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Long-COVID or long before? Neurocognitive deficits in people with COVID-19

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ABSTRACT

In connection with COVID-19 disease, evidence of persisting psychiatric and neurocognitive effects is accumulating. To examine long COVID symptoms, baseline data from 2015 (i.e., before the pandemic) and follow-up data from 2021 from 428 participants were compared. Participants with COVID-19 reported more subjective neurocognitive complaints in the follow-up, but this did not correspond to the test performance. Also, greater depressive symptoms compared with the no-COVID group were reported. However, these complaints must be put into perspective when considering the baseline data, since complaints were present before the COVID infection. Thus, premorbid performance as well as psychological factors should be considered when discussing long COVID.

Evidence is accumulating of psychiatric and neurocognitive sequelae in association with COVID-19 (Taquet et al., 2021). These persisting complaints are often referred to as the 'long COVID syndrome' (Sudre et al., 2021). Neurocognitive impairments, for example attention and memory deficits, are found in COVID-19 patients after the acute infection with SARS-CoV-2 for both hospitalized and non-hospitalized patients compared to persons without COVID-19 (Hampshire et al., 2021). Other self-reported deficits linked to persisting symptoms after acute COVID-19 are low energy, and disorientation (Rogers et al., 2020). However, more data is needed to clarify whether COVID-19 is causing neurocognitive deficits on a general level (Paterson et al., 2020). In addition to neurocognitive complaints, mood-related symptoms are also frequently reported in association with long COVID. Fatigue is one of the most common persisting symptoms following a SARS-CoV-2 infection and can also be found in milder COVID-19 cases (Townsend et al., 2020). Over 50% of patients surviving COVID-19 showed psychopathological symptoms of at least one psychiatric disorder one month after hospital discharge (Mazza et al., 2020). It is also discussed that COVID-19 leads to psychiatric disorders (Rogers et al., 2020). At the same time, it is known that mood disorders are linked to neurocognitive impairments. Depressive symptoms are often correlated with attention and memory deficits (Moritz et al., 2004). Mood variables seem to be a better predictor of self-reported neurocognitive complaints than neuropsychological test performance (Mascherek et al., 2020). Examining the possible association of neurocognitive complaints and psychiatric symptoms with COVID-19 is challenging, as individual-level comparative data for the patients' state before the SARS-CoV-2 infection are scarce, and most results therefore cannot be interpreted as causative (Hampshire et al., 2021). Longitudinal cohort studies are needed to better understand 'long COVID'. To approach this subject, we conducted a study to address whether neurocognitive complaints concerning attention and memory as well as objective attention and memory performance are related to a current or previous SARS-CoV-2 infection. We aimed to identify possible mediators that should be considered for differential diagnosis, particularly pre-COVID status and objective validation of cognitive complaints through neuropsychological testing.

The study was a follow-up on an evaluation of neurocognitive complaints and objective cognitive performance in relation to lifestyle and mood variables from March 2015 (Mascherek et al., 2020). The data were collected via the platform WisoPanel, an online data tool for recruiting representative samples for scientific research. We examined, among other variables, depressive symptoms, assessed with the depression module of the Patient Health Questionnaire (PHQ-9) and subjective cognitive complaints (i.e., "*I have trouble memorizing new things*" and "*I have trouble concentrating*"), rated on a scale from 1 ("*strongly disagree*") to 4 ("*strongly agree*"). Objective cognitive

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performance was evaluated as well; memory performance was assessed with the German version of the Auditory Verbal Learning Test (AVLT) adapted for online administration, and selective attention was assessed with a go/no-go task. The follow-up survey was conducted in April 2021. The sample included 675 individuals (mean age = 56.2 years; 57% women; 37.8% with a university degree or doctorate). Baseline data were available for 428 of the 675 participants (63%). With respect to mental health status, 68.5% reported never being diagnosed with a psychiatric disorder. Having received a current or previous diagnosis of depression was reported by 21.8%, and an anxiety disorder diagnosis was reported by 8.8% of the participants. Of the 675 individuals, 27 (4%) reported a current or previous SARS-CoV-2 infection (COVID-19 group). In the follow-up, participants in the COVID-19 group self-reported significantly more current attention complaints ($d = 0.56$, $p < 0.01$) but not more current memory complaints ($d = -.03$, $p = 0.89$) compared to people without current or previous SARS-CoV-2 infection (the no COVID-19 group). The COVID-19 group showed lower current objective memory performance ($d = 0.67$, $p < 0.001$) but not worse current attention performance ($d = 0.03$, $p = .87$). With respect to difference scores (baseline – follow-up), the comparison between the COVID-19 and no COVID-19 groups showed no significant difference in terms of subjective attention and memory complaints ($d = 0.05$–0.32, $p = 0.25$–0.86) or objective attention and memory performance ($d = 0.27$–0.51, $p = 0.06$–0.32). The COVID-19 group showed significantly more depressive symptoms at follow-up compared to the no COVID-19 group ($d = -0.59$, $p < 0.01$). Again, the difference score on depressive symptoms (baseline – follow-up) was comparable in both groups ($d = 0.14$, $p = 0.62$).

Overall, people with COVID-19 self-report more current complaints related to attention, but their objective test performance does not reflect a reduction in selective attention. Lower current memory performance, as well as higher current depressive symptoms in the COVID-19 group, are nullified when patients' pre-existing levels are taken into account. However, the findings of this study are potentially limited by the unequal group sizes and the fact that the participants' COVID-19 status was self-reported. Self-reported COVID-19 status can lead to an underestimation of the size of the COVID group since asymptomatic infections are possible and a positive status may remain unidentified. Moreover, long COVID is a new clinical picture that still needs to be researched in greater depth. At the same time, however, it is receiving a great deal of public attention. As a result of this heightened awareness, focusing attention on potential symptoms may intensify or even provoke complaints. It can be concluded that consideration of pre-COVID levels and psychological vulnerability factors (e.g., depression) is pivotal when examining cognitive deficits in COVID-19. Subjective complaints often reflect emotional problems rather than actual performance deficits. Thus, a thorough differential diagnostic assessment is important in order not to overlook, for example, protruding emotional problems or those resulting from another condition or pandemic-related stress (e.g., isolation). Emotional and neurocognitive complaints should be verified in this context.

CRediT authorship contribution statement

Anna Baumeister: Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Writing – original draft. **Anja S. Göritz:** Methodology, Investigation, Resources, Writing – review & editing. **Charles Benoy:** Conceptualization, Formal analysis, Writing – review & editing. **Lena Jelinek:** Conceptualization, Writing – review & editing. **Steffen Moritz:** Conceptualization, Methodology, Project administration, Formal analysis, Writing – review & editing.

Conflicts of interest

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2022.114822.

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