

# Multidisciplinary Approach to Brain Fog and Related Persisting Symptoms Post COVID-19

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Published online: 2 February 2022 © National Register of Health Service Psychologists 2022

#### Abstract

A third of patients who developed COVID-19 experience a persisting, diverse array of symptoms including respiratory, neurological, and psychiatric complaints referred to as post-acute sequelae of COVID-19 (PASC). Symptoms can last for months after the original infection and appear unrelated to the severity of the initial illness, which suggests that even patients who did not require extensive interventions at the acute stage may experience new and/or long-term symptoms. Brain fog is a colloquial term for a common complaint among patients with PASC and generally implies cognitive impairment in domains of attention and processing speed. There are multiple hypotheses for etiologies and explanations of mechanisms contributing to brain fog in PASC. In this paper, we describe some of the mechanisms associated with brain fog post COVID-19 and provide readers with treatment recommendations that encompass cognition, mood disorders, sleep disorders, and neuroinflammation.

**Keywords** Brain Fog · Covid-19 · Mood · Nutrition · Sleep

### **Clinical Vignette**

Ms. Ella Smith is a 35-year-old Critical Care Nurse who identifies as female. She tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 or COVID-19) about 3 months ago. She was hospitalized for 1 day but did not require mechanical ventilation. Initial symptoms included shortness of breath, cough, fever, fatigue, and difficulty sleeping, which have persisted. She also complains of significant "brain fog," which she defines as difficulty maintaining her attention and recalling information.

She reports significant fatigue and concerns about her work performance. Based on her cognitive complaints, she is referred for a neuropsychological evaluation. During the neuropsychological evaluation, Ms. Smith describes difficulty recalling details of conversations. She is more reliant on notes that she was before she had COVID-19. She sometimes feels drowsy during work hours and has made some inattentive mistakes. She is concerned about her ability to continue her current workload.

Ms. Smith discloses prior psychiatric history of major depressive disorder that was relatively stable prior to developing COVID-19. Her current mood includes reports of depressive and anxiety symptoms every day, nearly all day, such as feeling bad about herself, a loss of interest in her favorite hobbies, feelings of hopelessness, frequent worries about her recovery, and overeating to cope. She also describes insomnia and reports difficulty staying asleep. She says that she is frequently awoken by coughing and then tends to stay awake due to ruminating thoughts about her recovery.

Ms. Smith reports a 30-lb weight gain since she contracted COVID-19. She attributes this to decreased physical activity due to the shortness of breath and increased eating, which she associates with depressive symptoms. Her current body mass index is 31.2, classified in the obese range. Her primary medical history includes diabetes mellitus type II, hypertension, and hyperlipidemia. She rarely drinks alcohol and does not use tobacco or other substances.

Ms. Smith's neuropsychological test results reflected an individual with a high average baseline intelligence with variability in her test performance. Results were moderately impaired on tests assessing sustained attention and problem-solving and some aspects of processing speed. Simple attention, reasoning, language, memory, other aspects of



processing speed, and visuospatial function were generally within normal limits.

During the neuropsychology feedback session, the neuropsychologist provided psychoeducation about the impact of poor sleep, mood disorder, and changes in eating patterns on cognitive health. Using her neuropsychological evaluation as a guide, Ms. Smith was also provided with cognitive compensation strategies for inattention and difficulty problem-solving. Ms. Smith was then referred to specialists in psychology, integrated wellness, and sleep medicine to address other factors thought to be contributing to her chief complaint of brain fog.

## **Background on COVID-19 and Brain Fog**

The clinical presentation of COVID-19 resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily characterized by respiratory symptoms but can involve a diverse array of features including pulmonary (e.g., pneumonia, dyspnea on exertion), cardiac (e.g., ischemia, arrhythmias, myocarditis), gastrointestinal (e.g., anorexia, diarrhea), and neurological (e.g., headache, dizziness, ageusia, anosmia; Taquet et al., 2021). It is now well known that almost a third of patients across the world will experience persisting symptoms weeks and months, sometimes 1-year after diagnosis (Taquet et al., 2021). These findings are similar to recovery from SARS in 2000, especially for patients who experienced severe symptoms and spent weeks in intensive care. However, COVID-19 varies in that a large subset of patients who did not require hospitalization appear to experience reoccurring, persisting, or new symptoms months after the initial infection (Almeria et al., 2020).

The persisting symptoms after COVID-19 are referred to as "long COVID" or post-acute sequelae of COVID-19 (PASC). Of the diverse constellation of symptoms that constitute PASC, the neurological and psychiatric symptoms include fatigue, post-exertional malaise, cognitive complaints, sensorimotor symptoms, headaches, insomnia, depression, and post-traumatic stress disorder (Taquet et al., 2021). The mechanisms involved in developing PASC and factors affecting recovery from COVID-19 are still in the nascent stages. Current hypotheses include psychological factors, inflammatory and immune reactions, and physical deconditioning (Deng et al., 2021; Calabrese, 2020). The diversity in symptoms, involvement of multiple organ systems, and varying possible mechanisms suggest that a multi-pronged approach to treatment may be quintessential in recovery from PASC.

The colloquial term "brain fog" is among the top three symptoms reported by millions of individuals with PASC. While the term "brain fog" is used commonly by patients and the healthcare community, there is no widely accepted definition of this term. In general, it refers to a constellation of symptoms including inattention, short-term memory loss, and reduced mental acuity (Ocon, 2013; Garg et al., 2021). In the scientific literature, brain fog has been associated with disorders affecting the central nervous system (e.g., chronic fatigue syndrome and fibromyalgia) or treatments affecting the immune system such as chemotherapy for cancer (Ocon, 2013).

Subsequently, there are multiple theories on the etiology of symptoms that are associated with brain fog. Clinical observation and research in the last two years suggests severe COVID-19 disease is a consequence of the immune system producing excessive inflammatory proteins called cytokines, sometimes referred to as a cytokine storm, and PASC is a consequence of the exaggerated, prolonged immune response. This mechanism has the potential for crossing the blood–brain barrier and affecting neural regions and function, including cognition.

Brain fog and fatigue, commonly reported in patients with PASC, can be viewed as a consequence of neuroin-flammation. Other mechanisms suggest sleep disruption and psychiatric disorders that are impacted post-COVID have a secondary impact on cognition presenting as brain fog (Deng et al., 2021). Given that brain fog is among the top symptoms reported by patients with PASC and is often accompanied by presence of mood symptoms, mental health providers are likely to see patients who present with brain fog as a prominent concern post-recovery from the acute phase of COVID-19. This paper provides operationalization and general treatment recommendations for health service psychologists who are working with patients presenting with post-COVID-19 brain fog symptoms.

# Multidisciplinary Approach to Treating Brain Fog in COVID-19

In this section, we provide further background on symptoms and etiology associated with brain fog including (1) cognition, (2) sleep, (3) psychological factors, and (4) neuroinflammation.

#### Cognition

Studies evaluating cognitive deficits post COVID-19 generally illustrate impairments in cognitive domains of attention and executive function (Almeria et al., 2020). These deficits are primarily observed in the acute stages—typically in the first month after COVID-19 diagnosis. It is recognized that cognitive impairments in patients with PASC can exist even among those who did not require hospitalization or experience events associated with severe COVID-19. The pattern of cognitive deficits in domains of attention and executive



function is also present in these patients and recent research demonstrates presence of cognitive impairment even 4 months after COVID-19 (Hampshire et al., 2021). Possible contributors to impaired cognition, in the absence of any quantifiable neural involvement (e.g., stroke, hypoxia), include factors such as sleep quality, nutrition, and psychological function.

For Ms. Smith, the neurocognitive evaluation was used as a basis for quantifying the brain fog related cognitive complaints. In this case, the results assisted in ruling out possible causes of cognitive impairment from COVID-19 such as an anoxic injury or undiagnosed seizures. However, other factors were identified that could contribute to brain fog including sleep disruption, psychological symptoms (e.g., changes in mood), and possible neuroinflammation, especially given Ms. Smith's prior vascular history.

#### Sleep

Sleep disordered breathing (SDB) has been associated with comorbidities generally associated with increased risk of developing COVID-19, such as diabetes, obesity, hypertension, and older age. This association suggests a strong overlap between pre-existing SDB and adverse COVID-19 outcomes, including brain fog. Furthermore, consequences of COVID-19, such as hypoxia, are known to potentiate inflammation and may amplify symptoms associated with COVID-19 resulting in the worsening of existing sleep disorders and/or a new diagnosis of a sleep disorder (Orbea et al., 2021). Other factors to assess include history of insomnia prior to COVID-19, poor sleep hygiene, and previous history of obstructive sleep apnea. Lastly, patients experiencing psychological distress may manifest as insomnia or other SDB.

Sleep disorders are known to have an impact on cognition—especially in the domains of attention and processing speed. These cognitive domains are also affected in patients recovering from COVID-19. While research focuses on understanding the interplay between SDB and COVID-19, clinical evaluation and treatment plans for patients with brain fog post COVID-19 should include screening for sleep disorders and general sleep quality.

#### **Psychological Factors**

Disorders such as depression, anxiety, and post-traumatic stress disorder (PTSD) are all concerns for patients following infection with COVID-19 and should be considered when approaching a patient with brain fog. A recent meta-analysis (Deng et al., 2021) showed a pooled prevalence of 45% for depression and 47% for anxiety in patients diagnosed with COVID-19. A large retrospective cohort study of patients in the 6 months following COVID-19 diagnosis (Taquet et al., 2021) revealed higher incidence of first onset

mood, anxiety, and psychotic disorders for patients who had a COVID-19 diagnosis compared to patients with influenza or with another respiratory tract infection. Overall, this study reported prevalence of any mood, anxiety, or psychotic disorder at 23.98% and first onset of any of these disorders at 8.63%. Another study estimated prevalence for PTSD at 6.5% in patients diagnosed with COVID-19 within 2 months of infection, which is higher than for patients diagnosed with other respiratory illnesses (Horn et al., 2020).

Preliminary research suggests cognitive changes and mood symptoms are associated in patients recovered from COVID-19 (Almeria et al., 2020). In this small study of previously hospitalized patients diagnosed with COVID-19 assessed 10-35 days after discharge, cognitive complaints were associated with increased anxiety and depression. This association may indicate patients are experiencing distress because of cognitive symptoms, and this is consistent with our clinical observations. However, it also is important to note that poor concentration is a common diagnostic criterion for many mood and anxiety disorders. In addition, depression has been associated with a wide array of cognitive impairments including global cognition, episodic memory, executive functioning, processing speed, visuospatial memory, attention, and working memory as summarized in a recent systematic review (Jamieson et al., 2019). Therefore, a careful assessment of psychological factors is needed to disentangle symptoms when making a differential diagnosis.

#### Neuroinflammation

Recent clinical observations and research suggest much of the COVID-19 complications are also inflammatory-based (Calabrese, 2020). One treatment option is to reduce neuroinflammation by augmenting lifestyle practices, starting with nutrition to treat the symptoms associated with brain fog. Poor-quality food that is high in simple carbohydrates, trans fat, food additives and low in nutrient density has been associated with increased systemic inflammation and neuro-inflammation. Research on the gut-brain axis further demonstrates that the nervous system between the gut and brain are intimately connected. Nutrient deficiency is common among Americans four years and older. Even with fortified food and supplements, 70% of Americans remain vitamin D deficient (Drake, 2017).

Among patients with high risk for COVID-19 complications or PASC, those with a significant number of preexisting medical conditions are often treated with polypharmacy, which has also been related to micronutrient deficiency (Mohn et al., 2018). For example, long-term use metformin, a common antidiabetic medicine, has been associated with vitamin B12 deficiency, which is a nutrient critical for nerve health. These factors highlight the importance



of consideration of a referral to a qualified expert, such as a registered dietitian, for nutrition management following chronic illnesses, which could help in alleviating neuroinflammation associated with brain fog post COVID-19.

Ms. Smith in our vignette has multiple chronic illnesses prior to COVID-19, including hypertension, hyperlipidemia, and diabetes. Furthermore, she reported a recent diagnosis of vitamin B12 deficiency and had started taking supplements. She attributed her 30-pound weight gain to changes in her eating habits (i.e., increased intake of sweets and fried food) to cope with depressive symptoms, and decreased exercise. Thus, a referral to a registered dietitian is indicated. Decreasing her recently elevated BMI through work with a registered dietitian could help decrease some inflammation, which may help with symptoms of brain fog.

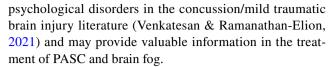
### Evidence-Based Assessment or Practice Considerations For Health Service Psychologists

Given the many facets of brain fog in COVID-19 and hypotheses on potential mechanisms, it can be difficult to design a pre-packaged intervention plan for health service psychologists that will work for all patients with PASC. However, there are some primary tenets to consider within each factor described below that are known to be associated with brain fog in COVID-19.

#### **Neuropsychological Evaluation**

Neuropsychological evaluations are designed to detect cognitive impairments compared to an individual's peer group. They can also serve as a measurable outcome to address the impact of interventions in the treatment of brain fog post COVID-19. Research on cognition in PASC suggests that patients with mild symptoms generally demonstrate minimal deficits in attention or executive function or may perform within the expected range (i.e., are cognitively intact). The latter can be attributed to the structured nature of the test setting with a quiet environment and minimal distractions. While it is possible that neuropsychological evaluations may be less sensitive to cognitive changes during the COVID-19 recovery process than detecting differences in functioning pre-illness, it is still worthwhile to assess throughout the treatment process. The cognitive complaints associated with psychological disorders, sleep disordered breathing, and signs of neuroinflammation may still be associated with notable changes for an individual patient and will inform the treatment process.

While the effects of COVID-19 on neural structures are still being investigated, there is a precedent for an association between self-reported cognitive symptoms and



For example, cognitive rehabilitation for traumatic brain injury is often recommended for individuals with cognitive complaints and includes a component of patient education or "psychoeducation" along with training of cognitive skills deemed to be a weakness for that individual. Clinicians may use this concept in treatment for individuals presenting with brain fog to include an educational component to provide an overview of brain fog. This psychoeducation can include the definition of brain fog, possible etiology, and general factors that can impact the recovery process. When this psychoeducation is supported with group intervention with patient's peers, the validation, reassurance, and access to qualified health care providers can facilitate the recovery process (Venkatesan & Ramanathan-Elion, 2021).

Another component of cognitive rehabilitation for traumatic brain injury that may apply to brain fog is remediation. This aspect relies on the neuropsychological assessment to determine areas of cognitive deficits or weaknesses. The goal here is to help the patient learn compensatory strategies consistent with the areas of cognitive impairment identified. For example, if attention is impaired, cognitive remediation would include providing cognitive strategies for poor attention such as prioritizing, reducing distractions, or working with patients on attention process training (Cicerone et al., 2019).

While patients with brain fog following COVID-19 are different from traumatic brain injury, there are some common characteristics in the rehabilitation of cognitive symptoms that can be generalized across disorders. Physical exercise is often a useful component in rehabilitation of attention and processing speed as well as mood symptoms. Patients with PASC are encouraged to increase physical activities, starting with gentle exercises such as walking, chair yoga, or stretching, and to increase their activity as tolerated. These suggestions may be helpful for health service psychologists to include in their resources to aid in the recovery from brain fog in PASC.

#### **Mental Health Assessment & Psychotherapy**

Assessment of mental health history prior to infection with COVID-19 is an important factor in understanding potential etiologies and interventions for cognitive symptoms. This can be completed using mental health screening measures such as the Generalized Anxiety Disorder–7 (GAD-7; Spitzer et al., 2006), Patient Health Questionnaire–9 (PHQ-9; Kroenke et al., 2001), and the Patient-Reported Outcomes Measurement Information System (PROMIS; Hays et al., 2009) Global Health Questionnaire. If patients indicate



suicidal ideation, the Columbia Suicide Severity Rating Scale (CSSRS; Posner et al., 2011) can be administered to assess for severity and risk. Additionally, if patients present with trauma symptoms such as nightmares, hyperarousal, and avoidance of anything that reminds them of their experience having COVID-19, a brief screening tool such as the Primary Care PTSD Screen for DSM-5 (PC-PTSD 5; Prins et al., 2015) can be given. These questionnaires provide measurable markers of mood symptoms, facilitate appropriate referrals to specialists, and assist in tracking change in symptoms over time. These screeners are recommendations for what is used frequently in our clinic. Health service psychologists may choose to use other screeners for assessing mood symptoms and suicide risk as they deem necessary.

Both patients with previous mental health history experiencing relapse of mental health symptoms following COVID-19 illness and patients with new onset mental health symptoms can benefit from evidence-based psychotherapy. For patients with previous mental health treatment, it can be helpful to review which evidence-based treatments were successful in the past to inform present treatment plans. For example, brief cognitive-behavioral therapy (CBT) may be considered for patients with primarily cognitive complaints without a clinically significant mental health condition to support adjustment to illness or disability. This brief CBT could include the application of skills to manage cognitive complaints. Additionally, patients with milder symptoms who are not interested in individual psychotherapy may benefit from support through formal or informal groups of other people experiencing persistent COVID-19 symptoms. Formal evidence-based group treatment can also help alleviate symptoms, while peer-led support groups may provide connection and decrease feelings of isolation.

Clinically, we have observed distress centered on performance at work in our patients with PASC. Patients often worry that problems with attention, word-finding, and memory will be noticed by supervisors and others at work. In addition to worrying about performance, patients may also report feeling embarrassment about cognitive changes and worry about the judgments of others. They may also feel down and self-critical about changes in perceived work-place performance even if these changes are not detected by others.

With some patients it can be helpful for health service psychologists engaged in evidence-based psychotherapy to determine if there is concrete evidence to support the patient's report of performance declines at work. When patients are experiencing self-consciousness or social anxiety about cognitive changes, taking steps to see if there is clear evidence for these changes may be beneficial. Then health services psychologists can consider engaging in cognitive restructuring with the patient to help shift the patient's focus to areas of strength. With patients who have been

unable to return to work or have returned with significant changes or limitations in their roles, evidence-based psychotherapy may focus more on self-acceptance, adjustment to change, and cognitive or behavioral strategies to manage or accommodate new limitations.

From a psychological perspective, Ms. Smith, the patient in the vignette, has a previous diagnosis of major depressive disorder and is currently experiencing symptoms of depression and anxiety. Given that, it is appropriate to consider cognitive-behavioral techniques in her treatment plan. This cognitive-behavioral treatment could include normalizing the frustration that she is experiencing, engaging in cognitive restructuring, and identifying healthy self-compassion behaviors that she can engage in when she is struggling.

#### Sleep Hygiene

Often, the first goal for health service psychologists with respect to sleep is to determine whether the patient's sleep is disrupted. This can be achieved through sleep questionnaires designed to assess sleep quality. Kong et al. (2019) provided a great overview of different sleep related questionnaires and their general purposes. For example, some are designed specifically to assess disorders such as insomnia, obstructive sleep apnea, or restless legs syndrome while others have a more general purpose. Results from the screen may warrant a referral to a sleep specialist for further diagnostic clarification. For example, the type of sleep disorder (e.g., insomnia, obstructive sleep apnea) often diagnosed through polysomnography may then determine further treatment. Health service psychologists can help initiate this important step and provide appropriate treatment options to address concerns for insomnia or poor sleep hygiene.

#### **Clinical and Ethical Challenges**

Given the multitude of symptoms that constitute brain fog and the diverse etiologies it may represent, patients often struggle to find appropriate resources for treatment. Developing a treatment plan that adequately addresses a patient's symptoms without overwhelming them can be challenging. From an individual patient perspective, the diversity and persisting nature of symptoms can be isolating. These symptoms can be compounded by the unknown trajectory of the recovery process with a relatively new problem, such as PASC. In addition, support from friends and family may wane over time due to the persisting and complex nature of brain fog.

Symptoms of fatigue that often accompany brain fog can make it challenging to seek professional help while also managing personal and professional demands. For example, patients with inflexible work schedules may not be able to



go to health care providers or join the shared appointments easily. This challenge is consistent with prior research on other disorders with chronic presentations (Ocon, 2013). Furthermore, patients may experience negative interactions with medical providers who suspect patients of exaggerating their symptoms. Lastly, PASC is often just one of the health issues a patient may be managing. Many patients often present with multiple prior medical and psychiatric comorbidities that also require ongoing treatment, compounding the recovery trajectory.

#### **Diversity Considerations**

The prevalence of COVID-19 is higher in Black, Hispanic, and other underrepresented communities—as are mortality rates. Racial disparities have been revealed in healthcare since the beginning of the pandemic highlighting the lack of access to appropriate healthcare facilities for preventative health (Rogers et al., 2020). In addition to inequitable access to healthcare, there may be stigma and lack of trust in the healthcare system preventing Black, Hispanic, and other underrepresented Americans from seeking mental health services if they are experiencing these challenges related to PASC. Furthermore, patients from low-income backgrounds may find it financially difficult to maintain key health behaviors, including those related to diet, that may not be covered by health insurance or feasible on a limited budget. When working with patients from underrepresented or low socioeconomic status backgrounds, health service psychologists should assess barriers to treatment including factors discussed here related to stigma and culturally informed care.

# **Conclusions and Lessons Learned Relating** to Vignette

In the vignette, Ms. Smith's brain fog evaluation began with an assessment of her cognition through neuropsychological tests, which helped determine areas of cognitive impairment and identify strengths and weaknesses. Possible etiologies for the brain fog were identified including undertreated mood disorder, possible sleep disorder, and changes in eating patterns, which prompted referrals to a psychologist, sleep disorder specialist, and a registered dietitian respectively.

Brain fog is a common symptom that patients may report to health service psychologists when recovering from COVID-19 infection. In fact, it is one of the most common complaints in PASC. Using our clinical practice as a model, this paper provides readers with a rubric of four factors to consider in patients with brain fog post COVID-19 that can aid in the recovery process. First, in some patients with complaints of brain fog, especially those who required intensive

care at the acute stage, it is important to rule out neurological causes of brain fog such as strokes and seizures that may warrant additional evaluation and medications. Second, when those factors are better controlled or have been ruled out, we advocate for a multi-prong approach for the evaluation of (1) cognition, (2) neuroinflammation markers, (3) psychological factors, and (4) sleep disorders in the treatment of brain fog. Each patient will likely need an individualized approach to treat brain fog as the four components may not be applicable to all. Third, we encourage health service psychologists to use the factors outlined here as a rubric for the initial evaluation and for determining further referrals based on two broad categories: (a) the patient—their medical and psychiatric history, current symptoms, their goals and motivation to improve, and their limitations (inflexible work schedules or financial constraints), and (b) the health service psychologist's ability to treat these symptoms or make appropriate referrals. Fourth, while some health service psychologists may be well-trained to manage sleep, mood, and related disorders, they should keep in mind referrals to specialists as outlined in this paper.

In conclusion, Ms. Smith's vignette represents many of the complications that patients are reporting when experiencing post-COVID-19 symptoms. These symptoms can be extremely distressing to patients and present unique challenges to health service psychologists because research is still developing in treating brain fog post COVID-19. Utilizing the information that we presented in this paper, it is encouraged that providers take a multi-disciplinary approach when assessing patients to make appropriate treatment recommendations. A team approach with appropriate referrals and opportunities for interdisciplinary consultation can provide optimal resources for the patient to receive services to recover from brain fog post COVID-19.

#### **Key Clinical Considerations**

- 1. Brain fog is a common symptom post COVID-19. A multi-disciplinary approach to addressing brain fog is paramount to a patient's success.
- 2. Cognitive impairment may be present in patients post COVID-19, even among those who did not require hospitalization at the acute stage.
- Appropriate psychological assessment and treatment of metal health conditions associated with and/or exacerbated by persistent symptoms post COVID-19 is important.
- 4. Neuropsychological evaluations may be helpful in quantifying the cognitive disorder.
- 5. Assessing adequacy of treatable lifestyle factors and educating patients with tools to optimize health behaviors including stress management, sleep quality, and



exercise is critical in managing chronic disease such as PASC and brain fog.

#### **Declarations**

**Statement of conflicts of interest** The authors do not have any conflicts of interest.

External funding, and other disclosures None

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**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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