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Subjective Neuropsychological Impairments after COVID-19: The Influencing Factors Obesity, Hypertension and Diabetes

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Abstract

Objective: Only few studies about cognitive impairments in the context of COVID-19 include subjective measurements in executive functions (EFs). The aim of the present study is to explore subjective impairments in EFs in a Dutch-speaking sample of post-COVID-19 participants. The term "subjective" refers to the fact that EFs are measured by participants' self-evaluation. Additionally, it aims to analyse the correlation between comorbidities (i.e., obesity, hypertension, diabetes), age, and perceived deficits in EFs. This research hypothesized that post-COVID-19 participants subjectively report more executive impairments in their everyday life than participants that did not suffer from COVID-19. Furthermore, it was hypothesized that post-COVID-19 participants suffering from either obesity, hypertension, or diabetes report more impairments in EFs compared to those without comorbidities. Finally, it was hypothesized that older post-COVID-19 participants experience more impairments in EFs compared to younger counterparts.

Methods: An online survey study was designed, and data was collected from individuals who suffered from COVID-19 (n = 105) and from healthy controls (n = 15). Participants completed the questionnaires BRIEF-A, BDI, and GAD-7 to assess executive functions, depression, and anxiety symptoms respectively. BRIEF-A scores were compared a) between post-COVID-19 participants and healthy controls using one-tailed Mann-Whitney U tests, b) between post-COVID-19 participants with and without comorbidities using one-tailed independent samples t-tests and Mann-Whitney U tests, and c) between different age groups using one-way ANOVA and Kruskal-Wallis H tests. Non-parametric alternatives to parametric tests were used when assumptions of normality and homogeneity of variance were violated.

Results: Post-COVID-19 participants had significantly higher BRIEF-A scores than healthy controls (i.e., GEC, mean rank: 63.98 vs. 36.13, $p < .01$; MI, mean rank: 64.38 vs.

33.33, p < .001; BRI, mean rank: 62.88 vs. 43.83, $p < .05$; Shift, mean rank: 64.10 vs. 35.33, $p < .01$; Working Memory, mean rank: 65.10 vs. 28.30, $p < .001$). Post-COVID-19 participants with comorbidities scored significantly higher than those without comorbidities on the Behavioural Regulation Index (mean rank: 62.25 vs. 49.64, $p < .05$). Statistically significant age effects were only observed in Working Memory scores: participants aged between 30 and 39 scored significantly higher than participants aged between 18 and 29 (*Mdn*: 20.00 vs. 15.00, $p < .05$) and participants aged between 30 and 39 scored higher than participants aged 65 and older (*Mdn*: 20.00 vs. 15.50, $p < .05$).

Conclusion: This research was one of a few to focus on the subjective perception of deficits in EFs. COVID-19 is associated with the experience of post-infectious cognitive impairments. Most importantly, the results raise some issues to the role of comorbidities in deficits in EFs after COVID-19. The results provide valuable information for clinical practice and possible areas of focus in treatment and rehabilitation planning of people who suffered from COVID-19.

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List of Abbreviations

BRI Behavioural Regulation Index

EFD Executive Function Deficits

EFs Executive Functions

GEC Global Executive Composite

MI Metacognition Index

Objective

Several Coronavirus Disease 2019 (COVID-19) studies conclude that many factors can contribute to regional differences in disease prevalence and symptom severity, such as average life expectancy and comorbidities (Shams et al., 2020; Wolff et al., 2020). Moreover, studies revealed various neurological symptoms of the infection (Halpin et al., 2021; Mao et al., 2020; Meinhardt et al., 2021). For example, there is evidence that the virus can affect executive functions (EFs), which are crucial for every-day functioning (Amalakanti et al., 2021; Helms et al., 2020; Pistarini et al., 2021). Yet, literature examining whether factors that contribute to cross-country differences in disease prevalence and symptom severity might also influence medium-to-long term consequences in post-COVID-19 patients, is scarce. It will be necessary to understand cross-cultural differences in post-infectious manifestations of COVID-19 to develop effective treatment and rehabilitation measures that are tailored to the respective population and region. Therefore, the aim of the present research is to explore post-infectious manifestations in individuals who suffered from COVID-19 with a focus on subjective impairments in EFs, and to analyse the correlation between comorbidities, age, and medium-to-long term consequences of SARS-CoV-2. In this respect, the term "subjective" refers to the fact that EFs are measured by asking participants to evaluate their problems they encounter in daily life.

Introduction

Due to its high transmissibility, the COVID-19 pandemic rapidly spread on a global scale. Reports of the World Health Organization confirm as of December 17th, 2021, that there have been more than 271 million cases diagnosed around the world and 5.331.019 confirmed deaths as a consequence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in about 190 countries (*World Health Organization*, 2021).

COVID-19 and Cross-Cultural Differences

In general, various risk factors have been reported that can lead to differences in the frequency and severity of COVID-19 among populations. Factors influencing cross-cultural differences include variance in demographics, income level, health infrastructure, government response, and cultural traits of different populations (Shams, Haleem, & Javaid, 2020). Another factor which influences the differences in the number and severity of COVID-19 cases is the average life expectancy in a country (Schetelig et al., 2020; Shams et al., 2020). Older people are more vulnerable to the disease because of weaker immune and respiratory systems and increasing number of underlying health conditions with age (Shams et al., 2020). Older age is associated with an increased risk of fatal and severe complications, and a decreased chance of recovery from COVID-19 (Iodice et al., 2021; Nijman et al., 2021). Thus, the number of COVID-19 cases and the fatality rates are likely to be higher in countries with higher life expectancy than in countries with lower life expectancy. In fact, a study which identified the top eighteen countries worst hit by COVID-19 cases found a positive correlation between average life expectancy and fatality rate (Shams et al., 2020). Five out of the six countries with the highest fatality rates had an average life expectancy above 80 years, among them France, Italy, and Spain (Shams et al., 2020).

There is evidence that older age may also be a risk factor for cognitive manifestations after infection with SARS-CoV-2: A study that included 1539 post-COVID-19 patients aged 60 years and older examined the long-term impact of COVID-19 six months after recovery (Liu et al., 2021). The results indicated that cognitive impairment was associated with SARS-CoV-2 infection and severity of COVID-19. Even more important, the findings of this study identified older age as a risk factor for post-infection cognitive impairment (Liu et al., 2021).

Apart from that, countries with a large percentage of individuals suffering from comorbidities such as hypertension, diabetes, and obesity are especially at risk for more

severe and fatal disease courses (Wolff et al., 2020). A population with a particularly large proportion suffering from precisely these factors is the Mexican population (Gutierrez & Bertozzi, 2020): Over 33% of Mexicans are overweight, which is the third-highest number among all "Organisation for Economic Co-operation and Development" member countries (OECD, 2017). Furthermore, many Mexicans suffer from hypertension and diabetes, 30% and 15% respectively (Campos-Nonato et al., 2013; OECD, 2017). The high prevalence of comorbidities is mirrored in the reported COVID-19 cases from Mexico (Gutierrez & Bertozzi, 2020). Statistics show that about one-third of COVID-19 patients in Mexico suffer from hypertension and diabetes, and nearly 24% are overweight (Hernandez-Galdamez et al., 2020).

COVID-19 and Executive Functions

Since the initial phase of COVID-19 pandemic, many studies revealed neurological symptoms of the infection. The most frequent symptoms include anosmia, a disturbance in smell, ageusia, a disturbance in taste, fatigue, headache, and impaired consciousness (Halpin et al., 2021; Mao et al., 2020; Meinhardt et al., 2021). These symptoms have been found to be strongly associated with impaired performance in neuropsychological assessment in attention, memory, and executive functions domains in COVID-19 patients (Almeria et al., 2020).

So far, EFs have only been the focus of a small amount of COVID-19 research. The term executive functions can be defined as an umbrella term that summarizes higher order cognitive processes that regulate the dynamics of human cognition and action, such as memory, planning, and attention (Miyake & Friedman, 2012). EFs can be considered core components of self-regulation and self-control ability and thus, have a great influence on individuals' mental and physical health, success in life, and cognitive and psychological development (Diamond, 2013). There is a general agreement that there are three to four core EFs (Botvinick et al., 2001; Lehto et al., 2003; Miyake & Friedman, 2012): inhibition of

prepotent responses (‘inhibition’), information updating and monitoring (‘updating’), and mental set shifting (‘shifting’), as well as conflict monitoring. Inhibition is the ability to “deliberately inhibit dominant, automatic, or prepotent responses when necessary” (Miyake et al., 2000, p. 57). Updating refers to monitoring and coding incoming information and appropriately replacing no longer relevant information with new information in the working memory (Miyake et al., 2000). Shifting relates to the ability to shift between multiple tasks, operations, or mental sets (Miyake et al., 2000). Conflic monitoring is the ability to evaluate levels of conflict and to adjust their influence on information processing (Botvinick et al., 2001). These components act together to guide higher-order cognitive constructs, such as planning and organizing, and are relevant for successful daily life functioning.

There are some studies that indicate that SARS-CoV-2 can affect EFs (Amalakanti et al., 2021; Helms et al., 2020; Pistarini et al., 2021). A study that observed neurological features in hospitalized COVID-19 patients reported that at discharge 15 out of 45 patients experienced loss of EFs, including inattention, disorientation, and disorganized movements (Helms et al., 2020). Moreover, there is evidence that even asymptomatic COVID-19 subjects have cognitive deficits in domains such as perception, naming, and fluency (Amalakanti et al., 2021). Another study investigated cognitive deficits among COVID-19 patients who required functional rehabilitation (Pistarini et al., 2021). The results showed that almost three quarters of the patients had cognitive deficits, including executive function deficits (EFD). Another study examined the symptom spectrum of COVID-19 and reported that 61.5% of patients showed cognitive impairments, including primarily EFD (Ermis et al., 2021).

EFD include ineffective planning and disorganization, problems with multitasking, poor decision-making, impaired concentration, and attention, as well as difficulties with problem-solving (Rabinovici et al., 2015). Moreover, EFs are significantly related to functional independence in older adults (Cahn-Weiner et al., 2002). Thus, EFD can have a great impact on everyday life.

Summarising previous studies, it has been shown that EFs have a major impact on everyday life (e.g., Rabinovici et al., 2015). Furthermore, studies conducted in the context of the COVID-19 pandemic indicate that people who were infected with SARS-CoV-2 report to suffer from EFD after recovery (e.g., Helms et al., 2020). Considering that especially people of older age and people with comorbidities are at higher risk for severe COVID-19 (Nijman et al., 2021; Wolff et al., 2020), it is possible that these people experience more EFD after COVID-19 than people without concomitant diseases and people of younger age who have a mild disease course.

Neuroinvasive Potential in Corona Viruses

Several mechanisms that could explain the acute and long-term effects of SARS-CoV-2 on the brain have been presented in recent studies (Iadecola, Anrather & Kamel, 2020; Miners, Kehoe & Love, 2020; Pereira, 2020; Uversky et al., 2021). To enter a human cell, SARS-CoV-2 needs to overcome the cell wall. The virus uses the spike protein and binds to the angiotensin-converting enzyme 2 (ACE2) receptor, which is localized in the cell wall (Hoffmann et al., 2020). Thereupon, host proteases, including transmembrane protease serine (TMPRSS2), participate in the processing of the spike protein and activate the cell entry of SARS-CoV-2. As ACE2 receptors are predominantly expressed in the lungs, COVID-19 is primarily recognized as a respiratory disease. However, ACE2 receptors are expressed in neural cells in the central nervous system, too (Chen et al., 2021; Khan & Gomes, 2020; Lukiw et al., 2020). Furthermore, there is evidence that SARS-CoV-2 is neurotropic, that is, the virus can invade and live-in neural tissue (Butler et al., 2020). Thus, the virus can enter the central nervous system and potentially cause neuropsychiatric syndromes affecting cognitive domains (Butler et al., 2020).

Before the COVID-19 pandemic, neuroinvasive potential has been reported in other coronaviruses, which caused two well-known worldwide outbreaks: the severe acute

respiratory syndrome by SARS-CoV in 2002, and the middle eastern respiratory syndrome by MERS-CoV in 2012. Both viruses have shown to be neuroinvasive (Arabi et al., 2015; Gu et al., 2005), and both caused neuropsychiatric short- and long-term consequences (Rogers et al., 2020). Empirical evidence from a meta-analysis of 72 studies on long-term symptoms in patients that recovered from either SARS or MERS, revealed memory and concentration deficits in more than 15% of the patients up to 39 months after the infection (Rogers et al., 2020). Additionally, results showed that during the acute illness, 27 to 41% of patients showed neuropsychiatric symptoms, including confusion, depressed mood, and anxiety. Han et al. (2003) designed a follow-up study of 69 patients who were clinically cured of SARS. Results showed that more than half of the patients still suffered from poor concentration and poor memory four months after hospital discharge.

Evidence of neuropsychological manifestations caused by MERS is available in two other studies. A study on 70 MERS-patients in Saudi Arabia revealed that a quarter of the patients (25.7%) developed confusion during the disease (Saad et al., 2014). Another study investigated the post-infectious neurological consequences of MERS in three patients (Arabi et al., 2015). Results showed new-onset changes on MRI imaging in all three patients, which were correlated to neurological manifestations, including altered levels of consciousness and confusions (Arabi et al., 2015). However, even though this is a very interesting study, the strength of the results should be interpreted with caution due to the small number of study participants.

The parallels to SARS-CoV-2 cannot only be drawn with previous coronaviruses but also with viral infections involving the Human Immunodeficiency Virus (HIV) and Zika Virus (ZIKV). Both have been shown to affect cognition, including attention, memory and learning defects (Kanmogne et al., 2020; Raper et al., 2020). Furthermore, viral infections are frequently associated with impaired EF. Like SARS-CoV-2, HIV is caused by RNA viruses and reached humans from animals (Sharp & Hahn, 2011; Zhang et al., 2020). In addition,

both viruses cause an increase in cytokine production, which is associated with secondary complications in infected individuals (Illanes-Álvarez et al., 2021). Kanmogne et al. (2018) examined the effect of HIV on EFs. Results revealed that HIV+ subjects performed significantly worse than their counterparts in all EFs tests. The authors concluded that HIV-1 infection can be associated with impaired EFs (Kanmogne et al., 2018). Similar results were reported in a study by Koekkoek et al. (2008), who evaluated neurocognitive functions of school-age children with HIV. The children performed significantly poorer on tests measuring EFs compared to age-appropriate norms (Koekkoek et al., 2008). Taken together, these results provide room to suspect that SARS-CoV-2 may also have an impact on EFs.

The Unresolved Issue

Current research on COVID-19 and studies about previous pandemics demonstrate two important things: Firstly, they highlight the need to perform detailed investigation of cognitive functions in post-COVID-19 patients. Impairments in EFs can have significant influences on everyday life, (e.g., Almeria et al., 2020; Helms et al., 2020). Secondly, literature points out the importance to understand regional risk factors in the neuropsychological manifestations of COVID-19 to develop effective treatment and rehabilitation measures that are tailored to the respective population (e.g., Gutierrez & Bertozzi, 2020; Shams, Haleem, & Javaid, 2020).

There is still a lack of clarity about how risk factors, such as average life expectancy and comorbidities, behave in the context of COVID-19. It is not sufficiently understood whether regional risk factors and associated more severe COVID-19 courses lead to more severe EFD. Potential associations need to be considered in patient management and treatment so that patients can be provided with cognitive training and psychological if needed.

Present Study

The aim of this thesis is to explore whether there are neuropsychological manifestations after COVID-19, focusing on impairments in EFs. Furthermore, possible influential factors in neuropsychological manifestations of COVID-19, such as age and comorbidities, are analysed. Additionally, self-reports of mood (depression and anxiety) are included to correct for possible mood-influences.

Hypothesis 1: Previous studies hint at possible mechanisms capable of causing cognitive alterations in patients who suffered from COVID-19 (Helms et al., 2020). Therefore, it is hypothesized that post-COVID-19 participants subjectively report more executive impairments in their everyday life than participants that did not suffer from COVID-19.

Hypothesis 2: Suffering from comorbidities is associated with a greater chance of having a severe course of COVID-19 (Wolff et al., 2020). Therefore, it is hypothesized that post-COVID-19 participants suffering from either obesity, hypertension, or diabetes report more impairments in EFs compared to those without comorbidities.

Hypothesis 3: Higher age is associated with more severe COVID-19 courses and post-infection cognitive impairment (Liu et al., 2021; Schetelig et al., 2020). Therefore, it is hypothesized that older post-COVID-19 participants experience more impairments in EFs compared to younger counterparts.

Methods

Design

This research is part of the Cognition and COVID-19 (Coco-19) research project led by Dr. S. Enriquez-Geppert, which was established to assess consequences of COVID-19 on neuropsychological and daily functioning. All participants were informed about the study and

gave informed consent. Data were collected anonymously and kept confidential. Ethical approval was obtained by the Ethics Committee of the Department of Psychology of the University of Groningen.

An online survey study was designed. Data collection was conducted between January 2021 and November 2021. Participants were recruited via convenience sampling, by collaborations with hospitals and general practitioners, by posting on social, by distributing flyers, and by asking acquaintances to participate.

Originally, this research thesis aimed to compare post-infectious manifestations of COVID-19 between a Mexican and Dutch sample to analyse possible cross-cultural differences in neuropsychological medium-to-long-term consequences. However, there were difficulties in recruiting Mexican participants. Several attempts were conducted to encourage Mexican individuals to participate. Despite all efforts, only 55 Mexicans started the test battery, of which 21 participants completed it. Among the completed questionnaires, three were filled out by individuals who suffered from COVID-19. The small sample size made it impossible to compare the results to the Dutch sample. Therefore, it was decided to focus the analyses on a single population. Only data of Dutch-speaking participants were considered in the analyses, focusing on comorbidities and age as possible factors that could lead to cross-cultural differences in post-COVID-19 manifestations.

Participants

In total, 477 Dutch-speaking participants started the test-battery. Inclusion criteria were a minimum age of 18 years and that participants stated to speak Dutch. Only respondents who gave informed consent were included. Participants who did not fill out either the demographics, the BRIEF-A, the BDI, or the GAD-7 were excluded from the dataset. In total, 357 participants were excluded, this resulted in a sample of 120 participants.

Comorbidities

The sample consisted of 103 female and 17 male participants (n = 120) of which 87.5% had suffered from COVID-19. In total, 13.3% (n = 16) of the participants reported suffering from psychological, neuropsychological, or psychiatric problems. Furthermore, participants reported suffering from comorbidities, namely, hypertension in 6.7% of cases (n = 8), obesity in 14.2% of cases (n = 17), and diabetes in 5.8% of cases (n = 7). Moreover, 22.5% (n = 27) of the participants reported taking medication against their physical or mental health condition (see Appendix A for details). A more detailed elaboration of the demographic data is presented in Table 1.

Table 1

Demographic Characteristics of the Study Population

		n	%
Age	18-29	18	15.0
	30-39	20	16.7
	40-49	27	22.5
	50-64	49	40.8
	65 or older	6	5.0
Sex	Female	103	85.8
	Male	17	14.2
	Other	0	0.0
	Prefer not to say	0	0.0
Marital status	Married / In a relationship	69	57.5
	Widowed	2	1.7
	Divorced	8	6.7
	Single	41	34.2
Highest educational qualification	Less than highschool degree	1	0.8
	Highschool diploma	4	3.3
	Education / Apprencieship	45	37.5
	Study without degree	2	1.7
	Bachelors degree	42	35.0
	Masters degree	24	20.0
	Doctorate	2	1.7
Employment status	Employed, working 1-39 hours per week	70	58.3
	Employed, working 40 or more hours per week	11	9.2
	Self-employed	11	9.2

		n	%
	Full-time student	6	5.0
	Part-time student	0	0.0
	Househusband/housewife	1	0.8
	Not employed, looking for work	2	1.7
	Not employed, not looking for work	2	1.7
	Retired	7	5.8
	Not able to work	10	8.3
Housing type	House	88	73.3
	Flat	28	23.3
	Residental home	3	2.5
	Assisted living facility	0	0.0
	Skilled nursing centre	0	0.0
	No single primary residence	0	0.0
	Other	1	0.8
Sport	Never	44	36.7
	1 time a week	27	22.5
	2-3 times a week	39	32.5
	Almost every day	10	8.3
Movement	30 minutes or less	51	42.5
	30 minutes to 2 hours	61	50.8
	2 to 4 hours	6	5.0
	More than 4 hours	2	1.7
Psychological illness	No	104	86.7
	Yes	16	13.3
Medication intake	No	93	77.5
	Yes	27	22.5
Health issues	Diabetes	7	5.8
	Obesity	17	14.2
	High blood pressure	8	6.7
	Stroke	0	0.0
	Heart attack	0	0.0
	Dementia	0	0.0
	Concussion	0	0.0
	No	88	73.3

Note. N = 120.

Procedure and Measures

Respondents were asked to complete the ‘COCO-19’ test battery. The COCO-19 test battery, standing for Cognition and COVID-19, was designed to assess the subjective impact

of SARS-CoV-2 infection on cognition. It was available online via the computer based Qualtrics Survey software and took about 80 minutes to complete. Participants had the option to complete the survey either in English, Dutch, German, Spanish, or French.

Respondents answered several demographic questions, such as age, gender, and educational level. Additionally, participants had to indicate whether they had COVID-19. If this was the case, participants were asked further questions regarding the course of the disease. For example, participants were asked whether they were hospitalized due to COVID-19, and whether they were treated with medication (see Table 2 for details).

Table 2

Information regarding COVID-19 Course of Disease

	Total	
	n	%
COVID-19	105	100.0
Symptoms typical of COVID-19	101	96.2
Hospitalization	8	7.6
Medication	40	38.1
	M	(SD)
Severity of disease course	68.37	21.06

Note. $n = 105$.

Furthermore, the COCO-19 test battery covers four different domains: neuropsychological, psychological, personality, and outcome measures. It is composed of 17 questionnaires, together covering each of the four domains (Table 3). This research only focused on the questionnaires relevant to answer the research question. The Behaviour Rating Inventory of Executive Functions for Adults (BRIEF-A; Roth et al., 2005) assessing EFs, the Beck's Depression Inventory (BDI; Beck et al., 1961) assessing depression, and the

Generalized Anxiety Disorder Scale-7 (GAD-7; Spitzer et al., 2006) assessing anxiety, were included.

Table 3

Summary of Questionnaires included in the COCO-19 Test Battery

Domain	Questionnaire	Process involved
Neuropsychological	Amnestic Subjective Cognitive Decline Questionnaire (ASCDQ)	Memory
	Behavior Rating Inventory of Executive Functions for Adults (BRIEF-A)	Executive functioning
	Cognitive Failure Questionnaire (CFQ)	General cognition
	Fragebogen erlebter Defizite der Aufmerksamkeit (FEDA)	Attention
	Fragebogen zur geistigen Leistungsfähigkeit (FLei)	General cognition
	Working Memory Questionnaire (WMQ)	Working memory
Psychological	Beck's Depression Inventroy (BDI)	Depression
	Fatigue Severity Scale (FSS)	Fatigue
	Generalized Anxiety (GAD-7)	Anxiety
	Kessler Psychological Distress Scale (K-10)	Distress
	Pittsburgh Sleep Quality Index (PSQI)	Sleep
	Positive and Negative Affect Schedule (PANAS)	General Health
	Short Form Health Survey (SF-12)	General Health
	University of California Los Angeles Loneliness Scale (UCLA)	Loneliness
Personality	NEO Five-Factor Inventory (NEO-FFI)	Personality
Outcome measures	WHO Quality of Life-BREF (WHOQOL-BREF)	Quality of life
	Functional Activity Questionnaire (FAQ)	Functional activity

Executive Functions

To subjectively assess EFs, participants were asked to rate their self-regulation in their everyday environment. Individuals' experiences of EFD in daily functioning may differ from results of objective neuropsychological assessment. Not all individuals who experience EFD in daily life show impairments in objective measurements (Koerts et al., 2011). Objective tests usually place the participant in a structured test situation in which the examiner instructs the participant what, when and how to do something (Lezak, 1982). By that, the non-distracting and structured test environment might circumvent participants' EFD (Manchester et al., 2004). Hence, the tests might not reflect difficulties with EFs, while impairments reveal themselves in situations when individuals need to organize their behaviour in daily structure. These discrepancies may have an impact on patient management and treatment (Koerts et al., 2011). To recognise and appropriately treat people who experience impairments in their everyday structure, although they do not show deficits in objective measurements, the subjective assessment of EFs is of particular importance.

EFs were assessed with the Behaviour Rating Inventory of Executive Functions for Adults (BRIEF-A; Roth et al., 2005). The BRIEF-A is suitable for participants aged between 18 and 90 years. It is composed of 75 items within nine non-overlapping scales that aim to measure aspects of EFs. These scales form two broader indexes, the Behavioural Regulation Index (BRI) and the Metacognitive Index (MI), which form a third overall score, the Global Executive Composite (GEC). On a 3-point Likert type scale (1 = *Never*, 2 = *Sometimes*, 3 = *Often*), participants were asked to indicate to what extent the items applied to them in the past month or since their COVID-19 diagnosis. Higher scores indicate greater difficulties in EFs. Example items and Cronbach's Alpha are presented in Table 4.

According to Miyake et al. (2000), response inhibition, working memory updating, shifting and conflict monitoring can be considered as separable but interrelated key

components of EFs. Therefore, besides the three overall scores, the subscales "Working memory", "Inhibit", "Shift", and "Self-Monitoring" are included to the analyses.

Table 4

BRIEF-A Scale, Example Items and Cronbach's Alpha of the Current Study

Scale	Example quote	Cronbach's Alpha
Global Executive Composite (GEC)		.96
Metacognition Index (MI)		.95
Initiate	"I must be reminded to start a task, even if I want to do it."	.76
Working memory	"In the middle of a task, I forget what I am actually doing."	.90
Plan / Organize	"I am overwhelmed by big tasks."	.84
Task Memory	"I make careless mistakes."	.77
Organization of Materials	"I am poorly organized."	.79
Behavioral Regulation Index (BRI)		.92
Inhibit	"I am impulsive."	.75
Shift	"I have difficulty moving from one task to another."	.79
Emotional Control	"I have tantrums."	.92
Self-Monitoring	"I do not notice when I do something that makes others feel bad before it is too late."	.77

While the BRIEF-A is an accepted tool to assess subjective problems with EFs, there is still debate about the use of self-reports to measure EFs. There is evidence that mood symptoms, such as depression and anxiety, are associated with the experience and subjective evaluation of EFs in daily life (Peters et al., 2014). A study by Hannsen et al. (2014)

investigated deterioration in EFs in day-to-day life and the relation to depression. Depression was the strongest predictor of subjective executive complaints, as measured by the BRIEF-A. Moreover, van der Hiele et al. (2012) found that patients characterized by more depression, anxiety, and psychological stress experienced greater impairments in EFs. Therefore, this research includes questionnaires that assess depression and anxiety symptoms.

Depression

To assess depressive symptoms, participants completed the Beck's Depression Inventory (BDI; Beck et al., 1961). The BDI is a self-report questionnaire including 21 items-groups, such as "I do not feel sad", "I feel sad", "I feel sad all the time and I can't snap out of it", and "I am so sad and unhappy that I can't stand it". Participants picked one statement of each group that best described how they felt in the past week or since their COVID-19 diagnosis. A total score of 0 to 13 is considered minimal to no depression, a total score of 14 to 19 is considered mild depression, a total score of 20 to 28 is considered moderate depression, and a total score of 29 to 62 is considered severe depression. Cronbach's alpha was 0.85.

Anxiety

The Generalized Anxiety Disorder Scale-7 (GAD-7; Spitzer et al., 2006) is a self-report measurement to assess anxiety symptoms. The questionnaire consists of seven items. Participants indicated on a 4-point Likert type scale (0 = *Not at all*, 1 = *Several days*, 2 = *More than half the days*, 3 = *Nearly every day*), how often they were bothered by the presented problems in the last two weeks or since their COVID-19 diagnosis. An example of an item is "Worrying too much about different things". A total score of 0 to 4 is considered minimal anxiety, a total score of 5 to 9 is considered mild anxiety, a total score of 10 to 14 is considered moderate anxiety, and a total score of 15 to 21 is considered severe anxiety. Cronbach's alpha was 0.83.

Statistical Design

Statistical analyses were performed using the software IBM SPSS 27 (IBM SPSS Statistics, New York, NY, United States). Data from Qualtrics Survey software were directly exported to SPSS. To answer the hypotheses, a series of statistical tests were performed, which are introduced in the following. Outliers were detected by visual inspection of box plots and were excluded from the analysis when they significantly affected the results. Assumptions of normality and homogeneity of variance were assessed by Shapiro-Wilk's test and Levene's *F* test respectively.

To answer the first hypothesis, group differences between post-COVID-19 participants and healthy controls were determined. Results from Shapiro-Wilk's test and Levene's *F* test suggested that there was a violation of the assumptions. Therefore, one-tailed Mann-Whitney *U* tests were applied. Similarity of distributions of scores of the groups was assessed by visual inspection. Differences in mean-ranks between groups were deemed statistically significantly when p-values were $\leq .05$. As the data did not meet the assumptions of normality and homogeneity, a one-tailed Kendall's tau-b correlation was run to determine the relationship between post-COVID-19 participants and healthy controls and GEC scores. A correlation was deemed statistically significantly when p-values were $\leq .05$.

To answer the second hypothesis, differences between post COVID-19 participants with comorbidities and those without comorbidities were determined. When assumptions of normality and homogeneity of variance hold, one-tailed independent-samples t-tests were performed with the relevant group as between subject factor. When assumptions of normality and homogeneity of variance did not hold, one-tailed Mann-Whitney *U* tests were performed. Differences between the groups were deemed statistically significantly when p-values were $\leq .05$. A one-tailed point-biserial correlation was run between post-COVID-19 participants with

comorbidities and post-COVID-19 participants without comorbidities and GEC scores. A correlation was deemed statistically significantly when p-values were ≤ .05.

To answer the third hypothesis, differences between the age groups were determined. When assumptions of normality and homogeneity of variance hold, one-way ANOVA was conducted. When the assumption of homogeneity of variance did not hold, the results of Welch's ANOVA was reported. When the assumption of normality did not hold, Kruskal-Wallis *H* test was performed. Distributions of scores were assessed by visual inspection of box plots. Differences between groups were deemed statistically significantly when p-values were ≤ .05. A Spearman's rank-order correlation was run to assess the relationship between age and overall BRIEF-A scores. A monotonic relationship was assessed by visual inspection of a scatter plot. A correlation was deemed statistically significantly when p-values were ≤ .05.

Results

Hypothesis 1: Post COVID-19 Participants versus Participants without COVID-19

There were 105 post-COVID-19 participants and 15 control participants that did not suffer from COVID-19. Mann-Whitney *U* tests were run to determine if there were differences in BRIEF-A scores between post-COVID-19 participants and controls. Looking at the overall scores of the BRIEF-A, Global Executive Composite (GEC) scores for post-COVID-19 participants (mean rank = 63.98) were statistically significantly higher than for controls (mean rank = 36.13), $U = 1153.00$, $z = 2.90$, $p < .01$, $r = 0.26$.

The same applied to Metacognition Index (MI) scores, which were statistically significantly higher for post-COVID-19 participants (mean rank = 64.38) than for controls (mean rank = 33.33), $U = 1195.00$, $z = 3.24$, $p < .001$, $r = 0.30$.

Behavioral Regulation Index (BRI) scores for post-COVID-19 participants (mean rank = 62.88) were statistically significantly higher than for controls (mean rank = 43.83), U = 1037.50, z = 1.99, $p < .05$, r = 0.18.

A closer analysis of the sub scales revealed that Shift scores for post-COVID-19 participants (mean rank = 64.10) were statistically significantly higher than for controls (mean rank = 35.33), U = 1165.00, z = 3.01, $p < .01$, r = 0.27. Working Memory scores for post-COVID-19 participants (mean rank = 65.10) were statistically significantly higher than for healthy controls (mean rank = 28.30), U = 1270.50, z = 3.85, $p < .001$, r = 0.35.

Despite being non-significant, there was a large correlation (r = .85) between the COVID-19 condition and the Inhibit scale, with post-COVID-19 participants scoring higher than the

Table 5

BRIEF-A Mann-Whitney U Test Results by COVID-19 Group and Control Group without COVID-19

	Group		Mann-Whitney *U* Test			
	COVID-19 Group (n = 105)	Control Group without COVID-19 (n = 15)				
Scale	mean rank	mean rank	*U*	*z*	*p*	*r*
GEC	63.98	36.13	1153.00	2.90	.002	.26
BRI	62.88	43.83	1037.50	1.99	.024	.18
MI	64.38	33.33	1195.00	3.24	.001	.30
Inhibit	61.61	52.70	904.50	9.34	.175	.85
Shift	64.10	35.33	1165.00	3.01	.002	.27
WM	65.10	28.30	1270.50	3.85	.001	.35
Self_Moni	62.03	49.77	948.50	1.30	.097	.12
Emo_Cont	63.37	40.40				
Initiate	63.39	40.30				
Plan_Orga	64.30	33.90				
Task_Moni	64.28	34.03				
Orga_Mat	62.90	43.67				

Note. Statistical analysis: one-tailed, Mann Whitney *U* test. Abbreviations: GEC = Global Executive Composite; BRI = Behavioral Regulation Index; MI = Metacognition Index; Inhibit = Inhibit; Shift = Shift; Emo_Cont = Emotional Control; Self_Moni = Self-Monitor; Initiate = Initiate; WM = Working Memory; Plan_Orga = Plan / Organize; Task_Moni = Task Monitor; Orga_Mat = Organization of Materials. *U* = Mann-Whitney *U* coefficient; *z* = standardized test statistic; *p* = *p*-value obtained; *r* = correlation.

Correlation between COVID-19 Condition and BRIEF-A scores

A Kendall's tau-b correlation was run to determine the relationship between a COVID-19 infection and GEC scores. There was a positive association between COVID-19 condition and GEC-scores, which was statistically significant, $\tau_b = .219$, $p < .01$.

COVID-19 Condition and GEC scores including Anxiety and Depression

Considering previous studies on the association between self-rated EFD and symptoms of depression and anxiety (Hannsen et al., 2014; Hiele et al., 2012; Peter et al., 2014), GAD-7 and BDI scores were added to the analysis. A one-tailed Spearman's rank-order correlation was run to assess the relationship between GEC scores and GAD-7 scores.

There was a statistically significant, strong positive correlation between GAD-7 scores and GEC scores, $r_s(103) = .502$, $p < .001$. Additionally, a one-tailed Spearman's rank-order correlation was run to assess the relationship between GEC scores and BDI scores. There was a statistically significant, strong positive correlation between BDI scores and GEC scores, $r_s(103) = .559$, $p < .001$.

A multiple regression was conducted to analyse what factors predict largest variance in GEC between post-COVID-19 participants and healthy controls. GAD-7 scores and BDI-scores were entered as independent variable. The multiple regression model statistically significantly predicted GEC scores $F(3, 116) = 36.135$, $p < .001$, adj. $R^2 = .47$. Except for COVID-19 condition, all variables added statistically significantly to the prediction, $p < .05$. Regression coefficients and standard errors can be found in Table 6.

Table 6

Multiple regression results for GEC scores

GEC Score	*B*	95% CI for *B*		*SE B*	*β*	R^2	ΔR^2	*p*
		LL	*UL*					
Model						.48	.47	
Constant	88.59	78.68	98.51	5.01				<.001
COVID-19 condition	8.73	-1.69	19.15	5.26	.12			.100
BDI	1.42	.78	2.05	.32	.40			<.001
GAD-7	2.20	.10	3.40	.61	.32			<.001

Note. Statistical analysis: one-tailed, multiple regression. Model = "Enter" method in SPSS Statistics; *B* = unstandardized regression coefficient; CI = confidence interval; *LL* = lower limit; *UL* = upper limit; *SE B* = standard error of the coefficient; *β* = standardized coefficient; R^2 = coefficient of determination; ΔR^2 = adjusted R^2.

Hypothesis 2: Post-COVID-19 Group suffering from either Obesity, Hypertension, or Diabetes versus post-COVID-19 Group without Comorbidities

In total, 28 post-COVID-19 participants with comorbidities and 77 post-COVID-19 participants without comorbidities. There were 17 post-COVID-19 participants that suffered from obesity, eight suffered from hypertension, and seven suffered from diabetes. A one-tailed independent-samples t-test was run to determine if there were differences in GEC scores between post-COVID-19 participants with either obesity, hypertension, or diabetes and post-COVID-19 participants without comorbidities. The difference in GEC scores between post-COVID-19 participants with comorbidities (M = 130.64, SD = 23.97) and post-COVID-19 participants without comorbidities (M = 125.57, SD = 21.95), was not statistically significant, M = -5.07, % CI [-14.92, 4.77], $t(103) = -1.02$, $p = .155$. Despite being non-significant, there was a small effect size for the difference between post-COVID-19 participants with comorbidities and post-COVID-19 participants without comorbidities (d = 0.23).

A one-tailed independent-samples t-test was run to determine if there were differences in the MI scores between the two groups. The difference in MI scores between post-COVID-19 participants with comorbidities (M = 77.07, SD = 13.77) and post-COVID-19 participants without comorbidities (M = 76.61, SD = 14.08), was not statistically significant, M = -0.46, % CI [-6.59, 5.67], $t(103) = -0.15$, $p = .441$.

A one-tailed Mann-Whitney U test was run to determine if there were differences in BRI scores between post-COVID-19 participants and controls. BRI scores for post-COVID-19 participants with comorbidities (mean rank = 62.25) were statistically significantly higher than for post-COVID-19 participants without comorbidities (mean rank = 49.64), U = 1337.00, $z = 1.88$, $p < .05$, $r = 0.18$, using an exact sampling distribution for U (Dineen &

Blakesley, 1973). Further analysis of the sub scales revealed no significant differences between the groups (see Tables 7 and 8 for details).

Table 7

BRIEF-A Mann-Whitney U Test Results by Post-COVID-19 Group with Comorbidities and Post-COVID-19 Group without Comorbidities

	Group		Mann-Whitney *U* Test			
	COVID-19 Group with Comorbidities (n = 28)	Control Group without Comorbidities (n = 77)				
Scale	mean rank	mean rank	*U*	*z*	*p*	*r*
BRI	62.25	49.64	1337.00	1.88	.030	.18
Inhibit	58.57	50.97	1234.00	1.14	.128	.11
Self_Moni	60.29	50.35	1282.00	1.50	.067	.15
WM	53.00	53.00	1078.00	.00	.500	.00
Emo_Cont	62.52	49.54				

Note. Statistical analysis: one-tailed, Mann-Whitney *U* test. Abbreviations: BRI = Behavioral Regulation Index; Inhibit = Inhibit; Emo_Cont = Emotional Control; Self_Moni = Self-MonitorWM = Working Memory. *U* = Mann-Whitney *U* coefficient; *z* = standardized test statistic; *p* = *p*-value obtained; *r* = effect size.

Table 8

BRIEF-A Independent-Samples t-Test Results by Post-COVID-19 Group with Comorbidities and Post-COVID-19 Group without Comorbidities

	Group				
	COVID-19 Group with Comorbidities (n = 28)	Control Group without Comorbidities (n = 77)	Independent-Samples *t*-Test		
Scale	*M* ± *SD*	*M* ± *SD*	*t*(103)	*p*	Cohen's *d*
GEC	130.64 ± 23.97	125.57 ± 21.95	-1.022	.155	0.23
MI	77.07 ± 14.08	76.61 ± 14.08	-0.15	.441	0.03
Shift	11.64 ± 2.71	10.86 ± 2.75	-1.30	.098	0.29
Initiate	14.61± 3.33	14.78 ± 3.19			
Orga_Mat	14.50 ± 3.43	14.30 ± 3.27			
Task_Moni	11.53 ± 2.17	11.75 ± 2.56			
Plan_Orga	18.93 ± 4.38	18.44 ± 3.97			

Note. Statistical analysis: one-tailed, independent-samples *t*-test. Abbreviations: GEC = Global Executive Composite; MI = Metacognition Index; Shift = Shift; Initiate = Initiate; Plan_Orga = Plan/Organize; Task_Moni = Task Monitor; Orga_Mat = Organization of Materials. *M* ± *SD* = mean ± standard deviation; *t* = observer *t*-value; *p* = *p*-value obtained.; Cohen's *d* = effect size.

Correlation between post-COVID-19 Participants with either Obesity, Hypertension, or Diabetes and post-COVID-19 Participants without Comorbidities and BRIEF-A Scores

A point-biserial correlation was run between post-COVID-19 participants with comorbidities and post-COVID-19 participants without comorbidities and GEC scores. There was no statistically significant correlation between comorbidities and GEC scores, $r_{pb}(103) = .100$, $p = .155$, with post-COVID-19 participants with comorbidities scoring higher on GEC scores than post-COVID-19 participants without comorbidities, $M = 130.64$ ($SD = 23.97$) vs. $M = 125.57$ ($SD = 21.95$). Comorbidities accounted for 1.0 % of the variability in GEC scores.

Hypothesis 3: Different Age Groups of Post-COVID-19 Participants

Participants were asked to indicate which age group they belonged to. Overall, 12 respondents identified as 18-29 years of age, 17 identified as 30-39 years of age, 27 identified as 40-49 years of age, 44 identified as 50-64 years of age, and 5 identified as 65 years of age or older (see Figure 1). A one-way analysis of variance (ANOVA) was conducted to determine if GEC scores were different for different age groups. The differences between age groups were not statistically significant, $F(4, 100) = 2.199$, $p > .05$. Despite being non-significant, there was a moderate effect size for the difference between the age groups ($\eta^2 = .08$).

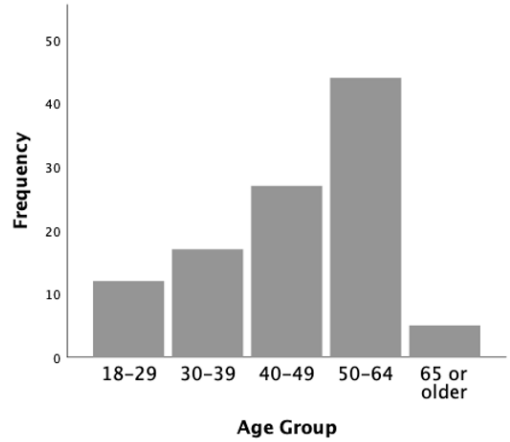

Fig. 1. Age Distribution of the Post-COVID-19 Participants.

A one-way ANOVA was conducted to determine if MI scores were different for the age groups. The differences between the age groups were not statistically significantly, F (4, 100) = 2.016, $p > .05$. Despite being non-significant, there was a moderate effect size for the difference between the age groups ($\eta^2 = .08$).

A Kruskal-Wallis H test was run to determine if there were differences in BRI scores between the five age-groups of participants. Median BRI scores were not statistically different between groups X^2 (4) = 7.496, $p > .05$. Despite being non-significant, there was a moderate effect size for the difference between the age groups ($\epsilon^2 = .07$).

A closer analysis of the sub-scales revealed significant differences in working memory scores between age-groups. A Kruskal-Wallis H test was run to determine the differences between the groups. Median working memory scores of the age groups 18-29 (15.50), 30-39 (20.00), 40-49 (17.00), 50-64 (18.50), and 65 and older (15.00) were statistically different $X^2(4) = 15.071$, $p < .01$. There was a moderate effect size for the difference between the age groups ($\epsilon^2 = .14$).

Subsequently, pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni correction for multiple comparisons. Adjusted p-values are presented. The post hoc analysis revealed statistically significant differences in working memory scores between the age groups 65 or older (Mdn = 15.00) and 30-39 (Mdn = 20.00) ($p < .05$) and 18-29 (Mdn = 15.50) and 30-39 (Mdn = 20.00) ($p < .05$), but not between any other group combination. Other than that, BRIEF-A scores did not significantly differentiate between the groups (see Tables 9 and 10 for details).

Correlation between Age and BRIEF-A Scores

A Spearman's rank-order correlation was run to assess the relationship between age and GEC scores. There was no statistically significant correlation between age and GEC scores, $r_s(103) = -.034$, $p = .732$.

Table 9

Medians and Kruskal-Wallis Test Results of BRIEF-A scores by Age Groups

	Age Group												
	18-29 (*n* = 12)		30-39 (*n* = 17)		40-49 (*n* = 27)		50-64 (*n* = 44)		65 or older (*n* = 5)		Kruskall-Wallis *H* Test		
Scale	*Mdn*	*SD*	*Mdn*	*SD*	*Mdn*	*SD*	*Mdn*	*SD*	*Mdn*	*SD*	$X^2(4)$	*p*	ϵ^2
BRI	43.50	10.60	51.00	10.30	49.00	10.35	49.50	10.75	44.00	8.70	7.496	.112	.07
Inhibit	10.00	2.94	12.00	3.46	13.00	2.65	12.50	3.03	11.00	3.21	5.007	.287	.05
Self_Moni	7.50	1.87	8.00	2.21	8.00	1.66	8.00	2.45	9.00	1.52	1.572	.814	.02
WM	15.50	3.82	20.00	3.32	17.00	4.04	18.50	3.27	15.00	2.51	15.071	.005	.14
Plan_Orga	18.00	3.61	21.00	3.55	20.00	4.34	18.00	4.06	14.00	3.56			
Task_Moni	11.00	2.16	12.00	2.40	11.00	2.72	12.00	2.46	10.00	0.89			
Orga_Mat	14.00	2.83	15.00	3.62	14.00	3.27	15.00	3.45	13.00	2.70			
Emo_Cont	15.00	5.91	19.00	5.63	16.00	5.67	19.00	4.76	14.00	3.11			
Initiate	12.50	1.81	15.00	3.16	14.00	3.86	14.00	3.00	15.00	2.92			

Note. Statistical analysis: two-tailed, Kruskal-Wallis test. Abbreviations: BRI = Behavioral Regulation Index; Inhibit = Inhibit; Emo_Cont = Emotional Control; Self_Moni = Self-Monitor; Initiate = Initiate; WM = Working Memory; Plan_Orga = Plan / Organize; Task_Moni = Task Monitor; Orga_Mat = Organization of Materials. *Mdn* = median; X^2 = *H*-statistic compared to a X^2-distribution; *p* = *p*-value obtained; ϵ^2 = effect size.

Table 10

Mean, Standard Deviation, and Analysis of Variance of BRIEF-A scores by Age Groups

	Age Group												
	18-29 (n = 12)		30-39 (n = 17)		40-49 (n = 27)		50-64 (n = 44)		65 or older (n = 5)		ANOVA		
Scale	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	$F(4, 100)$	*p*	η^2
GEC	116.83	21.17	138.06	20.39	125.22	23.90	127.86	22.19	114.20	13.95	2.20	.075	.08
MI	72.25	12.06	84.24	12.73	75.52	15.69	76.64	13.43	69.40	9.26	2.02	.098	.08
Shift	9.67	2.35	12.41	2.53	10.78	2.71	11.25	2.86	9.80	1.79	2.30	.064	.08

Note. Statistical analysis: one-way analysis of variance. *M* = mean; *SD* = standard deviation; *F* (df1, df2) = *F*-statistic; df1 = between groups degrees of freedom; df2 = within groups degrees of freedom; η^2 = effect size; *p* = *p*-value obtained

Discussion

The aim of the present research was to explore post-infectious manifestations of COVID-19 in terms of EFs and to examine the relationship between comorbidities, age, and medium-to-long term consequences of SARS-CoV-2 infection. This study compared post-COVID-19 participants to healthy controls who did not suffer from COVID-19. Most of the available studies of COVID-19 attributable symptoms use objective measurements to assess deficits. Few studies about subjective experience of impairments in EFs exist. This study tackles that very gap by using subjective self-report questionnaires to assess EFD, as well as depression and anxiety symptoms. Firstly, the effects of COVID-19 infection were assessed by comparing post-COVID-19 participants and healthy controls on BRIEF-A scores. Secondly, effects of comorbidities were assessed by comparing BRIEF-A scores from post-COVID-19 participants with and without comorbidities. Finally, age-related effects were assessed by comparing BRIEF-A scores of different age-groups of post-COVID-19 participants.

The main findings of this study are briefly summarized as follows: There were significant differences in post-COVID-19 participants and healthy controls. Participants that did suffer from COVID-19 had increased scores on self-reported EFD. Furthermore, there was a statistically significant difference between post-COVID-19 participants that suffered from comorbidities compared to post-COVID-19 participants without comorbidities. Post-COVID-19 participants who suffered either from obesity, hypertension, or diabetes scored higher on the composite score behaviour regulation index than post-COVID-19 participants without comorbidities. Furthermore, the results show some significant age differences of post-COVID-19 participants in EFs. Participants at the age of 30 to 39 most often reported difficulties in working memory. Apart from that, all age-groups scored equally on BRIEF-A scales.

In line with the first hypothesis, the findings of the present research show a considerable higher prevalence of subjective experience of EFD in post-COVID-19 participants compared to healthy controls. This pattern is consistent with early research on COVID-19 attributable symptoms. A study of 790 COVID-19 survivors investigated rates of cognitive impairment using well-validated neuropsychological measures and reported a relatively high frequency of cognitive impairments in post-COVID-19 participants, even several months after SARS-CoV-2 infection (Becker et al., 2021). In total, 18% of the participants showed deficits in processing speed and 16% had deficits in EFs. Another study assessed psychiatric and cognitive sequel in 226 hospitalized COVID-19 patients three months after discharge from hospital (Mazza et al., 2021). The results revealed that 78% of the sample performed poorly in at least one cognitive domain, with EFs being impaired in 50% of the sample. Apart from the fact that many studies report objective worsening of EFs in COVID-19 patients, this research adds information because it reports the subjective evaluation of EFD after COVID-19. The results make clear that there is not only objective EFD after infection with SARS-CoV-2, but that post-COVID-19 individuals notice the deterioration of EFs in their daily lives.

Interestingly, the results of the present research show that anxiety and depression scores were significantly correlated to GEC scores. There are two possible explanations for this. On the one hand, it is possible that infection with SARS-CoV-2 leads to more EFD, which then leads to more anxiety and depression symptoms. This association was demonstrated, in a study by Letkiewicz et al (2014). The authors examined whether EFD predicted worsening of depressive symptoms found that difficulties in EFs in daily life predicted an increase in depressive symptoms (Letkiewicz et al., 2014). Another study examined the association between COVID-19 and cognitive impairment and found that patients with cognitive complaints had significantly higher scores in anxiety and depression (Almeria et al. 2020).

On the other hand, it is possible that anxiety and depression symptoms are triggered by COVID-19 and that the symptoms lead to a deterioration of EFs. One argument in favour of this explanation is that previous literature shows that psychiatric symptoms are common in individuals who suffered from COVID-19 (Mazza et al., 2020). The study by Mazza et al. (2020) examined psychiatric symptoms in 300 hospitalized and 102 non-hospitalized COVID-19 survivors and found that 55.7% of the sample self-rated symptoms in the psychopathological range, with 31% for depression and 42% for anxiety. Additionally, previous literature shows that psychiatric symptoms are associated with neurocognitive impairment (Warren et al., 2021). Recent work compared EFs in healthy students to students with depression, anxiety, and stress symptoms (Ajilchi, 2017). Results indicated that students with symptoms of depression scored worse in terms of memory, inhibition control, planning, and flexibility compared to the healthy group. Additionally, it was found that students with anxiety symptoms had deficits in sustained attention (Ajilchi, 2017).

The results of the present study show, that participants subjectively experience more deficits in the EFs after the COVID-19 study compared to healthy controls. Therefore, the first hypothesis is accepted. Nevertheless, the results support the idea of a possible link between anxiety and depression symptoms and an increased subjective experience of EFD. It is important to consider these results in the treatment of COVID-19 patients. Thus, not only the treatment of physiological symptoms should be the goal, but also the rehabilitation of cognitive functions as well as the treatment of psychological symptoms should be considered. As long as the direction of the association between COVID-19, EFD and mood symptoms is not established, it is important to combine treatment to address underlying causes as well as symptoms.

In line with the hypothesized association between comorbidities and EFD in post-COVID-19 participants, there was a statistically significant difference between post-COVID-19 participants who either suffered from obesity, hypertension, or diabetes and post-COVID-

19 participants without comorbidities. Post-COVID-19 participants with comorbidities scored higher on the Behavioural Regulation Index compared to post-COVID-19 participants who did not suffer from comorbidities. The Global Executive Composite and the Metacognitive Index were not significantly different, indicating possibly more severe effects of comorbidities on behaviour rather than on cognition. Only few studies examine the association between known COVID-19 risk factors, such as hypertension, obesity, and diabetes and cognitive impairments. Nevertheless, a recent study found that comorbid COVID-19 survivors were more likely to experience problems performing usual activities, anxiety, and depression symptoms, as well as loss of concentration and memory, compared to those without any comorbidities (Mannan et al., 2021).

It is possible that the neuropsychological impairments experienced by individuals who suffered from COVID-19 could be a consequence of primary effects of SARS-CoV-2 on the central nervous system that are amplified by comorbidities (Hernandez-Galdamez et al., 2020). Severe COVID-19 can trigger a complex inflammatory response, which may result in a cytokine storm (Cothran et al., 2020). A cytokine storm can be defined as the uncontrolled release of proinflammatory cytokines (Tisoncik et al., 2012), which are suggested to act as key mediators in cognitive impairments after COVID-19 infection (Alnefeesi et al., 2021). Interestingly, a study by Zhou et al. (2020) reported that cognitive impairment after COVID-19 was positively correlated with the inflammatory level. Furthermore, a recently published study has found that fat cells themselves could contribute to inflammatory processes in COVID-19 (Martínez-Colón et al., 2021). For the study, researchers obtained and analysed autopsy specimens of various adipose depots in individuals who died from COVID-19. They concluded that the virus could trigger inflammatory processes in the body in the infected fatty tissue and, thereby, possibly contribute to severe clinical disease in obese individuals infected with SARS-CoV-2. Hence, a more severe course of the disease, triggered by comorbid conditions such as obesity, could be a risk factor for post-infectious cognitive deficits.

Apart from that, it is important to keep in mind that comorbid conditions such as hypertension themselves are associated with impairment of cognitive functioning like attention, concentration, working memory, and EFs (Bai et al., 2016; Gupta et al., 2008; Qiu et al. 2005). Thus, it is possible that comorbid post-COVID-19 participants experience more EFD than post-COVID-19 participants without comorbidities due to the direct effects of hypertension on cognitive functioning.

Furthermore, it is necessary to consider the possibility that the deficits in EFs result from secondary effects of anxiety and depression symptoms which result from a more severe course of COVID-19 (Ajilchi, 2017; Almeria et al. 2020; Warren et al., 2021). In line with this, a study that examined long-term health consequences in COVID-19 survivors reported that the risk of anxiety or depression is higher in patients with more severe COVID-19 disease course (Huang, 2021). Similar, the results of a study by Zhu et al. (2020) indicated that severe COVID-19 was the strongest risk factor for probable clinically relevant anxiety.

All things considered, the data from the present study indicate that people with comorbidities more frequently experience EFD. Therefore, the second hypothesis is accepted. Consequently, to improve treatment and rehabilitation planning, research is needed to further examine the relationship between comorbidities, COVID-19, and post-infectious neuropsychological manifestations.

Regarding the third hypothesis, it was expected that especially older participants would self-report more often to suffer from EFD. Several studies indicate that older populations are more vulnerable to get infected with COVID-19 (Shams, Haleem, & Javaid, 2020). Furthermore, people of older age showed to have an increased risk of dying and a decreased chance to recover from COVID-19 (Nijman et al., 2021). The results of the present study show some significant age differences of post-COVID-19 participants in executive functions. However, contrary to the hypothesis, participants at the age of 30 to 39 most often

reported difficulties in working memory. Apart from that, all age-groups scored equally on BRIEF-A scales.

The finding that participants aged between 30 and 39 years scored significantly worse on working memory compared to participants aged 65 or older might not be a cause of the direct action of SARS-CoV-2 on the central nervous system. A more plausible explanation could be that the deficits are caused by secondary symptoms, such as anxiety and depression, and that especially participants aged between 30 and 39 years suffered from these symptoms. In fact, when looking at the GAD-7 scores in the present study, participants aged 30 to 39 years self-rated their anxiety the highest (see Appendices B to D for details). This finding is consistent with previous studies that showed that younger age is a risk factor to suffer from both anxiety and depression (Hyland et al., 2020; Nwachukwu et al., 2020; Varma et al., 2021). More specifically, one study reported that especially the age-group of 21 to 40 is at risk for higher levels of anxiety (Moghanibashi-Mansourieh, 2020). It is possible that younger people may have perceived their social and economic prospects to be more threatened by COVID-19 pandemic compared to people of older age. As outlined previously, anxiety and depression can lead to deficits in EFs (Ajilchi, 2017; Almeria et al. 2020; Warren et al., 2021). This could explain why participants aged between 30 and 39 most often reported difficulties in working memory.

Taken together, the results of the present study do not support the third hypothesis. Consequently, it is rejected. However, the findings add information about the possible association between mood symptoms and EFs. The results reinforce the idea that cognitive impairment in post-COVID-19 participants is a result of secondary symptoms of depression and anxiety.

Limitations

This study has some limitations. First, it is worth mentioning that the research sample consisted of 15 healthy control participants that were compared to 105 individuals that suffered from COVID-19. The sample might not be representative of the general population and thus, caution needs to be taken when interpreting the reults (*World Health Organization*, 2021).

Secondly, the dropout rate of 75% could bias the present results. Dropouts might correspond to post-COVID-19 participants with higher disabilities. Participation in the study took about one hour. Studies show that COVID-19 patients have difficulties with attention and concentration (Vanderlind et al., 2021). Therefore, it is possible that especially people who suffered from great difficulties had problems completing the survey and therefore, dropped out prematurely. Consequently, this study may have only included people who experienced fewer difficulties. This could have led to the results of the study being biased and not representative of COVID-19 patients in general. If that was the case, the results of this study would possibly underestimate the true prevalence of the reported symptoms.

Finally, the results do not allow sufficient conclusions as to whether the reported EFD were caused by the direct action of SARS-CoV-2 on the central nervous system or whether they were the cognitive sequel of psychological reactions to a life-threatening illness, such as symptoms of anxiety and depression. Additional factors or mechanisms not explored in this study may further explain neurocognitive decline, such as potential neuroinvasion of SARS-CoV-2, blood-brain barrier disruption or neuroinflammation. Screening for cognitive changes in post-COVID-19 patients would possibly be an important tool for clinical practice. The collaboration of physicians and neuropsychologists, the monitoring of possible psychiatric symptoms and the recommendation of rehabilitation measures if needed will be beneficial for COVID-19 patients.

Future Implications

In general, for future research in the context of COVID-19 it would be preferable to have balanced data sets with equal numbers of post-COVID-19 participants and healthy controls participants who did not suffer from COVID-19. An equal distribution of post-COVID-19 participants and healthy controls would be more representative of the general population and thus, the results would be more generalizable (*World Health Organization*, 2021).

Apart from that, it would be worthwhile to identify possible additional risk factors underlying cognitive impairment: Future research could explore comorbidities, as well as possible biological mechanisms that were not explored in this study, such as potential neuroinvasion of SARS-CoV-2 and how they are related to deficits in EFs.

Furthermore, future studies are needed to identify possible secondary symptoms of COVID-19 disease, such as anxiety and depression, and to investigate the association with cognitive impairments. If the association between depression and anxiety symptoms and cognitive impairments in post-COVID-19 individuals proofs to be true, it will be essential to detect these symptoms in clinical settings to avoid later cognitive impairments. Therefore, future studies should try to include data on anxiety and depression symptoms before infection with SARS-CoV-2 and compare them with symptoms after infection. This would help to better understand the underlying cause of the EFD.

Conclusion

Despite some limitations, the findings of the present research raise specific issues to the role of comorbidities in neuropsychological manifestations in individuals who suffered from COVID-19. In addition, this study provides hints on a possible influence of anxiety and depression symptoms in the presentation of EFD after COVID-19 infection. The results have

reconfirmed findings regarding the presence of cognitive impairments in COVID-19 survivors. More than that, it is particularly noteworthy that this research represents an important addition to numerous studies that have investigated cognitive impairment based on objective measurements. This research was one of a few to focus on the subjective perception of deficits in EFs.

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Appendix A: Table of Medication Intake of Participants

Medication		*n*	%
Antidepressants		16	59.0
	Amitriptilyne	2	7.0
	Citalopram	3	11.0
	Paroxetine	2	7.0
	Sertraline	3	11.0
	Venlafaxine	2	7.0
	Not Specified	4	15.0
Antipsychotics		1	4.0
	Quetiapine	1	4.0
Treatment of Hypertension		3	11.0
	Bisoprolol	1	4.0
	Perindopril	1	4.0
	Cyress	1	4.0
Insulin		1	4.0
Metformin		1	4.0
Epilepsy pills		1	4.0
Deloratadine Teva		1	4.0
Airway dilator		1	4.0
Methylphenidate		2	7.0
Simvastatin		1	4.0
Esomeprazole		1	4.0

Note. $n = 27$.

Appendix B: Table of Mean and Standard Deviation of GAD-7 and BDI scores of post-COVID-19 Participants by Age Groups

	Age Group									
	18-29 (*n* = 12)		30-39 (*n* = 17)		40-49 (*n* = 27)		50-64 (*n* = 44)		65 or older (*n* = 5)	
Scale	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
GAD-7	5.42	4.32	6.35	4.43	4.52	3.48	4.16	2.57	4.20	3.19
BDI	14.17	8.41	16.18	6.42	12.04	5.77	13.20	6.47	14.00	7.18

Note. *n* = 105. M = mean; *SD* = standard deviation.

Appendix C: Table of GAD-7 scores of post-COVID-19 Participants

	Age Group									
	18-29		30-39		40-49		50-64		65 or older	
Scale	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Minimal anxiety	6	50.0	5	29.4	13	48.1	24	54.5	2	40.0
Mild anxiety	4	33.3	11	64.7	11	40.7	20	45.5	3	60.0
Moderate anxiety	1	8.3	0	0.0	3	11.1	0	0.0	0	0.0
Severe anxiety	1	8.3	1	5.9	0	0.0	1	2.0	0	0.0

Note. $n = 105$.

Appendix D: Table of BDI of post-COVID-19 Participants

	Age Group									
	18-29		30-39		40-49		50-64		65 or older	
Scale	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Minimal to no depression	7	58.3	8	47.1	18	66.7	26	59.1	3	60.0
Mild depression	0	0.0	5	29.4	4	14.8	9	20.5	0	0.0
Moderate depression	5	41.7	3	17.6	5	18.5	9	20.5	2	40.0
Severe depression	0	0.0	1	5.9	0	0.0	0	0.0	0	0.0

Note. $n = 105$.