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Cognition and Long COVID. Review.

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Abstract

Purpose of review: Provide an overview of current knowledge regarding cognitive issues in patients with long COVID, also termed brain fog or cognitive COVID.

Recent findings: Subjective cognitive symptoms in long COVID patients are common but often go undetected by traditional standardised cognitive test batteries. This discrepancy poses a major clinical and societal problem, given the prevalence, protracted course and impact of cognitive COVID on work functioning. New, online assessment methods for cognitive function are feasible and corroborate subjective self-report symptoms, finding executive function impairments in cognitive COVID. As vaccination protects against brain fog and not against anxiety and depression in long COVID, brain fog can be seen as a core symptom of long COVID, concerning executive functioning, and a direct effect of neurotropic viral brain infiltration. Depression and anxiety are comorbid conditions due to indirect factors associated with the pandemic, such as increased social isolation and loss of work.

Summary: Ongoing vaccination programs should not only target the elderly, but also working-age people. Online cognitive assessment batteries are recommended for assessment and treatment monitoring in long COVID. Integrated care is recommended given the high rate of multimorbidity. Future research might explore the effects of antiviral medication, modulation of the immune response, and GLP-1 agonists in long COVID.

Introduction

As many as 45% of COVID-19 survivors, regardless of hospitalisation status, may have a range of unresolved symptoms at 4 months [1]. This is called long COVID or post-COVID-19 condition. Coded as RA02 Post COVID-19 condition in ICD-11, it occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis [2]. Long COVID is a multisystem condition that can include neuropsychiatric symptoms like headache, insomnia, depression, sleep apnea, paresthesia, pain and fatigue, as well as brain fog [3,4]. Brain fog is a core symptom reported by long-COVID patients with a pervasive impact on daily life, such as normal daily activities, return to work, or maintaining social relationships [5].

Brain fog is a colloquial term that originated from patient discussions of their symptoms and has been adopted in medical literature. It can occur in many medical conditions and may present with symptoms such as poor concentration, feeling confused, thinking more slowly than usual, fuzzy thoughts, forgetfulness, lost words, and mental fatigue, as well as dissociative phenomena [6,7]. Cognitive dysfunction in long COVID may include impaired memory, attention and executive functions as well as decreased verbal fluency and reduced processing speed [8].

In terms of ICD-11 codes, brain fog is not listed as a mental disorder but under Chapter 21: Symptoms, signs or clinical findings, not elsewhere classified, subchapter *mental or behavioural symptoms, signs or clinical findings, involving consciousness (MB20)* in case of clouding of consciousness; *involving cognition (MB21)* in case of cognitive function issues like concentration, word finding, and orientation issues; and *involving motivation or energy (MB22)* in case of easy fatigability [2].

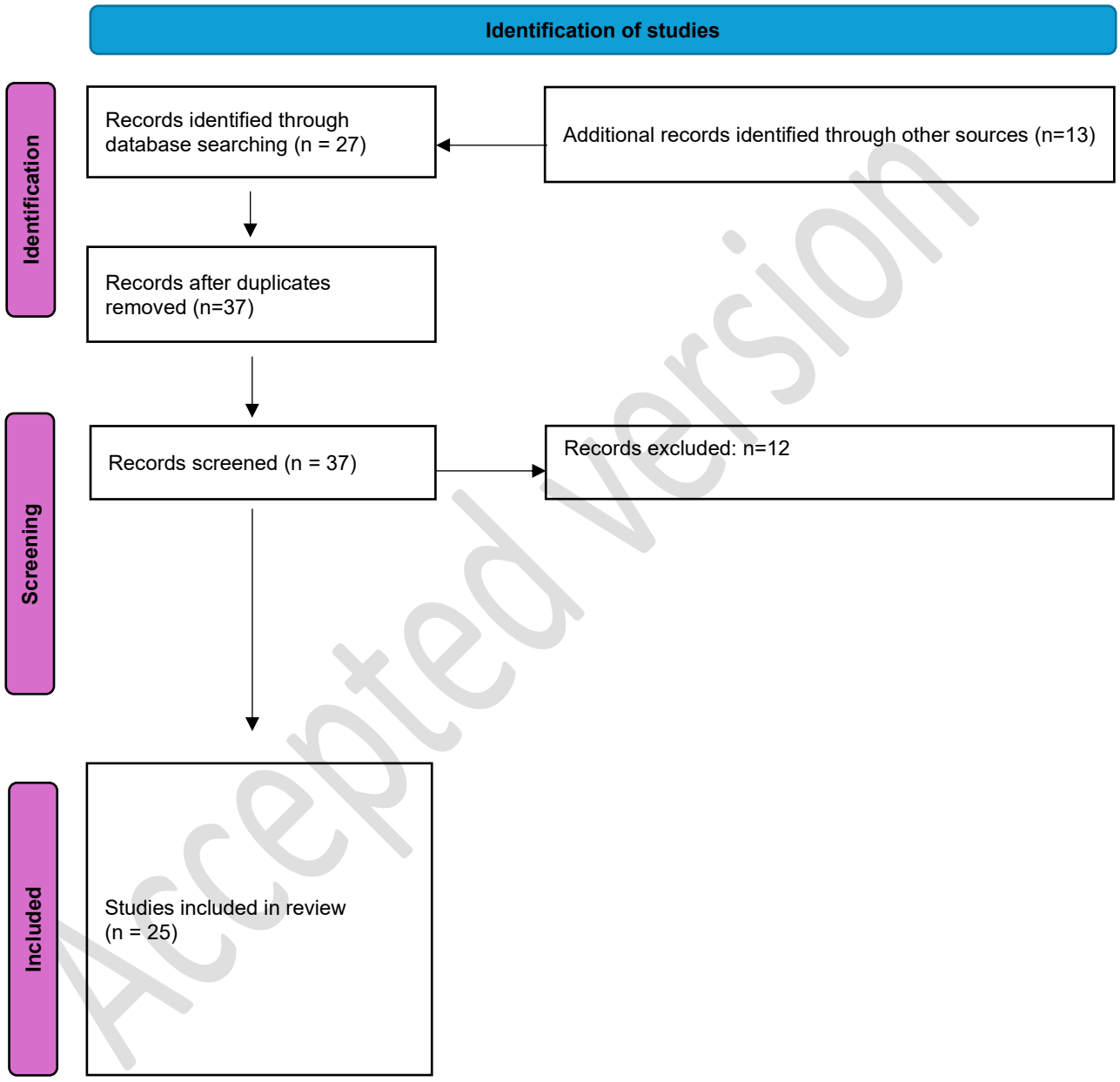
Research exploring the full range of composites of brain fog and specifics of cognitive dysfunction in long COVID by method of neuropsychological assessments is scarce and most studies reporting these symptoms are based on self-report. This review provides an overview of emerging knowledge on cognitive issues in patients with long COVID, also known as cognitive COVID, including their phenomenology, assessment, comorbidities, risk and protective factors, and suggestions for treatment and prevention.

Methods

A PubMed search was conducted to identify relevant literature on long COVID, cognitive symptoms, and brain fog published between 2022 and 2025. The search was conducted in October 2025 with the search terms "long COVID" OR “PASC” AND "brain fog" AND "cognitive symptoms". This yielded 27 hits. Also, experts were approached to indicate recent publications that might be relevant. This yielded 13 more hits. After duplicates removed, selected studies should focus on brain fog or cognitive symptoms in long COVID and report on their definition or phenomenology, risk or protective factors, prevention or treatment. Studies were excluded if they

did not consider cognitive function in long COVID or did not provide cognitive function outcome data. This yielded 25 selected studies [7,9,10,11,12,13,14,16,17,18,19,20,21,22,23,24,25,26, 27,28,29,30,35,37,39]. A flowchart is provided in Figure 1.

Figure 1. Flowchart selection of studies according to PRISMA statement [43].



Results

Phenomenology of cognitive symptoms in long COVID

Six studies [9,10,11,12,13,14] reported outcomes on the nature of cognitive symptoms as reflected by well-known neuropsychological tests, as shown in Table 1. The other studies are discussed throughout the article.

Table 1. Outcomes of cognitive tests in long COVID patients (N = 455)

Authors, year	Study design, population	Cognitive tests	Outcomes	Conclusion
Uncontrolled studies N = 280				
Krishnan et al. 2022 [9] USA	Cross-sectional. 20 Patients seropositive confirmed COVID-19 and persistent cognitive complaints without neurological or cardiovascular comorbidity. On average 5.5 months after infection.	Wechsler Memory Scale- IV (WMS-IV) Logical Memory, Rey Auditory Verbal Learning Test, and Brief Visuospatial Memory Test-Revised. Reading subtest from the Wide Range Achievement Test-IV Boston Naming Test-Second edition, lexical and semantic verbal fluencies. Judgment of Line Orientation. Digit Span, Matrix Reasoning, and Similarities subtests from the Wechsler Adult Intelligence Scale-IV (WAIS-IV; DKEFS Color-Word Interference. Trail Making Test, Wisconsin Card Sorting Test, and Conners Continuous Performance Test-3. Coding and Symbol Search subtests from the WAIS-IV and the Symbol Digit Modalities Test.	Twenty percent of patients or more showed impairment on the following tests: Trail Making Test A, Continuous Performance Test (Hit RT, Hit RT ISI Change, and Hit RT Block Change), Wisconsin Card Sorting Test Trials to First Category, and Brief Visuospatial Memory Test-Revised Recognition Discrimination.	Impairment in attention, processing speed, and executive functioning measures such as difficulty in abstract thinking, problem-solving and cognitive flexibility.
Ruzicka et al. 2024 [10] Germany	Cross-sectional. 78 Patients with a confirmed or highly suspected PC condition according to WHO definition. Median 183 days after infection.	Vocabulary tests (VT). The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Self-report questionnaire.	Self-report 80.3% impaired alertness, 68.6% confusion, 64.4% memory impairment, 35.1% of speech disorders. Intermediate/severe impairment of daily life in > 50%. None of the neurocognitive tests were significantly impaired EXCEPT • the TMT part A and B, that showed slight impairment across both tests (median ASV for TMT-A: 94.0, p=0.002; median ASV for TMT-B: 95.0, p=0.042); • the LNS (median ASV: 90.0, p<0.001) • and the d2-R section examining concentration capacity (d2-R—CC; median ASV: 88.0, p<0.001) • The sections List Recognition (LRg), Story Recall (SR), Figure Copy (FC), Digit Span	Overall, neurocognitive tests could confirm mild impairment in some but not all LC patients with cognitive symptoms. The cognitive domains most affected were working memory, attention, and concentration. **Nonetheless, pathological thresholds were exceeded only in few cases. Neurocognitive performance did not differ significantly between patients complaining of severe (n=26) versus non-severe (n=52) CS.** Patients reporting high severity of CS scored worse in the PHQ-9, FSS, WHOQOL-BREF, more often reported

			(DS) and Coding/Symbol-Number-Test (SNT). **However, the pathologic threshold (ASV of 85) was not underrun in any of the assessments by the median values to fall below the pathologic benchmark.**	impaired sleep, and had higher prevalence of psychiatric diagnoses. **CS in LC cannot be objectified by routine medical assessments such as neurocognitive testing (NCT) or brain imaging.** **Symptom severity of CS cannot be objectified by NCT.** Higher severity of CS is associated with worse patient reported outcomes such as anxiety, depression, sleep problems and Quality of Life.
Yamashita et al., 2025 [11] **USA**	Retrospective analysis of electronic medical record (EMR) clinical and test data. **182** People infected with SARS-Cov-2. On average 293 days post- infection.	Montreal Cognitive Assessment (version 8.2) (MoCA) and Trail Making Test-B (OTMT-B).	**94% of patients reported cognitive difficulties at their initial Long COVID clinic visit.** Long COVID-associated cognitive complaints included difficulties with short-term memory, attention, reading, and multi-tasking. Patients often referred to these symptoms as "brain fog." **However only 30% had abnormal MOCA tests.**	**Performance on standardized cognitive screening tests may not be consistent with frequently reported cognitive complaints in Long COVID patients.** Non-White race, less than 12 years of education, and a history of severe acute infection were associated with abnormal scores in the MoCA and the OTMT-B.
Controlled studies **N = 175**				
Rizzi et al., 2024 [12] **Switzerland**	Case-control design. **N=38** 14 People with serologically confirmed infection. 24 seronegative controls	CERAD 10 words list learning test. Trail Making test part A and B (TMT). Stroop test. Clock drawing test and bespoke standard questions about spatial-temporal orientation.	Cases obtained considerably lower scores in attention ($\beta = 0.428$, $p = 0.008$), executive functions ($\beta = 0.326$, $p = 0.046$), and memory tasks ($\beta = -0.367$, $p = 0.023$).	**Long COVID was associated with cognitive impairment in memory, attention, and executive functions in older adults, compared to people who were infected but did not develop Long COVID.**
Lawrence et al., 2025 [13] **USA**	Case-control design. **N=20** 10 LC patients. 10 controls without LC after infection.	WAIS-IV digit span. Symbol Digit Modalities Test (SDMT) Letter Fluency (COWAT) Semantic Fluency Rey-Osterrieth Complex Figure Test	Only letter fluency was significantly lower in LC patients.	**In LC patients reporting cognitive symptoms, robust neurocognitive testing showed normal attention, processing speed, visual planning, learning and memory, executive functioning. Language**

	6 months after infection.	California Verbal Learning Test (CVLT-II) Trail Making Test (TMT) Tower of London		(letter fluency) was significantly impaired in LC.
Cataldo et al., 2025 [14] Argentina	Cross-sectional study. N=137 109 LC patients. 28 healthy controls. Two years post infection.	Trail Making Test Parts A (TMT-A) and B (TMT-B) Stroop Color-Word Interference test includes Digit Span Forward (DGS-F) and Backward (DGS-B) tasks	21.1% of the LC group showed DGS-F impaired performance. 10–15% of the LC group showed impaired performance on the TMT-A, DGS-B, STROOP W, STROOP C and MoCA. However, similar impairment patterns were observed in the control group and no significant differences were found in terms of performance and net scores between the two groups.	Long COVID patients self- reported persistent cognitive symptoms such as memory problems and brain fog, with higher levels of fatigue and reduced quality of life compared to controls. However, despite such subjective cognitive complaints, cognitive tests did not reveal significant differences between groups, except for the TMT-A (p=0.05).

Legend: LC = long COVID. NCT = Neurocognitive tests. Neuropsychological test scores were compared to normalised scales of the local population and were considered to be "impaired" if they fell at least 1.5 SD below the mean. A loss of more than four points on the MoCA 8.2 was classified as 'abnormal' based on published literature, with one additional point being granted to patients with less than or equal to 12years of education. OTMT-B was considered abnormal if <25th percentile score.

Memory measures: Wechsler Memory Scale- IV (WMS-IV) Logical Memory, Rey Auditory Verbal Learning Test, Rey-Osterrieth Complex Figure Test and Brief Visuospatial Memory Test-Revised. CERAD 10 words list learning test. California Verbal Learning Test (CVLT-II). The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) which measures the following cognitive performance areas: Immediate memory: List Learning (LL), Memorized Words in the 4th Round (MW4), Story Memory (SM) Delayed memory: List Recall (LR), List Recognition (LRg), Story Recall (SR), Figure Recall (FR). Montreal Cognitive Assessment (MoCA): a quick, 10-minute screening tool used by healthcare professionals to detect mild cognitive impairment (MCI) by testing domains like memory, attention, executive function, language, and visuospatial skills.

Language tests: Reading subtest from the Wide Range Achievement Test-IV, Boston Naming Test-Second edition, Picture Naming (PN) and lexical and semantic verbal fluencies. Semantic and phonemic verbal fluency tasks (e.g. Number of words in 1 min). Letter fluency (COWAT). Verbal intelligence and estimate of the premorbid intelligence quotient (IQ): Vocabulary tests (VT).

Visuospatial testing: Judgment of Line Orientation. Clock drawing test and bespoke standard questions about spatial-temporal orientation. Figure Copy (FC).

Attention and executive functioning measures: Digit Span Forward (DGS-F) and Backward (DGS-B) tasks to evaluate verbal attention span and working memory, Matrix Reasoning, and Similarities subtests from the Wechsler Adult Intelligence Scale-IV (WAIS-IV, DKEFS Color-Word Interference, Trail Making Test, Wisconsin Card Sorting Test, and Conners Continuous Performance Test-3. Shortened version of the Stroop test. Letter Fluency (COWAT). Tower of London test. Stroop Color Word test to measure cognitive flexibility, cognitive inhibition, and information processing speed including word (STROOP W), colour (STROOP C), word-colour (STROOP WC) and interference (STROOP interf) tests. Coding/Symbol-Number-Test (SNT).

Visuomotor processing speed, cognitive flexibility and working memory: Coding and Symbol Search subtests from the WAIS-IV and the Symbol Digit Modalities Test; Trail Making Test. part A (TMT-A) and part B (TMT-B). CERAD 10 words list learning test.

Three of the six studies that reported outcomes of neurocognitive tests lacked controls [9,10,11]. They reported on a total of 280 patients with long COVID, two at approximately 6 months after infection [9,10], and one at approximately 9 ½ months [11]. The findings were rather similar for both timeframes. Compared to normalised population scores, the smallest study (N=20) reported impairment in attention, processing speed, and executive functioning measures [9]. However, the other two studies reported no significant difference from normal population scores or between patients complaining of severe versus non-severe cognitive symptoms [10,11]. The largest study suggested that performance on standardised cognitive screening tests may not align with the frequently reported cognitive complaints in Long COVID patients [11]. Higher severity of cognitive symptoms is, however, associated with worse patient-reported outcomes such as anxiety, depression, functional somatic syndromes and sleep problems [11]. The other three studies included a control group: two compared long COVID patients with healthy controls [12,14], and the other with patients who did not develop long COVID after SARS-CoV-2 infection [13]. They reported on a total of 195 patients with long COVID, one at approximately 6 months after infection [13], one at two years post-infection [14], and one with an unspecified time frame [12]. One study found cognitive impairment in memory, attention, and executive functions in older adults with long COVID, compared to people who were infected but did not develop long COVID [12]. The smallest study reported normal attention, processing speed, visual planning, learning and memory, and executive functioning, with only language (letter fluency) significantly impaired in Long COVID, compared with people who did not develop Long COVID after SARS-CoV-2 infection [13]. The largest controlled study found that despite subjective cognitive complaints, cognitive tests did not reveal significant differences between long COVID patients and healthy controls, except for the Trail Making Test-A ($p = 0.05$) [14].

From these studies, it is evident that subjective cognitive symptoms often cannot be confirmed with neurocognitive tests and can be associated with psychiatric comorbidity. In older adults with long COVID, significant impairment in memory, attention, and executive functions can be confirmed with neurocognitive tests. In adults, language (letter fluency) is significantly impaired in long COVID, and the Trail Making Test. which indicates impaired visuomotor processing speed, cognitive flexibility, and working memory. Furthermore, non-White race, less than 12 years of education, and a history of severe acute infection are associated with abnormal scores in the MoCA and the OTMT-B [11].

Other diagnostic tests for brain fog in long COVID

Given the finding that subjective cognitive symptoms, such as brain fog, often cannot be substantiated by standard cognitive tests, as shown in Table 1, there remains a need to explore them systematically and validly. A new and promising development is online cognitive testing that requires no in-person assistance and is shorter and more flexible than traditional cognitive tests, such as Cognitron [15]. It uses validated cognitive and neuropsychological tests and has been applied to people with long COVID, where it shows cognitive deficits in those reporting brain fog, especially in the executive functioning domain [16,17,18,19]. Another online cognitive assessment platform, accessible on a smartphone, focuses on memory function and was found to be feasible and valid for use in people with long COVID [20,44]. It shows results similar to another study exploring the course of memory problems in brain fog using self-report [21]. Given

that such tests have demonstrated greater sensitivity to cognitive differences in people with long COVID than traditional assessment scales, to subtle changes that occur in the early and prodromal stages of neurological conditions, their application in clinical practice seems warranted. They could support the diagnosis and monitoring of treatment outcomes.

Another method to explore cognitive function differently from traditional, extensive assistant-supported cognitive tests might be to apply the Mini Mental State Examination (MMSE). This well-known test has been shown to be feasible in patients with acute COVID who are no longer in the intensive care unit. It can discern difficulties in the attention and calculation domain, the memory domain, the temporal orientation and the language domain [22]. It can be administered by any clinician in contact with the patient and takes approximately 10 minutes. However, the feasibility or validity of assessing subjective cognitive symptoms with the MMSE has not been explored in long COVID.

So far, no validated questionnaires existed to explore self-reported subjective cognitive symptoms in long COVID. However, the newly developed self-report Brief Brain Fog Scale (BBFS) for post-COVID cognitive symptoms assesses whether a person experiences forgetfulness, difficulty thinking, difficulty focusing, cloudiness, and difficulty finding words or communicating. The scale demonstrated strong internal consistency, structural validity, and measurement precision [23]. Its clinical relevance still has to be evaluated.

Regarding brain imaging, studies report subtle white matter abnormalities, decreased grey matter volume, and reduced global brain size in long COVID [24,25,26]. One study found a statistically significant depletion of Cortical Grey Matter in long COVID patients with neurological symptoms [27], but another study showed no significant difference in thickness and volume of regions represented by the composite image-derived phenotype (IDP) z-scores between patients with NeuroCOVID and COVID [18]. Hence, so far, there is no support for the clinical diagnostic value of brain imaging for detecting cognitive symptomatology in long COVID patients [10].

Comorbidity with and difference from anxiety and depression

A systematic review and meta-analysis explored the prevalence of brain fog and mental health conditions in 17 studies reporting on 41,249 long COVID patients. The combined prevalence of mental health conditions such as anxiety and depression, and brain fog, was 20·4% (95% CI 11·1%-34·4%). The odds of mental health conditions and brain fog increased over time, which emphasises the need for preventive interventions and treatments. Odds of brain fog significantly decreased with increasing vaccination rates (p = ·000), but this was not the case for anxiety and depression [28]. This suggests that brain fog is a core symptom of long COVID and has a different etiological mechanism than mental health conditions, such as anxiety and depression.

Etiological factors for cognitive symptoms in long COVID

An ongoing pathophysiological process may contribute to cognitive symptoms in Long COVID. This is supported by virus RNA having been found in a brain autopsy of a post-COVID patient as late as 230 days following symptom onset [29], which suggests invasion of the central nervous system, causing neuroinflammation and ongoing neuromodulation. This would not be an unknown phenomenon. An adverse effect of respiratory virus infection on cognitive function,

accompanied by brain changes, has been documented during epidemics such as the 1918 influenza, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and the COVID-19 epidemic [30,31]. Furthermore, other viruses also affect the brain with a negative impact on cognitive function, notably the herpes zoster virus, where shingles vaccination has been found to be associated with lower incidence of Alzheimer [32]; Epstein-Barr virus, which damages the blood-brain barrier – a known cause of neurocognitive impairment [33], and possibly Cytomegalovirus[34]. An autoimmune response may play a role [18], and reactivation of latent viruses such as Herpes and Epstein-Barr Virus may also trigger neuropathology in long COVID [35]. The current evidence suggests cognitive problems in long COVID can be seen as a direct effect of neurotropic viral brain infiltration, associated with virus activity or their aftermath in the brain, influenced by factors like ethnicity, gender, severity of the acute infection, whether there is comorbid obesity [36], diabetes type 2 or hypertension, and characteristics of one's immune system such as a tendency to autoimmune disease. Over time, such symptoms may be aggravated by accompanying symptoms of mental health conditions such as depression and anxiety disorder, caused by social isolation and other impacts of the pandemic.

Impact on work functioning

A study exploring self-reported brain fog in a sample of 1,266 previously hospitalised patients due to COVID-19 during the first wave of the pandemic showed that it can persist over a period of 8 to 18 months post-COVID. Defined as self-perception of sluggish or fuzzy thinking, its prevalence fluctuated around 8%-5%; perceived memory loss, around 14.9%-12%. Concentration loss decreased from 6.9% at 8 months to 2.6% at 18 months [21]. Such prevalence rates and the finding that symptoms persist even at 18 months post-infection can affect work functioning. Moreover, another study based on a nonprobability internet population-based survey of 50-state US respondents aged 18 to 69 years conducted between February 2021 and July 2022 found higher rates. Among 2236 people who reported long COVID symptoms, 45.9% reported either brain fog or impaired memory. Long COVID was associated with a lower likelihood of working full-time (adjusted OR, 0.84 [95% CI, 0.74-0.96]) and a higher likelihood of unemployment (adjusted OR, 1.23 [95% CI, 1.02-1.48]). The presence of any cognitive symptom was associated with a lower likelihood of working full-time (adjusted OR, 0.75 [95% CI, 0.59-0.84]) [37]. This shows the urgency to prioritise the prevention and treatment of long COVID, not only in the elderly, but also in people of working age.

Prevention, management and policy implications

The NICE long COVID guideline emphasises the importance of screening for and treating cognitive symptoms. It recommends using a validated screener to assess such cognitive symptoms, without specifying which tests are available [38]. Given the extent and duration of cognitive COVID and its impact on workforce participation, this is certainly warranted, and the online tests discussed above may be recommended.

Regarding prevention, the reduced risk of brain fog associated with vaccination emphasises the need for ongoing vaccination programs that should not only target the elderly, but also working-age people. Training of cognitive function may improve execution speed, warranting further exploration of this treatment option [39]. Given the multimorbidity frequently encountered in long

COVID, treatment provision should integrate general, mental health, and revalidation services, as well as primary care, and include multidisciplinary diagnostic assessments, personalised treatment, and long-term follow-up to monitor progress and re-entrance into the workforce [40,41,42].

In future research, the effects of antiviral medication, immune-modulating medication, and GLP-1 agonists in long COVID may be explored - the latter given their effects on adiposity, a risk factor for long COVID and cognitive decline [36]. Furthermore, revalidation programs aimed at return to work, with a specific focus on cognitive problems, should be developed and evaluated in research.

Conclusion

Long COVID occurs frequently, and a main symptom is so-called brain fog. Brain fog is a much more widely defined concept than cognitive impairments identified by traditional cognitive test batteries. This review found only 6 studies, half of them uncontrolled, exploring this, in a total of 455 long COVID patients reporting cognitive symptoms. Performance on traditional cognitive tests is often inconsistent with subjective cognitive symptoms in patients with long COVID. This discrepancy between subjective symptoms and test results poses a major clinical problem, given the protracted course and the impact of cognitive COVID on work functioning. However, new online assessment methods for cognitive function corroborate subjective self-report symptoms, identify executive function impairments in cognitive COVID, and are feasible for long COVID. As vaccination protects against brain fog in long COVID, and not against anxiety and depression, this can be seen as a core symptom of long COVID, affecting executive functioning, and a direct effect of neurotropic viral brain infiltration and long-term neuromodulation. Depression and anxiety are comorbid conditions due to indirect factors associated with the pandemic, such as increased social isolation, including work loss and other impacts of the pandemic. Regarding prevention, the reduced risk of brain fog associated with vaccination emphasises the need for ongoing vaccination programs that should not only target the elderly, but also working-age people. Online cognitive assessment batteries are recommended for assessment and treatment monitoring in long COVID. Training of cognitive function may improve execution speed, warranting further exploration of this treatment option. Integrated care is recommended given the high rate of multimorbidity in long COVID. Future research should examine the effects of antiviral medications, immune response modulation, and GLP-1 agonists on cognitive function in long COVID.

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    - Large meta-analysis of long COVID epidemiological studies that substantiates the notion that brain fog is a core symptom of long COVID and has a different etiological mechanism than mental health conditions such as anxiety and depression.

Declarations

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Conflict of Interest

Dr. van der Feltz-Cornelis declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

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