The Negative Impact of Psychological Distress on Executive Functioning in COVID-19 Infection.

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Abstract

Objective: Previous studies on COVID-19 have established an association between SARS-CoV-2 infection and neuropsychological consequences. Increasing evidence shows prominent impairments in executive functioning (EF) and psychological functioning after COVID-19 infection. Recent findings suggest that psychological distress negatively impacts cognition in COVID-19. Therefore, the present study aims to get insight in self-reported EF impairments in COVID-19 infection, and the additional influence of psychological distress on these impairments in daily life. By using a subjective measure of EF, our study has the advantage of getting insight in the presence of EF impairments in daily life functioning. **Methods:** Our sample (N = 216, age range from 18 – 65 or older, 166 females and 50 males) consisted of 145 participants with previous COVID-19 infection and 71 participants without COVID-19 infection, who were recruited via convenience sampling. Participants completed the COCO-19 test battery, consisting of several existing questionnaires. This study focused on the BRIEF-A (measuring subjective EF), the GAD-7 (measuring anxiety) and BDI (measuring depressive symptoms); the latter two being individually assessed, as well as in a composite score to assess overall psychological distress. Stepwise regression analysis was used to assess the predictive value of COVID-19 infection and psychological distress on subjective EF impairments in daily life. Another stepwise regression analysis was used to assess the specific predictive value of depression and anxiety in COVID-19 infection on subjective EF impairments in daily life. **Results:** COVID-19 infection was a significant predictor of subjective impairments in EF in daily life, with a medium effect size (ES). Psychological distress in COVID-19 infection predicted a significant increase in subjective EF impairments, increasing the explained variance with 32.7% (large ES). Depressive symptoms were a significant stronger predictor of subjective EF impairments in daily life on top of COVID-19 infection (large ES), compared to symptoms of anxiety. The addition of anxiety only led to an

increase of 0.3% in the explained variance in the model with depressive symptoms and COVID-19 infection. Exploratory correlational analysis showed that sex, symptom severity and COVID-19 medication could be possible covariates since they are associated with either psychological distress and/or subjective EF impairments. **Conclusion:** The present study found that COVID-19 infection significantly predicts higher subjective EF impairments in daily life. Psychological distress seems to have an additional negative impact on subjective EF impairments in COVID-19 infection; depressive symptoms in COVID-19 infection have a stronger negative impact on subjective EF impairments than symptoms of anxiety. Therefore, our findings suggest that there is a specific association between COVID-19 infection, depression, and subjective EF impairments in daily life.

Keywords: COVID-19, cognition, executive functions, impairments in executive functions, daily life functioning, psychological distress, depression, anxiety

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The Influence of Psychological Distress on Executive Functioning in COVID-19 Patients

SARS-CoV-2, the virus that causes COVID-19, is primarily associated with clinical manifestations such as pneumonia, headache, and fatigue (Aghagoli et al., 2021; Asadi-Pooya & Simani, 2020). However, it recently has become apparent that SARS-CoV-2 also has neurological manifestations by spreading to the central nervous system (CNS) (Aghagoli et al., 2021; Liguori et al., 2021). Thus, SARS-CoV-2 has neurotropic and neurotoxic effects and therefore could lead to brain pathology, via direct or indirect infiltration pathways to the brain (Asadi-Pooya & Simani, 2020). In a recently published report on COVID-19 patients (N = 59) who have been admitted to intensive care units, almost 70% experienced neurological symptoms such as agitation, confusion and/or corticospinal tract signs; remarkably, 33% of the sample experienced executive dysfunction after hospital discharge with symptoms as inattention, impaired motor skills and disorientation (Helms et al., 2020). However, the exact infiltration mechanism of SARS-CoV-2 into the CNS is not clear yet. Proposed mechanisms are the direct invasion of SARS-CoV-2 into the brain, strong immune responses accompanied by high levels of cytokines and exposure to enduring psychological stress before and during SARS-CoV-2 infection, the latter two being indirect mechanisms (Fotuhi et al., 2020; Mazza et al., 2021). Consequently, the strong immune response caused by SARS-CoV-2 can trigger a cytokine storm which causes damage to the blood-brain barrier, whereas enduring exposure to psychological stress is also associated with heightened levels of cytokines; both are associated with an inflammatory state of the brain (Fotuhi et al., 2020). Based on the current knowledge on viral infections, it is suggested that this inflammation could lead to long term neuropsychological consequences with cognitive, behavioural, and affective symptoms (Mazza et al., 2021).

Neuropsychological Consequences of COVID-19 Infection

Persistent cognitive impairments are highly prevalent after COVID-19 infection, with executive dysfunctioning being the most pronounced (Helms et al., 2020; Mazza et al., 2021). Mazza et al. (2021) found that COVID-19 patients still showed high rates of cognitive complaints, three months after symptom onset. Based on equivalent scores, only 19% scored in the normal range of overall cognitive performance, regardless of illness severity. Executive functioning (EF) and psychomotor coordination were the most impaired, followed by working memory, information processing and verbal fluency; almost 50% of the participants experienced impairments in EF (Mazza et al., 2021). In line with these findings, Nalbandian et al. (2021) reported that COVID-19 infection is associated with impairments in concentration, memory, EF, and receptive language. Another study reported that 80% (N = 29) experienced significant cognitive impairments in their daily life functioning for at least three- or four-months after hospital discharge, with EF and verbal learning being most impaired (Miskowiak et al., 2021).

Emerging evidence suggests that psychiatric symptoms are associated with neuropsychological symptoms in COVID-19 patients; especially impairments in EF seem to be related to psychological distress (Liguori et al., 2021; Mazza et al., 2021). It is already known that psychological distress is often accompanied by EF impairments; executive dysfunctioning has even been proposed as a transdiagnostic cognitive impairment for general psychopathology because of the high prevalence of EF impairments across psychiatric disorders (Romer & Pizzagalli, 2021). In the context of COVID-19 infection, the amount of studies on the influence of psychiatric symptoms on cognitive functioning is scarce; this is surprising, given the high prevalence of psychiatric symptoms in COVID-19 patients. In the follow-up study of Mazza et al. (2021), 35.8% of their sample of COVID-19 patients (N = 226) still scored in the clinical range for at least one psychopathological dimension.

Interestingly, feelings of anxiety decreased, while depressive symptoms barely changed; 8.9% of the participants still met the criteria for a depressive episode. This percentage even rises to 28% when self-report measures were considered (Mazza et al., 2021). Partly in line with these findings, a large cohort study with discharged hospitalized COVID-19 patients (N = 1655) reported that 75% of their sample still experienced at least one neuropsychological symptom around six months after symptom onset (Huang et al., 2021). Among these, the most frequent reported symptoms were fatigue or muscle weakness (63%), sleep difficulties (26%), and depression or anxiety (23%). The latter finding is not in line with the results of Mazza et al. (2021); however, Huang et al. (2021) did not discriminate between anxiety and depression, so this discrepancy might be due to methodological differences. Given the high prevalence of psychological distress in COVID-19 infection and the already established association with EF impairments in non-COVID samples, these findings leave room to suggest that, on top of the negative impact of COVID-19 on cognition, an additional negative impact of psychological distress on impairments in EF could be suspected.

Depression and anxiety seem to be most persistent psychiatric symptoms in COVID-19 infection (Huang et al., 2021; Mazza et al., 2021). Studies on healthy participants have already illustrated that anxiety and depression are negatively correlated with EF (Banks & Boals, 2017; Beaudreau & O'Hara, 2008; O'Brien et al., 2004; Sliwinski et al., 2006; Snyder, 2013). Mazza et al. (2021) found that the presence of depressive symptomatology after COVID-19 infection seems to be related to executive dysfunctioning, especially attention and information processing; it should be noted that this association was more prevalent in woman than in men (Mazza et al., 2021). Previous research has already established that depression is related to impairments in EF, as they are both associated with insufficient levels of arousal in frontal regions in the brain (Warren et al., 2021). More specifically, working memory (WM), planning, cognitive flexibility and attention are often impaired in patients who suffer from

depression (DeBattista, 2005; Lockwood et al., 2002). These studies illustrate that depressive symptoms are directly related to impairments in EF, independent of the effects of COVID-19 infection. When taking this in consideration, it could be possible that depressive symptoms in COVID-19 infection exacerbate EF impairments.

Anxiety, on the other hand, is also related to impairments in EF, but through a different mechanism. Symptoms of anxiety are characterized by enduring hypervigilance, which is found to be associated with less available EF resources (Ajilchi & Nejati, 2017; Boals & Banks, 2020; Warren et al., 2021). The COVID-19 pandemic has a strong potential to trigger anxiety in the general population (e.g., constantly checking the news, worrying about the pandemic), leaving less available cognitive resources for EF (Boals & Banks, 2020). In addition, COVID-19 infection has been associated with worrying about disease course, financial stressors, and being isolated from family and friends (Dorman-Ilan et al., 2020). These findings suggest that COVID-19 infection is associated with additional psychological stressors (e.g., on top of the COVID-19 pandemic) that could lead to higher anxiety symptoms. Therefore, it could be suspected that symptoms of anxiety in COVID-19 infection have a negative impact on EF resources. However, depressive symptoms seem to be more directly related to EF impairments (e.g., both are related to insufficient arousal in the frontal lobes) than the more indirect impact of anxiety on EF (e.g., lower cognitive capacity for EF). Hence, depressive symptoms could be more strongly related to subjective EF impairments in COVID-19 infection than to anxiety.

Executive Functions

Impairments in EF seem to be one of the most prevalent and persistent cognitive complaints after COVID-19 infection (Helms et al., 2020; Ortelli et al., 2021). EF can be defined as the goal-directed neurocognitive processes that are necessary for coordinating and controlling cognition and behaviour (Luria, 1966; Miyake & Friedman, 2012; Welsh &

Pennington, 1988). Until now, EF is often used as an umbrella term (Barkley & Murphy, 2011; Bell & Meza, 2020; Jurado & Rosselli, 2007). In the present study, we include inhibition, working memory updating, conflict monitoring and task switching as the core EF, based on the findings of Miyake et al. (2000). Additionally, we adhere to the suggestion of Enriquez-Geppert et al. (2010) to split inhibition into motor inhibition and conflict monitoring.

EF are necessary to navigate successfully through daily life; for example, they help people to monitor their own behaviour and inhibit inappropriate behaviours (Garner, 2009; Romero-Ayuso et al., 2021; Snyder, 2013). Impairments in EF are associated with mental health problems (Romer & Pizzagalli, 2021), academic and occupational impairment (Rutherford et al., 2018). More generally speaking, EF is found to be a significant predictor of functional outcomes (Miyake et al., 2000; Wood et al., 2014). In conclusion, these studies illustrate the importance of EF in daily life functioning. However, the number of studies specifically studying EF in the context of COVID-19 is still scarce. Therefore, it seems reasonable that the present study is aimed at assessing EF in COVID-19 patients.

Present Study

Overall, the number of studies that focus on EF in COVID-19 patients is slowly increasing. In contrast to the merely subjective assessment of psychological functioning, most studies only include objective measures in the assessment of EF. However, research has established that objective EF tests have low ecological validity (Barkley & Murphy, 2011). More generally speaking, neuropsychological tests are often not sufficient to reflect everyday life (Roessler-Górecka et al., 2013). Next to this, several studies have reported that psychiatric symptoms and their subsequent psychological distress can negatively influence cognitive performances (Banks & Boals, 2017; Boals & Banks, 2020). When only using performance-based measures, this interference could lead to overestimations of cognitive impairments.

Research has illustrated the additional value of self-report measures to get more insight in daily life functioning (Roessler-Górecka et al., 2013). In addition, subjective measures of EF have high ecological validity, as shown by correlations with everyday functioning, participation levels and quality of life (Chaytor & Schmitter-Edgecombe, 2003; Vlagsma et al., 2017). Taken together, it is recommended to include a subjective measure of EF, such as the BRIEF-A, to get more insight in the consequences of EF impairments on everyday life. The BRIEF-A is found to be more sensitive to changes in EF and being less susceptible to the interference with psychiatric symptoms in comparison to other neuropsychological tests (Hagen et al., 2019; Rabin et al., 2006).

The present study aims to build further on the scarce knowledge on the influence of psychological distress on EF in daily life in COVID-19 infection. We will assess this by using subjective measures for both EF and psychological functioning, being one of the first studies doing so in the context of COVID-19. Until now, studies using objective measures suggest that there is an association between COVID-19 infection and impairments in EF (Helms et al., 2020; Mazza et al., 2021). Secondly, it is suggested that additional psychological stress in COVID-19 infection, specifically depressive symptoms, is related to even more impairments in EF (Mazza et al., 2021). Exploratory correlational analysis will be conducted to get insight in other possible covariates related to cognitive and psychological functioning in COVID-19 infection. Taken together, we hypothesize the following:

$H0_1$: There will be no significant prediction of self-reported impairments in EF in daily life by COVID-19 infection.

H1: COVID-19 infection predicts higher self-reported impairments in EF in daily life functioning.

$H0_2$: In the presence of COVID-19 infection, psychological distress will not improve the prediction of self-reported EF impairments in daily life.

H2: COVID-19 infection and psychological distress significantly improve the prediction of self-reported impairments in EF in daily life, compared to only considering COVID-19 infection.

$H0_3$: Depressive symptoms will not improve the prediction of self-reported impairments in EF in daily life more strongly than symptoms of anxiety in COVID-19 infection.

H3: The addition of depressive symptoms to COVID-19 infection improves the prediction of self-reported impairments in EF in daily life more strongly than the addition of anxiety symptoms.

Method

Participants

In the current study, the total sample size consisted of 294 participants (age range from 18 – 65 years). Among these, there were 234 female and 59 male participants; one participant chose the "other" gender category. Participants with- and without previous COVID-19 infection were recruited with convenience sampling, using the snowball method, our website (https://www.coco19-research.org/index.html), and distributing flyers on social media (i.e., Facebook groups) and in hospitals. Inclusion criteria for the current study were that participants had to be 18 years or older, speak English, Dutch, French, Spanish or German and either being infected with COVID-19 or not previously being infected with COVID-19. Participants were excluded if they did not give informed consent, if they scored outside the acceptable range of the validity scales of the BRIEF-A (i.e., Negativity score ≥ 4, Infrequency score ≥ 3, Inconsistency score ≥ 8) and if they did not fill out the questionnaire out entirely (below 98% progress). Participants did not receive any form of compensation for participating in our study. The study was conducted online, where participants could fill in the questionnaire in their own environment.

This research project was approved by the Ethics Committee of the Department of Psychology of the University of Groningen. Participants signed an informed consent prior to the study. Furthermore, the study is conducted according to the Declaration of Helsinki, which ensures that ethical principles regarding human participant research were obeyed.

Final Sample

Due to differences in the questionnaires, the present study only included German and Dutch participants (N = 294) to foster statistical analyses. After removing participants due to missing data and/or exclusion criteria, our sample size reduced to a total of 216 participants, consisting of 123 female and 22 male participants who were previously infected with COVID-19 (n = 145) and 43 female and 28 male participants (n = 71) who were not previously infected with COVID-19. Among these, there were 92 participants from Dutch nationality and 124 participants from German nationality, with an age range from 18 to 65 years or older. In total, 9 participants who were infected with COVID-19 were hospitalized. In addition, 67 of the 145 COVID-19 participants (46.2%) reported to have taken specific medication for their COVID-19 infection; the average self-reported symptom severity, with a range from 0 to 100, was 55.43 (n = 145). In total, 13.4% (n = 29) of the participants suffered from psychological, psychiatric, or neurological problems. Health problems that were reported were heart attacks (0.05%), high blood pressure (7.4%), obesity (8.3%), and diabetes (3.2%); 31 participants (14.4%) reported medication use for their (mental) health problems.

Procedure

The participants completed a computer-based test battery, which was designed using Qualtrics Survey software. The test battery is called COCO-19, which is an abbreviation for Cognition COVID-19. The participants were asked to complete this online test battery three times in total; a baseline measure and two follow-up measures, one after three and one after six months. Prior to starting with the test battery, the participants were asked to choose their

preferred language (German, Dutch, Spanish, French, or English). Participants then entered a screen with information on the study's objective and were presented an informed consent. Following this, participants were asked to fill out sociodemographic information such as age, gender, medication intake, educational level, and pre-existing conditions. Then participants were asked if they were previously infected with COVID-19; if they answered yes, they were forwarded to more specific questions regarding their illness, consisting of the date of diagnosis, disease severity, symptoms, inpatient stay, and medication intake. After these questions, the participants entered the main test battery. If participants answered that they were not previously infected with COVID-19, they directly entered the main test battery; the questionnaires and their specific sequence can be found in Table 1. In this paper the focus will be on three specific questionnaires; the Brief Rating Inventory of Executive Functions for Adults (BRIEF-A) to assess self-reported EF, the Generalized Anxiety Disorder-7 questionnaire (GAD-7) to assess anxiety and the Beck's Depression Inventory (BDI) for depressive symptoms; the latter two will also be merged into one measure of "psychological distress". At the end of the test battery, participants were asked to enter a personalized code to connect their responses of the baseline and follow-up measures.

Materials

Self-reported Executive Functioning

The Behavior Rating Inventory of Executive Functions for Adults (BRIEF-A) is used to get insight in the EF of the participants in an everyday life context; participants are asked to report on their EF and self-regulation in their daily life activities (Roth, 2005). The BRIEF-A is a self-report measure consisting of seventy-five items, divided in nine clinical scales, which are measured on a 3-point Likert scale (1 = *Never*, 2 = *Sometimes*, 3 = *Often*). The participants who were not infected with COVID-19 answer these questions regarding the past four weeks whereas the participants who were infected with COVID-19 answer these questions regarding

the period since their infection. The nine clinical scales result in three overarching scores, being one global executive composite (GEC), indicating overall functioning, and two index scores regarding metacognitive problems (MI) and behavioural regulation problems (BRI). The MI embodies five scales: Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials. The BRI contains four scales: Inhibit, Shift, Emotional Control, and Self-Monitor. In addition, the BRIEF-A includes three validity scales: Negativity, Infrequency, and Inconsistency. The Cronbach's alpha, as found in the present study, and examples for the items per scale can be found in Appendix A.

Psychological Variables

The General Anxiety Disorder-7 questionnaire (GAD-7) is used to assess the participants' level of general anxiety symptoms (Spitzer, 2006). The GAD-7 is a self-report measure, consisting of seven items that measured the participants' symptoms of anxiety regarding the past two weeks (group without previous COVID-19 infection) or the period since their infection (group with previous COVID-19 infection). The seven items are measured on a 4-point Likert scale, ranging from 0 (*not at all*) to 3 (*almost every day*). An example of an item is "Not being able to stop or control worrying". To calculate a total score, the scores on the seven items are added together. Total scores and their subsequent indication on severity of the anxiety can be found in Appendix B.

The Beck's Depression Inventory (BDI), developed by Beck (1961) is a self-report measure that is used to assess common depressive symptoms among the participants in the past two weeks (group without previous COVID-19 infection) or within the period since their diagnosis (group with previous COVID-19 infection). The BDI consists of 21 items, where each item is characterized by four different response options. An example of a response option is "I don't feel I am being punished". The response options have different scores; to calculate the total score on the BDI, all item scores are added up. Higher scores indicate a

higher amount and severity of depressive symptoms. Total scores and their associated severity indication of anxiety can be found in Appendix B.

Table 1

Content and Sequence of Test Battery "Coco-19"

Domain	Category	Test	Abbreviation
Life Outcome	Quality of Life	Quality of Life	WHO QoL BREF
	Functional Activity	Functional Activity Questionnaire	FAQ
Neuropsychological	General Cognition	Fragebogen zur geistigen Leistungsfähigkeit	FLEI
	General Cognition	Cognitive Failure Questionnaire	CFQ
	Executive Functioning	Behavior Rating Inventory of Executive Functions for Adults	BRIEF-A
	Working Memory	Working Memory Questionnaire	WMQ
	Attention	Fragebogen erlebter Defizite der Aufmersamheit	FEDA
	Memory	Amnestic Subjective Cognitive Decline Questionnaire	ASCDQ
Personality	Personality	NEO Five-Factor Inventory	NEO-FFI
Psychological	General Health	Short Form Health Survey	SF-12
	General Health	Positive and Negative Affect Schedule	PANAS
Sleep	Sleep	Pittsburgh Sleep Quality Index	PSQI
	Distress	Kessler Psychological Distress Scale	K-10
	Depression	Beck Depression's Inventory	BDI
	Anxiety	Generalized Anxiety	GAD-7
	Fatigue	Fatigue Severity Scale	FSS
	Loneliness	University of California Los Angeles Loneliness Scale	UCLA

Statistical analysis

Data preparation

To assess overall subjective impairments in EF, GEC sum scores of the BRIEF-A were calculated, where higher scores indicate more impairments in EF in daily life functioning. Sum scores of the GAD-7, measuring anxiety, and the BDI, measuring depression, were calculated to assess psychological distress. The GAD-7 and BDI sum scores were used independently to assess anxiety and depressive symptoms, as well as in a composite score to assess overall psychological distress in the context of COVID-19 infection.

Main analysis: regression analyses

Stepwise regression analyses were performed to test our hypotheses. Prior to performing the analysis, the assumptions for regression were checked for violations (e.g., linearity, normality, homogeneity, independence of observations), using Q-Q plots and tests (Casewise diagnostics and Durbin-Watson test); no violations were found. Using a correlational analysis, multicollinearity has been checked. Bivariate correlations should be below 0.7 to fulfil the multicollinearity requirement (Mukaka, 2012). As can be seen in Table 3, this requirement has also been fulfilled.

To be able to analyse the possible additive effect of psychological distress on executive impairments in COVID-19 infection, we used a stepwise regression analysis. As follows, GEC scores were used as the dependent variable. In the first step of the regression analysis, COVID-19 infection (0 = no, 1 = yes), was inserted as a predictor to test the first hypothesis. In the second step, psychological distress (composite score of the BDI and GAD-7) was added as the second predictor via the ‘Enter’ method to test our second hypothesis.

Then we performed another stepwise regression analysis to assess the independent predictive value of anxiety (measured with GAD-7) and depressive symptoms (measured with

BDI) on GEC scores in COVID-19 infection. Consequently, GEC scores were added as the dependent variable. Next, COVID-19 infection was inserted as the first predictor. BDI scores were more strongly associated to COVID-19 infection and GEC scores, compared to GAD-7 scores (see Table 3). Because of this, BDI scores were added as the second predictor in the second step via the Enter method. In the last step, GAD-7 scores were added as the third predictor via the Enter method; by comparing the second and third model, we tested our third hypothesis.

Exploratory Analysis

Finally, an exploratory correlational analysis was performed. First, correlations between sex and symptom severity were explored; several studies reported that, overall, women experienced more severe neuropsychological impairments after COVID-19 infection in comparison to men (Huang et al., 2021; Mazza et al., 2021). Secondly, we included subjective symptom severity in our analysis. Until now, most studies in the context of COVID-19 only included hospitalized patients, indicating high symptom severity (Helms et al., 2020; Zhou et al., 2020). However, Mazza et al. (2021) found that EF impairments were independent of symptom severity. To get further insight in this association, we aimed to explore the role of subjective symptom severity in cognitive functioning in the present study. Lastly, medicine intake was included in the analysis since research findings have shown that COVID-19 treatment, as well as other medications, could also influence cognitive performance and psychological functioning (García et al., 2020; Szcześniak et al., 2021). The data analysis is performed using SPSS (Version 26.0).

Results

Descriptive statistics for GAD-7, BDI, psychological distress, and GEC scores for both the group with previous COVID-19 infection and the group without COVID-19 infection can be found in Table 2. Regarding psychological distress, 33.8% of the group without any

previous COVID-19 infection reported severe depressive symptoms, whereas 71.7% of the group with a previous COVID-19 infection reported severe depressive symptoms; 19.7% of the group without COVID-19 infection reported severe anxiety, in comparison to 20% of the group with a previous COVID-19 infection. Mean standardized GEC scores were 41.94 for the group without COVID-19 infection and 50 for the COVID-19 group. Standardized GEC scores equal to or higher than 65 are considered clinically significant (Roth, 2005). In total, 4 participants of the group without COVID-19 infection and 10 of the group with previous COVID-19 infection had clinically significant GEC scores.

Table 2

Mean Scores and Standard Deviations for Psychological Distress and Self-reported EF in the Group with previous COVID-19 Infection and Group without COVID-19 Infection

	COVID-19 Infection Group		*No COVID-19 Infection Group*	
	M	*SD*	*M*	*SD*
Psychological Distress[a]	44.8	9.6	39.0	11.3
BDI (depression)	33.1	7.1	27.9	7.5
GAD-7 (anxiety)	11.7	3.4	11.0	4.4
GEC[b] (subjective EF)	122.4	21.2	105.4	25.6

Note. COVID-19 Infection Group n = 145 and No COVID-19 Infection Group n = 71.
[a] Sum score of the BDI and GAD-7
[b] Measured with the BRIEF-A

Main Analysis

The regression tables of the stepwise regression analyses can be found in Appendix C.

Hypothesis 1 and 2

COVID-19 infection was a significant predictor of GEC scores ($\beta = .33$, $t(214) = 5.18$, $p < .001$). Moreover, COVID-19 infection explained 10.7% of the total variance in GEC scores, with a medium effect size ($F(1, 214) = 26.87$, $p < .001$, $R^2_{adjusted} = .107$). These results indicate that COVID-19 infection leads to increased GEC scores ($r = .62$, $p < .001$). In total, these findings confirm our first hypothesis, being that COVID-19 infection a significant predictor of self-reported impairments in EF in daily life.

The addition of psychological distress further increased the explained variance in EF in daily life functioning with 32.7%, which significantly improved the prediction with a large effect size ($F(2, 213) = 83.18$, $p < .001$, $R^2_{adjusted} = .433$). Analysis of the parameter estimates showed that psychological distress ($\beta = .59$, $t(213) = 11.14$, $p < .001$), on top of COVID-19 infection ($\beta = .18$, $t(213) = 3.38$, $p < .001$), significantly increased GEC scores (also see Fig. 1). These results illustrate that psychological distress on top of COVID-19 infection significantly improves the prediction of GEC scores. These results confirmed our second hypothesis, being that the addition of psychological distress to COVID-19 infection improves the prediction of self-reported impairments in EF in daily life, in comparison to only considering COVID-19 infection.

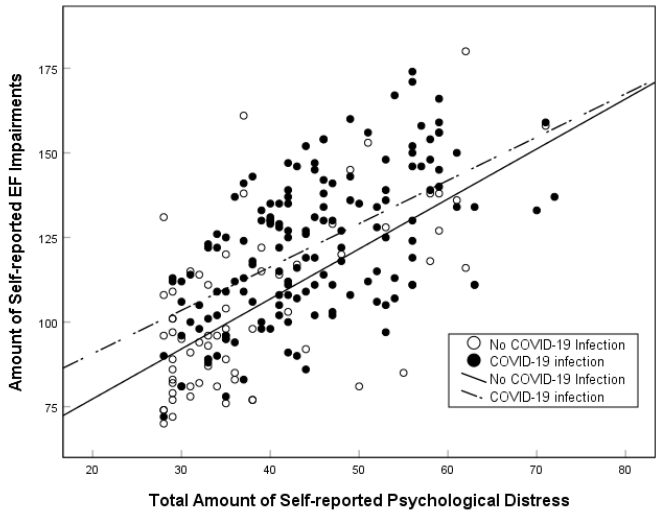
Hypothesis 3

BDI scores were a significant predictor of GEC scores ($\beta = .57$; $t(213) = 10.35$, $p < .001$) along with COVID-19 infection ($\beta = .15$; $t(213) = 2.73$, $p = .007$). The addition of BDI scores to the model with COVID-19 infection significantly increased the explained variance in GEC scores with 30%, showing a large ES ($F(2, 213) = 73.64$, $p < .001$, $R^2_{adjusted} = .403$).

GAD-7 scores were a significant predictor of GEC scores ($\beta = .23$, $t(212) = 3.36$, $p = .001$) in the model with COVID-19 infection ($\beta = .18$, $t(212) = 3.32$, $p = .001$) and BDI scores ($\beta = .42$, $t(212) = 5.80$, $p < .001$). These parameter estimates show that BDI scores on top of COVID-19 infection were a stronger predictor for GEC scores than GAD-7 scores (also see Fig. 2 and Fig. 3). Furthermore, the addition of GAD-7 scores to the regression model only led to an increase of 0.3% of the explained variance in GEC scores, with a small effect size ($F(3, 212) = 55.23$, $p < .001$, $R^2_{adjusted} = .431$). These results confirmed our third hypothesis, being that depressive symptoms in addition to COVID-19 infection improve the prediction of self-reported impairments in EF in daily life more strongly than symptoms of anxiety.

Figure 1

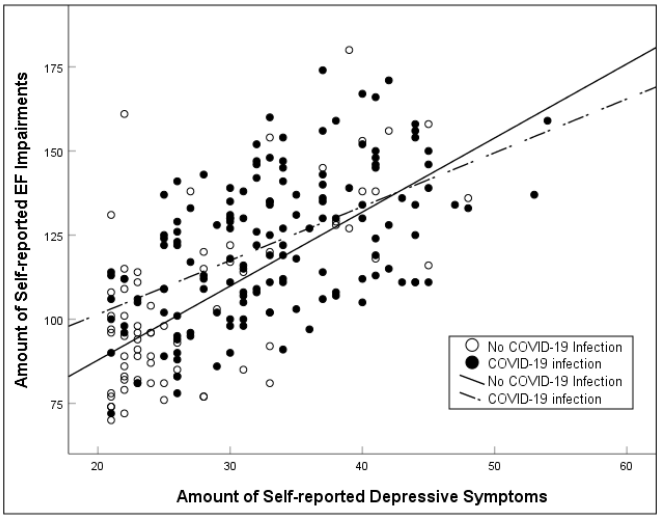
Scatterplot of the Changes in Self-reported EF Impairments as a Function of Total Psychological Distress and COVID-19 Infection



Note. Self-reported EF Impairments are measured with the GEC scale of the BRIEF-A. Psychological Distress is the composite score of total GAD-7 (anxiety) and BDI (depression) scores.

Figure 2

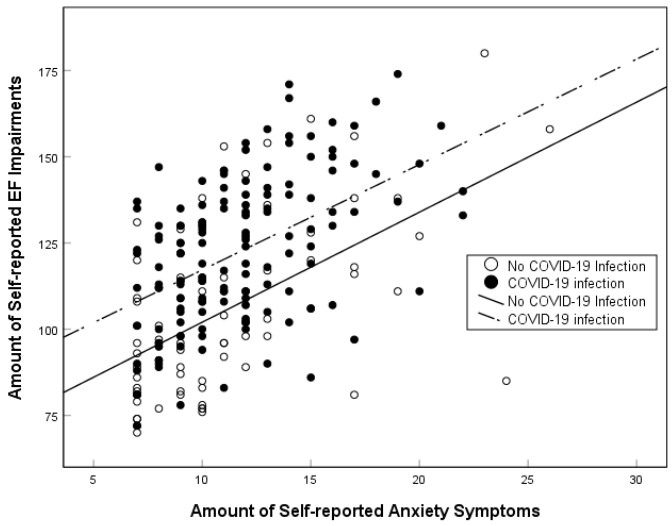
Scatterplot of the Changes in Self-reported EF Impairments as a Function of Depression and COVID-19 Infection



Note. Self-reported EF Impairments are measured with the GEC scale of the BRIEF-A. Depressive symptoms are measured with the total BDI scores.

Figure 3

Scatterplot of the Changes in Self-reported EF Impairments as a Function of Anxiety and COVID-19 Infection



Note. Self-reported EF Impairments are measured with the GEC scale of the BRIEF-A. Symptoms of anxiety are measured with the GAD-7 total scores.

Table 3

Pearson Correlations

	1.	2.	3.	4.	5.	6.	7.	8.
1. COVID-19 infection[a]	-							
2. Severity	c							
3. Sex[b]	-.27**	-.30**						
4. COVID-19 Medicine	.03	-.22**	.16					
5. GEC	.33**	.29**	-.25**	-.12				
6. Depression (BDI)	.32**	.42**	-.21**	-.20*	.62**			
7. Anxiety (GAD-7)	.08	.10	-.23**	-.21*	.51**	.65**		
8. Psychological Distress	.26**	.35**	-.23**	-.23**	.64**	.96**	.83**	

*. Correlation is significant at the 0.05 level.
**. Correlation is significant at the 0.01 level.
a. 0 = no, 1 = yes
b. 1 = female 2 = male
c. Cannot be computed because at least one of the variables is constant.

Exploratory correlational Analysis

In our explanatory analysis, we assessed severity, sex, and COVID-19 medication as possible covariates for our regression models (see Table 3). Correlations can be found in Table 3. Severity of symptoms had significant positive correlations to both GEC scores (medium ES) and psychological distress (medium ES). BDI, but not GAD-7, had a significant correlation to severity of symptoms, with a medium to large ES. Sex had significant negative correlations with all the assessed variables (GEC, psychological distress, GAD-7 and BDI), with small to medium ES. Lastly, COVID-19 medication did not correlate significantly to GEC scores but did have a significant positive correlation with psychological distress, with small to medium ES.

Discussion

The aim of the present study is to increase knowledge on neuropsychological consequences after COVID-19 infection. More specifically, the goal of the present study is to get more insight in the influence of psychological distress on EF in everyday life in COVID-19 infection. There are three key findings in the present study. First, our results provide supporting evidence for the negative impact of COVID-19 infection on subjective EF impairments in daily life. Secondly, our results provide supporting evidence that psychological distress in COVID-19 infection has an additional negative impact on subjective EF impairments in daily life. Thirdly, we found that depressive symptoms in COVID-19 infection more strongly predict self-reported EF impairments in daily life than anxiety symptoms. These findings will be more thoroughly discussed in the following paragraphs, ending with a discussion on the results from our exploratory correlational analysis. Lastly, we will discuss the limitations, implications, and conclusions of the present study.

As expected, our results indicate that participants who are previously infected COVID-19 infection report higher subjective impairments in EF in everyday life than

participants who are not previously infected with COVID-19. These results strongly imply that COVID-19 infection has a negative impact on subjective EF impairments in daily life. Since this is one of the first studies using a self-report measure for EF in COVID-19 infection, our results extend the merely objective findings on EF impairments after COVID-19 infection by creating more insight in the subjective burden of EF impairments in daily life functioning (Chaytor & Schmitter-Edgecombe, 2003; Vlagsma et al., 2017). Our findings suggest that participants who are previously infected with COVID-19 experience difficulties with performing daily life activities related to EF, which is consistent with the work of Miskowiak et al. (2021). They found that a large amount of their COVID-19 sample reported prominent EF impairments in their daily life, negatively impacting quality of life and functioning in work. Since it is already established that EF are a significant predictor of functional outcomes (Miyake et al., 2000; Wood et al., 2014), our results highlight the importance of considering the impact of EF impairments on daily life functioning in COVID-19 infection. Specifically, we recommend implementing more systematic cognitive screening in COVID-19 infection in combination with adequate treatment to decrease EF impairments and their subsequent impact on daily life functioning.

Secondly, our data shows that experiencing psychological distress in addition to COVID-19 infection significantly increases subjective EF impairments in daily life, in comparison to only COVID-19 infection. Whereas previous research has found that psychological distress is related to objective EF impairments in COVID-19 patients (Liguori et al., 2021; Mazza et al., 2021), the present study shows that this pattern of results is also present in subjective EF impairments, thereby highlighting the impact on daily life functioning. One interpretation of our findings is that psychological distress might exacerbate the impairments in EF, initially related to the COVID-19 infection itself, since previous research already established the negative effects of psychological distress on EF in non-

COVID samples (Banks & Boals, 2017; O'Brien et al., 2004; Sliwinski et al., 2006). However, bidirectionality cannot be ruled out; higher cognitive impairments could also increase psychological distress, so future research should further investigate this relationship. In conclusion, our findings indicate that it is important to pay attention to both cognitive and psychological symptoms in COVID-19 infection. Furthermore, we recommend implementing psychological support in the treatment of COVID-19 infection to improve mental health and possibly, indirectly, improve cognitive functioning.

At further examination, we found that depressive symptoms are significantly higher in participants who are previously infected with COVID-19 participants in comparison to participants who are not infected with COVID-19. However, we did not find significant differences in anxiety symptoms between these groups. A possible explanation for this could be the negative psychological impact of the COVID-19 pandemic on the general population, next to the impact of COVID-19 infection itself. While depressive symptoms seem to be specifically higher in COVID-19 infection (Mazza et al., 2021), anxiety symptoms are also found to be higher in the general population due to the psychological effects of the pandemic (such as social distancing, constantly reading the news on COVID-19, worrying about the pandemic, etc.; Boals & Banks, 2020), as well as in COVID-19 infection (social isolation, hospitalization and stigma; Fotuhi et al., 2020). In regard to our results, the psychological effects of the pandemic could be an explanation for the heightened anxiety symptoms in both groups. These findings implicate that future research should differentiate between psychological effects of COVID-19 infection or the pandemic, to be able to analyse the specific effects of COVID-19 infection on psychological distress.

Interestingly, our results show that depressive symptoms in COVID-19 infection have a stronger impact on subjective impairments in EF than symptoms of anxiety. On the contrary, symptoms of depression and anxiety are both strongly associated to subjective EF

impairments, independent of COVID-19 infection. Taken together, these results strongly imply that there is a specific connection between COVID-19 infection, depressive symptoms, and subjective EF impairments in daily life. These findings implicate that more attention should be given to the assessment and treatment of depressive symptoms in people who are infected with COVID-19. Furthermore, our findings extend the work of Mazza et al. (2021), who found that objective executive dysfunctioning after COVID-19 infection is related to the presence of depressive symptoms, by adding that subjective EF impairments are also related to depressive symptoms in COVID-19 infection. However, Mazza et al. (2021) noted that this relationship is more prevalent in women than in men. Since we only included gender in our correlational analysis, we cannot draw strong conclusions about this finding in our study. An important note, however, is that our sample is predominantly female, which could have led to biased results; this will be further discussed in the limitations. Nevertheless, our exploratory analysis suggests that women report higher psychological distress and executive impairments in comparison to men, with small to medium effect sizes. This finding is consistent with previous research, reporting that women, overall, seem to experience more impairments after COVID-19 infection than men (Huang et al., 2021; Mazza et al., 2021). Hormonal differences or differences in immune responses could be explaining these gender differences (Ancochea et al., 2020).

Secondly, in line with the findings of Mazza et al. (2021), we found that severity of symptoms is significantly correlated with subjective impairments in EF in our study, with a medium effect size. This is an important finding, because this implies that neuropsychological impairments are possibly present in more varying levels of symptom severity in people who are diagnosed with COVID-19. Therefore, we hypothesize that impairments in EF could also be assumed in people who experience less severe symptoms in their COVID-19 infection, stressing the importance of further research on neuropsychological variables amongst more

varying levels of symptom severity. Nevertheless, since we only included symptom severity in our correlational analysis, further research is necessary to gain further insight in this association. Lastly, we found that COVID-19 medicine intake is significantly correlated with psychological distress (medium effect size), but not with EF. This is partly contrasting previous research, where both cognition and psychological functioning was influenced by COVID-19 medication (García et al., 2020; Szcześniak et al., 2021). However, the possible influence of COVID-19 medications should be considered in future research in the context of COVID-19.

Limitations

Despite the strengths of the present study, there are also some limitations that should be taken into consideration. First, it is often assumed that impairments in EF are the consequence of psychopathology (Banks & Boals, 2017; Beaudreau & O'Hara, 2008; O'Brien et al., 2004; Sliwinski et al., 2006; Snyder, 2013), while it could also be possible that there is a bidirectional relationship or that EF impairments are associated with a vulnerability to develop and maintain psychiatric disorders. The current study was not aimed at determining causal relationships, so these possibilities cannot be ruled out.

Moreover, the BRIEF-A is normally complemented by an informant form to get insight in the awareness of the participants in their own difficulties regarding self-regulation in daily life functioning (Roth, 2005). This informant form is not included in the present study, due to technical restrictions regarding the online administration of our questionnaire. However, by not including this informant form, we were not able to get insight in the possible over- or underestimations in the self-reported impairments in EF, which could have led to biased results in our study.

Finally, there could be a gender bias in the present study. Our sample was predominantly female, indicating that the male gender might be underrepresented. Since there

are differences between sexes in diagnosis, clinical manifestations, and disease management of COVID-19 (Ancochea et al., 2020), this could have led to biased results. Therefore, it could be possible that the results of the present study are more generalizable to women than to men; several previous studies found that overall, women experienced more cognitive and psychological symptoms after COVID-19 infection (Huang et al., 2021; Mazza et al., 2021). Taken together, future research should account for sex differences in the context of COVID-19 research.

Implications

In general, our research findings contribute to the scarce knowledge on the neuropsychological consequences of COVID-19, and more specifically, the influence of psychological distress on subjective impairments in EF in COVID-19 infection. We have shown that psychological distress, on top of COVID-19 infection, has an additional negative effect on subjective EF impairments in daily life. Moreover, we found that depressive symptoms in COVID-19 infection more strongly impact subjective EF impairments in daily life than anxiety symptoms. Given the high prevalence and persistence of depressive symptoms and impairments in EF and after COVID-19 infection, more commonly grouped under “post-acute COVID-19 syndrome” (Nalbandian et al., 2021), our findings are highly relevant in this phase of the pandemic and stress the importance of further research in this relationship.

We suggest that future research in COVID-19 infection should also focus on lower levels of symptom severity, as the current research findings leave room to suspect that impairments in EF could also be present across lower levels of symptom severity; given the high prevalence of EF impairments after COVID-19 infection and the fact that EF are highly predictive for daily life functioning, we stress the importance of including more varying levels of symptom severity in COVID-19 research. Future research should therefore also focus on

non-hospitalized COVID-19 samples, using a validated symptom severity instrument, such as the COVID-19 symptom index (Lechien et al., 2021), to further analyse this association.

Secondly, we suggest that future research should focus on the association between depressive symptoms and impairments in EF in COVID-19 infection, as we found that especially depressive symptoms were strongly related to subjective EF impairments in the context of COVID-19 infection. Research on this matter could contribute to the development of more targeted interventions for people who suffer from the "post-acute COVID-19 syndrome", to improve their daily life functioning and overall quality of life.

Conclusions

In conclusion, we found supporting evidence for the negative impact of COVID-19 infection on subjective EF impairments in daily life. On top of that, our results demonstrated the additional negative impact of psychological distress in COVID-19 infection on subjective EF impairments in daily life. Furthermore, we found supporting evidence for the connection between COVID-19 infection, depressive symptoms, and subjective EF impairments in daily life. Taken together, our findings suggest the need for more systematic screening and treatment of both cognitive and psychological symptoms in COVID-19 infection, with special attention to depressive symptoms. Furthermore, we stress the importance of implementing psychological interventions in the treatment of COVID-19 infection. Future research should focus on further investigating the connection between depressive symptoms and EF in COVID-19 infection, with a focus on lower levels of symptom severity.

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Appendix A

BRIEF-A Examples of Items and Cronbach's Alpha per Scale of the Present Study

Scale	Item Example	Cronbach's Alpha
Global Executive Composite (GEC)		.90
Metacognition Index (MI)		.92
Initiate	"I have problems getting started"	.75
Working Memory	"I have difficulties with tasks that consist of several steps"	.90
Plan/Organize	"I have problems organizing activities"	.85
Task Monitor	"I have problems completing tasks (household, work)"	.78
Organization of Materials	"I leave the bathroom untidy"	.80
Behavioral Regulation Index (BRI)		.74
Inhibit	"I have difficulty sitting still"	.62
Shift	"I have difficulties to accept other ways of solving problems (work, friendship, tasks)"	.71
Emotional Control	"I overreact emotionally"	.87
Self-Monitor	"I do not notice when I do something that makes others feel bad before it is too late"	.65
Validity Scales		
Negativity	"I have difficulty moving from one task to another - Never"	.68
Infrequency	"I forget my name – Never" & "I have difficulty counting to three – Often"	.49
Inconsistency	"I make careless mistakes – Never" & "I make mistakes through carelessness – Often"	.50

Appendix B

Indication of Anxiety Severity of the GAD-7

Total scores	Indication
0 – 4	No anxiety
5 – 9	Mild anxiety
10 – 14	Moderate anxiety
15 – 21	Severe anxiety

Indication of Depressive Symptoms Severity of the BDI

Total scores	Indication
0 – 13	Minimal to no depressive symptoms
14 – 19	Mild depressive symptoms
20 – 28	Moderate depressive symptoms
29 – 62	Severe depressive symptoms

Appendix C

Stepwise Regression Analysis 1

Coefficients[a] of Stepwise Regression Analysis of COVID-19 Infection and Psychological Distress

Model	Predictors	*b*	SE	β	*t*	Sig.
1	(Constant)	105.37	2.70		39.07	.000
	COVID-19 infection[b]	17.06	3.29	.33	5.18	.000
2	(Constant)	52.35	5.22		10.02	.000
	COVID-19 infection	9.17	2.72	.18	3.38	.001
	Psychological Distress[c]	1.36	.12	.59	11.14	.000

Note. In the first step of the stepwise regression analysis, COVID-19 infection is forced in the model as covariate. In the second step, psychological distress is added via the Enter method.

[a] Dependent variable = GEC

[b] 0 = no and 1 = yes

[c] Psychological distress is the composite score of the GAD-7 (anxiety) and BDI (depression)

Stepwise Regression Analysis 2

Coefficients[a] of Stepwise Regression Analysis for COVID-19 Infection, Depression and Anxiety

	Model	*b*	SE	β	*t*	Sig.
1	(Constant)	105.36	2.70		39.07	.000
	COVID-19 infection[b]	17.06	3.29	.33	5.18	.000
2	(Constant)	54.74	5.37		10.20	.000
	COVID-19 infection	7.76	2.84	.15	2.73	.007
	Depression (BDI)	1.81	.17	.57	10.35	.000
3	(Constant)	52.52	5.28		9.94	.000
	COVID-19 infection	9.34	2.81	.18	3.32	.001
	Depression (BDI)	1.31	.23	.42	5.80	.000
	Anxiety (GAD-7)	1.46	.44	.23	3.36	.001

*Note***.** In the first step of the stepwise regression analysis, COVID-19 infection is forced in the model as covariate. In the second step, BDI scores were added via the Enter method. In the third step, GAD-7 scores were also added via the Enter method.

[a] Dependent variable = GEC

[b] 0 = no and 1 = yes