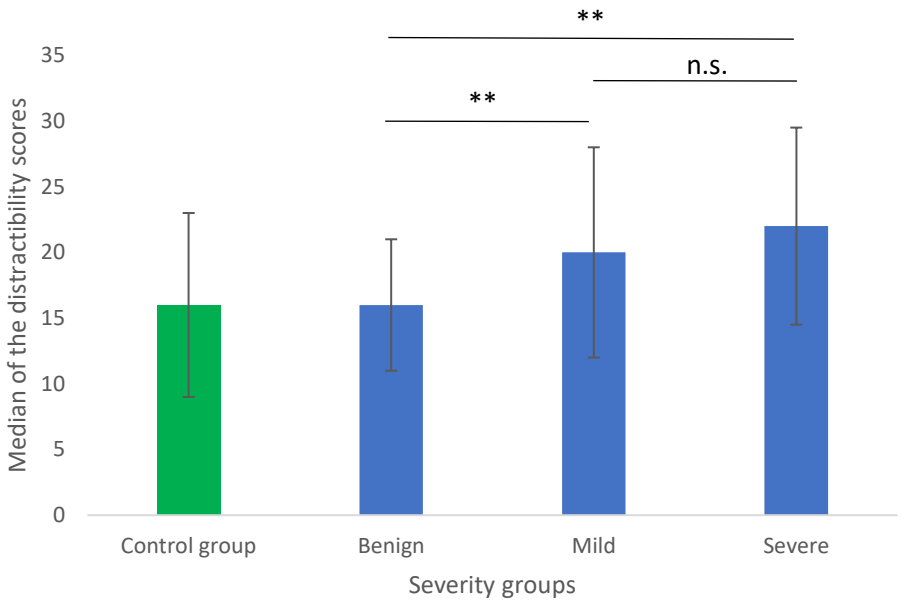


Note: Control group was added as a reference. The stars sympolizes the significance value. The interquatile range was used as error indicators.

For the distractibility domain of the CFQ, the distribution of scores differed significantly in the three severity groups, $H(2) = 12.54$, $p = .002$. The effect size, eta squared (η^2), was 0.05, indicating a small effect. Pairwise comparisons showed that severity group “benign” differed significantly from severity group “mild” ($p = .003$), severity group “benign” differed significantly from severity “severe” ($p = .001$), but severity group "mild” did not differ significantly from severity group “severe” ($p = .444$). Therefore, the second hypothesis can be assumed to be true. For an illustration, see figure 3.

Figure 3

Comparison of the CFQ distractibility composite scores medians between the severity groups



Note: Control group was added as a reference. The stars sympolizes the significance value. The interquatile range was used as error indicators.

Predicting the quality of life in COVID-participants

To test the final hypothesis, which states that the scores from the WMQ and CFQ forgetfulness and CFQ distractibility can predict the scores of the quality of life questionnaire within the long-COVID group, a forward stepwise regression analysis was conducted. The benefit of a forward stepwise regression is that it adds a variable that improves the model the most and so the best predictor is displayed. Assumptions for a regression analysis were met. Items three, four, and 26 were transformed due to negatively phrased items.

The dependent variable for the first regression was the WHOQoL composite score and the composite scores of WMQ, the CFQ forgetfulness scale, and the CFQ distractibility scale severed as predictors. To get the data from all independent variables, even if they are not significant, the stepping method criteria was adjusted. The probability of F was changed from an initial entry value of

.05 to .98 and from an initial removal value of .10 to .99. This way, also insignificant predictors were visible in the SPSS output.

To rule out multicollinearity, the variance inflation factor (VIF) was calculated. With the VIF being at its maximum at 3.185 and the coefficient standard error barely increasing with every predictor added, moderately correlation of the predictors could be assumed (Daoud, 2017).

The COVID-group exhibited lower WHOQoL scores (*Mdn* = 80.00, *IQR* = 18.50) than the Control group (*Mdn* = 102.00, *IQR* = 15.25), indicating a lower quality of life. Scores of WMQ predicted quality of life the best, with R^2 = .399, $F(1,183) = 121.400$, p = <.001 (model 1). Adding the CFQ forgetfulness scores to the regression analysis resulted in further explained variance (R^2 = .401, $F(2,182) = 60.967$) but not significantly, p = .398 (model 2). Adding the CFQ distractibility scale to the analysis the R^2 increased to .402, $F(3,181) = 40.554$, however not significant, p = .625 (model 3). In sum the R^2 value of the WMQ was .399, indicating that the WMQ scores explained 39,9% of the variance of the WHOQoL scores. Adding the forgetfulness and distractibility scores did not result in further explained variance.

Interpreting the ANOVA output, the three models are overall significant (p = <.001), meaning that there is a linear significant relationship between the dependent variable and independent variables. But looking at the Coefficients output and at the t-tests, one can clearly see that the only significant variable is the WMQ, see table 4.

A further regression analysis was carried out in which the composite values of the BDI and the GAD-7 were added. Now, the predictor explaining the most variance was the BDI (R^2 = .523, $F(1,183) = 200.261$, p = <.001. Adding the WMQ resulted in a R^2 of .619, $F(2, 182) = 147.942$, p = <.001. Adding the GAD-7, forgetfulness and distractibility scale did not result in further significant explained variance.

Table 4

Regression coefficients output, with WHOQoL as the dependent variable for the Long-COVID group

Model	Predictors	Unstandardized Coefficients		T	Sig.
		B	Std. Error		
1	(Constant)	108,523	2,591	41,878	<,001
	WMQ	-,337	,031	-11,018	<,001
2	(Constant)	109,742	2,965	37,015	<,001
	WMQ	-,305	,049	-6,288	<,001
	CFQ forgetfulness	-,158	,187	-,848	,398
3	(Constant)	110,067	3,045	36,151	<,001
	WMQ	-,297	,052	-5,751	<,001
	CFQ forgetfulness	-,111	,211	-,527	,599
	CFQ distractibility	-,103	,211	-,489	,625

Predicting the functional activity in COVID-participants

To test if the scores of WMQ, the CFQ forgetfulness scale, and the CFQ distractibility scale predict the values of the functional activity questionnaire, another forward linear regression was conducted, with the dependent variable being the composite score of the FAQ. Assumptions for a regression analysis were met. The FAQ values were transformed so that lower scores represent independency and higher scores dependency of others in everyday life. The same settings were retained as in the first analysis. The COVID-group exhibited higher FAQ scores (*Mdn* = 4.00, IQR = 8.00) than the Control group (*Mdn* = 0.00, IQR = 1.25), which indicates a higher impaired functional activity.

Just as in the first regression analysis, scores of WMQ predicted best functional activity, with R^2 = .487, $F(1,183) = 173.959$, p = <.001 (model 1). Adding the distractibility scale resulted in further variance explained (R^2 = .486) but insignificantly, p = .235 (model 2). Adding the forgetfulness scale

resulted in further variance explained (R^2 = .493) but insignificantly, p = .057 (model 3). With the VIF not exceeding 3.185, multicollinearity could be ruled out.

The ANOVA output indicates that the three models are overall significant (p = <.001) but looking at the Coefficient output the predictor WMQ is the only one staying significant with every model, implying that the WMQ is the best predictor for functional activity, see table 5.

Adding the BDI and GAD-7 scores as independent variables, resulted in the WMQ scores still explaining most of the variance of the FAQ with R^2 = .487, F(1, 183) = 173.959, p = <.001. Adding the BDI scores to the regression analysis, led to an increase of R^2 = .508, F(2,182) = 94.010, p = .006. Adding the GAD-7, forgetfulness and distractibility scale did not result in further significant explained variance.

Table 5

Regression coefficients output, with the FAQ as the dependent variable for the Long-COVID group

Model	Predictors	Unstandardized Coefficients		t	Sig.
		B	Std. Error		
1	(Constant)	-6,063	,947	-6,403	<,001
	WMQ	,148	,011	13,189	<,001
2	(Constant)	-5,520	1,050	-5,257	<,001
	WMQ	,162	,016	9,911	<,001
	CFQ distractibility	-,081	,068	-1,192	,235
3	(Constant)	-6,194	1,100	-5,630	<,001
	WMQ	,144	,019	7,718	<,001
	CFQ distractibility	-,148	,076	-1,948	,053
	CFQ forgetfulness	,146	,076	1,918	,057

Discussion

In the present study, an online survey with several questionnaires was conducted in which the life outcome as well as neuropsychological and psychological domains of 530 participants were examined, divided into a group of participants that have been infected with the SARS-CoV-2 virus and a group of participants who never been infected with the virus. 271 participants were included for the statistical analysis, 185 of them were assigned to the COVID-group and 86 to the healthy control group. This study investigated if the two groups differed in the domains of working memory, memory, and attentiveness and furthermore, if the severity of the illness influences the performance of the domains. Finally, it was investigated whether the three domains, together with measures of depression and anxiety, could predict quality of life and functional activity.

The performance of memory, working memory, and attentiveness was measured with the scores of the questionnaires WMQ, the CFQ forgetfulness scale and the CFQ distractibility scale. The quality of life and functional activity were measured with the questionnaires WHOQoL and FAQ. The level of depression and anxiety was measured using the BDI and GAD-7.

The results indicate that the COVID-group exhibited significantly more difficulties in the domains of memory, working memory, and attentiveness than the control group. Furthermore, for the WMQ, the CFQ forgetfulness scale and the CFQ distractibility the three severity groups benign, mild, and severe differed significantly from each other, see figure 1 – 3,

Testing for the third research question, the regression analysis supports the theory that impairments in working memory, memory, and attentiveness predicts the quality of life and functional activity for the COVID-group. In both regression analysis working memory performance explained most of the variance.

Performance in memory, working memory, and attentiveness and COVID-19

The COVID-group exhibited more working memory deficits, forgetfulness, and distractibility. Studies testing cognitive functions like working memory, memory, and attention found that COVID-19 patients exhibit deficits in these domains, even months after the acute infection (Delgado-Alonso et al., 2022; Cui et al.,2023; Jaywant et al., 2021; Mazza et al., 2021).

Reasons for neurocognitive impairments could be the infiltration of the virus into the central nervous system. SARS-CoV-2 is able to enter the brain and affect brain areas like the frontal lobe and the Hippocampus (Andriuta et al., 2022; Delorme et al., 2020; Donegani et al., 2021, Douaud et al., 2022). Since working memory is mostly associated with the frontal lobes (Panikratova et al., 2020; Stern et al., 2000), and memory with the Hippocampus (Barker & Warburton, 2011; Bird & Burgess, 2008), the impairments might be due to the infiltration of the virus. In a recent study of Díez-Cirarda et al. (2023), long-COVID patients underwent neuroimaging and cognitive testing, to determine possible correlations. It was found that in particular attention and working memory were impaired, followed by memory. Brain alterations in form of reduced functional connectivity in frontal areas as well as grey matter alterations in the parahippocampal areas were associated with attention, memory and working memory impairments. Further studies support the association between memory impairments and hippocampus alterations in long-COVID patients (Lu et al., 2020) and the virus affecting hippocampal regions (Douaud et al., 2022; Zorzo et al., 2023).

Furthermore, the neurological processes of neuroinflammation in the Alzheimer disease and in SARS-CoV-2 are similar (Ortiz et al., 2022), implicating the similar effects of neuroinflammation on the cognitive decline, like memory impairments. The hippocampus and temporal lobe are especially affected of the Alzheimer's disease, showing a remarkable similarity between the effect of COVID-19 and Alzheimer's disease on the brain (Zhao et al., 2021).

Literature regarding the influence of the virus on the CNS and resulting attention deficits also exists: Hypoxemic pneumonia, olfactory dysfunctions, and extensive cerebral white matter alterations correlated with impairments in attention, vigilance, and memory in COVID-19 patients (Delgado-Alonso et al., 2022; Dondaine et al., 2022; Silva et al., 2021). COVID-19 patients showing hypometabolism or other alterations in the frontal cortex are also exhibiting attentional dysfunctions (Kas et al., 2021; Yesilkaya et al., 2021).

Fatigue can have a negative impact on cognitive functions, since it has been associated with cognitive impairments (Graber et al., 2019; Kinsinger et al., 2010). Since fatigue is one of the main

symptoms of Long-COVID, it is very likely that it influences memory, working memory, and attention in a negative way (Bungenberg et al., 2022).

Influence of severity on cognitive impairments

The findings of this study illustrate that the severity of the course of illness of COVID-19 is associated with the severity of cognitive impairments. The three severity groups benign, mild, and severe differ significantly in working memory, memory, and attention deficits. This finding replicates studies that found cognitive impairments for severely affected COVID-19 patients (Ariza et al., 2023; Ollila et al., 2022; Vannorsdall et al., 2022). Ollila et al. (2022) found that patients that had a more severe infection exhibited more problems in attention, executive functions, and memory than patients with a less severe infection. The reason for this could be that the more severe the disease and the greater the impact of the virus on the CNS, the more pronounced the cognitive impairment: Studies show that patients with a more severe COVID-19 illness, suffer more from neurologic manifestations (Liotta et al., 2020; Mao et al., 2020), cytokine storm syndrome (Huang et al., 2020) and increased inflammation (Henry et al., 2020) and axonal injury (Virhammar et al., 2021), which are biomarkers of CNS infiltration. Perez Giraldo et al. (2023) found that hospitalized COVID-19 patients exhibited more markers of inflammation and more deficits in working memory and attention than non-hospitalized COVID-19 patients.

In this study and the study of de Groot et al. (2023) the cognitive differences of three severity groups were assessed for Long-COVID patients, which to the best of our knowledge, no study investigated before. The three severity groups all differ from each other in the working memory questionnaire, see figure 1. For the forgetfulness scale, severity group benign differed significantly from severe and severity group mild differed significantly from severity group severe, see figure 2. For the distractibility scale, participants with benign severity differed significantly from participants with mild severity and severity group benign differed significantly from severity severe, see figure 3. Feng et al. (2020) investigated clinical characteristics in three severity groups (moderate, severe, and critical) and found that the severe and critical group experienced multiple organ dysfunction,

impaired immune function, and more lung lobes in contrast to the moderate group in acute COVID-19 patients. Cognitive deficits were not assessed.

Predicting Quality of Life and functional activity

Furthermore, this study sheds light on cognitive impairments predicting the quality of life of COVID-19 patients. Memory, working memory, and attention deficits predicted the quality of life, whereas working memory being the strongest predictor with explaining 39.9 % of the variance of quality of life. The overall quality of life is impaired in COVID-19 patients (Rass et al., 2021). Memory and working memory deficits were associated with decreased quality of life in COVID-19 patients before (Miskowiak et al., 2023).

As discussed before, cognitive, and executive functions are necessary to master everyday life. It has been found that overall cognitive impairments negatively impact the quality of life in different patient groups (Mitchell et al., 2010), especially memory deficits (Castro-Lionard et al., 2011; Maki et al., 2014).

In addition, mental problems such as anxiety, depression, and fatigue can also lead to a reduced quality of life and acts as a mediator between cognitive problems and reduced QoL (Sohrabi et al., 2009). Since cognitive problems are associated with increased affective symptoms (Hill et al., 2016) and more quality of life is correlated with less anxiety and cognitive decline (Castro-Lionard et al., 2011), a meditating role is possible for COVID-19 patients. Méndez et al. (2021) found an association between impairments in memory, working memory, and anxiety, depression, and trauma symptoms for hospitalized COVID-19 patients. Rass et al. (2022) found that higher severity, impaired sleep, and anxiety were associated with reduced quality of life in COVID-19 patients. In this study, long-COVID participants experienced significantly more fatigue, anxiety, and depression symptoms than the control group. Adding depression and anxiety as possible predictors to the regression analysis led to depression being the strongest predictor and explaining 52.3 % of the variance. Depression, working memory, and anxiety together explained 62.5% of the variance.

Memory, working memory, and attention deficits predicted functional activity as well, with working memory being the strongest predictor. It has been found that cognitive impairments,

especially memory impairments, affect the people's ability to work (Davis et al., 2021; Miskowiak et al., 2023) and activities of daily living (Jaywant et al., 2024). Overall functional activity is impaired in Long-COVID patients (Nielsen et al., 2022). Research has revealed that working memory performance serves as a mediator for everyday functional activity (Borella et al., 2017; Guye et al., 2020), as working memory training improves functional ability (Cantarella et al., 2017). Looking at the FAQ individually, most of the activities that are queried require multiple steps and the ability to store information in the short-term memory while completing other tasks. A reason for working memory being the strongest predictor might be that the majority of questions querying working memory skills.

Memory and attention deficits were also found to predict everyday functional activity (Hyndman & Ashburn, 2003; Nakhla et al., 2022; Schmitter-Edgecombe et al., 2009), since they are crucial for living a structured and healthy life. Looking at the items of the FAQ, questions like "Paying attention to, understanding, discussing TV, book, magazine" or "Remembering appointments, family occasions, holidays, medications" query attention and memory.

Adding depression and anxiety as possible predictors in the regression analysis, working memory still proved to be the strongest predictor of functional activity, followed by depression.

Limitations and implications

Regarding the limitation, this study did not use a specific questionnaire only for memory and one for attention, rather two scales of the Cognitive Failure questionnaire were used. It is recommended to assess memory and attention with questionnaires specifically made to test these domains.

Furthermore, since the COVID-related questions were asked in the beginning of the questionnaire, response bias could be possible. COVID-19 participants may tend to give more extreme answers than if they had not been asked if they were infected with the virus. Winter and Braw (2022) found out that recovered COVID-19 patients reported more symptoms when they have been provided with information regarding the symptoms of Long-COVID prior to the subjective

assessment. It is recommended to ask COVID-related questions at the end of the questionnaire next time.

In general, with the form of assessment being subjective, subjective disease severity can influence the objectivity, reliability, and validity of the experiment. Subjective complaints do not necessarily reflect objective complaints. Ceban et al. (2022) pointed out that objective cognitive impairments and fatigue are more severe than the subjective assessment. This finding just demonstrates the subjectivity of reporting symptoms. Objective measurements like tests could be used to avoid subjectivity.

With more than double of COVID-participants than healthy participants, distribution is not balanced. Also, far more women took part in the study then men. Male COVID-19 patients show to have a higher severity and mortality than females (Ahrenfeldt et al., 2021; Jin et al., 2020). For future research, distribution of the two experimental groups should be more equal as well as sex.

Most of COVID-participants were between the age of 50 – 64. Cognitive impairment is associated with advanced age for Long-COVID patients (Hartung et al., 2022). In contrast, most of the healthy participants were between the age 18 – 29. Balanced distribution of age in both groups is recommended.

Conclusion

The current study demonstrated that Long-COVID patients exhibit significant more deficits in working memory, memory, and attentiveness than a control group. Furthermore, the more severe the course of the disease, the more the COVID participants showed deficits in working memory, memory, and attention. Working memory, memory, and attention predicted quality of life and functional activity for Long-COVID patients, with the working memory being the strongest predictor for both dependent variables. The results stress the neurocognitive impairments, Long-COVID patients have to face and the important effect on quality of life and everyday functioning. In addition, the results provide important implications for the handling of long-term COVID patients in the form of greater understanding of the extent and duration of symptoms, more support at work, in daily life and in interpersonal interactions. This paper used the data collected from de Groot et al. (2023).

References

Ahrenfeldt, L. J., Otavova, M., Christensen, K., & Lindahl-Jacobsen, R. (2021). Sex and age differences in COVID-19 mortality in Europe. *Wiener klinische Wochenschrift*, *133*(7-8), 393–398. https://doi.org/10.1007/s00508-020-01793-9

Aksoy, C. C., Saracoglu, İ., & Akkurt, L. (2022). Turkish Version of the Working Memory Questionnaire: Reliability and Validity. *Journal of Basic and Clinical Health Sciences, 6*(2), 401-407. https://doi.org/10.30621/jbachs.1003491

Alexopoulos, H., Magira, E., Bitzogli, K., Kafasi, N., Vlachoyiannopoulos, P., Tzioufas, A., Kotanidou, A., & Dalakas, M. C. (2020). Anti-SARS-CoV-2 antibodies in the CSF, blood-brain barrier dysfunction, and neurological outcome: Studies in 8 stuporous and comatose patients. *Neurology(R) neuroimmunology & neuroinflammation*, *7*(6), e893. https://doi.org/10.1212/NXI.0000000000000893

Alhusain, F., Alromaih, A., Alhajress, G., Alsaghyir, A., Alqobaisi, A., Alaboodi, T., & Alsalamah, M. (2021). Predictors and clinical outcomes of silent hypoxia in COVID-19 patients, a single-center retrospective cohort study. *Journal of infection and public health*, *14*(11), 1595–1599. https://doi.org/10.1016/j.jiph.2021.09.007

Ali Awan, H., Najmuddin Diwan, M., Aamir, A., Ali, M., Di Giannantonio, M., Ullah, I., Shoib, S., & De Berardis, D. (2021). SARS-CoV-2 and the Brain: What Do We Know about the Causality of 'Cognitive COVID?. *Journal of clinical medicine*, *10*(15), 3441. https://doi.org/10.3390/jcm10153441

Alquisiras-Burgos, I., Peralta-Arrieta, I., Alonso-Palomares, L. A., Zacapala-Gómez, A. E., Salmerón-Bárcenas, E. G., & Aguilera, P. (2021). Neurological Complications Associated with the Blood-Brain Barrier Damage Induced by the Inflammatory Response During SARS-CoV-2 Infection. *Molecular neurobiology, 58*(2), 520–535. https://doi.org/10.1007/s12035-020-02134-7

Andriuta, D., Si-Ahmed, C., Roussel, M., Constans, J. M., Makki, M., Aarabi, A., Basille, D., Andrejak, C., & Godefroy, O. (2022). Clinical and Imaging Determinants of Neurocognitive Disorders in Post-Acute COVID-19 Patients with Cognitive Complaints. *Journal of Alzheimer's disease : JAD*, *87*(3), 1239–1250. https://doi.org/10.3233/JAD-215506

Ariza, M., Cano, N., Segura, B., Adan, A., Bargalló, N., Caldú, X., Campabadal, A., Jurado, M. A., Mataró, M., Pueyo, R., Sala-Llonch, R., Barrué, C., Bejar, J., Cortés, C. U., NAUTILUS Project Collaborative Group, Garolera, M., & Junqué, C. (2023). COVID-19 severity is related to poor executive function in people with post-COVID conditions. *Journal of neurology*, *270*(5), 2392–2408. https://doi.org/10.1007/s00415-023-11587-4

Asadi-Pooya, A. A., Akbari, A., Emami, A., Lotfi, M., Rostamihosseinkhani, M., Nemati, H., Barzegar, Z., Kabiri, M., Zeraatpisheh, Z., Farjoud-Kouhanjani, M., Jafari, A., Sasannia, S., Ashrafi, S., Nazeri, M., Nasiri, S., & Shahisavandi, M. (2022). Long COVID syndrome-associated brain fog. *Journal of medical virology*, *94*(3), 979–984. https://doi.org/10.1002/jmv.27404

Awh, E., Vogel, E. K., & Oh, S. H. (2006). Interactions between attention and working memory. *Neuroscience*, *139*(1), 201–208. https://doi.org/10.1016/j.neuroscience.2005.08.023

Azouvi, P., Vallat-Azouvi, C., Joseph, P. A., Meulemans, T., Bertola, C., Le Gall, D., Bellmann, A., Roussel, M., Coyette, F., Krier, M., Franconie, C., Bindschadler, C., Diouf, M., Godefroy, O., & GREFEX Study Group (Groupe de Réflexion sur l'Evaluation des Fonctions Exécutives) (2016). Executive Functions Deficits After Severe Traumatic Brain Injury: The GREFEX Study. *The Journal of head trauma rehabilitation*, *31*(3), E10–E20. https://doi.org/10.1097/HTR.0000000000000169

Baddeley, A. (1992). Working memory. *Science*, *255*(5044), 556-559.

Barker, G. R., & Warburton, E. C. (2011). When is the hippocampus involved in recognition memory?.

The Journal of neuroscience : the official journal of the Society for Neuroscience, *31*(29), 10721–10731. https://doi.org/10.1523/JNEUROSCI.6413-10.2011

Beaud, V., Crottaz-Herbette, S., Dunet, V., Vaucher, J., Bernard-Valnet, R., Du Pasquier, R., Bart, P. A., & Clarke, S. (2021). Pattern of cognitive deficits in severe COVID-19. *Journal of neurology, neurosurgery, and psychiatry*, *92*(5), 567–568. https://doi.org/10.1136/jnnp-2020-325173

Bechara, A., Tranel, D., & Damasio, H. (2000). Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain : a journal of neurology*, *123 (Pt 11)*, 2189–2202. https://doi.org/10.1093/brain/123.11.2189

Benameur, K., Agarwal, A., Auld, S. C., Butters, M. P., Webster, A. S., Ozturk, T., Howell, J. C., Bassit, L. C., Velasquez, A., Schinazi, R. F., Mullins, M. E., & Hu, W. T. (2020). Encephalopathy and Encephalitis Associated with Cerebrospinal Fluid Cytokine Alterations and Coronavirus Disease, Atlanta, Georgia, USA, 2020. *Emerging infectious diseases*, *26*(9), 2016–2021. https://doi.org/10.3201/eid2609.202122

Bergman-Nutley, S., & Klingberg, T. (2014). Effect of working memory training on working memory, arithmetic and following instructions. *Psychological research*, *78*(6), 869–877. https://doi.org/10.1007/s00426-014-0614-0

Bird, C. M., & Burgess, N. (2008). The hippocampus and memory: insights from spatial processing. *Nature reviews. Neuroscience*, *9*(3), 182–194. https://doi.org/10.1038/nrn2335

Borella, E., Cantarella, A., Joly, E., Ghisletta, P., Carbone, E., Coraluppi, D., Piras, F., & De Beni, R. (2017). Performance-based everyday functional competence measures across the adult lifespan: the role of cognitive abilities. *International psychogeriatrics*, *29*(12), 2059–2069. https://doi.org/10.1017/S1041610217000680

Bridger, R. S., Johnsen, S. Å., & Brasher, K. (2013). Psychometric properties of the Cognitive Failures

Questionnaire. *Ergonomics*, *56*(10), 1515–1524. https://doi.org/10.1080/00140139.2013.821172

Broadbent, D. E., Cooper, P. F., FitzGerald, P., & Parkes, K. R. (1982). The Cognitive Failures Questionnaire (CFQ) and its correlates. *The British journal of clinical psychology*, *21*(1), 1–16. https://doi.org/10.1111/j.2044-8260.1982.tb01421.x

Brown, L. A., Ballentine, E., Zhu, Y., McGinley, E. L., Pezzin, L., & Abramoff, B. (2022). The unique contribution of depression to cognitive impairment in Post-Acute Sequelae of SARS-CoV-2 infection. *Brain, behavior, & immunity - health*, *22*, 100460. https://doi.org/10.1016/j.bbih.2022.100460

Bungenberg, J., Humkamp, K., Hohenfeld, C., Rust, M. I., Ermis, U., Dreher, M., Hartmann, N. K., Marx, G., Binkofski, F., Finke, C., Schulz, J. B., Costa, A. S., & Reetz, K. (2022). Long COVID-19: Objectifying most self-reported neurological symptoms. *Annals of clinical and translational neurology*, *9*(2), 141–154. https://doi.org/10.1002/acn3.51496

Burks, S. M., Rosas-Hernandez, H., Alejandro Ramirez-Lee, M., Cuevas, E., & Talpos, J. C. (2021). Can SARS-CoV-2 infect the central nervous system via the olfactory bulb or the blood-brain barrier? *Brain, behavior, and immunity*, *95*, 7–14. https://doi.org/10.1016/j.bbi.2020.12.031

Campos-Sousa, I. S., Campos-Sousa, R. N., Ataíde, L., Jr, Soares, M. M., & Almeida, K. J. (2010). Executive dysfunction and motor symptoms in Parkinson's disease. *Arquivos de neuro-psiquiatria*, *68*(2), 246–251. https://doi.org/10.1590/s0004-282x2010000200018

Cantarella, A., Borella, E., Carretti, B., Kliegel, M., & de Beni, R. (2017). Benefits in tasks related to everyday life competences after a working memory training in older adults. *International journal of geriatric psychiatry*, *32*(1), 86–93. https://doi.org/10.1002/gps.4448

Castro-Lionard, K., Thomas-Antérion, C., Crawford-Achour, E., Rouch, I., Trombert-Paviot, B.,

Barthélémy, J. C., Laurent, B., Roche, F., & Gonthier, R. (2011). Can maintaining cognitive function at 65 years old predict successful ageing 6 years later? The PROOF study. *Age and ageing*, *40*(2), 259–265. https://doi.org/10.1093/ageing/afq174

Ceban, F., Ling, S., Lui, L. M. W., Lee, Y., Gill, H., Teopiz, K. M., Rodrigues, N. B., Subramaniapillai, M., Di Vincenzo, J. D., Cao, B., Lin, K., Mansur, R. B., Ho, R. C., Rosenblat, J. D., Miskowiak, K. W., Vinberg, M., Maletic, V., & McIntyre, R. S. (2022). Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. *Brain, behavior, and immunity*, *101*, 93–135. https://doi.org/10.1016/j.bbi.2021.12.020

Chun, M. M., & Turk-Browne, N. B. (2007). Interactions between attention and memory. *Current opinion in neurobiology*, *17*(2), 177–184. https://doi.org/10.1016/j.conb.2007.03.005

Clark, D. B., Chung, T., Martin, C. S., Hasler, B. P., Fitzgerald, D. H., Luna, B., Brown, S. A., Tapert, S. F., Brumback, T., Cummins, K., Pfefferbaum, A., Sullivan, E. V., Pohl, K. M., Colrain, I. M., Baker, F. C., De Bellis, M. D., Nooner, K. B., & Nagel, B. J. (2017). Adolescent Executive Dysfunction in Daily Life: Relationships to Risks, Brain Structure and Substance Use. *Frontiers in behavioral neuroscience*, *11*, 223. https://doi.org/10.3389/fnbeh.2017.00223

Colom, Roberto & Martínez-Molina, Agustín & Shih, Pei-Chun & Santacreu, José. (2010). Intelligence, working memory, and multitasking performance. *Intelligence, 38*(6), 543–551. Doi:10.1016/j.intell.2010.08.002.

Cui, R., Gao, B., Ge, R., Li, M., Li, M., Lu, X., & Jiang, S. (2023). The effects of COVID-19 infection on working memory: a systematic review. *Current medical research and opinion*, 1–11. Advance online publication. https://doi.org/10.1080/03007995.2023.2286312

Daoud, J. (2017). Multicollinearity and Regression Analysis. *Journal of Physics: Conference Series 949*. Doi: 10.1088/1742-6596/949/1/012009.

Davis, H. E., Assaf, G. S., McCorkell, L., Wei, H., Low, R. J., Re'em, Y., Redfield, S., Austin, J. P., & Akrami,

A. (2021). Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine*, *38*, 101019. https://doi.org/10.1016/j.eclinm.2021.101019

de Groot, B. O., Biserni, C., Fuermaier, A. B. M., & Enriquez-Geppert, S. (2023). Untreated if unrecognized: A cognitive profile of sustained subjective executive dysfunctions in COVID-19. *Applied neuropsychology. Adult*, 1–11. Advance online publication. https://doi.org/10.1080/23279095.2023.2223329

Delgado-Alonso, C., Valles-Salgado, M., Delgado-Álvarez, A., Yus, M., Gómez-Ruiz, N., Jorquera, M., Polidura, C., Gil, M. J., Marcos, A., Matías-Guiu, J., & Matías-Guiu, J. A. (2022). Cognitive dysfunction associated with COVID-19: A comprehensive neuropsychological study. *Journal of psychiatric research*, *150*, 40–46. https://doi.org/10.1016/j.jpsychires.2022.03.033

Delorme, C., Paccoud, O., Kas, A., Hesters, A., Bombois, S., Shambrook, P., Boullet, A., Doukhi, D., Le Guennec, L., Godefroy, N., Maatoug, R., Fossati, P., Millet, B., Navarro, V., Bruneteau, G., Demeret, S., Pourcher, V., & CoCo-Neurosciences study group and COVID SMIT PSL study group (2020). COVID-19-related encephalopathy: a case series with brain FDG-positron-emission tomography/computed tomography findings. *European journal of neurology*, *27*(12), 2651–2657. https://doi.org/10.1111/ene.14478

Diamond A. (2013). Executive functions. *Annual review of psychology*, *64*, 135–168. https://doi.org/10.1146/annurev-psych-113011-143750

Díez-Cirarda, M., Yus, M., Gómez-Ruiz, N., Polidura, C., Gil-Martínez, L., Delgado-Alonso, C., Jorquera, M., Gómez-Pinedo, U., Matias-Guiu, J., Arrazola, J., & Matias-Guiu, J. A. (2023). Multimodal neuroimaging in post-COVID syndrome and correlation with cognition. *Brain : a journal of neurology*, *146*(5), 2142–2152. https://doi.org/10.1093/brain/awac384

Ding, Y., Liu, R. D., Liu, H., Wang, J., Zhen, R., & Jiang, R. H. (2019). Effects of Working Memory,

Strategy Use, and Single-Step Mental Addition on Multi-Step Mental Addition in Chinese Elementary Students. *Frontiers in psychology*, *10*, 148. https://doi.org/10.3389/fpsyg.2019.00148

Dondaine, T., Ruthmann, F., Vuotto, F., Carton, L., Gelé, P., Faure, K., Deplanque, D., & Bordet, R. (2022). Long-term cognitive impairments following COVID-19: a possible impact of hypoxia. *Journal of neurology*, *269*(8), 3982–3989. https://doi.org/10.1007/s00415-022-11077-z

Donegani, M. I., Miceli, A., Pardini, M., Bauckneht, M., Chiola, S., Pennone, M., Marini, C., Massa, F., Raffa, S., Ferrarazzo, G., Arnaldi, D., Sambuceti, G., Nobili, F., & Morbelli, S. (2021). Brain Metabolic Correlates of Persistent Olfactory Dysfunction after SARS-Cov2 Infection. *Biomedicines*, *9*(3), 287. https://doi.org/10.3390/biomedicines9030287

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

Doyle A. E. (2006). Executive functions in attention-deficit/hyperactivity disorder. *The Journal of clinical psychiatry*, *67 Suppl 8*, 21–26.

Dunn, O. J. (1964). Multiple comparisons using rank sums. *Technometrics, 6*(3) ,241-252. DOI: 10.1080/00401706.1964.10490181

Durston, S., Davidson, M. C., Tottenham, N., Galvan, A., Spicer, J., Fossella, J. A., & Casey, B. J. (2006). A shift from diffuse to focal cortical activity with development. *Developmental science*, *9*(1), 1–8. https://doi.org/10.1111/j.1467-7687.2005.00454.x

Erickson, M. A., Rhea, E. M., Knopp, R. C., & Banks, W. A. (2021). Interactions of SARS-CoV-2 with the

Blood-Brain Barrier. *International journal of molecular sciences*, *22*(5), 2681. https://doi.org/10.3390/ijms22052681

Espinar-Herranz, K., Delgado-Lima, A. H., Villatoro, B. S., Garaboa, E. M., Gómez, V. S., Vides, L. G., Bouhaben, J., & Delgado-Losada, M. L. (2023). Memory, Emotion, and Quality of Life in Patients with Long COVID-19. *Brain sciences*, *13*(12), 1670. https://doi.org/10.3390/brainsci13121670

Feng, J. F., Zhao, X., Gurkoff, G. G., Van, K. C., Shahlaie, K., & Lyeth, B. G. (2012). Post-traumatic hypoxia exacerbates neuronal cell death in the hippocampus. *Journal of neurotrauma*, *29*(6), 1167–1179. https://doi.org/10.1089/neu.2011.1867

Feng, Y., Ling, Y., Bai, T., Xie, Y., Huang, J., Li, J., Xiong, W., Yang, D., Chen, R., Lu, F., Lu, Y., Liu, X., Chen, Y., Li, X., Li, Y., Summah, H. D., Lin, H., Yan, J., Zhou, M., Lu, H., … Qu, J. (2020). COVID-19 with Different Severities: A Multicenter Study of Clinical Features. *American journal of respiratory and critical care medicine*, *201*(11), 1380–1388. https://doi.org/10.1164/rccm.202002-0445OC

Fiorenzato, E., Zabberoni, S., Costa, A., & Cona, G. (2021). Cognitive and mental health changes and their vulnerability factors related to COVID-19 lockdown in Italy. *PloS one*, *16*(1), e0246204. https://doi.org/10.1371/journal.pone.0246204

Fougnie, D. (2008). The Relationship between Attention and Working Memory. *New Research on Short-Term Memory, 1.*

Frontera, J. A., Yang, D., Lewis, A., Patel, P., Medicherla, C., Arena, V., Fang, T., Andino, A., Snyder, T., Madhavan, M., Gratch, D., Fuchs, B., Dessy, A., Canizares, M., Jauregui, R., Thomas, B., Bauman, K., Olivera, A., Bhagat, D., Sonson, M., … Galetta, S. (2021). A prospective study of long-term outcomes among hospitalized COVID-19 patients with and without neurological

complications. Journal of the neurological sciences, 426, 117486. https://doi.org/10.1016/j.jns.2021.117486

Fuermaier, A. B. M., Tucha, L., Koerts, J., Aschenbrenner, S., Kaunzinger, I., Hauser, J., Weisbrod, M., Lange, K. W., & Tucha, O. (2015). Cognitive impairment in adult ADHD--perspective matters!. *Neuropsychology*, *29*(1), 45–58. https://doi.org/10.1037/neu0000108

Gagliardi, S., Poloni, E. T., Pandini, C., Garofalo, M., Dragoni, F., Medici, V., Davin, A., Visonà, S. D., Moretti, M., Sproviero, D., Pansarasa, O., Guaita, A., Ceroni, M., Tronconi, L., & Cereda, C. (2021). Detection of SARS-CoV-2 genome and whole transcriptome sequencing in frontal cortex of COVID-19 patients. *Brain, behavior, and immunity*, *97*, 13–21. https://doi.org/10.1016/j.bbi.2021.05.012

García-Grimshaw, M., Chirino-Pérez, A., Flores-Silva, F. D., Valdés-Ferrer, S. I., Vargas-Martínez, M. L. Á., Jiménez-Ávila, A. I., Chávez-Martínez, O. A., Ramos-Galicia, E. M., Marché-Fernández, O. A., Ramírez-Carrillo, M. F., Grajeda-González, S. L., Ramírez-Jiménez, M. E., Chávez-Manzanera, E. A., Tusié-Luna, M. T., Ochoa-Guzmán, A., Cantú-Brito, C., Fernandez-Ruiz, J., & Chiquete, E. (2022). Critical role of acute hypoxemia on the cognitive impairment after severe COVID-19 pneumonia: a multivariate causality model analysis. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *43*(4), 2217–2229. https://doi.org/10.1007/s10072-021-05798-8

García-Sánchez, C., Calabria, M., Grunden, N., Pons, C., Arroyo, J. A., Gómez-Anson, B., Lleó, A., Alcolea, D., Belvís, R., Morollón, N., Mur, I., Pomar, V., & Domingo, P. (2022). Neuropsychological deficits in patients with cognitive complaints after COVID-19. *Brain and behavior*, *12*(3), e2508. https://doi.org/10.1002/brb3.2508

Gathercole, S.E., Alloway, T.P., Kirkwood, H.J., Elliott, J.G., Holmes, J., Hilton, K.A. (2008). Attentional

and executive function behaviours in children with poor working memory. *Learning and individual differences, 18*(2), 214–223. https://doi.org/10.1016/j.lindif.2007.10.003

Ghosh, R., Dubey, S., Finsterer, J., Chatterjee, S., & Ray, B. K. (2020). SARS-CoV-2-Associated Acute Hemorrhagic, Necrotizing Encephalitis (AHNE) Presenting with Cognitive Impairment in a 44-Year-Old Woman without Comorbidities: A Case Report. *The American journal of case reports*, *21*, e925641. https://doi.org/10.12659/AJCR.925641

González, D. A., Gonzales, M. M., Resch, Z. J., Sullivan, A. C., & Soble, J. R. (2022). Comprehensive Evaluation of the Functional Activities Questionnaire (FAQ) and Its Reliability and Validity. *Assessment*, *29*(4), 748–763. https://doi.org/10.1177/1073191121991215

Graber, M., Garnier, L., Duloquin, G., Mohr, S., Guillemin, S., Ramaget, O., Piver, A., Tainturier, C., Bret-Legrand, C., Delpont, B., Blanc-Labarre, C., Guéniat, J., Hervieu-Bègue, M., Osseby, G. V., Giroud, M., & Béjot, Y. (2019). Association Between Fatigue and Cognitive Impairment at 6 Months in Patients With Ischemic Stroke Treated With Acute Revascularization Therapy. *Frontiers in neurology*, *10*, 931. https://doi.org/10.3389/fneur.2019.00931

Guedj, E., Campion, J. Y., Dudouet, P., Kaphan, E., Bregeon, F., Tissot-Dupont, H., Guis, S., Barthelemy, F., Habert, P., Ceccaldi, M., Million, M., Raoult, D., Cammilleri, S., & Eldin, C. (2021). ^{18}F-FDG brain PET hypometabolism in patients with long COVID. *European journal of nuclear medicine and molecular imaging*, *48*(9), 2823–2833. https://doi.org/10.1007/s00259-021-05215-4

Guye, S., Röcke, C., Martin, M., & von Bastian, C. C. (2020). Functional Ability in Everyday Life: Are Associations With an Engaged Lifestyle Mediated by Working Memory?. *The journals of gerontology. Series B, Psychological sciences and social sciences*, *75*(9), 1873–1883. https://doi.org/10.1093/geronb/gbz056

Halder, S. K., & Milner, R. (2020). Mild hypoxia triggers transient blood-brain barrier disruption: a

fundamental protective role for microglia. *Acta neuropathologica communications*, *8*(1), 175. https://doi.org/10.1186/s40478-020-01051-z

Hartung, T. J., Neumann, C., Bahmer, T., Chaplinskaya-Sobol, I., Endres, M., Geritz, J., Haeusler, K. G., Heuschmann, P. U., Hildesheim, H., Hinz, A., Hopff, S., Horn, A., Krawczak, M., Krist, L., Kudelka, J., Lieb, W., Maetzler, C., Mehnert-Theuerkauf, A., Montellano, F. A., Morbach, C., … Finke, C. (2022). Fatigue and cognitive impairment after COVID-19: A prospective multicentre study. *EClinicalMedicine*, *53*, 101651. https://doi.org/10.1016/j.eclinm.2022.101651

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

Henry, B. M., de Oliveira, M. H. S., Benoit, S., Plebani, M., & Lippi, G. (2020). Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. *Clinical chemistry and laboratory medicine*, *58*(7), 1021–1028. https://doi.org/10.1515/cclm-2020-0369

Hess, C., Levy, B., Hashmi, A. Z., Hogan, J., Greenspan, S., Elber, A., Falcon, K., & Driscoll, D. F. (2020). Subjective Versus Objective Assessment of Cognitive Functioning in Primary Care. *Journal of the American Board of Family Medicine : JABFM*, *33*(3), 417–425. https://doi.org/10.3122/jabfm.2020.03.190265

Hill, N. L., Mogle, J., Wion, R., Munoz, E., DePasquale, N., Yevchak, A. M., & Parisi, J. M. (2016). Subjective Cognitive Impairment and Affective Symptoms: A Systematic Review. *The Gerontologist*, *56*(6), e109–e127. https://doi.org/10.1093/geront/gnw091

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia,

J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., … Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London, England)*, *395*(10223), 497–506. https://doi.org/10.1016/S0140-6736(20)30183-5

Hwang, K., Bertolero, M. A., Liu, W. B., & D'Esposito, M. (2017). The Human Thalamus Is an Integrative Hub for Functional Brain Networks. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *37*(23), 5594–5607. https://doi.org/10.1523/JNEUROSCI.0067-17.2017

Hwang, K., Bruss, J., Tranel, D., & Boes, A. D. (2020). Network Localization of Executive Function Deficits in Patients with Focal Thalamic Lesions. *Journal of cognitive neuroscience*, *32*(12), 2303–2319. https://doi.org/10.1162/jocn_a_01628

Hyndman, D., & Ashburn, A. (2003). People with stroke living in the community: Attention deficits, balance, ADL ability and falls. *Disability and rehabilitation*, *25*(15), 817–822. https://doi.org/10.1080/0963828031000122221

Ismail, I. I., & Salama, S. (2022). Association of CNS demyelination and COVID-19 infection: an updated systematic review. *Journal of neurology, 269*(2), 541–576. https://doi.org/10.1007/s00415-021-10752-x

Ivanov, I., Bansal, R., Hao, X., Zhu, H., Kellendonk, C., Miller, L., Sanchez-Pena, J., Miller, A. M., Chakravarty, M. M., Klahr, K., Durkin, K., Greenhill, L. L., & Peterson, B. S. (2010). Morphological abnormalities of the thalamus in youths with attention deficit hyperactivity disorder. *The American journal of psychiatry*, *167*(4), 397–408. https://doi.org/10.1176/appi.ajp.2009.09030398

Jaywant, A., Gunning, F. M., Oberlin, L. E., Santillana, M., Ognyanova, K., Druckman, J. N., Baum, M. A., Lazer, D., & Perlis, R. H. (2024). Cognitive Symptoms of Post-COVID-19 Condition and Daily Functioning. *JAMA network open*, *7*(2), e2356098. https://doi.org/10.1001/jamanetworkopen.2023.56098

Jaywant, A., Vanderlind, W. M., Alexopoulos, G. S., Fridman, C. B., Perlis, R. H., & Gunning, F. M. (2021). Frequency and profile of objective cognitive deficits in hospitalized patients recovering from COVID-19. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, *46*(13), 2235–2240. https://doi.org/10.1038/s41386-021-00978-8

Jiao, L., Yang, Y., Yu, W., Zhao, Y., Long, H., Gao, J., Ding, K., Ma, C., Li, J., Zhao, S., Wang, H., Li, H., Yang, M., Xu, J., Wang, J., Yang, J., Kuang, D., Luo, F., Qian, X., Xu, L., … Peng, X. (2021). The olfactory route is a potential way for SARS-CoV-2 to invade the central nervous system of rhesus monkeys. *Signal transduction and targeted therapy*, *6*(1), 169. https://doi.org/10.1038/s41392-021-00591-7

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

Johnson, J. A., Strafella, A. P., & Zatorre, R. J. (2007). The role of the dorsolateral prefrontal cortex in bimodal divided attention: two transcranial magnetic stimulation studies. *Journal of cognitive neuroscience*, *19*(6), 907–920. https://doi.org/10.1162/jocn.2007.19.6.907

Jueptner, M., Stephan, K. M., Frith, C. D., Brooks, D. J., Frackowiak, R. S., & Passingham, R. E. (1997). Anatomy of motor learning. I. Frontal cortex and attention to action. *Journal of neurophysiology*, *77*(3), 1313–1324. https://doi.org/10.1152/jn.1997.77.3.1313

Kane, M. J., Brown, L. H., McVay, J. C., Silvia, P. J., Myin-Germeys, I., & Kwapil, T. R. (2007). For whom the mind wanders, and when: an experience-sampling study of working memory and executive control in daily life. *Psychological science*, *18*(7), 614–621. https://doi.org/10.1111/j.1467-9280.2007.01948.x

Kas, A., Soret, M., Pyatigoskaya, N., Habert, M. O., Hesters, A., Le Guennec, L., Paccoud, O., Bombois,

S., Delorme, C., & on the behalf of CoCo-Neurosciences study group and COVID SMIT PSL study group (2021). The cerebral network of COVID-19-related encephalopathy: a longitudinal voxel-based 18F-FDG-PET study. *European journal of nuclear medicine and molecular imaging*, *48*(8), 2543–2557. https://doi.org/10.1007/s00259-020-05178-y

Kayaaslan, B., Eser, F., Kalem, A. K., Kaya, G., Kaplan, B., Kacar, D., Hasanoglu, I., Coskun, B., & Guner, R. (2021). Post-COVID syndrome: A single-center questionnaire study on 1007 participants recovered from COVID-19. *Journal of medical virology*, *93*(12), 6566–6574. https://doi.org/10.1002/jmv.27198

Kinsinger, S. W., Lattie, E., & Mohr, D. C. (2010). Relationship between depression, fatigue, subjective cognitive impairment, and objective neuropsychological functioning in patients with multiple sclerosis. *Neuropsychology*, *24*(5), 573–580. https://doi.org/10.1037/a0019222

Kofler, M. J., Sarver, D. E., Harmon, S. L., Moltisanti, A., Aduen, P. A., Soto, E. F., & Ferretti, N. (2018). Working memory and organizational skills problems in ADHD. *Journal of child psychology and psychiatry, and allied disciplines*, *59*(1), 57–67. https://doi.org/10.1111/jcpp.12773

Kumar, A., Pareek, V., Prasoon, P., Faiq, M. A., Kumar, P., Kumari, C., & Narayan, R. K. (2020). Possible routes of SARS-CoV-2 invasion in brain: In context of neurological symptoms in COVID-19 patients. *Journal of neuroscience research*, *98*(12), 2376–2383. https://doi.org/10.1002/jnr.24717

Lagarde, G., Doyon, J., & Brunet, A. (2010). Memory and executive dysfunctions associated with acute posttraumatic stress disorder. *Psychiatry research*, *177*(1-2), 144–149. https://doi.org/10.1016/j.psychres.2009.02.002

Lamontagne, S. J., Winters, M. F., Pizzagalli, D. A., & Olmstead, M. C. (2021). Post-acute sequelae of COVID-19: Evidence of mood & cognitive impairment. *Brain, behavior, & immunity - health*, *17*, 100347. https://doi.org/10.1016/j.bbih.2021.100347

Liotta, E.M., Batra, A., Clark, J.R., Shlobin, N.A., Hoffman, S.C., Orban, Z.S. and Koralnik, I.J. (2020), Frequent neurologic manifestations and encephalopathy-associated morbidity in Covid-19 patients. *Ann Clin Transl Neurol, 7*, 2221-2230. https://doi.org/10.1002/acn3.51210

Lu, Y., Li, X., Geng, D., Mei, N., Wu, P. Y., Huang, C. C., Jia, T., Zhao, Y., Wang, D., Xiao, A., & Yin, B. (2020). Cerebral Micro-Structural Changes in COVID-19 Patients - An MRI-based 3-month Follow-up Study. *EClinicalMedicine*, *25*, 100484. https://doi.org/10.1016/j.eclinm.2020.100484

Luck, D., Danion, J. M., Marrer, C., Pham, B. T., Gounot, D., & Foucher, J. (2010). The right parahippocampal gyrus contributes to the formation and maintenance of bound information in working memory. *Brain and cognition*, *72*(2), 255–263. https://doi.org/10.1016/j.bandc.2009.09.009

Lukiw, W. J., Pogue, A., & Hill, J. M. (2022). SARS-CoV-2 Infectivity and Neurological Targets in the Brain. *Cellular and molecular neurobiology*, *42*(1), 217–224. https://doi.org/10.1007/s10571-020-00947-7

Lyra E Silva, N. M., Barros-Aragão, F. G. Q., De Felice, F. G., & Ferreira, S. T. (2022). Inflammation at the crossroads of COVID-19, cognitive deficits and depression. *Neuropharmacology*, *209*, 109023. https://doi.org/10.1016/j.neuropharm.2022.109023

Maki, Y., Yamaguchi, T., Yamagami, T., Murai, T., Hachisuka, K., Miyamae, F., Ito, K., Awata, S., Ura, C., Takahashi, R., & Yamaguchi, H. (2014). The impact of subjective memory complaints on quality of life in community-dwelling older adults. *Psychogeriatrics : the official journal of the Japanese Psychogeriatric Society*, *14*(3), 175–181. https://doi.org/10.1111/psyg.12056

Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., Chang, J., Hong, C., Zhou, Y., Wang, D., Miao, X., Li,

Y., & Hu, B. (2020). Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA neurology*, *77*(6), 683–690. https://doi.org/10.1001/jamaneurol.2020.1127

Mathias, J. L., & Mansfield, K. M. (2005). Prospective and declarative memory problems following moderate and severe traumatic brain injury. *Brain injury*, *19*(4), 271–282. https://doi.org/10.1080/02699050400005028

Mazza, M. G., De Lorenzo, R., Conte, C., Poletti, S., Vai, B., Bollettini, I., Melloni, E. M. T., Furlan, R., Ciceri, F., Rovere-Querini, P., COVID-19 BioB Outpatient Clinic Study group, & Benedetti, F. (2020). Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain, behavior, and immunity*, *89*, 594–600. https://doi.org/10.1016/j.bbi.2020.07.037

Mazza, M. G., Palladini, M., De Lorenzo, R., Magnaghi, C., Poletti, S., Furlan, R., Ciceri, F., COVID-19 BioB Outpatient Clinic Study group, 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

Mazzola-Pomietto, P., Kaladjian, A., Azorin, J. M., Anton, J. L., & Jeanningros, R. (2009). Bilateral decrease in ventrolateral prefrontal cortex activation during motor response inhibition in mania. *Journal of psychiatric research*, *43*(4), 432–441. https://doi.org/10.1016/j.jpsychires.2008.05.004

Méndez, R., Balanzá-Martínez, V., Luperdi, S. C., Estrada, I., Latorre, A., González-Jiménez, P., Feced, L., Bouzas, L., Yépez, K., Ferrando, A., Hervás, D., Zaldívar, E., Reyes, S., Berk, M., & Menéndez, R. (2021). Short-term neuropsychiatric outcomes and quality of life in COVID-19 survivors. *Journal of internal medicine*, *290*(3), 621–631. https://doi.org/10.1111/joim.13262

Miskowiak, K. W., Johnsen, S., Sattler, S. M., Nielsen, S., Kunalan, K., Rungby, J., Lapperre, T., &

Porsberg, C. M. (2021). Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*, *46*, 39–48. https://doi.org/10.1016/j.euroneuro.2021.03.019

Miskowiak, K. W., Pedersen, J. K., Gunnarsson, D. V., Roikjer, T. K., Podlekareva, D., Hansen, H., Dall, C. H., & Johnsen, S. (2023). Cognitive impairments among patients in a long-COVID clinic: Prevalence, pattern and relation to illness severity, work function and quality of life. *Journal of affective disorders*, *324*, 162–169. https://doi.org/10.1016/j.jad.2022.12.122

Mitchell A. S. (2015). The mediodorsal thalamus as a higher order thalamic relay nucleus important for learning and decision-making. *Neuroscience and biobehavioral reviews*, *54*, 76–88. https://doi.org/10.1016/j.neubiorev.2015.03.001

Mitchell, A. J., Kemp, S., Benito-León, J., & Reuber, M. (2010). The influence of cognitive impairment on health-related quality of life in neurological disease. *Acta Neuropsychiatrica, 22*(1), 2–13. https://doi.org/10.1111/j.1601-5215.2009.00439.x

Moen, K. C., Miller, J. K., & Lloyd, M. E. (2017). Selective attention meets spontaneous recognition memory: Evidence for effects at retrieval. *Consciousness and cognition*, *49*, 181–189. https://doi.org/10.1016/j.concog.2017.02.003

Moradi, A. R., Doost, H. T., Taghavi, M. R., Yule, W., & Dalgleish, T. (1999). Everyday memory deficits in children and adolescents with PTSD: performance on the Rivermead Behavioural Memory Test. *Journal of child psychology and psychiatry, and allied disciplines*, *40*(3), 357–361.

Moriguchi, Y., & Hiraki, K. (2009). Neural origin of cognitive shifting in young children. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(14), 6017–6021. https://doi.org/10.1073/pnas.0809747106

Mukandala, G., Tynan, R., Lanigan, S., & O'Connor, J. J. (2016). The Effects of Hypoxia and

Inflammation on Synaptic Signaling in the CNS. *Brain sciences*, *6*(1), 6. https://doi.org/10.3390/brainsci6010006

Nakhla, M. Z., Banuelos, D., Pagán, C., Gavarrete Olvera, A., & Razani, J. (2022). Differences between episodic and semantic memory in predicting observation-based activities of daily living in mild cognitive impairment and Alzheimer's disease. *Applied neuropsychology. Adult*, *29*(6), 1499–1510. https://doi.org/10.1080/23279095.2021.1893172

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-z

Nielsen, T. B., Leth, S., Pedersen, M., Harbo, H. D., Nielsen, C. V., Laursen, C. H., Schiøttz-Christensen, B., & Oestergaard, L. G. (2022). Mental Fatigue, Activities of Daily Living, Sick Leave and Functional Status among Patients with Long COVID: A Cross-Sectional Study. *International journal of environmental research and public health*, *19*(22), 14739. https://doi.org/10.3390/ijerph192214739

Oh, E. T., Kim, C. W., Kim, H. G., Lee, J. S., & Park, H. J. (2017). Brusatol-Mediated Inhibition of c-Myc Increases HIF-1α Degradation and Causes Cell Death in Colorectal Cancer under Hypoxia. *Theranostics*, *7*(14), 3415–3431. https://doi.org/10.7150/thno.20861

Ollila, H., Pihlaja, R., Koskinen, S., Tuulio-Henriksson, A., Salmela, V., Tiainen, M., Hokkanen, L., & Hästbacka, J. (2022). Long-term cognitive functioning is impaired in ICU-treated COVID-19 patients: a comprehensive controlled neuropsychological study. *Critical care (London, England)*, *26*(1), 223. https://doi.org/10.1186/s13054-022-04092-z

Ortiz, G. G., Velázquez-Brizuela, I. E., Ortiz-Velázquez, G. E., Ocampo-Alfaro, M. J., Salazar-Flores, J.,

Delgado-Lara, D. L. C., & Torres-Sanchez, E. D. (2022). Alzheimer's Disease and SARS-CoV-2: Pathophysiological Analysis and Social Context. *Brain sciences*, *12*(10), 1405. https://doi.org/10.3390/brainsci12101405

O'Shea, A., Cohen, R. A., Porges, E. C., Nissim, N. R., & Woods, A. J. (2016). Cognitive Aging and the Hippocampus in Older Adults. *Frontiers in aging neuroscience*, *8*, 298. https://doi.org/10.3389/fnagi.2016.00298

Paneri, S., & Gregoriou, G. G. (2017). Top-Down Control of Visual Attention by the Prefrontal Cortex. Functional Specialization and Long-Range Interactions. *Frontiers in neuroscience*, *11*, 545. https://doi.org/10.3389/fnins.2017.00545

Panikratova, Y. R., Vlasova, R. M., Akhutina, T. V., Korneev, A. A., Sinitsyn, V. E., & Pechenkova, E. V. (2020). Functional connectivity of the dorsolateral prefrontal cortex contributes to different components of executive functions. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, *151*, 70–79. https://doi.org/10.1016/j.ijpsycho.2020.02.013

Patel, U. K., Mehta, N., Patel, A., Patel, N., Ortiz, J. F., Khurana, M., Urhoghide, E., Parulekar, A., Bhriguvanshi, A., Patel, N., Mistry, A. M., Patel, R., Arumaithurai, K., & Shah, S. (2022). Long-Term Neurological Sequelae Among Severe COVID-19 Patients: A Systematic Review and Meta-Analysis. *Cureus*, *14*(9), e29694. https://doi.org/10.7759/cureus.29694

Peräkylä, J., Sun, L., Lehtimäki, K., Peltola, J., Öhman, J., Möttönen, T., Ogawa, K. H., & Hartikainen, K. M. (2017). Causal Evidence from Humans for the Role of Mediodorsal Nucleus of the Thalamus in Working Memory. *Journal of cognitive neuroscience*, *29*(12), 2090–2102. https://doi.org/10.1162/jocn_a_01176

Percivalle, E., Sammartino, J. C., Cassaniti, I., Arbustini, E., Urtis, M., Smirnova, A., Concardi, M.,

Belgiovine, C., Ferrari, A., Lilleri, D., Piralla, A., & Baldanti, F. (2021). Macrophages and Monocytes: "Trojan Horses" in COVID-19. *Viruses*, *13*(11), 2178. https://doi.org/10.3390/v13112178

Perez Giraldo, G. S., Ali, S. T., Kang, A. K., Patel, T. R., Budhiraja, S., Gaelen, J. I., Lank, G. K., Clark, J. R., Mukherjee, S., Singer, T., Venkatesh, A., Orban, Z. S., Lim, P. H., Jimenez, M., Miller, J., Taylor, C., Szymanski, A. L., Scarpelli, J., Graham, E. L., Balabanov, R. D., … Koralnik, I. J. (2023). Neurologic Manifestations of Long COVID Differ Based on Acute COVID-19 Severity. *Annals of neurology*, *94*(1), 146–159. https://doi.org/10.1002/ana.26649

Perrin, P., Collongues, N., Baloglu, S., Bedo, D., Bassand, X., Lavaux, T., Gautier-Vargas, G., Keller, N., Kremer, S., Fafi-Kremer, S., Moulin, B., Benotmane, I., & Caillard, S. (2021). Cytokine release syndrome-associated encephalopathy in patients with COVID-19. *European journal of neurology*, *28*(1), 248–258. https://doi.org/10.1111/ene.14491

Peter, R. S., Nieters, A., Kräusslich, H. G., Brockmann, S. O., Göpel, S., Kindle, G., Merle, U., Steinacker, J. M., Rothenbacher, D., Kern, W. V., & EPILOC Phase 1 Study Group (2022). Post-acute sequelae of covid-19 six to 12 months after infection: population based study. *BMJ (Clinical research ed.)*, *379*, e071050. https://doi.org/10.1136/bmj-2022-071050

Petersen, M. S., Kristiansen, M. F., Hanusson, K. D., Danielsen, M. E., Á Steig, B., Gaini, S., Strøm, M., & Weihe, P. (2021). Long COVID in the Faroe Islands: A Longitudinal Study Among Nonhospitalized Patients. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *73*(11), e4058–e4063. https://doi.org/10.1093/cid/ciaa1792

Picton, T. W., Stuss, D. T., Alexander, M. P., Shallice, T., Binns, M. A., & Gillingham, S. (2007). Effects of focal frontal lesions on response inhibition. *Cerebral cortex (New York, N.Y. : 1991)*, *17*(4), 826–838. https://doi.org/10.1093/cercor/bhk031

Pilotto, A., Masciocchi, S., Volonghi, I., De Giuli, V., Caprioli, F., Mariotto, S., Ferrari, S., Bozzetti, S., Imarisio, A., Risi, B., Premi, E., Benussi, A., Focà, E., Castelli, F., Zanusso, G., Monaco, S., Stefanelli, P., Gasparotti, R., Zekeridou, A., McKeon, A., … Padovani, A. (2021). Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Encephalitis Is a Cytokine Release Syndrome: Evidences From Cerebrospinal Fluid Analyses. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *73*(9), e3019–e3026. https://doi.org/10.1093/cid/ciaa1933

Poliakoff, E., & Smith-Spark, J. H. (2008). Everyday cognitive failures and memory problems in Parkinson's patients without dementia. *Brain and cognition*, *67*(3), 340–350. https://doi.org/10.1016/j.bandc.2008.02.004

Pontelli, M. C., Castro, I. A., Martins, R. B., Veras, F. P., Serra, L., Nascimento, D. C., Cardoso, R. S., Rosales, R., Lima, T. M., Souza, J. P., Caetité, D. B., de Lima, M. H. F., Kawahisa, J. T., Giannini, M. C., Bonjorno, L. P., Lopes, M. I. F., Batah, S. S., Siyuan, L., Assad, R. L., Almeida, S. C. L., … Arruda, E. (2020). Infection of human lymphomononuclear cells by SARS-CoV-2. *bioRxiv : the preprint server for biology*, 2020.07.28.225912. https://doi.org/10.1101/2020.07.28.225912

Proust, A., Queval, C. J., Harvey, R., Adams, L., Bennett, M., & Wilkinson, R. J. (2023). Differential effects of SARS-CoV-2 variants on central nervous system cells and blood-brain barrier functions. *Journal of neuroinflammation*, *20*(1), 184. https://doi.org/10.1186/s12974-023-02861-3

Rass, V., Beer, R., Schiefecker, A. J., Kofler, M., Lindner, A., Mahlknecht, P., Heim, B., Limmert, V., Sahanic, S., Pizzini, A., Sonnweber, T., Tancevski, I., Scherfler, C., Zamarian, L., Bellmann-Weiler, R., Weiss, G., Djamshidian, A., Kiechl, S., Seppi, K., Loeffler-Ragg, J., … Helbok, R. (2021). Neurological outcome and quality of life 3 months after COVID-19: A prospective observational cohort study. *European journal of neurology*, *28*(10), 3348–3359. https://doi.org/10.1111/ene.14803

Rass, V., Ianosi, B. A., Zamarian, L., Beer, R., Sahanic, S., Lindner, A., Kofler, M., Schiefecker, A. J., Mahlknecht, P., Heim, B., Limmert, V., Sonnweber, T., Pizzini, A., Tymoszuk, P., Scherfler, C., Djamshidian, A., Kiechl, S., Tancevski, I., Seppi, K., Pfausler, B., … Helbok, R. (2022). Factors associated with impaired quality of life three months after being diagnosed with COVID-19. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*, *31*(5), 1401–1414. https://doi.org/10.1007/s11136-021-02998-9

Reynolds, J. L., & Mahajan, S. D. (2021). SARS-COV2 Alters Blood Brain Barrier Integrity Contributing to Neuro-Inflammation. *Journal of neuroimmune pharmacology : the official journal of the Society on NeuroImmune Pharmacology*, *16*(1), 4–6. https://doi.org/10.1007/s11481-020-09975-y

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. *Science (New York, N.Y.)*, *306*(5695), 443–447. https://doi.org/10.1126/science.1100301

Rubia, K., Russell, T., Overmeyer, S., Brammer, M. J., Bullmore, E. T., Sharma, T., Simmons, A., Williams, S. C., Giampietro, V., Andrew, C. M., & Taylor, E. (2001). Mapping motor inhibition: conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage*, *13*(2), 250–261. https://doi.org/10.1006/nimg.2000.0685

Salehinejad, M. A., Ghanavati, E., Rashid, M. H. A., & Nitsche, M. A. (2021). Hot and cold executive functions in the brain: A prefrontal-cingular network. *Brain and neuroscience advances, 5*, 23982128211007769. https://doi.org/10.1177/23982128211007769

Sapin, E., Peyron, C., Roche, F., Gay, N., Carcenac, C., Savasta, M., Levy, P., & Dematteis, M. (2015). Chronic Intermittent Hypoxia Induces Chronic Low-Grade Neuroinflammation in the Dorsal Hippocampus of Mice. *Sleep, 38*(10), 1537–1546. https://doi.org/10.5665/sleep.5042

Scarpina, F., & Tagini, S. (2017). The Stroop Color and Word Test. *Frontiers in psychology*, *8*, 557.

https://doi.org/10.3389/fpsyg.2017.00557

Schmitter-Edgecombe, M., Woo, E., & Greeley, D. R. (2009). Characterizing multiple memory deficits and their relation to everyday functioning in individuals with mild cognitive impairment. *Neuropsychology*, *23*(2), 168–177. https://doi.org/10.1037/a0014186

Schoechlin, C., & Engel, R. R. (2005). Neuropsychological performance in adult attention-deficit hyperactivity disorder: meta-analysis of empirical data. *Archives of clinical neuropsychology : the official journal of the National Academy of Neuropsychologists*, *20*(6), 727–744. https://doi.org/10.1016/j.acn.2005.04.005

Serrano, G. E., Walker, J. E., Arce, R., Glass, M. J., Vargas, D., Sue, L. I., Intorcia, A. J., Nelson, C. M., Oliver, J., Papa, J., Russell, A., Suszczewicz, K. E., Borja, C. I., Belden, C., Goldfarb, D., Shprecher, D., Atri, A., Adler, C. H., Shill, H. A., Driver-Dunckley, E., … Beach, T. G. (2021). Mapping of SARS-CoV-2 Brain Invasion and Histopathology in COVID-19 Disease. *medRxiv : the preprint server for health sciences*, 2021.02.15.21251511. https://doi.org/10.1101/2021.02.15.21251511

Sherman, S. M., & Guillery, R. W. (2002). The role of the thalamus in the flow of information to the cortex. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences*, *357*(1428), 1695–1708. https://doi.org/10.1098/rstb.2002.1161

Silva, L. S., Joao, R. B., Nogueira, M. H., Aventurato, I. K., de Campos, B. M., de Brito, M. R., et al. (2021). Functional and microstructural brain abnormalities, fatigue, and cognitive dysfunction after mild COVID-19. *Medrxiv*. 2021.03.20.21253414. doi: 10.1101/2021.03.20.21253414

Skevington, S. M., Lotfy, M., O'Connell, K. A., & WHOQOL Group. (2004). The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL group. *Quality of life research : an*

international journal of quality of life aspects of treatment, care and rehabilitation, *13*(2), 299–310. https://doi.org/10.1023/B:QURE.0000018486.91360.00

Smith, J. L., Mattick, R. P., Jamadar, S. D., & Iredale, J. M. (2014). Deficits in behavioural inhibition in substance abuse and addiction: a meta-analysis. *Drug and alcohol dependence*, *145*, 1–33. https://doi.org/10.1016/j.drugalcdep.2014.08.009

Snyder, H. R., Miyake, A., & Hankin, B. L. (2015). Advancing understanding of executive function impairments and psychopathology: bridging the gap between clinical and cognitive approaches. *Frontiers in psychology*, *6*, 328. https://doi.org/10.3389/fpsyg.2015.00328

Sohrabi, H. R., Bates, K. A., Rodrigues, M., Taddei, K., Martins, G., Laws, S. M., Lautenschlager, N. T., Dhaliwal, S. S., Foster, J. K., & Martins, R. N. (2009). The relationship between memory complaints, perceived quality of life and mental health in apolipoprotein Eepsilon4 carriers and non-carriers. *Journal of Alzheimer's disease : JAD*, *17*(1), 69–79. https://doi.org/10.3233/JAD-2009-1018

Stern, C. E., Owen, A. M., Tracey, I., Look, R. B., Rosen, B. R., & Petrides, M. (2000). Activity in ventrolateral and mid-dorsolateral prefrontal cortex during nonspatial visual working memory processing: evidence from functional magnetic resonance imaging. *NeuroImage*, *11*(5 Pt 1), 392–399. https://doi.org/10.1006/nimg.2000.0569

Tabacof, L., Tosto-Mancuso, J., Wood, J., Cortes, M., Kontorovich, A., McCarthy, D., Rizk, D., Rozanski, G., Breyman, E., Nasr, L., Kellner, C., Herrera, J. E., & Putrino, D. (2022). Post-acute COVID-19 Syndrome Negatively Impacts Physical Function, Cognitive Function, Health-Related Quality of Life, and Participation. *American journal of physical medicine & rehabilitation*, *101*(1), 48–52. https://doi.org/10.1097/PHM.0000000000001910

Taquet, M., Sillett, R., Zhu, L., Mendel, J., Camplisson, I., Dercon, Q., & Harrison, P. J. (2022).

Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. *The lancet. Psychiatry*, *9*(10), 815–827. https://doi.org/10.1016/S2215-0366(22)00260-7

Thai, M. L., Andreassen, A. K., & Bliksted, V. (2019). A meta-analysis of executive dysfunction in patients with schizophrenia: Different degree of impairment in the ecological subdomains of the Behavioural Assessment of the Dysexecutive Syndrome. *Psychiatry research*, *272*, 230–236. https://doi.org/10.1016/j.psychres.2018.12.088

The WHOQOL group. (1998). Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine, 28*(3), 551-558. doi:10.1017/S0033291798006667

Toepper, M., Markowitsch, H. J., Gebhardt, H., Beblo, T., Thomas, C., Gallhofer, B., Driessen, M., & Sammer, G. (2010). Hippocampal involvement in working memory encoding of changing locations: an fMRI study. *Brain research*, *1354*, 91–99. https://doi.org/10.1016/j.brainres.2010.07.065

Toniolo, S., Di Lorenzo, F., Scarioni, M., Frederiksen, K. S., & Nobili, F. (2021). Is the Frontal Lobe the Primary Target of SARS-CoV-2?. *Journal of Alzheimer's disease : JAD*, *81*(1), 75–81. https://doi.org/10.3233/JAD-210008

Vallat-Azouvi, C., Pradat-Diehl, P., & Azouvi, P. (2012). The Working Memory Questionnaire: a scale to assess everyday life problems related to deficits of working memory in brain injured patients. *Neuropsychological rehabilitation*, *22*(4), 634–649. https://doi.org/10.1080/09602011.2012.681110

Vannorsdall, T. D., Brigham, E., Fawzy, A., Raju, S., Gorgone, A., Pletnikova, A., Lyketsos, C. G., Parker,

A. M., & Oh, E. S. (2022). Cognitive Dysfunction, Psychiatric Distress, and Functional Decline After COVID-19. *Journal of the Academy of Consultation-Liaison Psychiatry*, *63*(2), 133–143. https://doi.org/10.1016/j.jaclp.2021.10.006

Varjačić, A., Mantini, D., Levenstein, J., Slavkova, E. D., Demeyere, N., & Gillebert, C. R. (2018). The role of left insula in executive set-switching: Lesion evidence from an acute stroke cohort. *Cortex; a journal devoted to the study of the nervous system and behavior*, *107*, 92–101. https://doi.org/10.1016/j.cortex.2017.11.009

Vélez-Santamaría, R., Fernández-Solana, J., Méndez-López, F., Domínguez-García, M., González-Bernal, J. J., Magallón-Botaya, R., Oliván-Blázquez, B., González-Santos, J., & Santamaría-Peláez, M. (2023). Functionality, physical activity, fatigue and quality of life in patients with acute COVID-19 and Long COVID infection. *Scientific reports*, *13*(1), 19907. https://doi.org/10.1038/s41598-023-47218-1

Versace, V., Sebastianelli, L., Ferrazzoli, D., Romanello, R., Ortelli, P., Saltuari, L., D'Acunto, A., Porrazzini, F., Ajello, V., Oliviero, A., Kofler, M., & Koch, G. (2021). Intracortical GABAergic dysfunction in patients with fatigue and dysexecutive syndrome after COVID-19. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*, *132*(5), 1138–1143. https://doi.org/10.1016/j.clinph.2021.03.001

Virhammar, J., Nääs, A., Fällmar, D., Cunningham, J. L., Klang, A., Ashton, N. J., Jackmann, S., Westman, G., Frithiof, R., Blennow, K., Zetterberg, H., Kumlien, E., & Rostami, E. (2021). Biomarkers for central nervous system injury in cerebrospinal fluid are elevated in COVID-19 and associated with neurological symptoms and disease severity. *European journal of neurology*, *28*(10), 3324–3331. https://doi.org/10.1111/ene.14703

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y., Zhao, Y., Li,

Y., Wang, X., & Peng, Z. (2020). Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*, *323*(11), 1061–1069. https://doi.org/10.1001/jama.2020.1585

Winter, D., & Braw, Y. (2022). COVID-19: Impact of Diagnosis Threat and Suggestibility on Subjective Cognitive Complaints. *International Journal of Clinical and Health Psychology, 22*(1), 1-9. https://doi.org/10.1016/j.ijchp.2021.100253

World Health Organization. (n.d.). *WHO COVID-19 Dashboard > Deaths*. World Health Organization Data. https://data.who.int/dashboards/covid19/deaths

World Health Organization. (2022, 07. December). *Post COVID-19 condition (Long COVID)*. https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition

Xie, R., Sun, X., Yang, L., & Guo, Y. (2020). Characteristic Executive Dysfunction for High-Functioning Autism Sustained to Adulthood. *Autism research : official journal of the International Society for Autism Research*, *13*(12), 2102–2121. https://doi.org/10.1002/aur.2304

Yang, Y., & Rosenberg, G. A. (2011). Blood-brain barrier breakdown in acute and chronic cerebrovascular disease. *Stroke*, *42*(11), 3323–3328. https://doi.org/10.1161/STROKEAHA.110.608257

Yao, W., Wang, T., Jiang, B., Gao, F., Wang, L., Zheng, H., Xiao, W., Yao, S., Mei, W., Chen, X., Luo, A., Sun, L., Cook, T., Behringer, E., Huitink, J. M., Wong, D. T., Lane-Fall, M., McNarry, A. F., McGuire, B., Higgs, A., … collaborators (2020). Emergency tracheal intubation in 202 patients with COVID-19 in Wuhan, China: lessons learnt and international expert recommendations. *British journal of anaesthesia*, *125*(1), e28–e37. https://doi.org/10.1016/j.bja.2020.03.026

Yesilkaya, U. H., Sen, M., & Balcioglu, Y. H. (2021). COVID-19-related cognitive dysfunction may be

associated with transient disruption in the DLPFC glutamatergic pathway. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*, *87*, 153–155. https://doi.org/10.1016/j.jocn.2021.03.007

Yin, X., Zhao, L., Xu, J., Evans, A. C., Fan, L., Ge, H., Tang, Y., Khundrakpam, B., Wang, J., & Liu, S. (2012). Anatomical substrates of the alerting, orienting and executive control components of attention: focus on the posterior parietal lobe. *PloS one*, *7*(11), e50590. https://doi.org/10.1371/journal.pone.0050590

Zalla, T., Joyce, C., Szöke, A., Schürhoff, F., Pillon, B., Komano, O., Perez-Diaz, F., Bellivier, F., Alter, C., Dubois, B., Rouillon, F., Houde, O., & Leboyer, M. (2004). Executive dysfunctions as potential markers of familial vulnerability to bipolar disorder and schizophrenia. *Psychiatry research*, *121*(3), 207–217. https://doi.org/10.1016/s0165-1781(03)00252-x

Zgaljardic, D. J., Borod, J. C., Foldi, N. S., Mattis, P. J., Gordon, M. F., Feigin, A., & Eidelberg, D. (2006). An examination of executive dysfunction associated with frontostriatal circuitry in Parkinson's disease. *Journal of clinical and experimental neuropsychology*, *28*(7), 1127–1144. https://doi.org/10.1080/13803390500246910

Zhang, L., Zhou, L., Bao, L., Liu, J., Zhu, H., Lv, Q., Liu, R., Chen, W., Tong, W., Wei, Q., Xu, Y., Deng, W., Gao, H., Xue, J., Song, Z., Yu, P., Han, Y., Zhang, Y., Sun, X., Yu, X., … Qin, C. (2021). SARS-CoV-2 crosses the blood-brain barrier accompanied with basement membrane disruption without tight junctions alteration. *Signal transduction and targeted therapy*, *6*(1), 337. https://doi.org/10.1038/s41392-021-00719-9

Zhao, Y., Li, W., & Lukiw, W. (2021). Ubiquity of the SARS-CoV-2 receptor ACE2 and upregulation in limbic regions of Alzheimer's disease brain. *Folia neuropathologica*, *59*(3), 232–238. https://doi.org/10.5114/fn.2021.109495

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

Zorzo, C., Solares, L., Mendez, M., & Mendez-Lopez, M. (2023). Hippocampal alterations after SARS-CoV-2 infection: A systematic review. *Behavioural brain research*, *455*, 114662. https://doi.org/10.1016/j.bbr.2023.114662

Zubair, A. S., McAlpine, L. S., Gardin, T., Farhadian, S., Kuruvilla, D. E., & Spudich, S. (2020). Neuropathogenesis and Neurologic Manifestations of the Coronaviruses in the Age of Coronavirus Disease 2019: A Review. *JAMA neurology*, *77*(8), 1018–1027. https://doi.org/10.1001/jamaneurol.2020.2065

Appendix

Checklist

General questions

- Do any of the authors have competing interests? If so, describe these here. If not, answer "The authors have no competing interests."

The authors have no competing interests.

- Did you obtain ethics approval to conduct this study? If so, provide the approval (IRB) number here. If not, explain why ethics approval was not obtained.

PSY-2021-S-0200

- Was the study preregistered prior to data collection? If so, provide a link to a public preregistration. If not, explain why you did not preregister the study.

No, it wasn't.

Archiving and accessibility

- Did you archive the data according to the Heymans Data Storage Protocol? If not, explain why you did not archive the data according to this protocol.

Yes, see the approval study number above.

- Did you make the raw (unprocessed) data publicly available? If so, provide a link to where the data can be found. If not, explain why you did not make the data publicly available.

No.

- Did you make the experimental and analysis scripts publicly available? If so, provide a link to where the experimental and analysis scripts can be found. If not, explain why you did not make the experimental and analysis scripts publicly available.

No.

Interacting with participants

- Was participant data made anonymous such that it cannot be traced back to individual participants? If so, explain how the data was made anonymous. If not, explain why the data was not made anonymous.

Data was pseuchonynymized.

- Were participants informed about the goal of the study (debriefed) after participating? If so, explain how participants were debriefed. If not, explain why participants were not debriefed.

The participants were informed about the goal of the study in the very beginning of the questionnaire. In order to use their data, they had to give their informed consent.

Sample size and statistical power

- Was the number of participants determined in advance? If not, explain why the number of participants was not determined in advance.

No, there was no determined number for this questionnaire study in advance. This is the first study in this direction, and power calculations could not be done, we used a convenience sample and try to gather as many participants within a specific range of time.

- How was the number of participants determined?

n.a.

- If applicable, was the number of observations per participant determined in advance? If not, explain why the number of observations per participants was not determined in advance.

n.a.

- If applicable, how was the number of observations per participant determined?

n.a.

- Did you conduct a power analysis beforehand? If so, provide the statistical power for the main outcomes. If not, explain why you did not conduct a power analysis beforehand.

See above.

Exclusion of participants and observations

- Were any participants excluded from the analysis? If so, explain why some participants were excluded.

Since we used eleven questionnaires for the analysis, we wanted to make sure that we have the data for every of these questionnaires for every participant. So participants that did not fill out these eleven questionnaires, were excluded from analysis.

- If applicable, were any observations (per participant) excluded from the analysis. If so, explain why some observations were excluded.

No.

- Were the exclusion criteria determined in advance? If not, explain why the exclusion criteria were not determined in advance.

The exclusion criteria were determined as soon as we agreed on which questionnaires to use for the analysis. There was some discussion about the ASCDQ and the SF-12, and they were later removed due to their low information value and the structure and coding of the questionnaire. However, removing the two questionnaires did not change the number of participants.

Reporting

- Were the outcome variables determined in advance?

The outcome variables were determined in advance. However, during the master thesis presentation there was a very useful and productive discussion and the outcome variable “memory” which was used to be measured with ASCDQ, was replaced with the CFQ forgetfulness scale.

- Did you report all outcome variables? If not, explain why some outcome variables were not reported.

Since the ASCDQ was replaced with the CFQ forgetfulness scale, it was not reported anymore. The reason was that the ASCDQ did not have a high informative value and therefore became redundant.

- Did you clearly identify exploratory analysis in the text? (An analysis is exploratory when the analysis procedure was not determined in advance

I tested for statistical differences in the psychological questionnaires between the Covid- and the control group and I added two independent variables in the regression analysis. Both analyses were not part of the research questions/hypotheses. I am not sure if that is meant by exploratory analysis?