Title

Memory alterations after COVID-19 infection: A systematic review

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Memory alterations in long-COVID: A systematic review

Abstract

SARS-CoV-2 infection has a wide range of both acute and long-term symptoms. Memory alterations have been frequently reported in studies that explore cognition. The main objective of the systematic review is to update and further analyze the existing evidence of objective memory impairments in long-COVID-19 considering sample and study design characteristics, as well as to explore associations between memory performance and their epidemiological, clinical, and pathological features. A total of 13 studies were identified by searching in PubMed, Web of Science, and PsycInfo databases up to May 6th, 2022. Most studies evaluated verbal component of memory in the short-term and long-term recall up to 30 minutes and mainly performed a single assessment completed at 4-6 months after the infection. The samples mainly consisted of middle-aged adults that required hospitalization. Samples were not stratified by sex, age, and severity. Poor verbal learning was reported in most cases (6-58%), followed by deficits in long-term (4-58%) and short-term (4-37%) verbal memory. Visuospatial component of memory was studied less than verbal component, showing impairment of long-term retention of visual items (10-49%). COVID-19 severity in the acute stage was not systematically associated with poor memory performance. Verbal memory deficits were associated with anxiety and depression. The existing literature on objective memory assessment in long-COVID suggests further research is warranted to confirm memory dysfunction in association with epidemiological, pathological, and clinical factors, using both verbal and visuospatial tests, and exploring in deep long-term memory deficits.

Keywords: long-COVID, post-acute COVID, memory, neuropsychology, cognition.

Introduction

Coronavirus disease 2019 (COVID-19) is a disease caused by the novel coronavirus severe acute respiratory syndrome 2 (SARS-CoV-2) which has had an important impact at social, economic, physical, and phycological levels (Hossain et al., 2020; Nicola et al., 2020). It is considered primarily a respiratory disease, but also a multisystemic disease with a wide range of long-term effects on almost all systems, including cognition (Daugherty et al., 2021; Kamal et al., 2021; Miners et al., 2020).

The acute phase of COVID-19 is accompanied by some combination of headache, fever, dyspnoea, non-productive cough, anosmia/ageusia, and myalgia, although a considerable proportion of patients may have mild symptoms or be asymptomatic. Moreover, this phase may be complicated by severe acute respiratory distress syndrome, hypoxia, respiratory failure, and multiple organ failure, as well as several neurological complications, including encephalopathy, delirium, inflammatory syndromes of the Central Nervous System (CNS), encephalitis, Guillain-Barré syndrome, and stroke, among others (Carod-Artal, 2021). However, irrespective of the severity of the neurological symptoms of COVID-19 in the acute phase, many patients who had mild or moderate COVID-19 present long-term neuropsychological alterations (Crook et al., 2021; Frontera et al., 2021).

Ten to twenty percent of subjects affected by the SARS-CoV-2 infection may present lasting symptoms after the acute episode (Carod-Artal, 2021; Greenhalgh et al., 2020). The term “long-COVID-19 syndrome” refers to symptoms extending beyond 12 weeks from the initial symptoms (WHO, 2021). In long-COVID, symptoms vary widely, and some of the most prevalent ones are respiratory. However, other reported symptoms include headaches, muscle pains and weakness, gastrointestinal upset, rashes,

metabolic disruption, thromboembolic conditions, mental health problems, and neurocognitive difficulties (Greenhalgh et al., 2020). Neurological symptoms, involving both the CNS and the Peripheral Nervous System (PNS), are present in long-COVID-19 (Ellul et al., 2020). Studies also reported psychological and neuropsychological difficulties in these patients, which are experienced even in those individuals who did not require hospitalization (Graham et al., 2021). The main underlying pathophysiological mechanisms of Long-COVID include viral persistence, endothelial dysfunction, coagulation activation, SARS-CoV-2 superantigen–mediated activation of the immune system, as well as autoimmunity (Brodin et al., 2022; Castanares-Zapatero et al., 2022). These mechanisms are complex and interrelated (Umesh et al., 2022). They can affect nervous system by virus neurotropism and subsequent neuroinflammation leading to pathophysiological impacts on several brain regions, including the cortex and the limbic system (Feizi et al., 2022), virus-mediated disruption of mitochondrial function in neurons and microglia (Stefano et al., 2021), hypometabolic state of brain (Guedj et al., 2021), immune-mediated destruction of the nervous system due to persistent antigens inflicting chronic damage (James & Georgopoulos, 2022), or microvascular thrombosis (Ahamed & Laurence, 2022).

The long-COVID-19 syndrome neuropsychological deficits affect attention, frontal/executive functions, memory, and visuospatial function (Ardila & Lahiri, 2020; Beaud et al., 2021; Jaywant et al., 2021). Four-month follow-up studies have observed deficits in immediate verbal memory, verbal working memory, visuospatial abilities related to visual searching, and sustained attention (Miskowiak et al., 2021). Factors affecting memory and executive deficits are not at all clear. Research on the relationship between cognitive impairments and the duration of mechanical ventilation or Intensive Care Unit (ICU) treatment has not found a significant correlation between cognitive

symptoms and severity of the acute episode of the disease (Beaud et al., 2021). Nevertheless, other studies have found an association between some persistent cognitive impairments and the degree of long-term pulmonary dysfunction and respiratory symptoms (Miskowiak et al., 2021). Memory sequelae have been mainly reported in older people with preexistent diseases and hospitalized during the infection, but they have also been observed in healthy young adults (<50 years) who have not required hospitalization during the infection (Daugherty et al., 2021). Some studies have observed a correlation between verbal working memory impairment and executive deficits and the severity of the infection (Di Pietro et al., 2021), whereas others have found that patients without severe infection (non-hospitalized) also showed cognitive complaints in working memory and attention at a ten-month follow-up (Graham et al., 2021). Long-COVID is frequently associated with mental health symptoms, such as low mood, hopelessness, anxiety, sleep disturbances, and post-traumatic stress disorder (PTSD) (Dorri et al., 2021; Greenhalg et al., 2020) and scientific evidence has not yet elucidated how these symptoms are related to memory disfunction. For this reason, to better understand the memory sequelae in these patients, it is important for the studies to include the stratification of patients infected by SARS-CoV-2 according to their clinical, pathological, and epidemiological features.

The scientific evidence on memory alterations in long-COVID-19 displays heterogeneity across studies. Samples differ in terms of their age and sex distribution (Nehme et al., 2021; Puchner et al., 2021). The severity of initial illness is also heterogeneous. Samples consisted of hospitalized patients, non-hospitalized patients, or both (Blomberg et al., 2021; Hosp et al., 2021; Taribagil et al., 2021). In studies that explore hospitalized patients, the severity of these patients varies in terms of the requirement of ICU treatment, oxygen therapy, endotracheal intubation, mechanical

ventilation, or other medical care, as well as mean days of hospitalization (Alemanno et al., 2021; Negrini et al., 2021; Olezene et al., 2021). Considering the time elapsed since the COVID-19 infection and the assessment, the assessment time-point also differ between studies. These studies include several methods for the assessment of memory, using different tests to assess several memory processes and including or not a control group in their design (Bliddal et al., 2021; Hugon et al., 2022).

The present review updates the existing evidence of memory impairments in long-COVID-19 and highlights specific patterns in the literature relative to long-COVID memory deficits; investigates variability in the sample characteristics, timing of assessment and experimental design, including analysis of associations between memory performance and clinical, pathological, and epidemiological variables; evaluates assessment-related variables such as the type of memory assessed, and the test employed for its evaluation. All these variables may account for variable findings that need to be reviewed to discuss similarities and differences across studies that can help address future studies attempting to better understand memory impairment in long-COVID syndrome.

Method

This review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

Search strategy

The search was performed in PubMed, Web of Science (WoS), and PsycInfo databases. No restriction on date of publication was applied. The final search was carried out on May 6th, 2022. The search was carried out using a search algorithm

combining terms for Long-COVID and memory assessment: (“long covid” OR “post covid” AND “memory”) OR (“long covid” OR “post covid” AND “cognit*”) OR (“long covid” OR “post covid” AND “learning”) OR (“long covid” OR “post covid” AND “neuropsychol*”) OR (“long covid” OR “post covid” AND “neurological symptom”).

Selection criteria

Inclusion criteria for this review were the following: (1) studies examining the presence of long-COVID symptoms, which occur 3 months from the onset of acute COVID-19 symptoms, last for at least 2 months and cannot be explained by an alternative diagnosis (WHO, 2021) and (2) studies which objective was memory assessment (immediate memory, short and/or long-term verbal memory/learning, short and/or long-term visuospatial memory/learning, verbal and/or visuospatial working memory, and procedural memory).

Exclusion criteria were: (1) articles not published in scientific journals, (2) articles lacking experimental results, (3) review articles, comments, or abstracts in congresses, (4) studies which assess memory with screening or brief tests, (5) articles which only include descriptive data and those which do not analyze memory performance in comparison with a control group or normative data, and (6) articles which do not specify the memory tasks employed.

Screening for inclusion

To select the studies that are included in this review, we deleted duplicate articles manually. Next, we screened titles and abstracts to discard articles not fulfilling the selection criteria. Then, we exhaustively analyzed the previously selected articles through full-text reading, and if any article failed to meet the inclusion criteria at this point, it was removed.

Results

Study selection

Pubmed, WoS, and PsycInfo yielded 554, 1653, and 57 articles, respectively, identifying a total of 2264 records. Then, after removing duplicates, 1817 records were selected. Then, after title and abstract reading, we selected 62 articles for full-text review. Of these 62 articles, 49 articles did not meet the selection criteria and were excluded. Consequently, 13 articles were selected for the systematic review. Figure 1 shows a flow chart diagram of the study selection.

[FIGURE 1 NEAR HERE]

Relevant information gathered from all retrieved studies is summarized in Table 1. Data included sample size, subjects ʾage, study design, memory assessed, evaluation tools, and relevant results.

[TABLE 1 NEAR HERE]

Sample characteristics

Most of the studies included a sample size of 60-90 participants (Crivelli et al., 2022; Ferrando et al., 2022; Ferrucci et al., 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Zhao et al., 2022). The lowest long-COVID sample size was 30 (Albu et al., 2021a), whereas the highest was 120 (Mattioli et al., 2021). All reviewed articles employed adult samples with a mean age over 45 years, being 27.4 the lowest-mean age (Zhao et al., 2021), and 60.8 the highest-mean age (Cecchetti et al., 2022). Sex distribution varied across studies, only one study presented a balanced distribution between males and females (Crivelli et al., 2022). In 53% of the studies the proportion of male participants was higher than females (Albu et al., 2021a, 2021b;

Cecchetti et al., 2022; Ferrucci et al., 2021, 2022; Voruz et al., 2022; Zhao et al., 2022); 38 % included more females than males in their samples (Ferrando et al., 2022; García-Sánchez et al., 2022; Mattioli et al., 2021; Vannorsdall et al., 2022; Whiteside et al., 2022). Except for the study of Zhao et al., (2022), most of the studies (92%) included hospitalized samples; 33% made comparisons between ICU and non-ICU patients (Albu et al., 2021a, 2021b; García-Sánchez et al., 2022; Vannorsdall et al., 2022). Only 38% of the studies revised subdivided long-COVID sample according to a classification of the severity of the illness (Crivelli et al., 2022; Voruz et al., 2022) or distinguished between patients on the basis of their clinical symptoms (Ferrando et al., 2022; Ferrucci et al., 2021; Voruz et al., 2022).

Objectives of the reviewed studies

There were studies (23%) whose main objective was to establish whether there were differences on memory performance between healthy subjects and long-COVID patients (Crivelli et al., 2022; Mattioli et al., 2021; Zhao et al., 2022), while others (53%) compared memory scores of long-COVID patients with standardized scores based on published normative data (Albu et al., 2021b; Ferrando et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Whiteside et al., 2022). Most studies (76%) differentiated subgroups of long-COVID patients to compare or better describe their memory performance. These subgroups of patients were stablished according to: (i) the severity of their illness in the acute stage (Albu et al., 2021a; Crivelli et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Voruz et al., 2022; Whiteside et al., 2022); (ii) their median age (Ferrucci et al., 2021); (iii) their acute or sub-acute-COVID manifestations, such as the presence of Acute Respiratory Distress Syndrome (ARDS) during hospitalization (Ferrucci et al., 2022) or post-acute cognitive complaints (Ferrando et al., 2022); (iv)

their clinical-long-COVID symptoms, including persistent symptoms such as dysgeusia or hyposmia (Cecchetti et al., 2022), or awareness of memory deficits (Voruz et al., 2022). Most of the studies performed a single neuropsychological assessment (84%) that was carried out either 4-5 months after hospital discharge or symptoms onset (55%) (Albu et al., 2021a, 2021b; Crivelli et al., 2022; Ferrucci et al., 2021; Mattioli et al., 2021; Vannorsdall et al., 2022) or in a later period (45%), 6-9 months after illness (Ferrando et al., 2022; García-Sánchez et al., 2022; Voruz et al., 2022; Whiteside et al., 2022; Zhao et al., 2022). Only two longitudinal studies aimed to explore the evolution of memory performance over time including baseline neuropsychological assessment measures 2 months (Cecchetti et al., 2022) and 5 months (Ferrucci et al., 2022) after hospital discharge and follow-up evaluation at 10 or 12-months, respectively. Half of the reviewed studies (46%) investigated associations between memory performance and mood disturbances such as depression (Albu et al., 2021a; Crivelli et al., 2022; García-Sánchez et al., 2022; Mattioli et al., 2021; Whiteside et al., 2022), anxiety (Albu et al., 2021a; Crivelli et al., 2022; García-Sánchez et al., 2022; Marrioli et al., 2021; Whiteside et al., 2022), and/or stress (Mattioli et al., 2021).

Evaluation tools

Most studies (84%) assessed verbal learning (Albu et al., 2021a, 2021b; Cecchetti et al., 2022; Crivelli et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Mattioli et al., 2021; Vannorsdall et al., 2022; Voruz et al., 2022; Whiteside et al., 2022). Verbal learning was tested, in the immediate and short term recall, by different tests, including the Rey Auditory Verbal Learning Test (RAVLT) (Albu et al., 2021a, 2021b; Cecchetti et al., 2022; Crivelli et al., 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022), the California Verbal Learning Test (CVLT) (Mattioli et al., 2021), the 16-item Grober and Buschke Free/Cued Recall Paradigm (FR/CR-16) (Voruz

et al., 2022), the Logical Memory subtest of the Wechsler Memory Scale-IV (WMS-IV) (Whiteside et al., 2022), and the Hopkins Verbal Learning Test-Revised (HVLT-R) (Whiteside et al., 2022). Some studies also assessed immediate and short-term recall of verbal items using the forward version of the Digit Span (DSf) subtest either in the Wechsler Adult Memory Scale-III and -IV (WAIS-III and WAIS-IV) (Albu et al., 2021a, 2021b; García-Sánchez et al., 2022; Voruz et al., 2022; Whiteside et al., 2022) or in different versions (Cecchetti et al., 2022; Crivelli et al., 2022; Vannorsdall et al., 2022), the subtests of verbal memory of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Ferrando et al., 2022), and the Selective Reminding Test (SRT) of the Brief Repeatable Battery of Neuropsychological Tests (BRBNT) (Ferrucci et al., 2021, 2022). Immediate and short-term recall of visuospatial items were assessed by forward versions of the Corsi Block Tapping test (Voruz et al., 2022; Zhao et al., 2022), Rey-Osterrieth Complex Figure (ROCF) (Cecchetti et al., 2022; Mattioli et al., 2021; Whiteside et al., 2022), and the Spatial Recall Test (SPART) of the BRBNT (Ferrucci et al., 2021, 2022). All the studies mentioned above that assessed verbal memory included a long-term memory assessment 20-30 minutes after learning. This long-term assessment was also included in some of the studies testing visuospatial component of short-term memory (Ferrando et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Mattioli et al., 2021; Voruz et al., 2022; Whiteside et al., 2022). The Benson Complex Figure Test (BCFT) was used in two studies with the only aim of assessing long-term visuospatial memory storage (Cecchetti et al., 2022; Crivelli et al., 2022). The ability to identify and discriminate among previously presented stimulus and distractors was studied by Zhao et al. (2022). This study assessed immediate and delayed visuospatial and verbal recognition of everyday objects and words.

Regarding working memory, most studies assessed this type of memory including verbal items (77%) using the backward version of the DS (DSb) subtest of WAIS-III and WAIS-IV (Albu et al., 2021a, 2021b; García-Sánchez et al., 2022; Voruz et al., 2022; Whiteside et al., 2022) or similar tasks (Cecchetti et al., 2022; Crivelli et al., 2022; Ferrucci et al., 2021, 2022; Vannorsdall et al., 2022). Only one study included visuospatial elements to be retained and manipulated, using a variant of the backward Corsi Block Tapping test (Voruz et al., 2022).

Main results

Subjective memory complaints

More than a third of long-COVID patients reported subjective cognitive complaints that include memory deficits, which were observed when tested by objective memory tests, even in a group of patients who do not report subjective deficits (Albu et al., 2021b). In this sense, the awareness of long-COVID patients memory condition was altered in most severe patients and those unaware of their own cognitive deficits presented worse execution on verbal memory than nosognosic patients (Voruz et al., 2022).

Objective verbal memory deficits

Studies which objectively assessed memory and aimed to compare memory performance of long-COVID patients with respect to healthy controls found significant differences in verbal learning (Crivelli et al., 2022) and long-term verbal memory (Crivelli et al., 2022). In contrast, the study of Zhao et al. (2022) showed no impairment of verbal recognition. In the same line, Mattioli et al., (2021) did not find differences between patients and controls on verbal memory when assessed with CVLT. Similarly to studies incorporating a control group, studies comparing long-COVID patients ’

memory performance with standardized scores based on published normative data found alterations in verbal learning and long-term retention of verbal information, with highly variable percentage of participants affected across studies. Thus, studies which have assessed verbal learning reported poor performance in 6-58% of cases (Albu et al., 2021b; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Whiteside et al., 2022) and long-term verbal memory resulted impaired in 4-58% of participants (Albu et al., 2021b; Ferrando et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Whiteside et al., 2022). Immediate or short-term verbal memory impairment was less reported, only presented in 4-37% of cases (Ferrando et al., 2022; García-Sánchez et al., 2022; Whiteside et al., 2022), followed by verbal recognition impairment, found in 19-23% of participants (Albu et al., 2021b; García-Sánchez et al., 2022), and verbal working memory deficits, described in 10-21% of cases (Albu et al., 2021b; García-Sánchez et al., 2022). Only the study of Whiteside et al. (2022), which followed the >2 standard deviations criteria, did not find verbal working memory deficits.

Objective visuospatial memory deficits

Contrary to verbal memory deficits, the impaired ability to retain visuospatial information was not predominant in the studies and was mainly reported when assessing the long-term retention of visuospatial items, 10-49% of cases (Ferrando et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2033; Whiteside et al., 2022), while, short-term retention of visuospatial information and visuospatial recognition resulted less impaired, as there were only reported in 8-16% of cases (Ferrucci et al., 2021; Whiteside et al., 2022) and 6% of cases (Whiteside et al., 2022), respectively. When comparing visuospatial memory of long-COVID patients with respect to controls, Crivelli et al., (2022) found significant impairment in long-term visuospatial memory

and more orientation-specific false alarms in the long-COVID patients comparing to controls were described during delayed object recognition (Zhao et al., 2022). However, Mattioli et al., (2021) did not find differences between patients and controls on visuospatial memory assessed with ROCF.

Relationship between clinical factors and memory function

The severity of the infection in the acute stage was not associated with poorly memory performance in some of the studies. Thus, some studies which assessed memory performance in association with the severity of the illness and/or other clinical factors, such as the average length of stay in the hospital, the admission to ICU, the duration of the acute symptoms of the disease or the presence of biomarkers, revealed that these factors are not relevant to the development of memory impairment when assessed 4-7 month later (Albu et al., 2021a; Cecchetti et al., 2022; Crivelli et al., 2022; García-Sánchez et al., 2022; Whiteside et al., 2022). However, others do not agree with these results. The study of Vannorsdall et al. (2021) observed significant differences between ICU and non-ICU patients on verbal learning. This study also reported that severe verbal memory impairment affecting learning, long-term maintenance and manipulation of verbal items was highly present in ICU patients. This study included a large sample size of hospitalized patients evaluated 4 months after diagnosis. Markers of acute respiratory failure or lungs condition during hospitalization of patients were associated with memory performance 5 months after hospital discharge in two studies. The (P/F) ratio, which is the relation between the arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2), the acute respiratory distress syndrome (ARDS), and the saturation of peripheral Oxygen (SpO_2) were predictors of verbal memory (Ferrucci et al., 2021, 2022), but showed no association with visuospatial learning (Ferrucci et al., 2022). Other biomarker, such as the elevated level of the liver enzyme

alanine transaminase (ALT) during hospitalization, was also associated with poor verbal memory, when assessing long-term recall (Ferrucci et al., 2022). The association between smell and taste alterations at 6 months and long-term visuospatial memory performance was also observed (Ferrucci et al., 2022). In this sense, dysgeusia and hyposmia were also relevant when assessing evolution of memory deficits, as patients suffering from these symptoms presented scarce improvement of memory (Cecchetti et al., 2022). This shows that long-term clinical symptoms of the disease were also relevant to predict memory performance. In this regard, Ferrando et al. (2022) found that long-COVID patients who had clinical symptomatology 6-8 months after illness, seeking care for post-acute cognitive complaints, showed deficits in immediate verbal memory and long-term verbal and visuospatial memories, whereas patients who did not have clinical symptomatology only presented immediate verbal memory deficits. Most of the patients of this study were not hospitalized and none were admitted to ICU or required ventilator support. However, memory impairment was more evident in those patients who had been evaluated closer to the infection (Zhao et al., 2022). In this sense, data from the scarce longitudinal studies assessing memory evolution over 7-8 moths supported memory improvement for verbal memory (Cecchetti et al., 2022; Ferrucci et al., 2022), whereas no significant improvements were found neither in visuospatial learning nor in long-term visuospatial memory (Ferrucci et al., 2022).

Mood disturbances and memory performance

The studies which explored the relationship between mood disturbances, experienced as symptoms of depression, anxiety, and stress, and memory performance showed association between these symptoms and verbal memory deficits in long-COVID patients. Many studies have found an association between depression and poor memory (80%) when assessing recognition, immediate, short-term and long-term

retention, and manipulation of verbal items (Albu et al., 2021a; Ferrucci et al., 2021; Mattioli et al., 2021; Whiteside et al., 2022), whereas only one study (García-Sánchez et al., 2022) failed to find any correlation between depression scores and verbal and visuospatial memory performance. Similarly, when exploring the relationship between anxiety symptoms and memory impairment, 80% of the studies found an association between anxiety symptoms and any type of verbal memory when measuring general cognition (Crivelli et al., 2022), immediate memory, short-term and long-term retention, and manipulation of verbal items (Mattioli et al., 2021; Whiteside et al., 2022). Only one study found associations between anxiety scores and both verbal and visuospatial memory deficits (Garcia-Sanchez et al. 2022). The absence of relationship between visuospatial memory, measured with the ROCF test, and anxiety, depression, and stress was found by Mattioli et al. (2021).

Discussion

Overall, the studies assessing memory in long-COVID devoted more particular attention to the verbal component of memory than the visuospatial one. The verbal component of memory has been studied in a more detailed way than the memory for visuospatial items. The studies meeting criteria for this review predominantly covered verbal learning that was tested in the long-term recall (20-30 minutes after learning) and in a single assessment performed 4-6 months after the acute episode of SARS-CoV-2 infection. In addition, their samples consisted of middle-aged adults that required hospitalization. However, these samples were not subdivided for analysis of memory according to their epidemiological, clinical, and pathological features. Yet, there is some consistency in findings across studies that can help to better understand memory deficits and their association with clinical features in long-COVID patients, as well as to direct future research.

The studies meeting criteria for inclusion in this review evaluated adult samples with no predominant female participants. This is striking, as current scientific evidence indicates that long-COVID predominantly affects adult females (Bai et al., 2022). In fact, women represent 80% of the sample of international studies assessing a large number of participants who reported to be experiencing prolonged symptoms of long-COVID in online surveys (Davis et al., 2021; Ziauddeen et al., 2022). Alteration of memory was the main cognitive symptom experienced by participants in these studies, being equally common across all ages (Davis et al., 2021; Ziauddeen et al., 2022). It is important to note that participants in both studies were between the ages of 40-60, as in the studies included in the present review. Davies et al. (2021) showed predominant short-term memory complaints across all age groups, while, in Ziauddeen et al. (2022), older long-COVID patients reported higher memory impairment than younger participants. Aging is characterized by cognitive decline (Olesen et al., 2020) and, therefore, it might be critical to study memory function in elderly COVID-19 survivors. This would contribute to better understand the effect of SARS-CoV-2 infection on vulnerable groups to cognitive impairment. Among the reviewed studies, the study of Ferrucci et al. (2021) is the only one to consider age subgroups. In this study, older adults (≥55 years) reported lower verbal memory compared to younger adults. However, it is important to note that younger patients have also shown memory deficits, as it was reported by Zhao et al. (2022), which include a young sample (27-year-old). Thus, more studies are needed to extract robust conclusions about how long-COVID affects memory at different ages.

As we mentioned above, most of the studies include a high number of male participants, despite the fact that recent research points to a high prevalence of neuropsychological long-COVID symptoms in female individuals (Michelutti et al.,

2022). Females are vulnerable to changes in their menstrual cycle as a consequence of the infection (Lebar et al., 2022). Sexual hormones and menstrual cycle exert an effect on the CNS and cognition (Pletzer et al., 2019). Nevertheless, clinical observation and literature on the relationship between female hormone dysregulations and cognitive symptoms in long-COVID are not yet available and more research is required to unveil this association.

The main deficits of memory were found in verbal learning and long-term recall of verbal and visuospatial information. The studies reviewed assessed mainly hospitalized samples, as in most studies assessing long-term effects of COVID-19 that were mainly done evaluating patients discharged from hospital (Rigoni et al., 2022). However, few studies subdivided their samples to make comparisons according to their severity and main symptoms, making difficult to draw conclusions about their role on the development of memory alterations. To include a stratification of patients according to their severity and predominant symptoms is very necessary when assessing memory performance. The development of long COVID symptoms may be linked to symptomatic COVID-19 infection, hospitalization, requirement of mechanical ventilation, and severity of the illness (Fernández-de-Las-Peñas et al., 2021; Rigoni et al., 2022; Taquet, Dercon et al., 2021). Self-reported memory complaints were associated with treatment modalities, more present in participants treated with steroids and antibiotics (Ahmed et al., 2022). However, any patient with COVID-19 may develop long-COVID, regardless of the severity of the infection and the intensity of the treatment (Crook et al., 2021). In fact, long-COVID with predominant memory impairment, dysgeusia and anosmia symptoms may occur even in patients with a mild course during the acute phase of infection (Grisanti et al., 2022). Even though few studies allow associations to be established, the reviewed studies indicate that COVID-

19 severity in the acute stage is not systematically associated with poorly memory performance. In this regard, severity of the illness (Cecchetti et al., 2022; Crivelli et al., 2022; Whiteside et al., 2022), hospitalization (García-Sánchez et al., 2022), admission to ICU (Albu et al., 2021a), duration of the acute symptoms and biomarkers of infection severity (García-Sánchez et al., 2022) were not associated with memory impairment in most of the studies meeting criteria for inclusion in this review. However, our review also includes evidence about the role of ICU requirement (Vannorsdall et al., 2022) and markers of acute respiratory failure or lungs condition (Ferrucci et al., 2021, 2022) as factors associated with poor verbal memory, but less or not related to visuospatial learning (Ferrucci et al., 2022). Visuospatial memory performance was associated with smell and taste alterations exclusively (Ferrucci et al., 2022).

The integrity of memory encoding and storage processes is attributed to the hippocampus and other medial temporal lobe areas, associated with episodic, long-term and visuospatial memories (Eichenbaum, 2000). Considering the susceptibility of the hippocampus to hypoxia (Maiti et al., 2006), the association of acute respiratory failure or lungs condition during hospitalization and memory performance could reflect a consequence of hypoxic damage on memory (Wang et al., 2022). Smell and taste alterations, that might reflect the access of the virus to the brain via olfactory pathways (Bougakov et al., 2021), were also associated with memory deficits in the reviewed studies (Ceccheti et al., 2022; Ferrucci et al., 2022). Visuospatial memory alterations were the most associated with anosmia and ageusia, which suggest an involvement of the olfactory tract and the entorhinal cortex. The latter is anatomically and functionally associated with the hippocampus (Canto et al., 2008). Dysgeusia and hyposmia were also relevant when assessing evolution of memory deficits, as were associated with scarce improvement (Cecchetti et al., 2022). The assessment protocols of the reviewed

studies account for memory function mainly at 4-6 months, and no later than 9 months, after the acute infection, performing only one evaluation, and few studies include longitudinal follow-up of the memory impairment (Cecchetti et al., 2022; Ferrucci et al., 2022). The reviewed studies permit to deduce that memory deficits persist for long-term (Cecchetti et al., 2022; Ferrando et al., 2022; Ferrucci et al., 2022; Voruz et al., 2022; Zhao et al., 2022) and visuospatial memory presented scarce improvement compared to verbal memory (Cecchetti et al., 2022; Ferrucci et al., 2022). This dissociation between verbal and visuospatial memory deficits could be consequence of different aetiologies. In this sense, hypoxic damage could account on general memory deficits and more verbal impairment, while alterations into the entorhinal pathway might be associated with visuospatial impairment and concomitant taste and smell symptoms. In this sense, hypometabolism of the olfactory gyrus and connected limbic and paralimbic brain regions was demonstrated in long-COVID patients with persistent functional complaints (Guedj et al., 2021).

Long-COVID patients were mainly evaluated in their verbal domain of memory, especially using DSf subtest of WAIS in the short-term recall (Albu et al., 2021a, 2021b; Cecchetti et al., 2022; Crivelli et al., 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022; Voruz et al., 2022; Whiteside et al., 2022) and examining the rates of forgetting of lists of 12-16 words that were tested after delay intervals of 20-30 minutes, using RAVLT in most studies (Albu et al., 2021a, 2021b; Cecchetti et al., 2022; Crivelli et al., 2022; García-Sánchez et al., 2022; Vannorsdall et al., 2022), but also other similar tests such as CVLT (Mattioli et al., 2021), FR/CR-16 (Voruz et al., 2022) or HVLT-R (Whiteside et al., 2022). All these tests make use of normative data in scoring, eluding the use of a group of healthy patients to compare results in most of the studies (Albu et al., 2021a, 2021b; García-Sánchez et al., 2022; Vannorsdall et al.,

2022; Whiteside et al., 2022). Long-term recall in these studies involved retention of information for only 20-30 minutes. This makes it impossible to draw any conclusions about the consolidation processes, which refer to a more stable, long-lasting form of memory vulnerable to interference (Squire et al., 2015). Other aspects of study design, such as whether a control group is used, can strongly affect results when assessing long-COVID, especially when participants are collected from hospital databases (Ledford, 2022). Memory for visuospatial items was assessed using forward versions of the Corsi Block Tapping test (Voruz et al., 2022; Zhao et al., 2022), the ROCF (Cecchetti et al., 2022; Mattioli et al., 2021; Whiteside et al., 2022), which is widely used to assess visual memory of brain injury or cognitive disorders (Zhang et al., 2021), and SPART of the BRBNT (Ferrucci et al., 2021, 2022). Most of these studies included not only an immediate recall, but also a delayed recall after 30 minutes (Ferrando et al., 2022; Ferrucci et al., 2021, 2022; García-Sánchez et al., 2022; Mattioli et al., 2021; Whiteside et al., 2022). However, only the Corsi Block Tapping test, which is conceptually similar to the Digit Span test, assesses spatial memory with minimal verbal mediation (Guariglia, 2007). Nevertheless, this test shows moderate reliability to detect mild or slight alterations of spatial memory (de Paula et al., 2016).

Reviewed articles that explored associations between memory and mood disturbances outline that long-COVID patients showing verbal memory impairment (Albu et al., 2021a; Ferrucci et al., 2021; Mattioli et al., 2021; Whiteside et al., 2022) present higher depression and/or anxiety scores, meanwhile visuospatial memory was not negatively associated with affective symptoms (Mattioli et al., 2021). However, more studies are needed to reach precise conclusions about the relationship between affective disorders and visuospatial and working memory deficits. It is known that post-COVID patients present a higher prevalence of anxiety and depression (Taquet, Geddes

et al., 2021). However, it is still a question to solve whether these symptoms are related to the experience of significant psychosocial stressors (e.g. severe illness or isolation, among others) or a consequence of virus infection (Whiteside et al., 2022). Although the purpose of this review is not to address these questions but to delve into affective associations and memory deficits, the former knowledge may be essential to understand the relationship between both cognitive and emotional processes. As mentioned above, the selection of the control group is an important variable deserving attention. The optimal control group for this purpose could be a non-clinical group of participants infected by SARS-CoV-2, as in Ferrando et al. (2022).

To the best of our knowledge, this review represents one of the few attempts to update the existing scientific literature on objective assessment of memory in long-COVID-19. Limitations of this review include risks of exclusion of studies which did not use long-COVID or post-COVID as descriptors but including results of long-term effect of the infection. It is also difficult to find consistency of results, as studies presented high clinical heterogeneity and different methods of analyses. Nevertheless, our review helps to highlight the gaps in the literature, including the small number of studies performing an objective memory assessment, scarce research on relevant epidemiological and clinical factors, lack of interest to understand how memory deficits evolve over time and poor use of healthy controls to establish comparisons. The existing literature on objective memory assessment in long-COVID suggests more research is warranted investigating memory dysfunction and its evolution in these patients, including aged patients. The studies reviewed reported overall patterns of memory impairment compared to normative data, as few studies include a control group, particularly in long-term and short-term verbal memory. Such patterns are especially evident in studies assessing a large sample of hospitalized patients. Future studies that

specifically examine long-term retention are needed to better define the frequency and consequences of memory deficits in patients with long-COVID. In this regard, it is important to conduct studies using complex cognitive tasks, including relevant covariates, and assessing the consolidation of memories and the effect of interference of both verbal and visuospatial items. Additionally, it is necessary to include a group of healthy controls to make comparisons. Future research must also aim to establish the sensitivity and specificity of memory tests in differentiating between groups of patients according to their sex, age, severity, main symptoms, and evolution. This would allow neuropsychological testing of memory in long-COVID to be useful toward identification and prediction of memory deficits and their etiology, thereby enabling professionals to better understand neuropsychological needs of long-COVID patients to design their interventions.

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The authors report there are no competing interests to declare.

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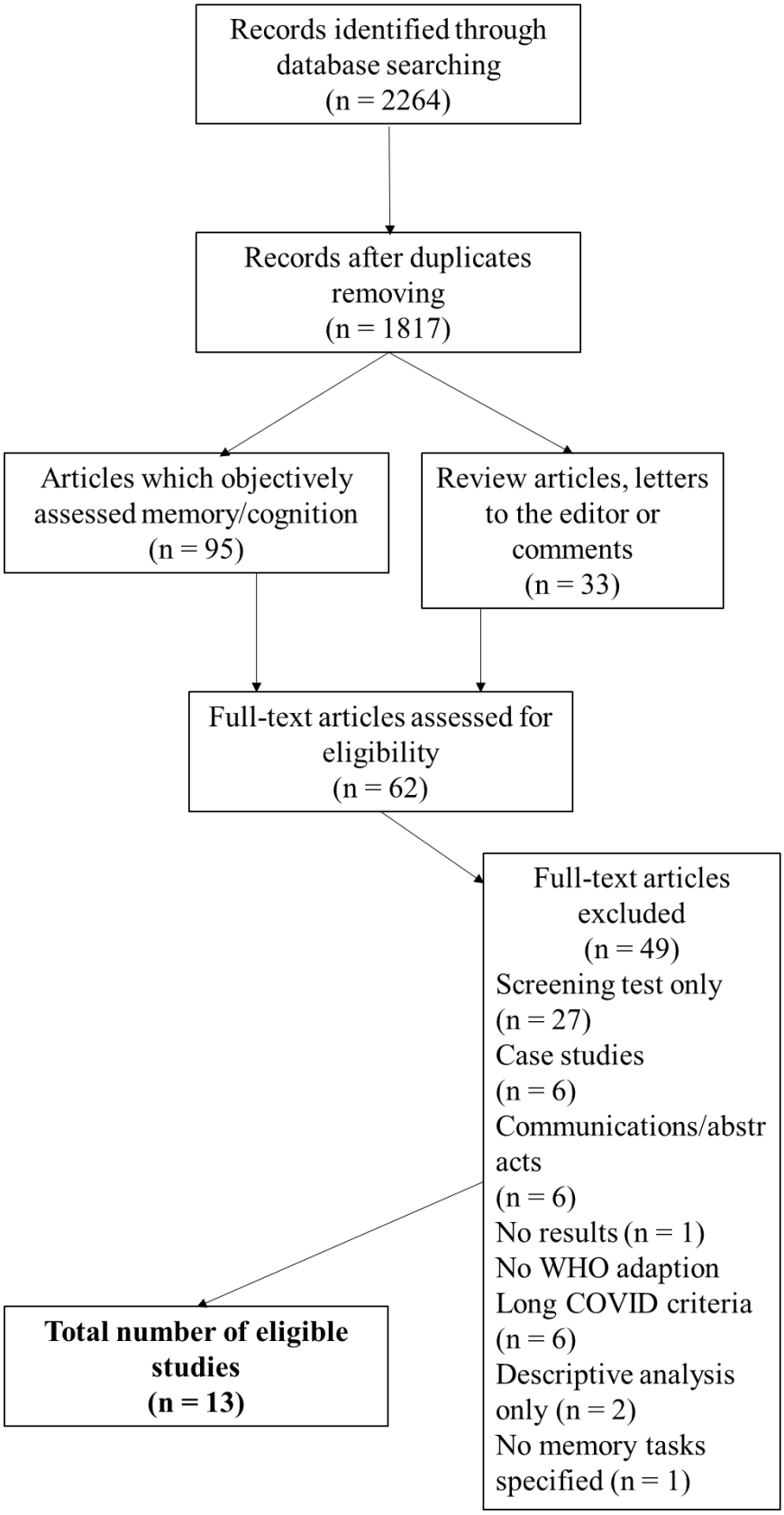

Figure 1. Flowchart of literature search and study selection process.

Table 1. Characteristics and main results of studies assessing memory in Long-COVID patients

First author, year	Sample characteristics	Experimental design	Type of memory assessed	Tests employed	Main outcomes
Albu et al. (2021a)	N = 30 (M.A.* 54, 11 F*) 16 ICU* patients (M.A. 61.5, 3 F) 14 non-ICU patients (M.A. 43.5, 8 F) Assessment time: >3 months since symptoms onset	Comparison of memory performance between ICU and non-ICU patients. Associations between memory and mood disturbances.	Verbal learning Long-term verbal memory Verbal recognition Verbal working memory	RAVLT* DSb* (WAIS*-III)	There were no significant differences between ICU and non-ICU patients on verbal learning, long-term verbal memory, verbal recognition or working memory. There was an association between depressive symptoms and altered verbal recognition functions (p=0.023).
Albu et al. (2021b)	N= 40 (M.A. 52 ± 11.4, 16 F) 30 hospital admission patients (21 ICU, 9 non-ICU) 10 home confined patients. Assessment time: >3 months since symptoms onset	Descriptive analysis. Comparison between memory performance and standardized scores based on normative data.	Verbal learning Long-term verbal memory Verbal recognition Verbal working memory	RAVLT DSb (WAIS-III)	37.5% of patients reported subjective cognitive complains, including difficulties in short-term memory. Patients showed alterations of verbal learning (58.1%), long-term verbal memory (51.6%), verbal recognition (19.4%), and working memory (9.7%).
Cecchetti et al. (2022)	N = 49 C-19* baseline: n = 49 (M.A. 60.8 ± 12.6, 13 F, M.E.* 11.1 ± 3.9) C-19 follow-up: n = 33 (M.A. 60.6 ± 12.9, 8 F, M.E. 11.3 ± 3.9) Admission to ER* due to respiratory symptoms Assessment times: 2 and 10 months after hospital discharge	Comparison of memory performance across time (2 and 10 months). Comparison between patients with and without dysgeusia/hyposmia during the acute illness.	Verbal learning Immediate verbal recall Long-term verbal memory Short-term verbal memory Verbal working memory Long-term Visuospatial memory	RAVLT DSf* DSb ROCF* BCFT*	6% of patients showed memory impairment at 10 months. Scores of immediate verbal recall improved after 10 months (p<0.001). Other type of memories did not improve. Patients with dysgeusia/hyposmia showed lower improvement at immediate verbal recall relative to patients without dysgeusia/hyposmia (p=0.003).

Crivelli et al. (2022)	N = 90 H.C.* group: n = 45 (M.A. 57, 20 F, M.E. 17) C-19 group: n = 45 (M.A. 50, 22 F, M.E. 17) Composite scores groups: H.C. group: n = 29 C-19 group: n = 29 C-19 sub-groups: - Mild disease: n= 19 - Moderate and severe disease: n= 9 Assessment time: 4-5 months after illness	Comparison of memory performance between H.C. and C-19 patients. Comparison of memory composite scores between H.C. and C-19 patients. Comparison of memory composite scores between C-19 severity groups. Associations between memory performance and mood disturbances.	Short-term verbal memory Verbal working memory Verbal learning Long-term verbal memory Long-term visuospatial memory	DSf DSb RAVLT BCFT	Scores in verbal learning ($p<0.05$), long-term verbal memory ($p=0.007$), long-term visuospatial memory ($p=0.009$), and working memory ($p<0.001$) differed between the groups. Composite scores results showed deficits in memory in C-19 patients, compared to H.C. ($p=0.016$), with intermediate effect size (0.734). Memory composite scores did not differ across the severity groups. There was an association between anxiety and cognitive impairment ($p=0.043$).
Ferrando et al. (2022)	N = 60 C-19 non-clinic group: n = 28 (M.A. 33.7 ± 11.0, 16 F, M.E. 16.4 ± 2.2) C-19 clinic group: n = 32 (M.A. 48.1 ± 12.8, 25 F, M.E. 15.8 ± 2.1) Assessment time: 6-8 months after illness	Overall sample, non-clinic group and clinic-group memory performances were compared to standardized scores based on normative data.	Immediate verbal memory Long-term verbal memory Long-term visuospatial memory	RBANS*	Clinical group reported more subjective memory complaints than non-clinical group ($p=0.002$). Non-clinical group scored lower than normative values on immediate verbal memory ($p=0.01$). Clinical group scored lower than normative values on immediate verbal memory ($p=0.001$) and long-term memory ($p=0.001$).

Ferrucci et al. (2021)	N = 38 (M.A. 53.45 ± 12.64, 11 F, M.E. 12.39 ± 3.24) Hospitalized patients 2 sub-groups based on median age: - ≥55 years (n = 20) - <55 years (n = 18) 2 subgroups based on the presence of ARDS* during hospitalization: - No ADRS (n = 21) - ADRS (n = 12) Assessment time: 4-5 months after hospital discharge	Comparison between memory performance and standardized scores based on normative data. Associations between memory performance and clinical factors. Linear regression analysis was performed when significant correlations were found. Associations between memory performance and mood disturbances. Association between the presence/absence of ARDS during hospitalization and memory performance.	Verbal learning Long-term verbal memory Visuospatial short-term memory Long-term visuospatial memory Verbal working memory	BRBNT*	Participants showed deficits in verbal learning (10.5%), long-term verbal memory (26.3%), visuospatial short-term memory (15.8%), visual long-term memory (18.4%), and working memory (5.3-10.5%). Participants aged ≥ 55 obtained lower scores in verbal memory, when compared to aged < 55 ($p=0.025$). There was a positive correlation between the lowest P/F* ratio during hospitalization and verbal learning ($r=0.404$; $p=0.027$), being a predictor of verbal learning score (adjusted $R^2=0.133$; $p=0.027$). SpO_2* levels upon hospital arrival correlated positively with long-term verbal memory performance ($r=0.373$; $p=0.042$). Depression scores correlated negatively with long-term verbal memory performance ($r=-0.0372$; $p=0.023$). ARDS was associated with a lower performance in both verbal learning ($p=0.007$) and long-term verbal recall ($p=0.029$).

Ferrucci et al. (2022)	N = 76 C-19 baseline: n = 76 (M.A. 56.24 ± 12.08, 20 F) C-19 follow-up: n = 53 (M.A. 58.51 ± 10.29, 15 F) Hospitalized patients Assessment times: 5 (baseline) and 12 (follow-up) months after hospital discharge	Comparison between memory performance and standardized scores based on normative data. Comparison of memory performance across time (5 vs 12 months). Associations between memory performance and clinical factors, after controlling for age, sex, education, and discharge. Linear regression analysis.	Verbal learning Long-term verbal memory Visuospatial short-term memory Long-term visuospatial memory Verbal working memory	BRBNT	At baseline, patients presented impairment in long-term verbal memory (26.3%), verbal learning (17.1-19.7%) and long-term visuospatial memory (18.2%). At follow-up, long-term visuospatial and verbal memory were impaired in 18.9% and 15.1% of patients, respectively. Long-term verbal memory ($p=0.047$), verbal learning ($p<0.05$) and working memory ($p<0.05$) improved compared to baseline. No improvements were shown in visuospatial learning and long-term visuospatial memory. A greater P/F ratio during hospital stay was a positive predictor of verbal ($p=0.029$; $r_{partial}=0.271$) and visuospatial learning ($p=0.041$; $r_{partial}=0.252$) at baseline. Patients who reported hyposmia ($p=0.020$; $\eta_p^2=0.077$) or dysgeusia ($p=0.037$; $\eta_p^2=0.062$) at baseline had worse long-term visuospatial memory. ARDS resulted nor relevant. Serum ALT* during hospitalization was inversely associated with long-term verbal memory ($p=0.014$) at baseline.
Garcia-Sanchez et al. (2022)	N = 63 (M.A. 51.1 ± 12.5, 41 F, M.E. 14.4 ± 3.1) 33 hospitalized patients (15 required ICU) Mean assessment time: 6-7 months after diagnosis	Raw scores were transformed into standardized scores (T-scores) based on normative data, and then transformed into Pc* (Impairment= Pc < 25) PCA* to analyze multiple cognitive domains. Association of memory impairments and hospitalization, disease duration, biomarkers, and affective scores.	Verbal learning Long-term verbal memory Verbal recognition Long-term visuospatial memory Short-term verbal memory Verbal working memory	RAVLT ROCF DSf (WAIS-IV) DSb (WAIS-IV)	60.3% of patients showed multiple-domain impairment and 39.7% showed single-domain impairment. Patients show impairment in short-term verbal memory (36.51%), verbal working memory (20.63%), verbal learning (52.38%), long-term verbal memory (39.68%), verbal recognition (23.33%) and long-term visuospatial memory (49.21%). Memory deficits did not correlate with hospitalization, duration of the disease, biomarkers, anxiety or depression.

Mattioli et al. (2021)	N = 150 H.C. group: n = 30 (M.A. 45.73, 22 F, R.E.* 8-18) C-19 group: n = 120 (M.A. 47.86, 90 F, R.E. 8-18) Assessment time: 4 months after diagnosis	Comparison of memory performance between H.C. and C-19 patients. Associations between memory and mental health scores.	Long-term visuospatial memory Verbal learning Immediate verbal memory Long-term verbal memory	ROCF CVLT*	Both verbal and visuospatial memory tasks did not differ between groups. There was an association between anxiety and lower immediate (p=0.000) and long-term verbal memory (p=0.044), as well as depression and stress with lower immediate memory, (p=0.016) and (p=0.038) respectively. Long-term visuospatial memory was not associated with anxiety, depression, or stress.
Vannorsdall et al. (2021)	N = 82 (M.A 54.5 ± 14.6, 48 F M.E. 14.7 ± 3.1) ICU group (n = 48: M.A. 58 ± 14.8, 25 F, M.E. 14 ± 3) Non-ICU group (n = 34: M.A. 49.5 ± 13, 23 F, M.E. 15.7 ± 3.1) Assessment time: 4 months after diagnosis	Comparison of memory performance between ICU and non-ICU groups. Comparison between memory performance and standardized scores based on normative data. Mild/moderate and severe memory impairment were defined as performances ≥1.5 and ≥2 SD* below normative data.	Verbal learning Long-term verbal memory Short-term verbal memory Verbal working memory	-Telephone assessment- RAVLT DSf DSb	ICU and non-ICU patients differed on verbal learning (p<0.001). 32% of non-ICU patients presented severe memory impairment of verbal learning and long-term verbal memory. 58% of ICU patients showed severe memory impairment of verbal learning, long-term verbal memory and verbal working memory. More than 33% of ICU patients presented mild/moderated impairment of verbal learning and long-term verbal memory.
Voruz et al. (2022)	N = 102 Anosognosic C-19 group: n = 26 (7 F, M.A. 56.58 ± 13.12) Anosognosic C-19 subgroups: -Mild: n = 7 -Moderate: n = 11 -Severe: n = 8 Nosognosic C-19 group: n = 76 (30 F, M.A. 56.49 ± 9.60) Nosognosic C-19 subgroups: -Mild: n = 38 -Moderate: n = 23 -Severe: n = 15 Assessment time: 6-9 months after diagnosis	Relationship between anosognosia for memory dysfunction and the severity of the infection in the acute phase. Comparison of memory performance between anosognosic and nosognosic patients.	Verbal learning Short-term verbal memory Long-term verbal memory Verbal working memory Short-term visuospatial memory Long-term visuospatial memory Visuospatial working memory	FR/CR-16* ROCF DSf (WAIS-IV) DSb (WAIS-IV) Corsi forward Corsi backward	15.6% of patients who presented mild disease displayed anosognosia for memory dysfunction, compared with 32.4% of patients with moderate disease and 34.8% of patients with severe disease. Anosognosic patients presented worse performance than nosognosic patients on verbal learning (p=0.008), long-term (p=0.001) and short-term (p=0.016) verbal memory. Long-term and short-term visuospatial memory, and working memory did not differ between groups.

Whiteside et al. (2022)	N = 49 (41 F, M.A. 49.65 ± 12.43, M.E. 14.47 ± 2.16) 15 hospitalized patients (13 in ICU, 9 with ventilation) Assessment time: 6 months after diagnosis	Comparison between memory performance and standardized scores based on normative data. Borderline and impaired performances were defined as 1.0-1.9 SD and >2.0 SD below normative data. Associations between memory performance and clinical characteristics. Associations between mood disturbances and memory performance.	Verbal learning Verbal immediate memory Short-term and working verbal memory Long-term verbal memory Short-term visuospatial memory Long-term visuospatial memory Visuospatial recognition	Logical memory (WMS*-IV) DSf (WAIS-IV) DSb (WAIS-IV) HVLT-R* ROCF	Low number of patients presented memory impairment when using >2 SD criteria (verbal learning: 6.1%; verbal immediate memory: 4.1%; short-term and working verbal memory: 0%; long-term verbal memory: 4.1-6.1%; short-term visuospatial memory: 8.2%; long-term visuospatial memory: 10.2%; visuospatial recognition: 6.1%). Verbal learning and visuospatial recognition were borderline in 24.5% and 20.4% of patients, respectively. Severity of the illness is not associated with memory performance. Depressive and anxiety scores were negatively associated with verbal short-term and working memory performance, (r=-0.30) and (r=-0.31) respectively.
Zhao et al. (2022)	N = 80 H.C. group: n = 44 (M.A. 26.3 ± 8.0, 17 F) C-19 group: n = 36 (M.A. 27.4 ± 8.6, 14 F) Non-hospitalized patients Mean assessment: 7-8 months after diagnosis	Comparison of memory performance between H.C. and C-19. Associations between memory impairment and time from COVID-19 diagnosis.	Immediate and delayed Object recognition memory Immediate and delayed verbal recognition memory Short-term visuospatial memory	-Tasks provided by Cognitron- Object episodic memory Word memory Spatial span	C-19 group showed a significant decrement in delayed object recognition memory compared to immediate object recognition memory (p=0.0003). C-19 group presented more object orientation-specific false alarms in delayed recognition than H.C. (p=0.02). Poor delayed recognition is associated with more recent infections (r=0.6; p=0.001).

Abbreviations* ALT: Alanine Transaminase; **ARDS**: Acute Respiratory Distress Syndrome; **BCFT**: Benson Complex Figure Test; **BRBNT**: Brief Repeatable Battery of Neuropsychological Tests; **C-19**: COVID-19; **CVLT**: California Verbal Learning Test; **DSb**: Digit Span backward; **DSf**: Digit Span forward; **E.R.**: Emergency Room; **F**: Female; **FR/CR-16**: 16-item Grober and Buschke Free/Cued Recall Paradigm; **H.C**: Healthy Control; **HVLT-R**: Hopkins Verbal Learning Test-Revised; **ICU**: Intensive Care Unit; **M.A.**: Mean Age; **M.E.**: Mean Education; **Pc**: Percentile; **PCA**: Principal Component Analysis; **P/F**: arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2); **RAVLT**: Rey Auditory Verbal Learning Test; **RBANS**: Repeatable Battery for the Assessment of Neuropsychological Status; **R.E.**: Range Education; **ROCF**: Rey-Osterrieth Complex Figure; **SD**: Standard Deviation; **SpO_2**: Saturation of peripheral Oxygen; **WAIS**: Wechsler Adult Intelligence Scale; **WMS**: Wechsler Memory Scale.