ÖSSZEFOGLALÓ KÖZLEMÉNY

REVIEW ARTICLE

Cognitive impairment in long-COVID

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Background – Long Covid is a complex condition characterised by symptoms that persist for weeks and months after the Covid infection, accompanied by cognitive impairment that negatively affects daily life. Understanding this complex condition is important for the development of diagnostic and therapeutic strategies.
Purpose – This article aims to provide a comprehensive overview of cognitive impairment in long-COVID, including its definition, symptoms, pathophysiology, risk factors, assessment tools, imaging abnormalities, potential biomarkers, management strategies, long-term outcomes, and future directions for research.
Methods – The search methodology used in this review aimed to include a wide range of research on cognitive impairment related to both COVID-19 and long-COVID. Systematic searches of PubMed and Google Scholar databases were conducted using a mixture of MeSH terms and keywords including 'cognition', 'cognitive impairment', 'brain fog', 'COVID-19' and 'long-COVID'. The search was restricted to studies published in English between 1 January 2019 and 11 February 2024, which presented findings on neurological manifestations in human participants.
Results – Long-COVID is characterized by persistent symptoms following COVID-19 infection, with cognitive impairment being a prominent feature. Symptoms include brain fog, difficulties with concentration, memory issues, and executive function deficits. Pathophysiological mechanisms involve viral persistence, immune responses, and vascular damage. Risk factors include age, pre-existing conditions, and disease severity. Cognitive assessment tools such as the Montreal Cognitive Assessment (MoCA) are essential for diagnosis. Imaging studies,

Kognitív károsodás hosszú Covid esetén
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Háttér – A hosszú Covid összetett állapot, amit a Covid-fertőzést követően hetekig és hónapokig fennmaradó tünetek jellemeznek, és a mindennapi életet negatívan befolyásoló kognitív károsodás kísér. Ennek az összetett állapotnak a megértése fontos a diagnosztikus és terápiás stratégiák kifejlesztéséhez.
Cél – E cikk célja, hogy átfogó áttekintést nyújtson a hosszú Covidban jelentkező kognitív károsodásról, beleértve a definíciót, a tüneteket, a patofiziológiát, a kockázati tényezőket, az értékelési eszközöket, a képalkotó eljárásokkal felfedezhető eltéréseket, a lehetséges biomarkereket, a kezelési stratégiákat, a hosszú távú kimeneteket és a kutatás jövőbeli irányait.
Módszerek – Az áttekintés keresési módszertanának célja az volt, hogy a Covid-19-hez és a hosszú Covidhoz kapcsolódó kognitív károsodással kapcsolatos kutatások széles körét tartalmazza. A PubMed és a Google Scholar adatbázisokban végeztünk szisztematikus keresést a MeSH terminusok és kulcsszavak – beleértve a „kogníció", „kognitív károsodás", „agyi köd/brain fog", „COVID-19" és „long-COVID" kifejezéseket – kombinációjának felhasználásával. A keresést azokra a 2019. január 1. és 2024. február 11. között angol nyelven megjelent tanulmányokra korlátoztuk, amelyek humán neurológiai megnyilvánulásokra vonatkozó eredményeket mutattak be.
Eredmények – A hosszú Covidot a Covid-19-fertőzést követően fennmaradó tartós tünetek jellemzik, amelyek közül kiemelkedik a kognitív károsodás. A tünetek közé tartozik az agyi köd, a koncentrációs nehézségek, a memóriaproblémák és a végrehajtó funkciók hiányosságai. A patofiziológiai mechanizmusok a vírusperzisztenciát, az immunválaszt és az érrendszeri károsodást foglalják magukba. A kockázati tényezők közé tartozik az életkor,

including MRI, PET, and SPECT, reveal structural and functional brain alterations. Potential biomarkers include C-reactive protein, interleukin-6, and neuron-specific enolase. Management strategies encompass cognitive rehabilitation, occupational therapy, medications, and lifestyle modifications.
Discussion – Long-COVID poses a multifaceted challenge, and cognitive impairment significantly impacts patients' lives. A multidisciplinary approach, including cognitive rehabilitation and medication when appropriate, is essential for effective management. Future research should focus on validating biomarkers and understanding long-term cognitive outcomes.
Conclusion – Long-COVID is a global health concern, and cognitive impairment is a distressing symptom. While pharmacological interventions have potential, they require careful consideration. Continued research is crucial for improving the understanding and treatment of cognitive impairment in long-COVID.

Keywords: COVID-19, long-COVID, cognition, cognitive impairment, brain fog

a már meglévő betegségek és a Covid-19-fertőzés súlyossága. A diagnózis felállításához elengedhetetlenek a kognitív értékelő eszközök, mint például a Montreal Cognitive Assessment (MoCA). A képalkotó vizsgálatok, beleértve az MRI-t, a PET-et és a SPECT-et, strukturális és funkcionális agyi elváltozásokat tárnak fel. A potenciális biomarkerek közé tartozik a C-reaktív fehérje, az interleukin-6 és a neuronspecifikus enoláz. A kezelési stratégiák közé tartozik a kognitív rehabilitáció, a foglalkozásterápia, a gyógyszeres kezelés és az életmódváltás.
Megbeszélés – A hosszú Covid sokrétű kihívást jelent, és a vele járó kognitív károsodás jelentősen befolyásolja a betegek életét. A hatékony kezeléshez elengedhetetlen a multidiszciplináris megközelítés, beleértve a kognitív rehabilitációt és adott esetben a gyógyszeres kezelést. A jövőbeli kutatásoknak a biomarkerek validálására és a hosszú távú kognitív kimenet megértésére kell összpontosítaniuk.
Következtetés – A hosszú Covid, aminek a kognitív károsodás aggasztó tünete, globális egészségügyi problémát jelent. Bár a farmakológiai beavatkozásokban rejlik potenciál, használatuk alapos megfontolást igényel. A további kutatás elengedhetetlen a hosszú Covid esetében jelentkező kognitív károsodás megértése és kezelésének javítása érdekében.

Kulcsszavak: Covid-19, hosszú Covid, kogníció, kognitív károsodás, agyi köd

The emergence of COVID-19, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), had led to a global health crisis with a myriad of long-term effects. Among these, long-COVID, a syndrome characterized by lingering symptoms post-recovery, presents a significant challenge. Notably, cognitive impairment has emerged as a pivotal concern within long-COVID, affecting a substantial portion of recovering individuals.

This review aims to provide a comprehensive overview of cognitive impairment in long-COVID, drawing on current scientific literature. While this review synthesizes the latest findings, it is important to acknowledge the limitations inherent in our current understanding. Several aspects of long-COVID's cognitive impairments, including their pathophysiology and long-term impact, remain under investigation. Therefore, some of the claims and hypotheses presented are speculative and based on indirect evidence.

Our focus encompasses the pathophysiology of long-COVID, specifically its impact on cognitive functions, alongside an examination of risk factors, assessment tools, and potential management strategies. By presenting an integrated view of existing knowledge, this review seeks to aid clinicians in managing the cognitive aspects of long-COVID. However, we emphasize the necessity for further experimental research to validate these insights and to fill the gaps in our understanding of this complex post-viral syndrome.

Methodology

The search strategy for this review was designed to capture a comprehensive range of studies on cognitive impairment associated with COVID-19 and long COVID-19. We conducted systematic searches in PubMed and Google Scholar, utilizing a combination of the following MeSH terms and keywords: "cognition", "cognitive im-

pairment", "brain fog", "COVID-19", and "long COVID". The search was limited to studies published in English between January 1, 2019, and February 11, 2024, that reported on neurological symptoms in human subjects.

Our study selection process involved a two-step screening method. Initially, titles and abstracts were reviewed to identify studies meeting our inclusion criteria. Subsequently, full-text articles were assessed for eligibility. The inclusion criteria were specifically designed to capture studies focusing on cognitive impairments related to COVID-19 and long COVID. Exclusion criteria were applied to studies not focusing on human subjects or those not in the English language. Disagreements regarding study inclusion were resolved through a democratic voting process among the three authors. Given the heterogeneity of the studies identified, a narrative synthesis approach was employed to synthesize the findings. This method allowed for a comprehensive examination of the varied manifestations of cognitive impairment in long-COVID, including the prevalence, nature, and potential mechanisms of cognitive deficits. A limitation of the methodological framework of our study is the lack of analyses with permutations including the keyword 'post-COVID syndrome'.

Definition of long-COVID

Long-COVID, also known as post-COVID-19 syndrome, is defined as a range of symptoms that continue for weeks or months beyond the initial recovery from COVID-19. The Centers for Disease Control and Prevention (CDC) and the National Institute for Health and Care Excellence (NICE) acknowledge the persistence of symptoms post-COVID-19, which cannot be explained by alternative diagnoses[1, 2]. Studies such as *Sudre* et al. have characterized long-COVID by symptoms such as fatigue, headache, dyspnea, and anosmia, and identified risk factors like age, BMI, and gender[3]. The prevalence of long-COVID symptoms varies, with estimates suggesting that 13.3% to 16.1% of COVID-19 patients experience persistent symptoms. The study by *Bohn* et al. provides empirical evidence on cognitive impairment in long-COVID, examining over 500 individuals to correlate cognitive deficits with demographics and clinical history[4]. The findings highlight the importance of considering age, BMI, and hospitalization status in understanding cognitive impairment post-COVID-19[5–7].

Symptoms

Long-COVID is a complex condition characterized by a wide range of persistent symptoms that can significantly impact daily life. Understanding its prevalence, symptoms, and risk factors is crucial for developing effective management strategies. The primary symptoms of long-COVID include fatigue, shortness of breath, cognitive impairment ("brain fog"), anxiety, and depression. Fatigue is reported as the most common symptom, followed by dyspnoe, joint pain, and difficulty in concentrating. For instance, a study by *Whitaker* et al. found that 37.7% of symptomatic post-COVID-19 patients experienced at least one long-COVID symptom, with 14.8% experiencing three or more symptoms lasting 12 weeks or more[8]. These findings are consistent with a meta-analysis that identified fatigue, cognitive impairment, joint pain, anxiety, and depression as primary clinical symptoms of long-COVID. It is important to note that some patients with underlying cognitive impairment present with accelerated rate of cognitive decline. Longitudinal study by *Matsui* et al. examining cognitive decline in older persons post-COVID-19, provides insights into the long-term cognitive impacts, particularly in older individuals with cognitive impairment[9].

Pathophysiology

The pathophysiology of long-COVID is complex and multifaceted, involving a range of biological processes and mechanisms. While the current understanding is continually evolving, several key aspects have been identified, albeit with varying levels of evidence.

Long-COVID may result from a combination of direct viral effects, persistent immune responses, and multi-organ system damage. One proposed mechanism involves the persistence of SARS-CoV-2 or its fragments in the body, contributing to ongoing inflammatory responses[10]. This prolonged immune activation can lead to a range of symptoms characteristic to long-COVID, including fatigue, cognitive impairment, and muscle weakness.

The virus's ability to directly invade neural tissue has also been a subject of study. The SARS-CoV-2 virus can potentially enter the brain, affecting neurological functions[11]. This neuroinvasion might contribute to cognitive symptoms seen in long-COVID, such as memory and concentration difficulties. Additionally, the role of microglia, the brain's resident immune cells, is increasingly recognized in the context of long-COVID's neurological manifestations[12].

Furthermore, cytokine profiles in long-COVID patients indicate a heightened inflammatory state. Proinflammatory cytokines like IL-6 and TNF-alpha, elevated in severe COVID-19 cases, are believed to play a role in the pathophysiology of long-COVID[13]. These cytokines can contribute to systemic inflammation and potentially cross the blood-brain barrier, affecting cognitive functions. Vascular damage and microclot formation, resulting from the body's response to the virus, have also been suggested as contributors to long-COVID symptoms. This vascular involvement can lead to reduced oxygenation in tissues, including the brain, further complicating the clinical picture[14, 15].

In summary, the pathophysiology of long-COVID is not entirely understood and likely involves multiple interrelated mechanisms, including direct viral effects, immune responses, and systemic inflammation. Further research is necessary to fully elucidate these processes and their implications for the management and treatment of long-COVID.

Risk factors for long-COVID

Understanding the risk factors for long-COVID is crucial for both prevention and management strategies. While the literature identifies several factors associated with an increased risk of developing long-COVID, it is important to interpret these findings within the context of evolving research. Age has been identified as a risk factor, with individuals aged 50 and above exhibiting a higher likelihood of developing long-COVID[16–18]. However, this association is complex and not uniformly consistent across studies. For instance, other research indicates that while older age is a risk factor for severe acute COVID-19, it does not necessarily correlate with an increased risk of long-COVID[19].

Pre-existing health conditions such as hypertension, asthma, psychiatric illness, and immune system diseases have also been associated with a higher risk of long-COVID[20, 21]. These conditions may exacerbate the severity of initial COVID-19 infection or contribute to the persistence of symptoms. However, the direct relationship between these conditions and long-COVID needs further investigation.

It is also noted in some studies that there is no clear evidence supporting a direct correlation between the severity of initial COVID-19 infection and the likelihood of developing long-COVID[22, 23]. This highlights the need for more comprehensive research to understand the full spectrum of risk factors and their interactions.

In summary, while certain factors such as older age, pre-existing conditions, and the severity of the initial infection have been associated with an increased risk of long-COVID, the exact nature of these relationships remains a subject of ongoing research. Continued studies are essential to better understand these risk factors, which will aid in developing more effective prevention and management strategies for long-COVID.

Cognition in long-COVID

Cognitive impairment, often termed as ‘brain fog’, is a prevalent symptom in long-COVID patients. Studies have found a substantial occurrence of cognitive impairment, with incidences varying widely. *Miskowiak* et al. reported that 59-65% of patients exhibited clinically significant cognitive impairments four months after COVID-19 hospitalization, with verbal learning and executive functions being most affected[24]. Additionally, *Dressing* et al. observed that long-COVID patients self-reported uniform symptoms like impaired attention and memory, but neuropsychological testing revealed minor impairments only at individual level, approximately six months post-infection[25]. The cohort study by *Liu* et al. focused on the one-year trajectory of cognitive changes in older COVID-19 survivors; it revealed a significant incidence of cognitive impairment and its association with the severity of the initial COVID-19 infection, thereby contributing to the understanding of cognitive sequelae in long-COVID[26].

The spectrum of cognitive impairments in long-COVID is diverse, affecting various domains such as attention, memory, fluency, and executive function. This variability is highlighted in the study by *Blazhenets* et al., which found a significant reduction in frontoparietal and temporal metabolism, accompanied by improvement in cognition in COVID-19 patients over time[27]. The cognitive impact of long-COVID is multifaceted and can manifest differently from one individual to another. Studies like that of *Cavaco* identified predictors of cognitive decline post-COVID-19, emphasizing the need for tailored interventions based on individual profiles[28].

The pervasiveness of cognitive impairments in long-COVID patients has significant implications for clinical management. A rational and data-driven approach to understand these cognitive symptoms is paramount in advancing our comprehension of long-COVID and devising effective strategies for treatment and rehabilitation.

Cognitive assessment tools in long-COVID

Accurate assessment of cognitive impairment in long-COVID is essential for effective management and treatment. While initial discussions in this review included tools such as the MoCA, the Mini-Mental State Examination (MMSE), and the Frontal Assessment Battery (FAB), a closer examination reveals that these tools, though useful, might not fully capture the subtleties of cognitive changes in long-COVID. Originally developed for identifying mild cognitive impairment (MCI) and dementia, their sensitivity to the specific cognitive impairments experienced by long-COVID patients can be limited, especially in those who were cognitively intact prior to infection[29–31]. *Hammerle* et al. found that cognitive tests like the Symbol Digit Modalities Test (SDMT) were more sensitive than others like the Mini-Mental State Exam 2 (MMSE-2) in detecting cognitive changes in long-covid[32].

The need for a more comprehensive approach is evident. The Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV), with its detailed subtests covering various cognitive domains, provides a more nuanced assessment. Employing a selection of these subtests can offer insight into specific areas of cognitive impairment, aligning with the approach utilized in studies such as that by

Lauria et al., which applied a wide range of tests for a thorough cognitive evaluation[33].

In clinical practice, a strategy that combines general screening tools like MoCA with the more detailed assessments available through WAIS-IV subtests can lead to a more accurate and comprehensive understanding of a patient's cognitive status. This approach allows for initial broad screening, followed by targeted evaluation of identified areas of concern, thereby facilitating the development of individualized treatment plans. *Vakani* et al. underscore the need for comprehensive cognitive assessments in long-COVID, supporting the use of tools like WAIS-IV for a nuanced understanding of cognitive impairments[4, 34].

In summary, while general cognitive screening tools serve as a valuable initial step in cognitive assessment for long-COVID patients, they should be complemented by more specific tests that allow for a detailed evaluation of the various cognitive domains. This balanced approach enhances the accuracy of cognitive assessments and supports the formulation of tailored therapeutic interventions for long-COVID patients.

Imaging abnormalities

The integration of Magnetic Resonance Imaging (MRI) findings with other imaging modalities provides a comprehensive view of the neurological implications of long-COVID. These insights are crucial for understanding the pathophysiology of long-COVID and guiding future research and treatment strategies.

Magnetic Resonance Imaging

MRI studies have emerged as essential tools in unraveling the neurobiological underpinnings of cognitive impairment and other neurological symptoms observed in long-COVID patients. These imaging investigations have shed light on various structural and functional alterations within the brain that correlate with clinical manifestations experienced by individuals grappling with the aftermath of COVID-19 infection. One notable MRI finding is the increased incidence of small vessel disease observed in long-COVID patients[35]. This phenomenon, characterized by the dysfunction or damage of small blood vessels in the brain, has been linked to a spectrum of symptoms, including cognitive impairment, headaches, and even stroke-like manifestations. The identification of small vessel disease through MRI underscores its potential role in contributing to the complex cognitive landscape of long-COVID. In addition to structural changes, MRI studies have provided insight into inflammatory processes occurring within the brain of long-COVID patients[36]. The increased signal intensity observed on specific MRI sequences, such as T2-weighted and fluid-attenuated inversion recovery (FLAIR), suggests the presence of neuroinflammation. This inflammatory response within the brain points to the intricate interplay between the immune and the central nervous system, possibly contributing to the cognitive impairment and other neurological symptoms[37].

Furthermore, white matter changes detected through MRI have garnered attention due to their potential association with cognitive impairment, fatigue, and other symptoms characteristic of long-COVID. White matter alterations, often indicated by changes in diffusion tensor imaging (DTI) metrics, reflect disruptions in the connectivity and integrity of neural pathways[38]. These changes may contribute to the observed cognitive deficits and further highlight the complexity of the brain's response to COVID-19. Recent MRI studies have also reported the presence of cerebral small vessel disease in subsets of long-COVID patients[39]. This particular form of small vessel disease can lead to a range of symptoms, including headaches, cognitive impairment, and stroke-like manifestations. The identification of such vascular abnormalities emphasizes the need for a comprehensive understanding of the vascular-brain interplay in long-COVID related neurological symptoms.

Other imaging modalities

Beyond MRI, investigating the effects of long-term COVID on the brain requires the incorporation of advanced imaging modalities such as PET and SPECT. PET, often using radiotracers such as FDG, visualises regional cerebral glucose metabolism[40] and provides insight into metabolic changes underlying cognitive deficits[41]. SPECT captures cerebral blood flow dynamics and reveals perfusion abnormalities in patients with long COVID[42], particularly in cognitive processing areas. The integration of these modalities provides a holistic view of the neurological manifestations of long-COVID, aiding in the identification of biomarkers[43–46]. Studies show decreased FDG uptake in cortical areas in long-COVID patients[43], and MRI shows grey matter loss in the olfactory bulb and hippocampus[45]. FDG-PET shows bilateral hypometabolism in specific brain regions in long COVID patients[41]. MRI scans of mild COVID patients show no significant differences compared to negative cases[46]. The combination of these findings improves understanding and guides interventions in cognitively impaired long-COVID patients.

Biomarkers for long-COVID

The identification of biomarkers for long-COVID is an area of significant interest, as these markers can provide insight into the underlying mechanisms and aid in the diagnosis and management of the condition. However, it is important to approach this area with caution, recognizing that the research is still evolving.

One of the key biomarkers under investigation is C-reactive protein (CRP), a marker of inflammation that has been linked to long-COVID. Elevated levels of CRP have been associated with more severe cases of COVID-19, suggesting a potential role in the persistence of symptoms[47]. However, the direct relationship between CRP levels and specific long-COVID symptoms, including cognitive impairment, requires further investigation. Interleukin-6 (IL-6), another inflammatory marker, has garnered attention for its potential association with long-COVID. Elevated IL-6 levels have been observed in patients with severe COVID-19 and may play a role in the development of long-COVID symptoms[48]. However, further studies are needed to establish a definitive link between IL-6 levels and long-COVID.

Neuron-specific enolase (NSE), an enzyme found in neurons, is being explored as a biomarker for cognitive impairment in the context of COVID-19. While studies have reported elevated NSE levels in patients with COVID-19, the correlation with cognitive functions specifically remains to be clarified[49]. Additionally, other markers such as TNF-α and IL-1β are being studied for their potential role in long-COVID[50]. These markers are known to be involved in inflammatory responses and may contribute to the pathophysiology of long-COVID.

In summary, while various biomarkers are being investigated for their potential roles in long-COVID, the evidence supporting their utility is still emerging. Ongoing research is crucial to validate these biomarkers and to understand their implications fully in the diagnosis and management of long-COVID.

Management

Cognitive rehabilitation therapy

Cognitive rehabilitation therapy, as primary intervention for cognitive impairment in long-COVID, incorporates structured training to promote neuroplasticity and functional recovery. Recent studies emphasize the need for individualized cognitive rehabilitation programs to target specific deficits, enhancing attention, memory, and executive functions in long-COVID patients. For example, Liu et al. found cognitive impairment in COVID-19 survivors 12 months post-discharge and emphasised the importance of immediate interventions to address these challenges. Large-scale and long-term studies are needed to demonstrate the potential of cognitive rehabilitation interventions[26].

Occupational therapy

Occupational therapy plays a crucial role in enabling individuals with cognitive impairment to manage their daily activities. Tailored strategies developed in collaboration with patients can optimize attention, memory, and executive functions. This approach is supported by findings from Matsui et al., who observed accelerated cognitive decline in individuals with cognitive impairment during the COVID-19 pandemic, indicating the importance of personalized occupational therapy interventions[9].

Medications

While there are no specific medication approved for cognitive impairment in long-COVID, certain drugs may be considered for managing associated symptoms. For instance, Liu et al. highlight the association between severe COVID-19 and increased risk of cognitive decline, suggesting a potential role for pharmacological interventions in severe cases[26].

Lifestyle modifications

Lifestyle modifications such as adequate rest, a balanced diet, regular exercise, sleep hygiene, and stress management are vital for managing cognitive impairment in long-COVID patients. This is corroborated by the study of Dressing et al., which indicates the potential benefit of lifestyle interventions on cognitive functions in long-COVID patients[25].

Managing cognitive impairment in long-COVID requires a comprehensive approach, integrating cognitive rehabilitation, occupational therapy, potential pharmacological interventions, and lifestyle modifications. It is essential to tailor these interventions based on individual assessments and evolving research findings to optimize outcomes for long-COVID patients.

The importance of a multidisciplinary team approach

Collaborative decision-making between patients and healthcare providers remains essential. This process should be grounded in comprehensive assessments, balancing the potential benefits and risks of any intervention. As the landscape of long-COVID continues to evolve, ongoing research is critical for understanding the impact and efficacy of both pharmacological and non-pharmacological treatments. Future research directions should focus on understanding the mechanisms behind cognitive impairment post-COVID and to develope targeted interventions.

In conclusion, the future direction for managing cognitive impairment in long-COVID involves a balanced exploration of pharmacological and non-pharmacological interventions, underpinned by cautious consideration and collaborative decision-making. A data-driven approach will guide our understanding of the most effective strategies for addressing cognitive deficits in the context of long-COVID.

Long-term outcomes

The heterogeneity in cognitive outcomes among long-COVID patients is a significant finding. *Costa* et al. emphasized the potential long-term risk of cognitive impairment and dementia following severe COVID-19, indicating variability in cognitive trajectories and potential for severe outcomes[51]. Recent studies have deepened our understanding of the chronicity and impact of cognitive impairment in long-COVID. For example, Dressing et al. found that long-COVID patients reported uniform symptoms such as impaired attention, memory, and multitasking abilities, highlighting the persistence of cognitive challenges[25]. This study suggests minor impairments on a single-patient level approximately 6 months after infection, offering a nuanced view of cognitive recovery.

Understanding the factors influencing the persistence and severity of cognitive deficits is critical. Research by Cavaco et al. on COVID-19 patients one year after hospital discharge identified predictors of cognitive decline, such as age, sex, previous dementia diagnosis, frailty, and delirium, offering valuable insights into the complex nature of long-term cognitive impairment[28].

The long-term cognitive impairment in long-COVID patients underlines the need for ongoing research and comprehensive clinical strategies. These insights from recent studies emphasize the multidimensional impact on individuals' lives and the importance of tailored interventions. It is crucial to continue exploring the long-term outcomes of cognitive impairment in long-COVID to develop effective strategies for mitigating its impact and fostering cognitive well-being.

Future directions

While exploring pharmacological treatments for cognitive impairment in long-COVID, it is crucial to proceed with caution. The use of medications, especially off-label, requires a thorough understanding of potential benefits and risks. For instance, research by Miskowiak et al. highlights the need for systematic cognitive screening and targeted treatments for persistent cognitive impairment in COVID-19 survivors, emphasizing a careful approach to pharmacological interventions[24].

Exploring non-pharmacological interventions is equally vital. *Hausswirth* et al. demonstrated the positive impact of a neuro-meditation program on cognitive function in long-COVID patients, suggesting the potential of alternative, non-pharmacological methods to address cognitive deficits[52].

Conclusion

Long-COVID is a significant global health problem and may lead to cognitive impairment in some individuals. The pathophysiology of cognitive symptoms is poorly understood, and currently there is no specific treatment for this condition. Clinicians should be aware of the potential for cognitive impairment in patients with long-COVID and treat the underlying symptoms appropriately. Further research is needed to better understand the long-term consequences of cognitive impairment in long-COVID.

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