Original Article

What We Know About Neurocognitive Outcomes in Long-/Post-COVID-19 Adults

A Comprehensive Scoping Review

Susan Seibert[1,2,3], Alexander Hanke[2], Michelle Wieberneit[2,4], Luzie Bieler[2], Robin Gräfenkämper[2,5], Katrin Klatt[2], and Catherine Nichols Widmann[1,2,3]

1 Center for Neurology, Medical Center, University of Bonn, Germany
2 Department of Neurodegenerative Diseases and Geriatric Psychiatry, Medical Center, University of Bonn, Germany
3 German Center for Neurodegenerative Diseases, Bonn, Germany
4 University of Western Australia, Law School, Perth, Australia
5 University of Witten/Herdecke, Department of Clinical Psychology & Psychotherapy, Witten, Germany

Abstract: This review assesses neurocognitive studies on long-/post-COVID-19 adult patients, highlighting the research gaps. We categorize populations by infection severity, demographics, inclusion of controls, and psychological/biological factors. Methodologically, we analyzed 73 studies (95,600 subjects) from December 2019 to October 2022 using PRISMA-ScR guidelines and the PICO framework. Our findings revealed that most studies lacked control groups (88%) and reported unclear overall cognitive outcomes (73%). While the studies frequently assessed executive functions (86%) and attention (85%), there were few longitudinal studies. Varied reporting on sample sizes further complicated the analysis. The identified gaps encompass convenience sampling, limited longitudinal studies, and inadequate use of cognitive test batteries, leading to a discrepancy between expected and reported outcomes. The absence of standardized comparisons and inconsistent statistical methods exacerbated these gaps.

Keywords: neuropsychology, cognition, long-COVID, post-COVID, postacute COVID-19 syndrome

Was wissen wir über neurokognitive Ergebnisse bei Erwachsenen mit Langzeit-/Post-COVID: Ein umfassender Scoping-Review

Zusammenfassung: In dieser Übersichtsarbeit werden neurokognitive Studien über Long-/Post-COVID-Patienten_innen bei Erwachsenen ausgewertet und Forschungslücken aufgezeigt. Die Populationen wurden nach Infektionsschwere, Demografie, Kontrollen und psychologischen/biologischen Faktoren kategorisiert. Unter Anwendung der PRISMA-ScR und PICO-Richtlinien wurden 73 Studien (95.600 Probanden), veröffentlicht zwischen Dezember 2019 bis Oktober 2022, analysiert. Die Ergebnisse zeigen, dass bei den meisten Studien Kontrollgruppen fehlten (88%) und unklare kognitive Gesamtergebnisse berichtet wurden (73%). Während exekutive Funktionen (86%) und Aufmerksamkeit (85%) häufig bewertet wurden, gab es nur wenige Längsschnittstudien. Schwankende Stichprobengrößen erschwerten die Analyse zusätzlich. Zu den festgestellten Mängeln gehören willkürliche Stichproben und die unzureichende Verwendung standardisierter kognitiver Testbatterien. Das Fehlen standardisierter Vergleiche und einheitlicher statistischer Methoden sind zusätzliche Defizite.

Schlüsselwörter: Neuropsychologie, Kognition, Long-COVID, Post-COVID, Post-COVID-Syndrom

Introduction

Since the emergence of the severe acute respiratory syndrome Coronavirus type 2 (SARS-CoV-2) and the consequent Coronavirus disease 2019 (COVID-19), a subset of individuals recovering from COVID-19, estimated between 2% and 45%, have exhibited persistent cognitive alterations. These alterations present a significant challenge in understanding the full spectrum of post-COVID-19 cognitive impacts (Chen et al., 2022; Quinn et al., 2022). These changes are recognized by the World Health Organization (WHO) as part of the "U09.9 Post-COVID-19 Condition" (Soriano et al., 2021). Recent guidelines by the Association of the Scientific Medical Societies

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in Germany (Koczulla et al., 2022) and the National Institute for Health and Care Excellence (NICE) define long-/post-COVID-19 syndrome as characterized by symptoms that persist or worsen for more than 12 weeks after infection and significantly impact daily life (Miskowiak et al., 2021; Venkatesan, 2021).

Patients affected by COVID-19 frequently report experiencing cognitive difficulties that persist beyond the acute phase of the infection, irrespective of the severity of the initial infection (Pinzon et al., 2022). These cognitive complaints, often accompanied by concurrent psychiatric and physical symptoms, are typically described with terms such as "brain fog." Although this term effectively conveys the cognitive cloudiness experienced by patients, it lacks the precision required for a definitive clinical diagnosis (Peper & Schott, 2021; Schou et al., 2021). This discrepancy underscores a gap between the subjective experiences of individuals suffering from post-SARS-CoV-2 cognitive impairments and the formal classifications of neuropsychological conditions.

Current reviews and meta-analyses have struggled to provide detailed insights into the evidence of cognitive impairments or map the long-term effects extending beyond 6 months (Jacot de Alcântara et al., 2023; Nalbandian et al., 2023). Factors complicating the understanding of cognitive deficits include fatigue, psychiatric burden, and neurological changes. Furthermore, the existing research is limited, often marked by biased sampling methods, and exhibits considerable heterogeneity – approaching 100 % in some analyses (Chen et al., 2022). This heterogeneity and the scarcity of longitudinal studies highlight the urgent need for gathering and analyzing objective data to identify risk factors predisposing individuals to specific types and levels of cognitive challenges following infection in the long term.

This scoping review provides a comprehensive overview of the neurocognitive outcomes observed in COVID-19 survivors, adhering to stringent criteria. It is important to clarify that the purpose of a scoping review is not to draw definitive conclusions but rather to map the existing research landscape, identifying the types of data available and pinpointing gaps in the current knowledge. This effort aligns with Pollock et al.'s (2023) best-practice recommendations and is of vital importance for neuropsychologists and related professionals. By identifying underexplored areas and articulating existing knowledge gaps, this scoping review endeavors to enhance our understanding of the long-term cognitive sequelae of COVID-19. It aims to serve as a foundational step for future research, guiding the direction of subsequent in-depth studies that can address these gaps and contribute to the development of targeted interventions.

Methods

We preregistered this scoping review on the *Open Science Framework* (https://osf.io/cj2qn) on 22 March 2023, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-SCR; Tricco et al., 2018).

Our search strategy, rooted in the PICO framework (Schardt et al., 2007), aimed to identify studies examining cognitive outcomes (O) in adult patients (P) infected with SARS-CoV-2 who had undergone objective neuropsychological assessments (I). We targeted cognitive domains, including memory, learning, attention, verbal ability, executive function, and visuospatial ability (C). A comprehensive list of the key terms related to cognition and COVID-19, including free-text and MeSH terms, is detailed in Electronic Supplementary Material (ESM 1).

We conducted our primary search on PubMed on 31 October 2022 and included material from 1 December 2019 to 31 October 2022. We excluded reviews, editorials, and nonhuman studies. We manually entered all search results into a spreadsheet, without using automated search or extraction methods. To ensure thoroughness, we conducted manual cross-referencing with two databases and performed additional manual searches of reference lists.

We included studies that (a) were published after 1 December 2019 (the onset of the COVID-19 pandemic), (b) included adult participants (18 years and older), and (c) were available in English or German.

Two authors (CNW and SuS) screened the articles. We excluded studies not meeting our inclusion criteria (see Table 1). The analysis phase involved a comprehensive evaluation of study samples, cognitive tests administered, and additional assessments from related fields like neurology. We focused on describing the cohorts, including sample size, sex distribution, age, types of cognitive testing, inclusion of healthy controls, and recruitment methods. This analysis went beyond mere data collation and involved a critical appraisal of the findings.

Results

Overall Results

The search yielded 790 studies, including 32 obtained through manual searches and reference screenings. We managed the findings using the Zotero Reference Manager. After removing one duplicate, we excluded 710 based on title and abstract reviews. Following a full-text assessment, we excluded 6 more studies, leaving 73 that met the inclusion criteria, as shown in Figure 1.

Table 1. Screening questions for exclusion at two levels of the review process

Level of review	Question	Answer
1 (Title and abstract)	Did an objective neurocognitive assessment (including short cognitive screenings) take place?	No
	Were only subjective self-reported or proxy ratings of cognitive ability used?	Yes
	Were only assessments of health-related quality of life, emotional health employed?	Yes
	Were patients included who had been verifiably infected with the Sars-CoV-2 virus?	No
	Were humans the subject of study?	No
	Were adults 18 and over the subject of study?	No
	Language of article English or German?	No
	Was the date of the article before the pandemic?	Yes
	Is the article a review, study protocol, commentary, case report, letter to the editor, editorial, or personal view?	Yes
	Is the article an RCT, NRCT, test-retest (independent variable)?	Yes
2 (Full article)	Should the article be excluded for any of the reasons listed above?	Yes

Note. NRCT: Nonrandomized controlled trial; RCT: randomized control trial.

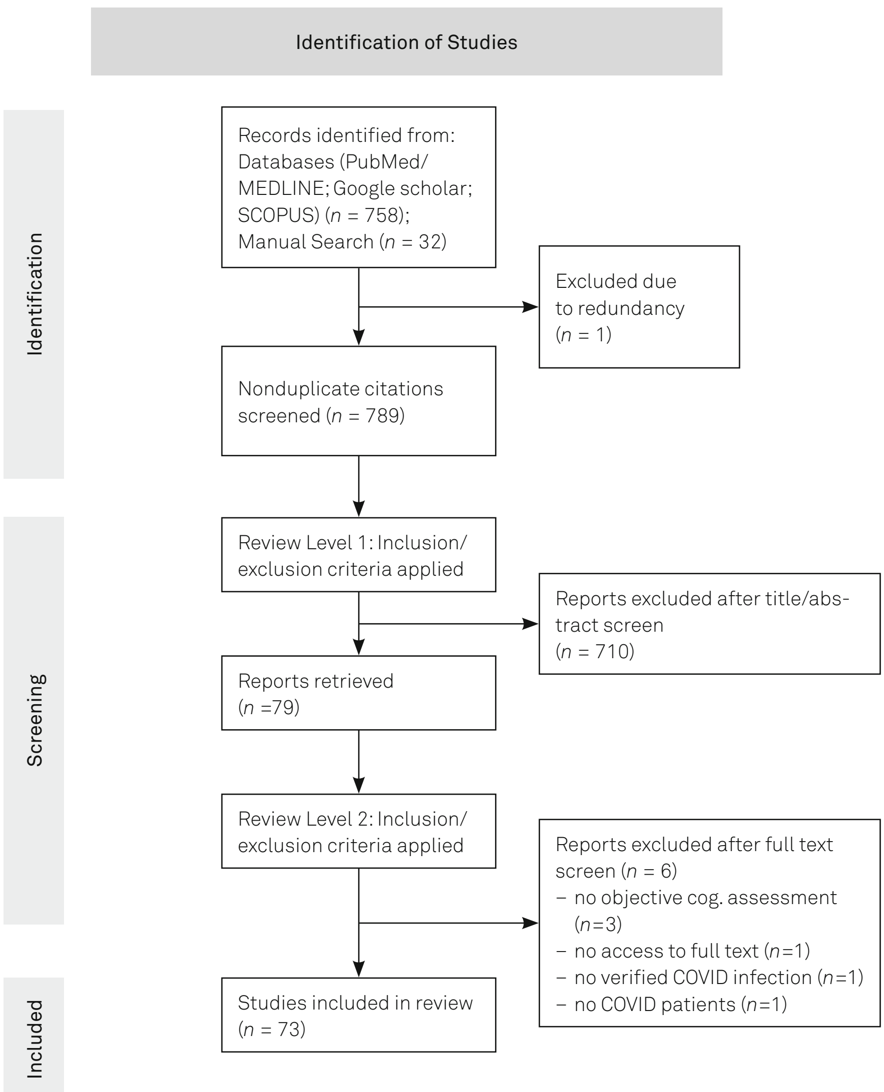

Figure 1. PRISMA flow diagram for inclusion and exclusion of publications.

Characteristics of the Included Studies

The included studies encompassed various regions: 50 from Europe, 3 from the Middle East, 2 from East Asia, and 18 from North, Central, and South America; for additional details, refer to ESM 2.

Regarding the length of follow-up after a SARS-CoV-2 infection, half of the studies did not specify any duration; one-third indicated a follow-up period ranging from 6–12 months; a small proportion (3%) had a follow-up period extending from 12–18 months.

Study Sample and Design

Most studies (86%) focused on clinically-based samples, 10% on population-based, and 4% on occupational-based samples, with some overlaps. Study designs included 40% cross-sectional, 34% cohort, and 12% longitudinal, with no randomized clinical trials or primarily imaging studies. The sample sizes varied from 8 to 84,285, with the largest proportion of studies (34%) having 51–100 participants, followed by 22% that had fewer than 50 participants. 7% had over 1,000 participants. Overall, the gender distribution was approximately 45% males and 55% females.

Regarding cognitive scores, 73% of the studies did not specify the type used. Of the remaining, 8% used unique composite scores, 7% employed domain/subscale scores, and 5% reported global scores from a cognitive test battery. Executive function (EF) and attention were the most assessed domains (86% and 85%, respectively), followed by verbal abilities, including learning and memory (74–77%). Visuospatial abilities were less frequently examined (30%). However, there was little consistency in outcome reporting, with variations in assigning tests to cognitive domains, as few tests exclusively measure a single domain. Control groups were absent in 64% of studies, 23% used actively recruited controls, and 12% relied on historical norms, potentially conflating pandemic and COVID-19 effects, as discussed in section "Healthy Controls Under Pandemic Situation".

Specific COVID-19 Subgroups

Severity of COVID-19/Hospitalization Status

Around half of the studies reviewed (52%) stratified their samples according to initial COVID-19 severity. This stratification followed official guidelines (e.g., the WHO Clinical Progression Scale, see Evans et al., 2021), or the Brescia-COVID Respiratory Severity Scale (Cristillo et al., 2022), the requirement for oxygen and hospitalization (Alemanno et al., 2021), or the number of symptoms during infection (Stavem et al., 2022). Of these studies, 94% relied on purely clinically-based cohorts, which did not allow for further within-study stratification because of their heterogeneity.

Among these, 37% identified a correlation between initial disease severity and cognitive performance, noting lower scores in cognitive screenings or verbal memory tests for more severely affected patients, particularly those hospitalized or in the ICU (Arica-Polat et al., 2022; Becker et al., 2021). Conversely, 61% found no significant cognitive differences among severity groups or between hospitalized and nonhospitalized individuals (see Braga et al., 2022; Crivelli et al., 2021).

Subjective Impairment

In this review, 27% of studies reported rates of subjective cognitive impairment. A quarter of these studies specifically recruited COVID-19 patients presenting with cognitive complaints in clinical settings, inherently limiting the scope of comparison with healthy controls or the broader affected population. Assessment methods varied greatly, from validated questionnaires or simple dichotomous items to no formal assessment at all.

Studies like Blackmon et al. (2022) consistently reported self-identified neurocognitive deficits in early post-COVID-19 patients. However, the longitudinal aspect of cognitive complaints presents a complex picture. For instance, Miskowiak et al. (2021) observed self-reported cognitive problems among 80% 3–4 months postdischarge, whereas Schild et al. (2023) reported persistent problems at 15 months postinfection.

A striking pattern emerged from these studies: Subjective cognitive complaints often did not correlate with objectively measurable impairments.

Objective Impairment

The vast majority of studies (95%) focused on objective cognitive performance in COVID-19 patients, notably those by Arica-Polat et al. (2022) or Ferrucci et al. (2021). Despite extensive investigations, a critical gap identified was the lack of uniform comparative standards, complicating the assessment of cognitive impairment rates.

The timing of assessments varied, and there was a notable lack of consensus in defining cognitive impairment. Thirteen studies (18%) used the Montreal Cognitive Assessment (MoCA) with a cut-off of ≤26 points, while others employed a telephone-based MoCA with different thresholds (≤18 ($n = 2$) to ≤19 ($n = 1$)). Other studies used z-scores as a metric, with cut-offs of ≤-1.5 and ≤–2. Ranges of standard deviations (*SD*) were also utilized as criteria for impairment: –1 *SD* ($n = 2$), –1.5 *SD* ($n = 3$), and –2 *SD* ($n = 5$). The lack of a unified definition for impaired percentile ranks (PR) further contributed to the difficulty in interpreting results. The remaining studies either gave no definition or indicated test-specific cut-offs without a detailed explanation, leaving the interpretation of these thresholds ambiguous.

About 14 % of the studies adopted composite scores to detect impairment (e.g., Andriuta et al., 2022; Crivelli et al., 2021). 8 % of the studies used alternative approaches like exploratory factor analysis. Remarkably, all six studies that utilized these techniques reported either single or multidomain cognitive impairments (e.g., Blackmon et al., 2022; García-Sánchez et al., 2022). These diverse methodological approaches underscore the multifaceted impact of COVID-19 on cognitive functions.

There were prevalent methodological challenges, such as high false-positive rates (reported in 32 %) because of multiple statistical tests and underreporting of power analyses (reported by a mere 8 %), specificity (0 %), and sensitivity (4 %) of tests. Only a few studies addressed these concerns, and even fewer reported on validation or provided effect sizes and confidence intervals. Aspects of symptom or performance validity were seldom reported (5 %). Similarly, reports of effect sizes (19 %) and confidence intervals (18 %) were rare, limiting the reliability of results.

Pre- and Comorbid Conditions

The influence of premorbid conditions on cognitive outcomes after COVID-19 is a critical but underresearched topic. Our review of 12 academic articles indicates that premorbid conditions like hypertension and diabetes may hinder cognitive recovery after COVID-19 (Ferrando et al., 2022), although the link between comorbidity prevalence and cognitive outcomes is not universally supported. For example, Hadad et al. (2022) and Frontera et al. (2021) found no significant association between most pre-existing conditions and cognitive impairment, except in cases of pre-existing dementia.

Studies like Bungenberg et al. (2022) and Ortelli et al. (2020) highlight the impact of fatigue on cognitive performance. Fatigue refers to a pervasive sense of tiredness or exhaustion not relieved by rest, which has been speculated to cause a sense of brain fog or cognitive impairment in some COVID-19 patients. Hartung et al. (2022) revealed that, while fatigue could be predicted by female gender, younger age, pre-COVID-19 neuropsychiatric comorbidity, pre-COVID-19 depression, and the number of acute COVID-19 symptoms, they found no connection between fatigue and cognitive impairments.

Variations in study designs, such as differences in hospitalization status and diagnosis methods, contribute to inconsistent findings. Future research needs to consider these variables to offer reliable patient care and therapy insights.

Assessment Tools

Screening Tools

The most commonly used screening tools across the 22 studies that used them were the MoCA ($n = 14$), followed by the Mini-Mental State Examination (MMSE; $n = 2$), and, for telephone-based screenings, the modified Telephone Interview of Cognitive Status (TICS-m; $n = 3$) and the t-MoCA ($n = 3$), with varying results.

These tools produced a wide range of reported impairment prevalence, varying from 10 % to 80 %, in studies with sample sizes ranging from 8 to 1,077 subjects (e.g., see Evans et al., 2021; Frontera et al., 2021).

The reported pattern of cognitive deficits varied across studies, with EFs, attention, and memory most frequently implicated (see Beaud et al., 2021; Blazhenets et al., 2021; Nersesjan et al., 2022). Both the MoCA and the Frontal Assessment Battery (FAB) were effective in distinguishing cognitive differences between patients and healthy control or normative samples, particularly in EF, attention, and language indices (Hadad et al., 2022; Ortelli et al., 2022).

A consensus emerged that the MoCA was more sensitive than the MMSE in detecting mild cognitive deficits (Aiello, Fiabane, et al., 2022; Bonizzato et al., 2022). However, these studies also noted that screenings might not capture all cognitive deficits, suggesting the need for more comprehensive performance measures (Frontera et al., 2021). A recent review emphasizes the subtle nature of cognitive deficits, which may escape detection by both current screening methodologies and more in-depth neurocognitive assessment tools (Widmann et al., 2023).

Short and Extensive Cognitive Test Batteries

Short cognitive test batteries, lasting 30 minutes or less, were used in 27 studies (37 %). These tests identified significant cognitive impairments in patients, regardless of hospitalization status, across various domains. The deficits included, but were not limited to, EFs and memory, often aligning with findings from screening tools (Hampshire et al., 2021; Hosp et al., 2021).

Several studies found preservation of other cognitive abilities, such as working memory (Hampshire et al., 2021; Poletti et al., 2022). Despite their brevity, these cognitive tests could detect cognitive fatigue and reduced occupational capacity in some individuals who recovered from COVID-19, even up to 1 year postinfection. This was evidenced by longer reaction times or lower performance scores on tasks requiring higher-order cognitive functions such as attention and EFs (Andrei Appelt et al., 2022; Damiano et al., 2022).

A minority of studies additionally incorporated brief evaluations of neuropsychiatric symptoms (e.g., Mazza et al. 2021; Ferrando et al. 2022), demonstrating that depressive symptomatology could independently predict poor neuropsychological test performance.

The results from 24 studies (33 %) that employed extensive neuropsychological test batteries largely reflected the patterns of results from shorter cognitive tests.

Specific Cognitive Areas

Complex Attention

Various methods were employed in the 65 studies on complex attention, including the MoCA, the Trail-Making Test (TMT), and computer-based tests such as the Continuous Performance Test (Becker et al., 2021; Bungenberg et al., 2022). Eleven used computer-based assessments, whereby only one study which used the perception and attention subtest of the Vienna Test System reported effect sizes, which were small and ranged from Cohen's d = .01 to .46 (Delgado-Alonso et al., 2022).

Four studies revealed worse performance on selective and sustained attention tasks in patients compared to controls, indicated by higher omission and error rates and slower reaction times (Delgado-Alonso et al., 2022; Dondaine et al., 2022; García-Sánchez et al., 2022; Zhou et al., 2020). Seven of the 15 studies using screenings found persistent attentional deficits in COVID-recovered individuals, compared with controls or a normative population. The sample sizes for these studies ranged from 46 to 1,077 individuals, with varying effect sizes noted in different studies from d =.63 to 1.80 (García-Grimshaw et al., 2022; Hadad et al., 2022).

Results from 30 studies using paper-pencil tasks like TMT-A and Wechsler Adult Intelligence Scale – IV (WAIS-IV) Coding showed inconsistent findings on attentional deficits, depending on the test and time postinfection (Crivelli et al., 2021; Zhou et al., 2020). These diverse methodologies led to varied conclusions about attentional repercussions in COVID-19 survivors.

Verbal Learning

Verbal learning was a primary focus in 46 (77 %) studies on COVID-19, with 37 using cognitive batteries but only 15 providing concrete outcomes. Initially, Almeria et al. (2020) noted low (3 to 6 %) pathological scores on verbal learning tests, whereas Cian et al. (2022) observed significant differences between COVID-19 patients and healthy controls approximately 20 days postdischarge, using the Rey Auditory Verbal Learning Test (RAVLT).

Subsequent studies like Méndez et al. (2021) and Hosp et al. (2021) reported varying degrees of impairment, with the latter noting the greatest effects. Different cut-off scores led to diverse impairment rates, as seen in studies by Serrano-Castro et al. (2022) and Priftis et al. (2022). Three to 4 months postinfection, Miskowiak et al. (2021) and Vannorsdall et al. (2022) found significant verbal learning deficits, particularly between ICU and non-ICU patients. However, Mattioli et al. (2021) saw no significant disparities at this stage.

Notably, Cecchetti et al. (2022) observed marked improvement in verbal learning 8 months after the initial assessment. These findings highlight the variability in cognitive outcomes post-COVID-19, influenced by methodology and patient demographics.

Verbal Memory and Recall

In our review of 54 studies on verbal memory post-COVID-19, 31 used cognitive test batteries, with over half reporting domain-specific outcomes. *Objective* verbal memory was typically assessed through word-list tasks like the RAVLT, the Hopkins Verbal Learning Test (HVLT), or the Free and Cued Selective Reminding Test (FCSRT) (Mattioli et al., 2021, 2022).

Early postinfection stages showed minimal deficits in verbal memory and recall (Almeria et al., 2020; Dressing et al., 2022), whereas mild to severe impairments emerged 1–4 months later, with studies like Serrano-Castro et al. (2022) reporting 35 % with borderline clinical deficits (z ≤–1) in severe patients. At 6 months postdischarge, severe impairments were noted in studies like Costas-Carrera et al. (2022). At 8 months, Becker et al. (2021) found that 23 % of patients (n = 170) had deficits in the HVLT-recall, especially among hospitalized patients. Ferrucci et al. (2022) reported improvements in long-term verbal memory over 5–12 months but noted it as one of the most affected domains (15 %). Three studies (Hadad et al., 2022; Mattioli et al., 2021; Poletti et al., 2022) found no differences in verbal memory compared to controls.

Notably, *subjectively* reported memory complaints across studies range from 7 % (Mattioli et al., 2021) to 100 % (Bungenberg et al., 2022; Dressing et al., 2022).

Visuospatial Learning and Memory

The 20 studies focusing on visuospatial learning post-COVID-19 mostly used tests like the Rey Complex Figure Test (RCFT), involving multiple trials and delayed retrieval. Sixteen studies provided objective outcomes, with Priftis et al. (2022) showing over 80 % average performance on the RCFT around 80 days postinfection. Serrano-Castro et al. (2022) noted that visuospatial abilities were less affected by cognitive deficits assessed 90 to 120 days postinfection.

Hospitalization appeared to affect performance, with four studies noting lower scores in hospitalized patients (e.g., Arica-Polat et al., 2022; Blackmon et al., 2022). However, Bungenberg et al. (2022) found no differences between hospitalized and nonhospitalized groups regarding delayed recall. Two studies highlighted visual memory as the most impaired domain, with deficits observed in 22–18 % of patients (Dressing et al., 2022; Ferrucci et al., 2022).

Delgado-Alonso et al. (2022) reported COVID-19 patients scored significantly worse than controls on a computerized figural memory test 3 months postinfection. Crivelli et al. (2021) and Cecchetti et al. (2022) supported these findings, although the latter noted this difference diminished at a 10-month follow-up.

Language

Nearly half of the 58 studies that assessed language abilities post-COVID-19 revealed variable impairments in tasks like the Boston Naming Test (BNT) and verbal fluency. Any complications regarding poor foreign language abilities were systematically precluded from the findings. The studies included in the review specifically excluded participants not fluent in the languages of interest.

Of these studies, 26 reported specific outcomes. Early posthospitalization, Almeria et al. (2020) found minimal impairment in naming ability (n = 1). Serrano-Castro et al. (2022) reported naming and verbal fluency were less impaired than memory and attention, with 17 % and 34 % of patients scoring ≤ 1 SD, respectively, 1–4 months postinfection.

Vannorsdall et al. (2022) observed significant impairments in phonemic fluency in post-ICU patients 4 months postdischarge. At 6 months, García-Sánchez et al. (2022) found that 11 % scored below average on the BNT, with verbal fluency impairment affecting 25–30 % of patients. Across various studies, language and EFs were identified as the most affected cognitive domains up to 8 months postinfection (see Andriuta et al., 2022; Braga et al., 2022; Hadad et al., 2022).

Executive Functions

While a substantial number of studies (n = 66) included measures of EFs, only 27 reported specific outcomes. Commonly used assessments included the Stroop task or the Trail Making Test-Part B (TMT-B). Most studies conducted neuropsychological assessments 3–4 months after COVID-19 onset. These investigations indicated that EFs were the most impaired cognitive domain in 25–65 % of patients (n = 29 to n = 226) (Henneghan et al., 2022; Mazza et al., 2021).

Clinical studies show varied effects of COVID-19 on EFs. For instance, Jaywant et al. (2021) found no link between intubation duration and dysexecutive symptoms, while Vannorsdall et al. (2022) observed slowed EFs in ICU-treated patients. Comparisons with healthy controls (n = 4) revealed significant EF impairments in post-COVID-19 patients, with persistent deficits noted 6–10 months after onset. Becker et al. (2021) and others suggest a dysexecutive syndrome, with about 16 % of recovered patients showing EF and phonemic fluency impairments, indicative of frontal brain network deficits (Aiello, Radici et al., 2022; Bonizzato et al., 2022).

General Effects

Psychopathology and Cognition

Research indicates that individuals who survive the acute phase of a COVID-19 infection may still experience an array of negative mental health outcomes, including but not limited to, mood and sleep disorders (Xie et al., 2022). Long-term data on these outcomes, however, remain limited. Our review identified five studies that explicitly reported such outcomes concerning objective cognitive performance.

In an extensive study, Taquet et al. (2022) found considerable variability in the risk patterns for these outcomes after a COVID-19 infection. Most psychiatric disorders showed a return to baseline after 1–2 months postinfection. However, the risk for cognitive impairments, dementia, and psychotic disorders remained elevated at the end of the 2-year follow-up period (Taquet et al., 2022). Sahanic et al. (2023) identified three recovery patterns in COVID-19 survivors, including a group with persistent mental symptoms. Krishnan et al. (2022) noted that preexisting mood symptoms might worsen post-COVID.

These data suggest that, while the risk of mood disorders generally returns to baseline quickly among COVID-19 survivors, a distinct subset remains at increased risk for mood and anxiety disorders as well as cognitive impairment, dementia, and psychotic disorders, particularly those prone to developing post-COVID-19 syndrome (PCS).

Age Effects

The age range in the reviewed studies spanned from 18 to 93 years. Thirteen studies mentioned age effects, but only eight provided specific outcomes. Of these, two found no significant age-related long-term cognitive deficits, while seven noted difficulties in older cohorts. Three studies showed that older age correlated with lower MoCA and verbal memory performance (Alemanno et al., 2021; Larsson et al., 2021). Older age is a known risk factor for survival and cognitive deficits post-COVID-19 (Cheng et al., 2021). However, Evans et al. (2021) observed a different pattern, with middle-aged patients (40–59 years) showing less recovery compared to younger (<30) and older (≥70) patients. In some studies, age was not a significant factor in long-term cognitive deficits post-COVID-19 (Hadad et al., 2022; Hampshire et al., 2021). Age interactions with sex or gender effects are also notable (see below "Sex and Gender Effects").

Sex and Gender Effects

Only four studies directly addressed the role of biological sex in cognitive outcomes post-COVID-19. Women reported more subjective cognitive deficits post-COVID-19 hospitalization than men, possibly because of greater openness about limitations (Bai et al., 2022; Brody, 2000). Female sex was initially considered a risk factor for post-COVID-19 syndrome, with women facing a 1.4 to 3.0 higher risk, including symptoms like "brain fog" (Asadi-Pooya et al., 2022). Neuropsychological test findings vary; some show no sex differences, while others indicate worse male performance on tasks like the Stroop task (Ferrucci et al., 2021; Ollila et al., 2022). Lifespan differences between sexes should be considered in these comparisons (Hirnstein et al., 2019).

Time Effects

Studies exploring the temporal effects on cognitive outcomes post-COVID-19 (*n* = 28), through follow-ups or measures like intubation duration, showed mixed results (Cristillo et al., 2022; Pilotto et al., 2021). While six studies, such as the one by Mattioli et al. (2022), reported no significant time-related cognitive effects, others observed stagnation or decline in cognitive functions postinfection, affecting even young, active individuals (Cristillo et al., 2022; Holdsworth et al., 2022). However, most studies (*n* = 21) noted changes in cognitive performance over time, with none reporting complete cognitive recovery at follow-ups (Cecchetti et al., 2022; Shanley et al., 2022). Acute symptoms were generally reduced 6 months to 1 year postinfection, with both subjective and objective cognitive complaints declining (Del Brutto et al., 2022).

Education and Cognitive Reserve

In six studies, educational background and cognitive reserve (CR) were key to cognitive performance post-COVID-19. Less education (<12 years) was linked to worse outcomes, particularly in attention, EFs, and memory (Ollila et al., 2022; Valdes et al., 2022). Costas-Carrera et al. (2022) found that high CR individuals had superior neuropsychological performance 6 months posthospitalization. Educationally disadvantaged individuals faced higher risks of COVID-19 infection and hospitalization. Higher education correlated with higher vaccination rates and reduced hospitalization risk.

Minority Communities and Effects of Socioeconomic Status

Only infrequently did the studies report ethnic and socioeconomic disparities in cognitive outcomes post-COVID-19, revealing a gap in the literature. Most study participants were white, female, and well-educated, primarily from clinical settings, potentially biasing conclusions. Only Abramoff et al. (2023) in the United States addressed these factors, finding worse outcomes among lower socioeconomic groups and Black individuals (*n* = 324). Broader research consistently shows ethnic and socioeconomic disparities in disease exposure and healthcare access. More comprehensive studies considering these factors are urgently needed for a holistic, global understanding of post-COVID-19 cognitive outcomes (see Cheng et al., 2021; Dragano et al., 2021).

Healthy Controls Under Pandemic Situation

Data regarding the cognitive effects of the pandemic on healthy controls are limited, as most studies focused on patient groups like those with mild cognitive impairment or lacked healthy comparison groups (Baschi et al., 2020). The most frequently reported psychological symptoms were increased anxiety, stress, and depressive symptoms (Dragano et al., 2022). The research findings demonstrated a spectrum of cognitive outcomes in healthy individuals, ranging from negligible differences to noticeable declines in cognitive performance, particularly in memory, attention, and EFs (Manfredini et al., 2023; Pisano et al., 2021). The overall impact of the pandemic extends beyond cognitive function, as measures such as lockdowns and social distancing have compounded mental distress in the general population (Favieri et al., 2021).

Discussion

This scoping review comprises 73 cognitive studies with a collective sample size of 95,600 subjects globally and critically examines the neuropsychological sequelae of SARS-CoV-2. It highlights the multifaceted nature of these effects and underscores methodological diversity, variable study populations, and observation periods. The review stresses the need for extended longitudinal research for a deeper understanding of the implications of COVID-19 beyond the initial 6 months postinfection. A notable gap is the lack of standardized reporting in cognitive assessments, which hampers the comparability and reliability of neuropsychological research findings.

Furthermore, the current review also shows that a standard of outcome reporting needs a clear characterization of recruited patients, actively recruited healthy controls, and clear timelines. This is alarming since national policies necessarily rely on the circumscribed set of relatively biased and largely short-term studies with often unreliable outcomes. Research needs to account for various demographics, socioeconomic statuses, and cultural backgrounds to make findings more representative and applicable to diverse populations. In addition, overreliance on clinical samples limits our understanding of long-term effects, since "post-COVID-19" (i.e., the recovery phase after COVID-19) and PCS may be inadvertently lumped together (Nicotra et al., 2023).

We need an accounting of how the pandemic itself and associated societal changes, such as increased remote work or social isolation, have also influenced cognitive and mental health. Now that COVID-19 is endemic, we might expect the long-term outcomes of current and future variants to have less consequence for the population as a whole.

The review identifies impairments in attention and executive functions, indicating potential disruptions in the fronto-parietal network (Bendella et al., 2023), especially in populations requiring these functions in daily life, like middle-aged individuals. Furthermore, the review discusses how these impairments may intertwine with psychological burden, sleep disturbances, and fatigue, often overlooked in clinical populations. Note that these cognitive domains require more deliberate and careful examination than is generally possible in cognitive screenings.

While potentially easier to assess, the effects on language and verbal fluency present a less consistent picture, warranting further investigation (Bertuccelli et al., 2023; Crivelli et al., 2022). Such cognitive deficits tend to be mild and show a diminishing trajectory over time (Cecchetti et al., 2022). The findings of this review agree with newer research, such as that of Zhao et al. (2023), who identified four clusters, including the following impairment gradations: without or mild (44 %), moderate and physical (30 %), moderate and cognitive and mental health (10 %), and severe group (16 %).

A particularly salient observation is the heightened cognitive impairment and, particularly, delayed recall observed among hospitalized and ICU patients, which suggests a correlation between the severity of the initial illness and subsequent cognitive outcomes, though such correlations exhibit considerable variability (Klinkhammer et al., 2023). The review also highlights a frequent disconnect between self-reported cognitive difficulties and objective impairments, with cognitive screenings often inadequate in capturing the complexity of these deficits (Goldstein et al., 2023).

Psychiatric distress emerges as a common symptom and distinct risk factor for months postinfection (Taquet et al., 2022), with additional risks including low education and pre-existing conditions (Ceban et al., 2023). The information provided here is valuable as researchers investigate pathophysiologies underlying PCS, including direct and indirect immune and inflammatory effects, virus variants, genetics, critical illness, biomarkers, and vaccination effects (Ceban et al., 2023).

It would not be a complete review without once more drawing attention to the distinction between the concept of "brain fog" as a subjectively lived experience and "cognitive impairments," which can be objectively measured by a neuropsychologist, something crucial to assess to understand the patient's condition and create appropriate interventions. Further, understanding the nature of cognitive impairment after COVID-19 infection requires studies that adequately and equally address objective cognitive performance and known or surmised factors that may worsen cognitive performance, such as sleep disorders, anxiety, and fatigue. Additionally, we need longitudinal studies with a dual focus on neuropsychological assessment and intervention.

The review elucidates the individual-specific nature of cognitive deficits post-COVID-19, emphasizing the complexity and diversity of these impairments. Additionally, it identifies a significant gap in our understanding of the cognitive impact of the pandemic on healthy individuals, an issue that merits urgent attention. While the pandemic has induced mental distress affecting broad populations and negatively impacting cognitive functions, its comprehensive effects require further examination.

Limitations

This scoping review faces several limitations that warrant consideration. Firstly, the heterogeneity in methodologies across the included studies limits the generalizability of our findings. Key unknowns persist, such as the specific timelines for cognitive recovery in the general population and the duration of various cognitive deficits postrecovery. Furthermore, how outcomes observed in clinical settings translate to the general recovery process remains unclear, especially considering the ongoing research into the broad spectrum of post-COVID-19 symptoms.

Another significant limitation is the temporal scope of the literature search. The rapidly evolving nature of research into the neurocognitive consequences of COVID-19 means that newer studies could challenge or overturn the conclusions drawn here. Additionally, excluding studies published in languages other than English and German narrows the breadth of our analysis, potentially overlooking valuable insights from regions such as Africa, which remain largely unaccounted for.

A notable gap in the current body of literature is the lack of substantial data on social cognition, a critical domain within the DSM-5, which points to an urgent need for further research in this area. Moreover, the absence of findings related to postvaccination cognitive outcomes represents another crucial avenue for future study, particularly in understanding the long-term impact of COVID-19 vaccines on cognitive health.

Relevance for Practice

Interdisciplinary, methodologically sound research is crucial to deepening our understanding of the long-term phenotypes associated with post-COVID-19 condition. Research endeavors must adopt longitudinal designs with regular follow-ups. Adherence to best practices in neuropsychology is essential across all phases: from study conceptualization to selection of metrics and statistical methodologies. Existing inquiries into the cognitive sequelae of COVID-19 exhibit discernible limitations regarding design integrity, statistical power, and methodological rigor, with a conspicuous absence of neuropsychological expertise (Becker et al., 2023).

Active recruitment of healthy controls, alongside comprehensive neuropsychological assessments, is essential, particularly when cognition is a primary outcome measure. COVID-19 affects cognitive domains differently among individuals, emphasizing the necessity for targeted, large-scale studies focusing on specific risk groups and symptomatic clusters. These clusters could focus on post-COVID-19 subtypes such as chronic fatigue/postexertional malaise, and post-ICU phenomena (Gloeckl et al., 2023) or based on the severity of symptoms (Kisiel et al., 2023). This is crucial for developing effective patient care strategies and interventions. It is also essential to take the needs of patients seriously and offer appropriate neuropsychological assessment after initial screening (Koterba et al. 2024). Professional neuropsychologists and cognitive researchers can provide specific expertise for this. Considering the broader societal impact of the pandemic, it is necessary to reevaluate assumptions about post-COVID-19 cognitive health, particularly compared to historical norms. Lastly, assessment tools must be inclusive and account for diverse demographics and societal factors affecting infection risks and long-term effects (Dragano et al., 2022). Further detailed, longitudinal neuropsychological assessments are essential to grasp the full scope of aftermath of COVID-19 among specific groups and unravel associated biological and psychological mechanisms.

Electronic Supplementary Material

The electronic supplementary material (ESM) is available together with the online version of the article at https://doi.org/10.1024/1016-264X/a000395

ESM 1. Search strings (Tables).

ESM 2. Overview of studies (Tables).

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ORCID
Susan Seibert
https://orcid.org/0000-0003-4736-4488
Alexander Hanke
https://orcid.org/0000-0001-5766-4148
Michelle Wieberneit
https://orcid.org/0000-0002-2935-3446
Lucie Bieler
https://orcid.org/0000-0002-1216-6046
Robin Gräfenkämper
https://orcid.org/0000-0001-9649-8373
Katrin Klatt
https://orcid.org/0000-0001-5651-7357
Catherine Nichols Widmann
https://orcid.org/0000-0001-8889-8385

Catherine Nichols Widmann
University of Bonn Medical Center
Center for Neurology
Venusberg-Campus 1/C80
53127 Bonn
Germany

catherine.widmann@ukbonn.de